



2018 ABSTRACT BOOK

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Vitiligo
International
Symposium



Friday



001

How do Keratinocytes Behave in the Apparently Normal Skin of Vitiligo Patients?

Dr. Daniela Kovacs

San Gallicano Dermatologic Institute, IRCCS, Rome, Italy

Friday, November 9, 2018, 9:02:00 AM - 9:12:00 AM

TAKE HOME MESSAGE:

The presence of alterations in the cytoarchitecture and functionality of keratinocytes located in apparently normal vitiligo skin highlights how the interplay between keratinocytes and melanocytes may be affected even in non macroscopically involved areas contributing, over time, to deregulate the epidermal organization per se and the appropriate functions of the surrounding melanocytes.

Overall our data underline, once again, how in vitiligo there is an involvement both of the whole skin and of all its cell populations.

ABSTRACT:

Functional alterations in vitiligo skin have been detected not only in melanocytes themselves but in all cutaneous cell populations. This broad involvement now seems to embrace also apparently normal skin and the presence of a disadvantageous microenvironment may contribute, over time, to exhaust melanocytes functionality, thus promoting their depletion. In this context, data from our laboratory have shown the predisposition to a stress-mediated premature senescence phenotype both in melanocytes and fibroblasts of non lesional vitiligo skin areas.

In this study we analyzed primary cultures of vitiligo keratinocytes collected from normal appearing skin to highlight features of the epidermal compartment that may impact on melanocyte homeostasis, yet earlier their disappearance. We evaluated the expression of a panel of parameters associated to inflammation and stress-related senescence. The results showed the up-modulation of inflammatory-related mediators (e.g. CXCL9, CXCL10, IL-1 alpha, IL-1 beta) in non lesional keratinocytes in comparison to control cells matched for age, gender and anatomic site. Non lesional vitiligo keratinocytes exhibited also an enlarged size with respect to control, a hallmark usually associated to a senescent phenotype. A defect in the cytoskeletal actin reorganization and a deregulation in the expression of markers related to keratinocyte differentiation and adhesion properties was also observed. The parallel ex vivo analysis of non lesional skin biopsies collected from vitiligo patients revealed an increase in the thickness of the total epidermis associated to a high number of keratinocytes displaying positive reactivity for the senescence marker p16. The presence of deregulated cytoarchitectonic and functional features in non lesional keratinocytes may contribute to alter, even in apparently normal skin, both the structure of the epidermis in toto and the interactions of keratinocytes with the neighboring melanocytes, crucial for the survival and functionality of the latter.

002

Linking the Melanocytorrhagy Hypothesis and the Immune Response in Vitiligo

Dr. Katia Boniface

Bordeaux University, Bordeaux, France

Friday, November 9, 2018, 9:12:00 AM - 9:22:00 AM

TAKE HOME MESSAGE:

Our work identified a new mechanism to explain melanocyte loss in vitiligo : inflammatory cytokines (in particular TNF α and IFN γ), produced by T cells locally in perilesional skin of vitiligo patients, will act directly on melanocytes to downregulate E-cadherin expression, the main protein involved in melanocyte attachment to keratinocytes. In addition, these cytokines will act on epidermal cells to induce MMP9 production, which will be involved in E-cadherin cleavage and the release of soluble E-cadherin and subsequent detachment of melanocytes. MMP9 inhibition could contribute to melanocyte stabilization to the basal layer of the epidermis in vitiligo patients.

ABSTRACT:

Melanocyte loss is the pathological hallmark of vitiligo; yet, whether such disappearance results from melanocyte death due to a cytotoxic activity of CD8 T cells and/or their detachment, the so-called melanocytorrhagy hypothesis, due to a defect of the melanocyte adhesion system, involving in particular E-cadherin, still remains debated. Multiple combinatorial factors have been involved in disease development, with a prominent role of the immune system, in particular T cells. We recently showed that vitiligo skin harbors melanocyte specific resident memory T cells that produce elevated levels of the inflammatory cytokines IFN γ and TNF α , while displaying moderate cytotoxic activity. Therefore, we further explored the interplay between the inflammatory response characterizing vitiligo disease and the loss of melanocytes. Using an in vitro model of reconstructed pigmented human epidermis, we found that the combined activity of IFN γ and TNF α induced melanocyte detachment rather than their death through disruption of membrane E-cadherin expression, the major protein involved in melanocyte attachment to keratinocytes, and the release of soluble E-cadherin.. Such phenomenon further confirmed in vivo following dermal injection of both cytokines, and was also undeniably observed in vitiligo patients perilesional skin. Importantly, IFN γ and TNF α induced the production of matrix metalloproteinase 9 (MMP9) by epidermal cells, leading to E-cadherin cleavage and melanocyte detachment from the basal layer of the epidermis. In vitiligo patients, MMP9 levels were found upregulated both in the skin and blood flow and positively correlated with the body surface area involved. Lastly, MMP9 inhibition allowed melanocyte stabilization to the basal layer of the epidermis both in vitro and in vivo. These results highlight an uncovered role of MMP9 and a new mechanism to explain depigmentation associated with inflammation and targeting MMP9 could represent an attractive strategy in vitiligo, a disease that still suffers from a lack of effective treatment.

003

Activation of Melanocytic CXCR3B Initiates the Auto-immune Response in Vitiligo

Prof. Thierry Passeron

Université Côte d'Azur Nice, Department of Dermatology & INSERM, Nice, France

Friday, November 9, 2018, 9:22:00 AM - 9:32:00 AM

TAKE HOME MESSAGE:

Innate immunity plays a key role in the initial steps of vitiligo

Melanocytes expressed the isoform B of CXCR3

Activation of CXCR3B on melanocytes by CXCL10 induces their initial apoptosis

Activated by the local production of IFN γ , the remaining melanocytes expressed co-stimulatory molecules and present their own antigens to the T cells attracted by the chemokines and initiate the adaptive response

Targeting CXCR3B appears as a new therapeutic target to prevent and to treat vitiligo

ABSTRACT:

Increasing evidence has shown that the disappearance of melanocytes in the skin of vitiligo patients is secondary to an adaptive T-cell mediated immune response. However, the initial steps involved in the anti-melanocytic specific immune response remain unknown. Here we demonstrated, using skin and blood samples extracted from vitiligo patients and compared to healthy controls, that non-lesional skin and blood of vitiligo patients has a significant increase in natural killer and type 1 innate lymphoid cells that initially produce interferon gamma (IFN γ). Upon IFN γ stimulation melanocytes and keratinocytes are producing chemokines such as CXCL9, 10 and 11, that attract T cells. We show that melanocytes extracted from non-lesional skin of vitiligo patients have a strong basal expression of Chemokine (C-X-C motif) receptor 3 (CXCR3) isoform B while melanocytes from healthy volunteers have a low expression and keratinocytes lack CXCR3B. CXCR3B activation by CXCL10 at the surface of melanocytes induces their initial apoptosis. The remaining melanocytes, activated by the IFN γ production, start expressing markers of activated presenting cells and present their own antigen to the attracted T cells, thus initiating the specific anti-melanocytic immune reaction. Inhibiting the CXCR3B activation prevents this initial apoptosis and the further activation of T cells in co-culture of melanocytes of vitiligo patients with their autologous peripheral blood mononuclear cells.

These results emphasize the key role of CXCR3B in the initial apoptosis of melanocytes and identify CXCR3B as a new target to prevent and to treat vitiligo by acting at the very early steps in their destruction.

004

NKG2D/NKG2D Ligands Axis: Implication During Initiation and Inflammatory Occurrence Phases in Vitiligo

Dr. Katia Boniface

INSERM U1035-ImmunoDermatology Team, Bordeaux, France

Friday, November 9, 2018, 9:32:00 AM - 9:42:00 AM

TAKE HOME MESSAGE:

- Vitiligo perilesional skin CD8+TEM cells highly express NKG2D.
- CD8+TEM NKG2D+ cells express markers of residency and display increased expression of the cell proliferation and activation associated markers with higher capacity to produce elevated levels of IFN γ and TNF- α , compared to the negative NKG2D counterpart
- Melanocyte-specific vitiligo CD8+TEM cells are enriched within the NKG2D+ T cell population
- In vitro Mo-DC cultured in the presence of IFN γ display increased expression of the NKG2D Ligands MICA/MICB.

ABSTRACT:

Vitiligo is an autoimmune disease that results from the loss of epidermal melanocytes, with a prominent role of both innate and adaptive immune cells. We have recently shown that vitiligo perilesional skin is infiltrated by CXCR3+ CD8+ resident memory T cells producing both IFN γ and TNF α , two pro-inflammatory cytokines found important for the progression of the disease. However, the mechanism that could promote such production of type 1 cytokines remains unclear. Natural Killer (NK) Group 2D (NKG2D) is an activating receptor mainly found on immune cells, including NK, NKT and CD8+ T cells. CD8+NKG2D+ T cells play a major role during immune surveillance and are involved in the excessive immune response occurring in autoimmune diseases. However, the involvement of NKG2D in vitiligo pathogenesis remains to be elucidated. Here, we show that expression of NKG2D is up-regulated on skin CD8+ effector memory T (TEM) cells in perilesional skin of progressive vitiligo compared to stable vitiligo, psoriasis or control skin. A thorough analysis of extracted skin T cells revealed that CD8+NKG2D+ TEM cells express markers of residency such as CD69, and/or CD103, and display increased expression of the cell proliferation-associated marker Ki-67 but also of activation markers including HLA-DR, and Inductible T-cell CO-Stimulator (ICOS). This NKG2D+ T cell subset produces elevated levels of both IFN γ and TNF- α compared to the NKG2D- counterpart. Moreover, more than 60% of the skin CD8+NKG2D+ T cells showed specificity for melanocyte antigens in progressive vitiligo. Interestingly, we found that T cells expressing NKG2D are characterized by an increased intensity of expression of the T cell receptor (TCR) and that NKG2D expression is not altered following TCR activation or after stimulation with multiple pro-inflammatory cytokines or chemokines such as IFN γ , TNF- α , CXCL9 and CXCL10, suggesting that NKG2D expression is stable during the inflammatory events occurring during the progression of the disease. Additional experiments showed that monocytes derived myeloid dendritic cells (Mo-DCs) stimulated by IFN- α induce NKG2D Ligand expression by Mo-DCs, notably MHC class I chain-related protein A and B (MICA and MICB), suggesting that these pro-inflammatory DCs could potentiate the local activation of skin NKG2D+ CD8+ T cells. All together, these data highlight NKG2D as a potential marker of pathogenic CD8+TEM subset important for vitiligo progression, which could be therapeutically exploited for the management of this near-orphan disease.

005

Advances in the Role of Metabolism in Vitiligo

Dr. Emanuela Bastonini

IFO San Gallicano Dermatologic Institute, IRCCS, Italy

Friday, November 9, 2018, 9:42:00 AM - 10:52:00 AM

TAKE HOME MESSAGE:

Our data argue for an intrinsic metabolic impairment involving the cells of both dermal and epidermal compartment. Thus, the metabolic machinery may be considered as a possible innovative target for therapy.

ABSTRACT:

A growing number of studies supports the existence of intrinsic metabolic defects in vitiligo melanocytes that lead to an intracellular oxidative stress acting as a main intracellular signal transduction in cell degeneration. Recently, we demonstrated that, compared to healthy melanocytes, cultured non lesional vitiligo melanocytes present an impaired mitochondrial energy metabolism manifested as increased mitochondrial mass associated to a paradoxical lower level of ATP production and mitochondrial DNA (mtDNA) quantity. Evidence argues for a dynamic interplay between cellular energy and autophagy balance and defines autophagy induction as an adaptive metabolic response under several stress conditions. Autophagy which is a sensor of redox signaling, may be considered a metabolic process that can restore energy balance. Autophagy is an evolutionarily conserved catabolic process of recycling that guarantees cellular homeostasis by a selective removal of aberrant misfolded or long-lived proteins, damaged lipids and dysfunctional organelles. Here, we show that autophagic activity occurs in melanocytes and fibroblasts derived from non lesional skin of vitiligo patients. Moreover, this activation is correlated with AMPK signaling, PI3K-mammalian target of rapamycin (mTOR) pathway and SIRT1 expression. Some autophagy-related genes are up-regulated in primary cultures of melanocytes and fibroblasts derived from non lesional skin of vitiligo patients respect to healthy subjects. In parallel LC3-II, the most used biomarker of autophagosome formation, is significantly increased in vitiligo cells and we show that its activation can be due to the augmented intracellular ROS content since the expression of LC3-II decreased following the treatment with the ROS scavenger N-acetyl-L-cysteine in non lesional vitiligo melanocytes. On the other hand, in normal melanocytes tert-butyl hydroperoxide-induced oxidative stress increased autophagy as shown by the over-expression of Atg genes and LC3-II. We have confirmed that mtDNA copy number is significantly reduced in vitiligo melanocytes compared to sex- and age-matched healthy subject. Moreover, the mRNA level of expression of specific mitochondrial DNA polymerase- β (POL- β), an important regulator of mitochondrial biogenesis, displayed no significant difference in the vitiligo group compared with healthy donors. Overall, data indicated that in vitiligo melanocytes, due to impaired mitochondrial functionality that does not correlate with augmented mitochondriogenesis, the increases of mtDNA mass and the occurrence of autophagy may represent a compensatory mechanism to maintain normal energetic level.

006

Validity and Feasibility of the Self Assessment Vitiligo Extent Score (SA-VES) Among Egyptian Patients

Prof. Marwa Abdallah

Ain Shams University, Faculty of Medicine, Cairo, Egypt

Friday, November 9, 2018, 10:57:00 AM - 11:07:00 AM

TAKE HOME MESSAGE:

Self-administered vitiligo extent score (SA-VES) demonstrated excellent feasibility (easily comprehensible to physician and patient, easily administered to the patient, short completion time) in an Egyptian patient population. It showed validity with physician's vitiligo extent score (VES) (high significant correlation and high internal consistency). SA-VES is a user-friendly vitiligo extent score in patients of different cultural and educational backgrounds.

ABSTRACT:

Background:

Self Assessment Vitiligo Extent Score (SA-VES) was previously validated allowing patients to score their vitiligo extent in an easy way. Conducting similar studies on a wider range, darker skin types, patients with more extensive vitiligo and of different settings could add to the value of the new scoring system. In addition, feasibility aspects (ease of application of a Patient Reported Outcome Measure in its intended context of use) are considered to be important in the selection of the most appropriate instrument.

Aim of work:

To describe the feasibility of using of SA-VES among Egyptian vitiligo patients of different educational levels. Furthermore, validity of the SA-VES was evaluated in this Egyptian patient population.

Patients and methods:

Vitiligo patients of different age groups attending the vitiligo clinic at Ain Shams University Hospitals from October 2017 to April 2018 were enrolled. All patients were subjected to evaluation of VES by the physician and SA-VES by the patients or their parents (children). Validity for SA-VES was determined by comparing the results of both SA-VES and VES, while feasibility was determined by recording the completion time, patient's required mental ability level, ease of administration, and comprehensibility of using the SA-VES.

Results:

Vitiligo patients (n=207; 128 females & 79 males; age range 1- 79 y mean 23.78, SD 18.49 y) with Fitzpatrick skin types II-VI (II (4,3%), III (33.3%), IV (45.9%), V (8.2 %) & VI (4.8%)) were included in our study. Patients had different educational levels ranging from illiterate to postgraduate. The mean VES was 1.92 (SD 3.54, range 0.003-

31.13) and SA-VES was 1.78 (SD 3.62, range 0.01-36.69). VES and SA-VES showed a significant positive correlation ($p < 0.05$). The test was easily administered and only 19.1% ($n=33$) of adults needed physician's assistance during completing the SA-VES.

Conclusion:

SA-VES demonstrated excellent feasibility and highly significant correlation with VES in an Egyptian patient population. SA-VES is a user friendly vitiligo extent score in patients of different cultural and educational backgrounds.

007

Interpretation of the Self Assessment Vitiligo Extent Score (SA-VES) by Suggesting Severity Strata by Use of Anchor-Based Methods

Prof. Nanja van Geel

Ghent University Hospital, Ghent, Belgium

Friday, November 9, 2018, 11:07:00 AM - 11:17:00 AM

TAKE HOME MESSAGE:

This study provides the first guide for the interpretation of the numerical output obtained by the SA-VES (vitiligo extent) and enables the translation into a global vitiligo severity grade.

ABSTRACT:

Background:

The self assessment vitiligo extent score (SA-VES) is a validated, patient derived assessment measure for monitoring vitiligo extent. Information on how to translate the obtained extent scores into disease severity strata based on patient global assessment categories (limited to severe) is still lacking. The patients' perception is utmost important when defining these cut off points. Stratification is needed to define inclusion criteria for clinical trials, epidemiological research and is important for correct comparison and pooling of trial results.

Objectives:

The first aim was to develop severity strata for the SA-VES for use in patients with vitiligo. The second aim was to investigate the role of several factors on patients' interpretation of severity and extent (e.g. disease impact, skin type, number of involved areas and location of lesions).

Methods:

In total 607 patients with vitiligo (non segmental) completed a questionnaire at the Ghent University Hospital (consecutively) including 2 patients-assessed anchor questions. These anchor questions consisted of 2 of our

validated 5-point Patients Reported Global Assessment (PR-GA) scores for severity (PR-Gas) and extent (PR-GAe), ranging from not severe/no involvement to very severe/very extensive. The relationship between these PR-GAs and the SA-VES was determined in order to stratify the SAVES scores. Furthermore, the role of several factors on patients' interpretation of severity were in addition assessed by evaluating the correlation coefficients between the PR-Ga for severity and several factors (e.g. BSA, impact, photo skin type, location of lesions, age...)

Results:

The median SA-VES score per category for PR-GA of extent was 0.74% for limited, moderate 2.46%, extensive 8.25% and very extensive 29.21%. Cut-off value (SA-VES) based on ROC analysis between limited and moderate extensive was 1.26%; between moderate and extensive 3.97%; and between extensive and very extensive 19.70%. The median SA-VES score per category for PR-GA of severity for limited was 0.60%, moderate 1.92%, severe 5.42% and very severe 8.44%. Cut-off value (SA-VES) based on ROC analysis between limited and moderate severe was 0.92%, between moderate and severe 2.72% and between severe and very severe 20.22%. Significant correlating factors regarding patients' severity perception (PR-GA for severity) were: total affected Body Surface Area, disease impact, involvement hands, age and number of involved areas.

Conclusion:

This study provides the first guide for the interpretation of the numerical output obtained by the SA-VES (vitiligo extent) and enables the translation into a global vitiligo severity grade. Patients' interpretation of vitiligo severity and extent will probably vary amongst patients worldwide. Future studies are therefore necessary to get further insight into this variation.



008

Establishing the Fingertip Unit as a Measurement to Assess BSA Across Diverse Ethnic Populations

Dr. Raheel Zubair

Henry Ford Hospital, Detroit, MI, USA

Friday, November 9, 2018, 11:17:00 AM - 11:27:00 AM

TAKE HOME MESSAGE:

The study compared palm and finger sizes and found that the palm measured 18 FTUs and the hand measured 32 FTUs. By setting 32 FTU, the area of the hand unit, equivalent to 1% BSA, it was found that 1 FTU corresponds to 0.03% BSA. Among the 58 patients in the study, hand to palm area ratios were close to constant among both children and adults. While the Seoul study used a homogenous population, a follow-up study in Detroit, MI aims to determine whether FTU to hand area ratios are constant across a diverse population.

ABSTRACT:

Vitiligo is a common dermatologic disease characterized by skin depigmentation that results from melanocyte destruction. One of the most widely used instruments used to assess vitiligo severity and treatment response is the Vitiligo Area Scoring Index (VASI).¹ In this instrument, the hand unit, which is the entire palmar surface of one hand and digits, corresponds to 1% body surface area (BSA). Like similar instruments, VASI has a limited ability to evaluate pigment changes in small areas. A study in Seoul, South Korea raised the possibility of using the fingertip unit (FTU) to measure small areas of BSA. 1 FTU was defined as the area of the palmar surface between the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joint, the PIP and distal phalangeal (DIP) joint, or the DIP and the tip of the finger. The study compared palm and finger sizes and found that the palm measured 18 FTUs and the hand measured 32 FTUs. By setting 32 FTU, the area of the hand unit, equivalent to 1% BSA, it was found that 1 FTU corresponds to 0.03% BSA. Among the 58 patients in the study, hand to palm area ratios were close to constant among both children and adults. While the Seoul study used a homogenous population, a follow-up study in Detroit, MI aims to determine whether FTU to hand area ratios are constant across a diverse population. 5-10 subjects, both adults and children, in 6 racial categories, will have their dominant hand photographed with an object of known size for calibration purposes. Ratio of FTU and palm areas to that of the hand will be compared using image analysis. The results will be presented and will help to conclude if FTU can be used as an adjunct to the hand unit when evaluating BSA. This could lead to improvements in the accuracy and speed of VASI. s



009

Vitiligo Surface Area Smartphone Application

Conor Vickers

Lewis Katz School of Medicine at Temple University, Philadelphia, USA

Friday, November 9, 2018, 11:27:00 AM - 11:37:00 AM

TAKE HOME MESSAGE:

Smartphone technology allows for new methods to perform surface area measurements of vitiligo skin involvement and track changes over time.

ABSTRACT:

Introduction:

Precise assessment of the surface area involvement of vitiligo is an important part of clinical research and treatment. Due to involvement of different anatomic sites, calculation of the total area involved presents a challenge. Currently, the standard technique involves taking a picture of a lesion or a tracing of a lesion next to a ruler for scale, uploading that image onto a computer, and using an image software to calculate the area. Presented here is a novel technique using a smartphone application to perform surface area measurements.

Methods:

Ten different shapes were cut out, and photos were acquired using the smartphone app. Images were acquired from a short distance (10 cm) and a farther distance (30 cm) with a ruler in view. The shapes included 3 shapes with easily calculated geometrical areas (square, circle, triangle) and 7 abstract shapes with largest diameters ranging from 2cm to 7cm. Surface area measurements were made with both the smartphone app and ImageJ software; Pearson correlation analysis was used to evaluate the agreement between the measurements. In addition, the paired t-test was performed to evaluate an upward or downward shift in the measured areas as detected by the app compared to that by imageJ software.

Results:

A statistically significant ($p < 0.05$) between App and imageJ measured surface areas.

Discussion:

A high correlation coefficient between app measurements and ImageJ measurements imply excellent agreement between the area measurements obtained by both techniques. Also, there were no statistically significant differences between the measurements implying that the app can serve as an accurate and reliable alternative for performing surface area measurements. It will allow physicians and researchers to take pictures of cutaneous lesions with their smartphones and save the image with surface area measurements which can be used at follow up visits to account for improvement or worsening. This app can potentially be utilized for other skin conditions.

010**Quantitative Assessment of Vitiligo in Vivo Using Multimodal Optical Spectroscopy**

Dr. Harvey Lui

Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

Friday, November 9, 2018, 11:37:00 AM - 11:47:00 PM

TAKE HOME MESSAGE:

Noninvasive optical analysis of vitiligo reveals additional potential pathophysiologic changes beyond the absence of melanin from the skin.

ABSTRACT:**Background:**

Reduced epidermal pigmentation is considered the primary pathophysiological difference between vitiligo and normal skin. Morphologic variants of vitiligo are based qualitatively on the distribution of lesions and their clinical appearances. The objective of this study is to quantitatively assess vitiligo in terms of its pathophysiological changes using multimodal spectroscopy.

Patients and Methods:

Thirty-seven patients (17 male, 20 female) were recruited in this study with a mean age of 42 (range: 18-74) years, and covering skin types I (4), II (9), III (13), IV (7) and V (4). Lesions of vitiligo and the adjacent normal skin were measured using diffuse reflectance and Raman spectroscopy. Skin color was calculated from the diffuse reflectance spectrum in the CIE L*a*b* color space. Biophysical properties including melanin, oxy-hemoglobin and deoxy-hemoglobin and scattering were calculated using the empirical Kollias algorithm. Lesion versus normal properties were analyzed statistically using the two-tailed non-parametric paired Wilcoxon test.

Results:

Vitiliginous skin exhibits significantly higher L*, lower a* and b* than adjacent normal skin (p

011**Treatment of Severe Vitiligo Using Apremilast: a Double Blind Placebo Controlled Study in 80 Patients****Prof. Thierry Passeron**

Université Côte d'Azur. CHU Nice, Department of Dermatology & INSERM U1065, team 12, Nice, France

Friday, November 9, 2018, 1:22:00 PM - 1:32:00 PM

TAKE HOME MESSAGE:

- Apremilast acts on the adaptive immune response occurring in vitiligo
- Apremilast, by activating on the cAMP pathway, could enhance the repigmentation process
- Results of this clinical study will allow to determine the clinical efficacy of this treatment in combination to UVB

ABSTRACT:

The role of the adaptive immunity in the depigmentation process of vitiligo lesions is now well demonstrated. Apremilast is a phosphodiesterase 4 inhibitor that showed efficacy and good tolerance in rheumatoid arthritis and psoriasis. Apremilast induces a potent activation of the cyclic AMP (cAMP) pathway leading to a decrease activation of the Th1 and Th17 pathway along with a decreased production of CXCL10. Interestingly, the cAMP pathway is well demonstrated to be the main pathway for inducing proliferation of melanocytes and melanogenesis. Indeed, it induces the phosphorylation of the transcription factor CREB that in return activates MITF. MITF is the key transcription factor of melanocyte regulating proliferation process and inducing melanogenesis by increasing the

transcription of tyrosinase and DCT enzymes. Thus apremilast appears of interest not only to halt the depigmentation process but also to potentiate the repigmentation in vitiligo.

We conducted a monocentric prospective randomized trial. 80 patients with vitiligo on more than 5% of the total body surface area were included. The study was divided in 2 phases. In the first phase of 24 weeks, patients were randomized (1:1) to receive UVB (twice weekly) and 30mg BID apremilast or UVB (twice weekly) and placebo. All patients achieving more than 30% of repigmentation were then enrolled in the second phase of the study. In this second phase the responding patients were re-randomized and received UVB (twice weekly) and 30mg BID apremilast or UVB (twice weekly) and placebo, for 24 additional weeks. The evaluation was performed by two independent physicians on standardized pictures. The main criteria of evaluation was the VASI score. VETF, VES and DLQI were also assessed.

The statistical analysis of the first phase is ongoing. The results of the phase 1 will be presented during the meeting.

012

Qualitative and Quantitative Comparison of Two Methods of Cell-based Therapies in Vitiligo

Prof. Somesh Gupta

All India Institute of Medical Sciences, New Delhi, India

Friday, November 9, 2018, 1:32:00 PM - 1:42:00 PM

TAKE HOME MESSAGE:

Non-cultured epidermal cell suspension (NCECS) and non-cultured extracted hair follicle outer root sheath cell suspension (NC EHF ORS CS) provide comparable results even though the number of transplanted cells in NC EHF ORS CS was one tenth of NCECS. This may be due to higher proportion of melanocytes and their precursor stem cells in hair follicles as compared to epidermis.

ABSTRACT:

Introduction:

Non-cultured epidermal cell suspension (NCECS) and non-cultured extracted hair follicle outer root sheath cell suspension (NC EHF ORS CS) are the commonly used procedures for cell-based therapy in vitiligo; however, there is limited data available on the quantitative and qualitative aspects of these cell suspensions, such as cell yield and cell viability.

Aim:

Quantitative and qualitative assessment of NCECS and NC EHF ORS CS.

Methods:

Each patient underwent both the procedures on different comparable patches or, when a large patch was present, the patch was divided into two equal halves and randomized to receive either NCECS or NC EHF ORS CS. Patients were followed up for six months and percentage repigmentation was calculated.

Results:

Thirty patients (24 female and 6 male) with stable vitiligo were included in the study. The average number of cells obtained using NC EHF ORS CS was $349,643 \pm 532,701.7$ and NCECS was $3,553,750 \pm 3,327,956.2$. The average cell viability was found to be 79.05% in NCECS and 80.80% in NC EHF ORS CS. Repigmentation was noted at weeks 16 and 24. Repigmentation in NCECS group was $48.6 \pm 35.4\%$ and $52 \pm 36.6\%$ at 16 and 24 weeks, respectively. In NC EHF ORS CS group, the repigmentation was $37.7 \pm 33.2\%$ and $52 \pm 35.4\%$, at 16 and 24 weeks, respectively.

Conclusions:

Our study shows encouraging results with the use of NC EF ORS CS and NCECS in the treatment of stable vitiligo. Although the mean number of cells transplanted in NC EF ORS CS is approximately 1/10th of the cells transplanted through NCECS, percentage re-pigmentation using both methods was found to be comparable at the end of 6 months.

013**Lessons from Healthcare Big Data Analyses for Vitiligo and Phototherapy**

Prof. Jung Min Bae

Department of Dermatology, College of Medicine, The Catholic University of Korea, Gyeonggi-do, South Korea

Friday, November 9, 2018, 1:42:00 PM - 1:52:00 PM

TAKE HOME MESSAGE:

Using the Korean NHI Claims database, we performed a series of statistical analyses on the associations between vitiligo and various autoimmune diseases, the pregnancy outcome of patients with vitiligo, the risk of skin cancer following long-term phototherapy, and the effects of long-term phototherapy on cardiovascular and bone health. Big data has the potential to answer the clinical queries that could not be solved in the clinical practice. In this session, we will discuss recent findings from healthcare big data analyses for special issues on vitiligo and phototherapy.

ABSTRACT:**Introduction:**

Vitiligo is a common autoimmune depigmentation skin disorder affecting 1% of the population. Phototherapy has been the mainstay of treatment for vitiligo over decades, and frequently requires long treatment durations for more than a few years. However, little is known about vitiligo and the effects of long-term exposure to ultraviolet light on skin and health during phototherapy. Korea runs one of the largest National Health Insurance (NHI) systems

worldwide, which covers up to 98% of the 50 million people in Korea. The Korean NHI database contains all claims information from the NHI program and the Korean Medical Aid program for the past 10 years. It includes all information on the use of medical services of more than 100,000 patients with vitiligo.

Objective:

To explore the effects of long-term exposure to ultraviolet light on skin and health during phototherapy including the risk of skin cancer, cardiovascular and bone health.

Methods:

Using the Korean National Health Insurance (NHI) Claims database, we performed a series of statistical analyses on the associations between vitiligo and various autoimmune diseases, the pregnancy outcome of patients with vitiligo, the risk of skin cancer following long-term phototherapy, and the effects of long-term phototherapy on cardiovascular and bone health. The database includes all information on the use of medical services of more than 100,000 patients with vitiligo in Korea for the past 10 years.

Results:

We demonstrated that pregnant women with vitiligo had a significantly lower rate of full-term pregnancy rate (OR 0.870, 95% CI 0.816-0.927) and higher incidence of spontaneous abortion (OR 1.250, 95% CI 1.148-1.362) than pregnant women without vitiligo. Compared to the no narrow-band UV-B phototherapy group, patients treated more than 100 sessions showed reduced risks of cardiovascular events (HR 0.599, 95% CI 0.369-0.971), cerebrovascular events (HR 0.808, 95% CI 0.671-0.974), and all major osteoporotic fractures (HR 0.699, 95% CI 0.576-0.849), respectively.

Conclusion:

Big data has the potential to answer the clinical queries that could not be solved in the clinical practice.



014

Study of Serum IL-23 Level in Active, Stable and NB:UVB Treated Non-segmental Vitiligo

Dr. Fathy Ghada Muhammad

Ain Shams faculty of Medicine, Ain Shams University, Cairo, Egypt

Friday, November 9, 2018, 1:52:00 PM - 2:02:00 PM

TAKE HOME MESSAGE:

- Altered serum IL-23 level might have a role in immunopathogenesis of non-segmental vitiligo through initiation of inflammation (activity) rather than maintenance and progression (duration) of the vitiligo.

- NB-UVB treatment decreased serum level of IL-23 in patients with active non-segmental vitiligo which might further intensify the role of NB-UVB as an immunomodulatory agent.

ABSTRACT:

Background:

Limited studies regarding the participating role of interleukin 23 (IL-23) in the pathogenesis of vitiligo, have been performed on few numbers of vitiligo patients which lead to contradictory results.

Objective:

to determine the potential participation of IL-23 in the pathogenesis of vitiligo in active, stable and narrow band ultra violet B (NB: UVB) treated vitiligo.

Methods:

a case control study which was carried out on 40 patients with non-segmental vitiligo; twenty patients with active vitiligo, twenty with stable vitiligo versus age and sex matched healthy controls. All patients were subjected to 40 NB-UVB sessions, 3 sessions/week (13 weeks). Serum IL-23 levels were measured by ELISA technique before and after treatment.

Results:

Before treatment, compared to serum IL-23 level in controls (mean 35.50 ± 20.21) pg/ml, a significant higher serum IL-23 levels in active vitiligo patients (mean 76.39 ± 37.55) pg/ml, however stable vitiligo patients had a non-significant difference (mean 40.45 ± 27.14) pg/ml ($P=0.463$). Comparison between active versus stable vitiligo revealed a high significant difference ($P=0.002$). A significant positive correlation was found between serum IL-23 levels with disease activity and body surface area (VETI score). After NB: UVB treatment sessions, a significant reduction in serum IL-23 levels in active vitiligo patients (mean 53.65 ± 18.48) pg/ml ($P=0.002$) was detected, however no significant difference was detected in stable vitiligo patients (mean 40.45 ± 27.14) pg/ml compared to with the NB-UVB treated group ($P=0.080$).

Conclusion:

Altered serum IL-23 level might have a role in immune-pathogenesis of non-segmental vitiligo through initiation of inflammation (activity) rather than maintenance and progression (duration) of the vitiligo.

015

Depigmentation with Q-switched Nd:YAG Laser in Universal Vitiligo: A Long-term Follow Up Study of 4-years

Dr. Imran Majid

CUTIS Institute of Dermatology, Srinagar Kashmir, India

Friday, November 9, 2018, 2:02:00 PM - 2:12:00 PM

TAKE HOME MESSAGE:

QS Nd:YAG laser is an effective tool for treating residual pigmentation in universal vitiligo and the therapeutic effect can be maintained in most cases with regular sunscreen use and need-based topical therapies.

ABSTRACT:

Purpose:

Q-switched (QS) lasers are used for depigmentation in universal vitiligo but there is limited data on long-term results after laser treatment. This study was conducted to assess the safety and long-term follow up results of QS Nd:YAG laser treatment in combination with need based topical depigmentation therapy universal vitiligo.

Methods:

A retrospective study was performed on patients of universal vitiligo who had received QS Nd:YAG laser treatment from 2010 to 2013. All these patients were contacted and called for follow-up. Patients who reported were assessed clinically and information regarding adverse effects and relapse (repigmentation) in the follow-up period was obtained. Any need for topical depigmenting creams or other interventions and overall satisfaction to treatment was also documented.

Results:

Records of 34 patients were retrieved out of whom 28 cases reported for the follow-up visit. Duration of follow-up ranged from 2-years to 5-years (mean 2.78). No long-term adverse effects were reported and majority of cases were highly satisfied with treatment. Satisfactory results with >90% clearance of pigment was reported by 89.3% (25/28) cases out of whom 72% (18/25) cases had retained the therapeutic effect with the use of sunscreens with/without intermittent topical depigmentation therapies. In 7 cases partial to complete relapse was observed.

Conclusions:

QS Nd:YAG laser is an effective tool for treating residual pigmentation in universal vitiligo and the therapeutic effect can be maintained in most cases with regular sunscreen use and need-based topical therapies.

016

Knowledge, Habits, and Risk Perception Associated with Sun Exposure in Vitiligo Patients

Dr. Bhavnit Bhatia

Henry Ford Health System, Detroit, MI, USA

Friday, November 9, 2018, 3:50:00 PM - 4:02:00 PM

TAKE HOME MESSAGE:

The photoprotection habits of patients as well as the understanding of the effects of UV light on vitiligo differs significantly between those patients who participate in support groups and those who do not. For male patients and those who are not part of support groups, physician counseling should include discussion of photoprotective behaviors such as applying and reapplying sunscreen, seeking shade, wearing protective clothing, avoiding prolonged sun exposure, and avoiding exposure during peak sun hours. They should be counseled that vitiligo does not predispose them to higher rates of skin cancer, and may in fact be protective. All patients should be educated about gradual exposure to the sun, particularly as an adjunct therapy to topical and systemic therapies, such as JAK inhibitors.

ABSTRACT:

Importance:

Despite ultraviolet light exposure being one of the main treatments of vitiligo, no previous studies have thoroughly investigated the sun-related habits of vitiligo patients.

Objective:

To determine the knowledge and perception of risk regarding sun exposure in vitiligo patients according to their participation in a vitiligo support group.

Design:

Prospective cross-sectional study using a semi-directed questionnaire. We compared patients based on membership in support groups. The study was initiated on June 20, 2017 and ended on December 20, 2017.

Setting:

Multicenter, cross-sectional study with patients from vitiligo support groups and dermatology referral centers based in France and the US. Patients who were attending the vitiligo clinics of all participating centers were systematically proposed to participate.

Participants:

Vitiligo patients age 18 and older. Participants were recruited using volunteer sampling. A total of 479 vitiligo patients participated. Of these, 361 patients completed the SA-VES.

Results: A total of 479 vitiligo patients out of the 501 patients who were proposed to participate in the study agreed to do so and responded to the questionnaire. Of these, 62% declared to belong to a support group and 38% declared not to. A total of 363 patients responded to the SA-VES, of whom 244 were considered to have severe disease (SA-VES>6%). Patients belonging to a support group had safer habits and behavior towards sun exposure; i.e. reapplying sunscreens (OR, 2.11; P=0.02 for two applications per day and OR, 2.09; P=0.04 for three application a day). Similarly, patients belonging to a support group declared less often to believe that sun exposure of vitiligo leads to increased risk of skin cancer (OR, 0.4; P

017

Examining the Relationship Between Vitiligo and Obesity

Dr. Sheena Nguyen

Western University of Health Sciences, Huntington Beach, CA, USA

Friday, November 9, 2018, 4:02:00 PM - 4:14:00 PM

TAKE HOME MESSAGE:

Though our data set demonstrated a negative study for the direct link between vitiligo and obesity, this may still have value in directing future studies towards examining other factors of metabolic syndrome to vitiligo - both of which are burdening on multiple levels for the patient. With more data emerging on vitiligo being related to pro-inflammatory conditions, further studies are also needed to not just examine obesity being related to vitiligo severity but also activity as well potentially being used as a predictor of disease course.

ABSTRACT:

Though there is growing evidence that vitiligo is related to pro-inflammatory conditions such as metabolic syndrome and obesity, very few publications address any direct linkage and a review of current literature does not reveal any insightful information into the connection between vitiligo and obesity. For our study in examining a potential link between vitiligo and obesity, we extracted data from a cohort of patients with vitiligo seen in clinic. Using both the Vitiligo Assessment Severity Index (VASI) and calculating each patient's Body Mass Index (BMI) from our sample size of 67 patients ranging in age from two to 69 years, we were able to analyze the correlation between these variables. Though our data set demonstrated no relationship for the direct link between vitiligo and obesity, this may still have value in directing future studies towards examining other factors of metabolic syndrome to vitiligo - both of which are burdening on multiple levels for the patient.

018

Phenotypic Influence of Atopic Diathesis in Adult Vitiligo

Prof. Julien Seneschal

University of Bordeaux, Department of Dermatology, Saint-André Hospital, Bordeaux, France

Friday, November 9, 2018, 4:14:00 PM - 4:26:00 PM

TAKE HOME MESSAGE:

- Vitiligo is frequently associated with autoimmune diseases such as autoimmune thyroiditis and atopy.

- Atopy is associated with elevated levels of serum IgE.
- The presence of high IgE levels in patients with vitiligo is negatively associated with autoimmune background. The presence of high IgE levels in patients with vitiligo is associated with Koebner Phenomenon type 1.
- High levels of IgE might be protective for the development of other chronic autoimmune inflammatory disorders in vitiligo.
- The benefit of surgical procedures for the treatment of vitiligo in patients with high IgE levels should be carefully weighted with the risk of depigmentation at the donor site.

ABSTRACT:

Vitiligo is a chronic inflammatory skin depigmenting disorder that is often associated with other autoimmune disease such as thyroiditis.¹ Moreover, there is growing evidence that vitiligo is also associated with atopy, a genetic tendency to develop allergic hypersensitivity reactions, with production of immunoglobulin E (IgE). Patients with vitiligo have a higher prevalence of atopic dermatitis; however, the link between IgE levels and vitiligo has not been yet investigated. We sought to compare clinical and demographical factors between vitiligo patients with or without elevated IgE levels. To this end, we conducted a monocentric observational retrospective study including consecutive adult vitiligo patients attending the vitiligo clinic. Demographic characteristics and clinical features were recorded using the Vitiligo European Task Force (VETF) questionnaire. Total IgE levels, thyroid function and the presence of thyroid antibodies were measured routinely. A total of 256 patients were included. Forty-six (17.97%) had elevated total IgE and 210 (82.03%) had normal total IgE levels. Elevated IgE levels were positively associated with atopy and Koebner phenomenon type 1 (depigmentation on site of trauma) (OR, 2.15 [1.07-4.76] ; p=.0405). There was a negative association with autoimmune background (OR, 0.36 [0,15;0,86] ; p=.0222). These observations suggest that the presence of high levels of total IgE in patients with vitiligo might be protective for the association of vitiligo with other chronic inflammatory or autoimmune disorders.



019

Quality of Life in Vitiligo Support Groups

Zoe Smith

Wayne State School of Medicine, Detroit, MI, USA

Friday, November 9, 2018, 4:26:00 PM - 4:38:00 PM

TAKE HOME MESSAGE:

This survey demonstrates that vitiligo support group members are more likely to report a worse quality of life than

non-support group members. Vitiligo support group members also report an increased prevalence of poorer QoL indicators and more severe overall disease involvement in exposed portions of the body (face). Our data suggests that vitiligo patients with a worse quality of life seek out psychosocial support systems. There may be a potential protective effect and benefit of support group participation. Considering the risk of psychological co-morbidities in vitiligo patients, it is recommended to utilize support groups to promote the physical and psychological health of these patients.

ABSTRACT:

Introduction:

Vitiligo places a physical and psychological burden on many patients. Current literature suggests a greater risk of psychiatric morbidity and a significant effect on a person’s health-related quality of life (HRQL). Preliminary evidence suggests that support groups are helpful in reducing stress and improve quality of life (QoL). Although a small number of cohorts and case reports have used the vitiligo-specific instrument to capture disease-targeted concerns and issues, no study has compared QoL of vitiligo patients who are support group members versus those who are non-support group members.

Objective:

We sought to evaluate and compare the QoL in support group members versus non-support group members with vitiligo.

Methods:

Support group members were recruited through the Global Vitiligo Support Group Community (GVSC), an international network of 25 support group chapters, including members of Henry Ford Hospital-sponsored, Southeast Michigan Vitiligo Support Group (VSTRONG). Non-support group members were recruited from the clinics of Henry Ford Health System, New York University, and Albert Einstein College. Subjects completed the Vitiligo Specific Quality of Life (VitiQoL) instrument. This survey included a pool of vitiligo-specific items, created based on in-depth interviews with patients with vitiligo and their responses to items in several previously validated HRQL measures.

Results:

135 support group members and 135 non-support group members completed the survey. Support group members reported a higher total QoL score, indicating a worse quality of life (48.6) compared to non-support group members (31.5), P-value

020

A Retrospective Analysis of Vitamin D in Vitiligo Compared to Other Skin Disorders

Dr. Pearl Grimes

Vitiligo & Pigmentation Institute of Southern California, Los Angeles, CA, USA

Friday, November 9, 2018, 4:38:00 PM - 4:50:00 PM

TAKE HOME MESSAGE:

This data expands our knowledge regarding vitamin D levels in a spectrum of skin disorders, race, and autoimmunity.

ABSTRACT:

Introduction:

The aim of this retrospective analysis was to investigate the relationship between Vitamin D levels in vitiligo and a spectrum of other skin disorders. 448 patients with skin disorders and 40 healthy control subjects were included in the study, including 185 Caucasians (38%), 77 Hispanics (16%), 65 Asians (13%), and 161 African Americans (33%). The median age of patients was 35. Of the group, 257 patients had vitiligo. Approximately two-thirds of the study population was female (307/488, 63%). Labs were performed on initial consultation prior to any treatment.

Results:

There were no statistically significant differences between Vitamin D levels recorded via seasonal analysis of the data. The duration of disease also had no significant effect on Vitamin D levels. Vitiligo patients had significantly higher Vitamin D levels compared with other skin diseases. The proportion of patients diagnosed with vitiligo who had low Vitamin D levels (

021

New Techniques in Sequential Treatment of Acral Vitiligo Using Electrodessication With or Without Topical TCA

Dr. Hasan El-Fakahany

Minia Faculty of Medicine, Minia, Egypt

Friday, November 9, 2018, 4:50:00 PM - 5:02:00 PM

TAKE HOME MESSAGE:

Acral vitiligo treatment is easier by electrodissection machines with or without TCA. This new technique does not

need expensive equipment, special experience or time consuming procedures. It provides a new hope in treatment of acral vitiligo patients.

ABSTRACT:

Introduction

Acral vitiligo is considered a challenge for dermatologists to treat. Usually acral areas are poorly responding to topical treatments or phototherapy. Once stable, surgery is the best treatment option for acral vitiligo.

Patients and methods

Electrodessication device is used for the treatment of two groups of acral vitiligo. In the first group, it was used to prepare the recipient area for epidermal grafts. In the second group, sequential repigmentation was achieved using electrodesiccation and topical TCA.

Results

In both groups, successful repigmentation was achieved using both techniques.

Conclusion

Electrodessication with or without topical TCA can be an easy, safe, effective and not expensive method for treatment of acral vitiligo.

Saturday



022

Estimation of Melanocyte Count in Different Donor Areas in Non-segmental Vitiligo Before and After NB-UVB Phototherapy

Prof. Samia Esmat

Cairo University, Cairo, Egypt

Saturday, November 10, 2018, 5:02:00 PM - 5:14:00 PM

TAKE HOME MESSAGE:

Both the gluteal region and the thigh are equally suitable for harvesting donor tissue for surgery in NSV cases since the melanocytic count is similar in both areas. This count was significantly increased in a similar manner in both sites after 18 sessions of NB-UVB therefore it is recommended to expose the donor area to NB-UVB a few weeks before the scheduled surgery.

ABSTRACT:

Background:

Commonly used donor sites during surgical treatment of stable non-segmental vitiligo (NSV) include the gluteal region or the thigh. Higher melanocyte density in the donor site could improve the outcome of transplantation. Estimation of melanocytic count and assessment of the effect of NB-UVB exposure on this count in both sites was not performed previously.

Objectives:

To compare the melanocytic count in the gluteal region and thigh; and assess the effect of NB-UVB phototherapy on the number of melanocytes in both sites.

Methods:

Twenty stable NSV patients and 5 controls were enrolled in this study. Two 3 mm punch biopsies were taken from normal skin of the gluteal region and thigh before and after 18 sessions of NB-UVB. Immunohistochemical staining by Melan A was done and melanocytes were counted in all samples.

Results:

There was no significant difference in melanocytic count between the gluteal region and thigh before NB-UVB therapy in NSV cases ($P=0.777$) as well as between cases and controls. In NSV cases, NB-UVB induced a significant increase in the melanocytic count in both gluteal region and thigh ($P=0.002$ for both) with no difference found between both sites ($P=0.430$). A significant positive correlation was found between the percentage change of melanocytic count and skin phototype ($P=0.001$, $r=0.677$) and total cumulative joules ($P=0.025$, $r = 0.511$) in the gluteal region.

Conclusion:

Melanocytic count is similar in normal skin of gluteal region and thigh in NSV cases. This count was significantly increased in a similar manner in both sites after NB-UVB. Both sites are equally suitable for harvesting donor tissue for surgery in NSV cases preferably after NB-UVB phototherapy.

023

Melanocyte Fall into The Dermis (Melanocytopsis) Could Trigger The Activation of Autoimmune Process

Dr. Yvon Gauthier

Vitiligo and Melasma Research Association, Le Bouscat, France

Saturday, November 10, 2018, 8:52:00 AM - 9:02:00 AM

TAKE HOME MESSAGE:

- Melanocyte autoimmune destruction is probably the main cause of depigmentation.
- Triggering of autoimmune activation in vitiligo skin is not clearly understood.
- A melanocyte defective adhesion could play a crucial role in vitiligo pathogenesis.
- Histologically, melanocyte detachment following two directions (upwards in the epidermis ; Â« Melanocytorrhagy Â» and downwards into the dermis ; Â« Melanocytopsis Â») was demonstrated.
- Apoptotic(?) melanocytes in the dermis ,preferentially identified by MITF and SOX 10, are rapidly destroyed by surrounding inflammatory cells including lymphocytes and macrophages
- In perilesional pigmented skin, mechanical,oxidative,chemical stress could locally promote a chronic detachment into the dermis of vulnerable and mis attached melanocytes.
- Antigenic material is released , engulfed within macrophages,carried by dendritic cells and finally presented to T cells draining lymph nodes to initiate autoimmune cascade.
- Melanocytopsis could be the missing link between melanocyte adhesivity impairment in pigmented vitiligo skin and autoimmune response at the edges of the lesion.

ABSTRACT:

Background

Melanocyte autoimmune destruction in vitiligo skin seems to be the main cause of the depigmentation. Nevertheless a well demonstrated melanocyte defective adhesion could play a crucial role in vitiligo pathogenesis. Actually the mechanisms of innate and adaptive immunity leading to melanocyte destruction are better known. But the processes which could trigger the autoimmune activation in vitiligo skin are not clearly understood. In pigmented perilesional skin several direct or indirect adhesivity impairments which could be implicated in melanocyte detachment. were reported such as : E- Cadherin-beta-catenin system down expression, positivity of anti-alpha 5 beta integrin antibody, Aquaporine down regulation, Tenascin C overexpression and Wnt beta-catenin pathway impairment. Moreover focal gaps and multiple replications or layering of basement membrane existing in perilesional skin could weaken

melanocyte attachment. Finally it was suggested, but not demonstrated until now, that under various stress vulnerable and mis-attached melanocytes could be chronically detached into the dermis.

Objective :

To search possible histological links between melanocyte adhesion defects and cell mediated autoimmune process in vitiligo skin.

Patients and Method:

4mm punch biopsies were taken from pigmented perilesional skin in 20 patients with non segmental vitiligo. The skin samples were routinely processed and many serial sections (> 10) were performed. All the sections were immunostained with the following antibodies: HMB45, TRP1, and MITF,SOX10 antibodies for melanocyte detection, E-Cadherin antibody for keratinocytes- melanocytes interconnexions, Aquaporine 3, Collagen IV antibodies, and finally CD8 and CD4 lymphocytes antibodies for the assessment of inflammatory infiltrate.

Results:

Various adhesion defects were found. E- cadherin down expression of the epidermis basal layer was associated to upwards melanocyte detachment and their transepidermal elimination (Melanocytorrhagy) in 18% of cases. Focal abnormalities of basement membrane with gaps and disruption of Collagen IV expression seemed to facilitate melanocyte protrusion (68% of Cases) through the basement membrane and in some cases the fall of MITF+ and SOX 10 + melanocytes into the dermis .In that cases we observed successively : a release of nuclear material from these detached melanocytes which is engulfed by macrophages included in surrounding inflammatory infiltrate

Discussion:

Melanocyte fall into the dermis (melanocytoposis) is not easy to demonstrate and can pass easily unnoticed for several reasons : melanocytes into the dermis are exclusively identified through specific nucleus immuno- stainings (MITF and SOX 10), they are rapidly destroyed as foreign cells by the inflammatory infiltrate and this brief phenomenon is only located to some parts of pigmented perilesional skin.So we suggest that mechanical ,oxidative or chemical stress could locally promote a chronic detachment into the dermis of vulnerable or damaged melanocytes. Then antigenic material could be released, engulfed within macrophages,carried by dendritic cells and finally presented to T cells draining lymph nodes to initiate autoimmune T cell-mediated killing of melanocytes.

« Melanocytoposis » ,demonstrated for the first time,could be the « missing link » between the adhesivity impairment in pigmented skin , the activation of cell mediated autoimmunity and the autoimmune response at the edges of the lesion.

Possible Role of HMGB1 in Melanocyte Apoptosis in Vitiligo Pathogenesis

Prof. Sang Ho Oh

Department of Dermatology, Yonsei University College of Medicine, Seoul, South Korea

Saturday, November 10, 2018, 9:02:00 AM - 9:12:00 AM

TAKE HOME MESSAGE:

HMGB1, which is associated with melanocyte apoptosis is known to be linked to vitiligo pathogenesis. This study tries to identify target receptors or signalings in HMGB1-mediated melanocyte apoptosis and we will suggest their probabilities of future target molecules for vitiligo treatment or activity markers of vitiligo.

ABSTRACT:

Background:

High mobility group box 1 (HMGB1) is a well-known chromatin protein that is located in the nucleus and released to extracellular space. HMGB1 acts as damage-associated molecular pattern molecules (DAMPs) after it is released from cells. HMGB1, which can induce melanocyte apoptosis, is known to be involved in vitiligo pathogenesis.

Objective:

In this study, the role of HMGB1 in association with vitiligo development was examined using control melanocyte cell line (PIG1) and vitiligo melanocyte cell line (PIG3V).

Methods:

To evaluate effect of HMGB1 on cell viability, MTT assay was utilized. Then, apoptosis signaling molecule (caspase-3) was evaluated and melanogenesis-associated signalings were checked after HMGB1 treatment using western blot analysis, melanin contents quantification, and confocal microscopy. RNA sequencing analysis was done to find out the related signaling and molecules.

Results:

To apply the previous findings that HMGB1 induces melanocyte apoptosis to vitiligo models, the negative effect of HMGB1 was examined in control melanocyte cell line (PIG1) and vitiligo melanocyte cell line (PIG3V) to verify the role of HMGB1 in vitiligo pathogenesis through cell viability and apoptosis markers. And the related signaling and molecules in HMGB1-induced melanocyte apoptosis were screened out through RNA sequencing. And receptors for HMGB1-mediated cell apoptosis were discovered.

Conclusion:

This experiments elucidate the more detailed target molecules and pathways for HMGB1-induced melanocyte apoptosis, which can be connected with vitiligo pathogenesis.

025

Interrater Reliability of a Physician Global Assessment (PGA) Tool for Vitiligo: Results of an International Vitiligo Expert Meeting

Prof. Nanja van Geel

Ghent University Hospital, Ghent, Belgium

Saturday, November 10, 2018, 9:12:00 AM - 9:22:00 AM

TAKE HOME MESSAGE:

The study demonstrated an acceptable interrater reliability of a Physician Global Assessment tool for vitiligo extent. The Interpretation seems to correspond quite well amongst physicians worldwide. This study also provide a first guide for the interpretation (based on severity strata) of the numerical output of the Vitiligo Extent Score (VES) from a physician's point of view.

ABSTRACT:

BACKGROUND

A Global Assessment score for vitiligo extent including a 5-point scale can be useful to define inclusion criteria for clinical trials and is important for stratification and interpretation of other physician reported outcome measures. It can also be used in guidelines to steer the decision making process.

Objectives:

The first aim was to investigate the interrater reliability of a Physician Global Assessment (PGA) tool for vitiligo in an international setting.

The second aim was investigating possible severity strata for Vitiligo Extent Score (VES)

Methods:

The interrater reliability of a PGA for vitiligo extent was assessed during an international vitiligo workshop at the San Gallicano Institute in Rome (Vitiligo Global Issues Consensus Conference Workshop "Outcome measurement instruments" Nov 30-1 Dec 2016). The workshop was based on a series of photographs (mainly with UV) of 20 patients with vitiligo (non segmental) including different degrees of extent. Patients were randomly selected from a pool of consecutively included patients. Photographs were also presented in a randomized order. Participating physicians (vitiligo experts) were asked to score the grade of extent on the 5-point global assessment scale for each patient (ranging from no involvement to very extensive vitiligo). To gather more information regarding possible severity strata for extent the total affected Body Surface Area (BSA) was assessed by an expert using the Vitiligo Extent Score (VES).

Results:

A total of 29 vitiligo experts from 5 continents participated in the workshop. Twenty-eight scoring sheets were suitable for analyses [Europe (7), Asia (9), Africa (4), North America (6), South America (2)]. Based on weighted kappa analyses, fair to good interrater agreement [Intraclass Correlation Coefficient (ICC)] were observed within each separate continent (differences not significant): North America (0.817; 95% CI 0.694-0.911), South America (0.720; 95%CI 0.424-0.878), Europe (0.675; 95%CI 0.481-0.836), Africa (0.658; 95%CI 0.462-0.824) and Asia (0.630; 0.464-0.796). The overall ICC between all raters was 0.686 (95% CI 0.544-0.830). Mean (median) BSA

values per category for disease extent were for limited 0.87% (1.06%), moderate 3.86% (3.36%) and extensive 13.12% (12.23%) (very extensive could not be determined, n=1).

Conclusion:

The study demonstrated an acceptable interrater reliability of a PGA for vitiligo extent. The Interpretation seems to correspond quite well amongst physicians worldwide. This study also provide a first guide for the interpretation (based on severity strata) of the numerical output of the Vitiligo Extent Score (VES) from a physician's point of view. These severity strata for vitiligo extent seem to be situated mainly within the first 15% body surface area affected. Future studies are necessary to confirm these results.

026

Tissue Expression of Aquaporin 3 In Different Sites of Vitiligo: An Immunohistochemical Study

Prof. Samia Esmat

Faculty Of Medicine Cairo University, Cairo, Egypt

Saturday, November 10, 2018, 9:22:00 AM - 9:32:00 AM

TAKE HOME MESSAGE:

vitiligo keratinocytes show abnormalities in adhesion apoptosis and cytokine production. aquaporins play an important role in keratinocyte differentiaion and adhesion. aquaporin 3 is defective in all vitiligo lesions while acral lesiona have a peculiar pattern of expression. since vitiligo is not a disease of melanocytes alone, abnormalities of its mileau is possibly behind the resistance of acral lesions to repigmentation even after grafting of melanocytes.

ABSTRACT:

Background:

The role of epidermal keratinocytes in the pathogenesis of vitiligo has proved to be crucial. Aquaporin 3 (AQP3) is a glycerol water channel that is expressed in epithelial tissues and is involved in the regulation of keratinocyte proliferation, cell migration, and tumorigenesis. A role of AQP3 has been proposed in vitiligo.

Objective:

To assess AQP3 expression in keratinocytes of vitiliginous skin in different anatomical sites to evaluate the possible role of AQP3 in the pathogenesis of vitiligo and its possible relation to resistence of repigmentation in acral vitiligo.

Methods:

This study included 15 patients with both acral and non-acral vitiligo lesions, 15 subjects as control. four punch biopsies (2 mm) were taken from acral, and non-acral skin (lesional and perilesional). Two (2 mm) biopsies were

taken from each control subject (acral and non acral). AQP3 tissue expression was analyzed immunohistochemically.

Results:

AQP3 expression was completely absent in the granular layer in all biopsies of vitiligo patients, while it was found in all biopsies of normal skin (P

027

Depigmentation of Remaining Normal Skin Using Monobenzyl Ether of Hydroquinone (MBEH) In Vitiligo: Patient Selection, Tolerability, and Effect on Quality of Life.

Dr. Wedad Mostafa

Cairo University, Cairo, Egypt

Saturday, November 10, 2018, 9:32:00 AM - 9:42:00 AM

TAKE HOME MESSAGE:

Depigmentation of residual normal skin can be a very important upgrade to a better quality of life for patients with extensive resistant vitiligo. The face and the hands are very critical areas that might require depigmentation even if the rest of the body is not extensively involved. Using MBEH as a topical cream provides a practical and relatively easy way to achieve depigmentation. Although the process might take a long time the results are always very encouraging. Development of erythema and irritation is a problem that can delay the response however it can be avoided by using lower concentrations and lower frequencies of application. Strict solar protection is mandatory to maintain the achieved depigmentation,

ABSTRACT:

Background:

Depigmentation is sometimes the final resort for patients with widespread or resistant to treat vitiligo. Cryoablation, Q-switched lasers as well as chemical peels are used with variable degrees of success. The topical use of Monobenzyl Ether of Hydroquinone (MBEH) could be the most practical way to get rid of the remaining normally pigmented skin especially in relatively large areas. Controlled trials in this field are very limited with minimal evidenced based data about the recommended concentrations, precautions and guidelines for using it.

Objective:

Comprehensive clinical evaluation of the efficacy and tolerability of two different concentrations of MBEH in patients demanding depigmentation of face and hands highlighting the relation to type and distribution of the remaining pigmented skin and its reflection on the patient's quality of life.

Methods:

forty patients with extensive facial and hand vitiligo assigned for depigmentation were randomly divided into 2 groups; A and B treated with MBEH 20 and 40%, respectively. All patients applied physical sunscreens. Assessment was performed every two weeks until complete depigmentation was achieved or for 12 months, by clinical evaluation, photography, point counting as well as biometric measurement of melanin and erythema using a colorimetric tool dermacatch. Dermatology Life Quality Index (DLQI), Visual Analogue Scale (VAS) for patient satisfaction were performed at baseline and end of study.

Results:

A significant dilution of color, reduction of the pigmented area and decrease of melanin content were obtained in all cases. Initial response started at 4+2.1 months while complete depigmentation was achieved after 7.2+3.21 months. Erythema and irritation developed in 70% of cases and was minimized by lowering the frequency of application. DLQI and VAS scores improved significantly. Incidence of relapse was significantly related to insufficient solar protection. When the two groups were compared, group B showed higher incidence of irritation and lower incidence of relapse but the difference did not reach statistical significance.

Conclusion:

MBEH depigmentation has a significant influence on vitiligo patients quality of life. Efficient solar protection is essential for maintenance of depigmentation. Compared to 40% MBEH 20% concentration is recommended especially for the face.

028**Melanocyte-Keratinocyte Transplantation Procedure****Dr. Sanjeev Mulekar**

Mulekar Vitiligo Clinic, Mumbai, India

Saturday, November 10, 2018, 11:18:00 AM - 11:30:00 AM

TAKE HOME MESSAGE:

Learning points for participants: Selection criteria, procedure steps, anesthesia techniques, differences in childhood and adult vitiligo.

ABSTRACT:

Vitiligo is a chronic disorder, primarily believed to be of autoimmune origin. The natural course of the disease is characterized by periods of progression and remission, which remains unpredictable in spite of many advances in its pathogenesis and treatment. Until about 30 years ago, vitiligo was treated exclusively by medical therapies. Earliest references to surgical treatment for vitiligo can be traced to reports by Behl and Falabela. They used split thickness

graft and epidermal graft to treat amelanotic patches. Initial studies were attempted to treat leucodermas other than vitiligo.

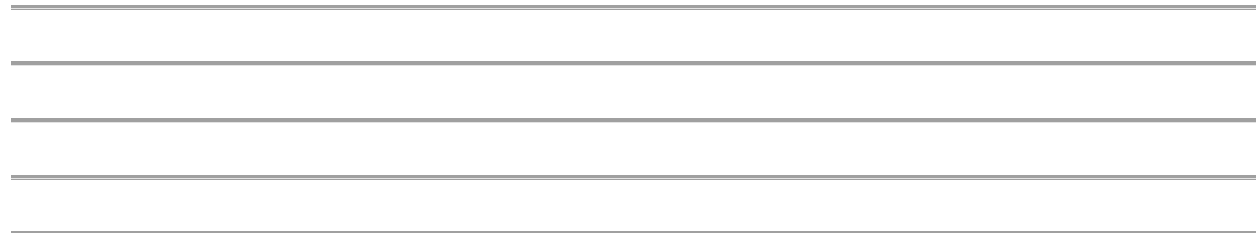
Medical therapies are considered as first choice to treat all types of vitiligo. However, it is increasingly known and documented that segmental vitiligo, lesions located on glabrous skin and with leukotrichia respond poorly to medical therapies. Surgical methods are useful to restore pigment in such cases and are being used more often.

Surgical methods can be divided into tissue grafting such as punch graft, blister graft, and split thickness skin graft and cellular grafting which include cultured and non-cultured cell transplantation. Non-cultured melanocyte-keratinocyte transplantation (MKTP) has many advantages over other methods and gives excellent cosmetic results in most of the treated cases. It is available only at select centers due to regulatory issues and lack of training. In addition to vitiligo, post burn leukoderma, piebaldism, chemical leukoderma, post DLE depigmentation, halo nevus were treated successfully with MKTP. The technique is being practiced for more than 17 years at our center. Recent techniques use cellular suspensions instead of grafts. The epidermal cells are separated from the shave biopsy, and then transplanted on to the derm abraded vitiliginous area as a cell suspension. This process can be accomplished either by culturing them in vitro or using non-cultured cell suspension.

Recent techniques use cellular suspensions instead of tissue grafts. They have many advantages. It is a day care procedure. Large areas can be treated in one operative session with much better cosmetic results, immobilization is not required, repeat surgeries are easy. However, they are more complex, require specialized instruments and high level of training, thus making them expensive compared to established methods.

The scope of surgical therapies has expanded to include difficult to treat areas and localized vitiligo in childhood due to the technological advances and increasing evidence in the literature.

Recently many indicators of good and bad prognosis with MKTP have been observed. Fingertip involvement, large areas of vitiligo is bad prognostic factors. Children respond poorly compared to adults to surgical therapies as observed.



029

New Techniques in Tissue Grafting for Vitiligo: Smash Grafting and its Modifications in the Management of Resistant Stable Vitiligo

Dr. Imran Majid

CUTIS Institute of Dermatology, Srinagar Kashmir, India

Saturday, November 10, 2018, 11:30:00 AM - 11:42:00 AM

TAKE HOME MESSAGE:

Smash grafting and its modification serve as useful alternatives to cellular grafting techniques in resistant stable vitiligo

ABSTRACT:**Background:**

The biggest advantage of cellular grafting over tissue grafting procedures is that a relatively much larger surface area of the recipient skin can be treated with a smaller sized graft. Among tissue grafting procedures, smash grafting is the only technique that can repigment a recipient vitiligo lesion that is 5-10 times the size of the donor graft.

Aim:

This report describes smash grafting and some modifications in smash grafting technique by which the procedure can be converted into a procedure almost similar to a non-culture epidermal cell suspension technique with an easier application and a uniform spread of the graft material.

Methods:

Over 1-year, more than 50 patients have been treated with smash grafting at our institute and among these, 20 patients were treated with the modified smash grafting procedure. Two modifications were done in the standard procedure; first modification was to mix the smashed graft with any viscous solution like hydroxymethyl-propyl cellulose or hyaluronic acid to improve the consistency and convert the grafted material into a uniform suspension. Second modification was to cover the recipient area with dry collagen dressing first and then apply the graft suspension under the dressing by using a spatula or a pipette.

Results:

Most of the patients (more than 80%) could achieve excellent results with smash grafting. More importantly, the repigmentation achieved was uniform and perigraft halo was seen in only 4 cases.

With the addition of hydroxymethyl-propyl cellulose or hyaluronic acid the smashed graft could be converted into a suspension very similar to a trysinized non-culture epidermal cell suspension (NCES). The consistency and even appearance of the 'smashed suspension' was almost similar to NCES. With this modification it was really easy to spread the suspension evenly and uniformly on the dermabraded recipient area. The application of a collagen dressing before application of the smashed graft further improved the uniformity and ease of the application.

Of the 20 patients treated with the modified procedure, about 80% (16/20) patients were able to achieve at least 75% repigmentation of the grafted lesions. No adverse effects were noted with the use of hyaluronic acid or hydroxymethyl-propyl cellulose on the dermabraded recipient skin.

Conclusions:

Smash grafting and its modifications can serve as excellent alternatives to cellular grafting techniques in resource poor settings.

030

Evaluation of the Effect of Needling on the Outcome of Autologous Punch Grafting in Vitiligo Patients

Prof. Mona Atwa

Faculty of Medicine, Suez Canal University, Ismailia, Egypt

Saturday, November 10, 2018, 11:42:00 AM - 11:54:00 AM

TAKE HOME MESSAGE:

Although punch grafting represents a simple and effective surgical procedure in treatment of vitiligo, the occurrence of depigmented rim around the treated lesions reduces patients satisfaction. We tried needling with NB-UVB after punch grafting to prevent the occurrence of depigmented rim around the treated lesions. However, needling has no significant improving effect on the outcome of punch grafting. Moreover, it might have a deteriorating effect on some cases leading to lesser degree of repigmentation and higher incidence of depigmented rim.

ABSTRACT:

Background:

punch grafting represents a simple and effective surgical procedure in treatment of vitiligo with few manageable side effects except the residual depigmented rim. Needling can cause micro-inoculations of epidermal melanocytes from pigmented islands of vitiligo lesion into the depigmented areas.

Objectives:

this study aimed to investigate whether needling with NB-UVB after punch grafting could prevent the occurrence of depigmented rim around the treated lesions.

Subjects and methods:

seventeen patients with generalized bilateral non-segmental stable vitiligo were enrolled. In each patient, two bilateral and symmetrical vitiligo patches were subjected to punch grafting then randomly assigned to treatment by NB-UVB alone or by needling followed by NB-UVB. The study duration was 3 months.

Results:

needling with NB-UVB after punch grafting resulted in a higher rate of depigmented rim (41.2% of lesions) than NB-UVB alone (28.5% of lesions) ($P=0.453$). The overall transplantation survival and repigmentation was observed in 88.2% of lesions treated by needling with NB-UVB versus 94.1% of lesions treated with NB-UVB only ($P=0.185$).

Conclusion:

needling has no significant improving effect on the outcome of punch grafting. Moreover, it might have a deteriorating effect on some cases leading to lesser degree of repigmentation and higher incidence of depigmented rim.



031

Six-year Follow-up of Vitiligo Patients Successfully Treated with Autologous Non-cultured Melanocyte-Keratinocyte Procedure

Dr. Saad Altalhab

IMAM University, Riyadh, Saudi Arabia

Saturday, November 10, 2018, 11:54:00 AM - 12:06:00 PM

TAKE HOME MESSAGE:

Patient with fingertip involvement and disease flare-up are the main cause of relapse in patients successfully treated with MKTP. Mechanical dermabrasion should be preferred over laser dermabrasion for the recipient area.

ABSTRACT:

Although autologous non-cultured melanocyte-keratinocyte transplantation (MKTP) is considered a successful procedure in the treatment of stable vitiligo, there is lack of long-term maintenance data for this specific treatment.

Objective:

To search for factors associated with long-term maintenance of patients with stable vitiligo successfully treated with MKTP

Design, Setting, and Participants:

This was a single-center retrospective study including stable vitiligo patients who underwent successful MKTP at the National Center for Vitiligo and Psoriasis, Riyadh, Saudi Arabia, between January 1st 2004 to June 30th 2017. Cox proportional hazard model was used to estimate factors associated with relapse at 6 years of follow-up. Co-variables included, gender, type of vitiligo, age at vitiligo onset, age at surgical procedure, disease duration, disease stability, affected body surface area, treated surface area, fingertip involvement, type of recipient area treatment and recurrence defined as the onset of new lesions on previously untreated areas.

Main Outcomes and Measures:

Risk of developing relapse defined as re-appearance of more than 10% depigmentation in a previously treated and re-pigmented site (Cox proportional hazards regression).

Results:

In total, 602 patients were included in the study of whom 410 (67%) were women. Mean age was 24.25 years [4.0-67.0]. Affected body surface area (adjusted HR = 0.37; P = 0.04), type of vitiligo (adjusted HR = 2.11; P = 0.03), fingertip involvement (adjusted HR = 3.75; P = 0.01) and mechanical dermabrasion (adjusted HR = 0.26; P = 0.03) were retained as independent variables associated with relapse.

Conclusions and Relevance:

Patient with fingertip involvement and disease flare-up are the main cause of relapse in patients successfully treated with MKTP. Mechanical dermabrasion should be preferred over laser dermabrasion for the recipient area.

032

A Simplified Transplantation of Basal Cell Layer Suspension Using a Dermarolling/Dermastamp System in Vitiligo

Prof. Laila Benzekri

Mohammed V University, Rabat Maroc, Morocco

Saturday, November 10, 2018, 12:06:00 PM - 12:18:00 PM

TAKE HOME MESSAGE:

- Until now, all the melanocyte transplantation techniques proposed for repigmenting the vitiligo skin need a previous destruction of the depigmented epidermis.
- The dermarolling/dermastamp system causing microinjuries in the epidermis offered for the first time a minimally invasive method of transepidermal melanocyte transplantation.
- Histologically, the melanocytes introduced into the microfissures can survive and can move towards the basal layer.
- The healing is obtained quickly with minimal inflammatory reaction.
- The repigmentation is earlier, more efficient at 1 month and equally efficient at 6 months compared to direct cell delivery on dermabraded or laserabraded patches.
- It is a good and safe option for non acral and stable vitiligo patches not exceeding 100 cm².

ABSTRACT:

Background:

Since the first description of a transplantation technique of basal cell layer suspension in 1992 (1), several modified methods were proposed for repigmenting the skin of selected vitiligo patients. All these invasive methods need a previous destruction of the depigmented epidermis. Recently, intralesional injections of autologous epidermal cells were reported as an alternative and successful treatment (2). So, a minimally invasive and less painful method of melanocyte transplantation could be offered by the dermarolling/dermastamp system with needles causing tiny microinjuries in the epidermis.

Aim of the study:

to develop and to histologically analyze a simple method for transepidermally delivering keratinocytes and melanocytes into vitiligo skin (3).

Patients and method:

13 patients with stable vitiligo including 11 segmental vitiligo and 2 generalized vitiligo were recruited. The technique involves a preparation of keratinocyte/melanocyte by trypsinization from patient's scalp skin and a transepidermal delivery using a dermaroller/dermastamp equipped with 0.2 mm needles. Dermarolling and dermastamp use leads to less painful epidermal microinjuries. The efficacy of cell delivery was analysed histologically and repigmentation was evaluated clinically and photographically at 1, 4 and 6 months. The scores represented the repigmentation percentage as follows 0(0), I (1-24%), II (25-49%), III (50-74%) and IV (75-100%).The trial was registered at NIH clinical trials NCT02962180.

Results:

Histologically, the transplanted keratinocytes rapidly degenerated, leading to keratinization, but melanocytes survived and integrated appropriately into the basal layer. Clinically, the onset of repigmentation was earlier with dermastamp compared to dermaroller. The mean repigmentation score was III at 6 months of dermaroller use whereas, with dermastamp, it was II at 1 month and IV at 4 months. There was no repigmentation in acral vitiligo. No adverse events were observed in recipient and in donor site.

Discussion:

Compared to direct cell delivery on dermabraded patches, the repigmentation with trans-epidermal transplantation is earlier and more efficient at 1 month and equally efficient at 6 months.

Conclusion:

Trans-epidermal melanocyte delivery appears to be a simple, safe and effective therapeutic option for non acral and stable vitiligo patches.

References

- 1:Gauthier Y. J.Am. Acad.Dermatol 1992.26(2)191-194.
- 2:Khodadadi L. Arch. Dermatol. Res 2010;302(8):593-599
- 3:Benzekri L. Pigment Cell Melanoma Res. 2017 Sept;30(5):493-497



033

Melanocytes Keratinocytes Transplantation Surgery In Depth: T Cells Impact Outcomes

Dr. Maggi Ahmed

UMASS Dermatology, Worcester, MA, USA

Saturday, November 10, 2018, 12:18:00 PM - 12:30:00 PM

TAKE HOME MESSAGE:

Autoreactive T cells remain in the clinically stable vitiligo lesions and might explain poor surgical outcomes of the melanocyte transplantation as well as the preferential responses among different vitiligo subtypes. Pre/post-operative treatment of the vitiligo lesions undergoing surgery with immunosuppressive light or medical therapies may improve the success of the transplantation.

ABSTRACT:

Vitiligo is an autoimmune disease of the skin mediated by cytotoxic CD8+ T cells that kill melanocytes and result in

disfiguring depigmentation. Despite optimal selection of surgical candidates in vitiligo, outcomes can be unpredictable in terms of post-surgical repigmentation and its durability. Moreover, variable surgical responses among different vitiligo subtypes have been reported. Even in successful surgeries, a rim of depigmentation called a “halo”, may remain at the outer margin of the grafted vitiligo lesion and is difficult to expect or to explain. Here we performed modified suction blister biopsies on 17 patients undergoing melanocyte keratinocytes transplantation surgery. We sampled lesions undergoing the surgery as well as non lesional skin from clinically stable subjects with non segmental, segmental or mixed vitiligo as well as one Pibaldism patient as a control. The cellular immune infiltrate in the skin interstitial fluid was phenotyped and quantified by flow cytometry and inflammatory cytokines were measured by ELISA. Subjects were followed up for a minimum period of 6 months and the reported values were correlated with their post-surgical score of repigmentation. Three out of the seventeen subjects developed depigmented halos, which were subsequently sampled for similar analyses. We found significant CD8+ T-cell infiltration in most of the vitiligo patients, but was higher in the non segmental lesions and in the poorly responding ones. Interestingly, lesional CD8+ T-cell number didn’t correlate with the duration of stability but negatively correlated with post-surgical score of repigmentation. Subtyping analysis of T cells revealed a predominant resident memory (CD69+/CD103+) phenotype in vitiligo lesions which may explain their recalcitrant nature. Perigraft depigmented halo revealed very high CD8 T-cell number as well as CXCL9 and CXCL10 levels when compared to the successfully repigmenting portion of the same lesion. In conclusion, autoreactive T cells remain in the clinically stable vitiligo lesions and might explain poor surgical outcomes of some melanocyte transplantation. Pre/post-operative treatment of the vitiligo lesions undergoing surgery with immunosuppressive light or medical therapies may improve the success of the transplantation.

034

Developing the VASI for Vitiligo: Historical and Methodologic Perspectives

Dr. Harvey Lui

Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

Saturday, November 10, 2018, 4:02:00 PM - 4:12:00 PM

TAKE HOME MESSAGE:

Vitiligo scoring systems such as the VASI are designed to quantify the objective visible appearance of vitiligo on the skin, and reflect specific aspects of the clinical disease presentation.

ABSTRACT:

Over the last 15 years several novel clinical scoring systems have been developed and evaluated for assessing vitiligo including the VASI (Vitiligo Area Scoring Index). The evolution of these clinical evaluation tools has paralleled an increased awareness within the dermatology community of the importance of providing care for

affected patients and generating data to guide evidence-based approaches to management. The VASI was designed as a simple bedside technique for objectively quantifying the visible extent of vitiligo by taking into account two equally important aspects the disease: (1) the overall area of involvement by vitiligo as an index of the visible degree of disease/disfigurement, and (2) the very slow, and gradual nature of its repigmentation which proceeds in one or more relatively consistent patterns (i.e. freckling, concentric repigmentation from the border, or homogeneous repigmentation). VASI was also developed at a time when vitiligo therapies were, and continue to be, relatively modest in clinical efficacy, and thus fulfilled the need for a sensitive clinical tool that could detect smaller, but relevant treatment effects. The area of involvement is estimated using conventional clinical rules, while the scoring of repigmentation takes into account the understanding that the visual quantification of repigmentation is more apparent towards either polar end of the continuum from zero to complete repigmentation. Although digital photography has essentially become an almost indispensable and ubiquitous tool of daily life, and is very helpful for qualitative monitoring of skin diseases that respond slowly to therapy, reliable methods for quantifying these images for research purposes remains challenging. The simplicity and versatility of the VASI system is based on basic principles and realities that enable its reliability, validity, and reproducibility.

035

Stress Response Pathways In Vitiligo Pathogenesis

Dr. Prashiela Manga

New York University School of Medicine, New York, NY, USA

Saturday, November 10, 2018, 4:12:00 PM - 4:22:00 PM

TAKE HOME MESSAGE:

Dysfunctional stress responses may play a role in the onset of vitiligo. We have determined that three key pathways, the unfolded protein stress response, the NRF2-regulated antioxidant response and the nuclear factor-kappa B pathway are activated by agents known to trigger vitiligo. These pathways may play a role in determining melanocyte survival and may be disrupted in melanocytes from individuals with vitiligo.

ABSTRACT:

Interfollicular epidermal melanocytes are continually subjected to environmental challenges and activate protective stress responses for survival. Dysregulation of these responses may increase susceptibility to autoimmune-mediated destruction resulting in progressive skin depigmentation typical of vitiligo. We delineated the response of melanocytes from normally pigmented individuals (NMs) to challenge with monobenzone (MBEH) and 4-tertiary butyl phenol (4-TBP), chemicals known to trigger vitiligo. We identified three survival pathways that were activated following exposure: the unfolded protein stress response (UPR), the NRF2-regulated antioxidant response and the nuclear factor-kappa B (NFkB) pathway. We are now investigating the role of these pathways in determining

melanocyte viability and their activity in melanocytes from individuals who developed vitiligo (VMs). To date, we have demonstrated that the PERK-eIF2 β arm of UPR is active in NMs at baseline, but not in keratinocytes and dermal fibroblasts. PERK downregulation substantially reduced NM viability (p

036

Skin Seeding Technique Using a Motorized 0.5-mm Punch for Refractory Vitiligo: A Method Free From the Direction of Punch Grafting

Prof. Jung Min Bae

Department of Dermatology, College of Medicine, The Catholic University of Korea, Gyeonggi-do, South Korea

Saturday, November 10, 2018, 4:22:00 PM - 4:32:00 PM

TAKE HOME MESSAGE:

Punch grafting for vitiligo has limitations of the time-consuming nature and the possibility of a cobblestone appearance. The skin seeding technique (SST) using a motorized 0.5-mm punch overcame the limitations and showed excellent treatment results. Since the outcome of the SST was not influenced by the direction of punch grafting, it can substantially shorten the treatment time. Also, the use of 0.5-mm punch can minimize the risk of cobblestoning. The SST is promising to treat refractory vitiligo on an outpatient basis, particularly in patients with small lesions and in patients who are unlikely to tolerate prolonged surgery.

ABSTRACT:

Background:

Punch grafting is a simple technique for the treatment of stable vitiligo, resistant to medical therapy. However, the time-consuming nature and frequent cobblestoning remain the limitation of the procedure. We devised a skin seeding technique (SST) using a motorized 0.5-mm punch to overcome these limitations.

Objectives:

To show the effectiveness of the SST for refractory vitiligo, and to compare the treatment outcome of the SST according to the direction of punch grafting.

Methods:

This was a prospective split-body clinical study. A total of 100 lesions in 50 patients (6 to 67 years old) with stable vitiligo refractory to nonsurgical treatment were included between June 2017 and May 2018. In each patient, two lesions in the same body area were divided into the right-side-up and upside-down group, respectively. A stainless steel punch of 0.5 mm in diameter loaded into the handpiece of micromotor was used for skin graft from both donor and recipient sites. At recipient sites, the skin was removed to create chambers for planting grafts at intervals of 4 mm using the motorized micro-punch. At donor sites, the grafts were harvested at intervals of 1 mm using the

motorized micro-punch. In the right-side-up group (n = 50), the grafts were placed into the chambers of the recipient site in the right direction, and in the upside-down group (n = 50), the grafts were placed upside down. After 1-week of steri-strip fixation, the lesions were treated with excimer laser for 3 months.

Results:

Treatment success (defined as ≥75% repigmentation) was achieved in 72% of the right-side-up group and 76% of the upside-down group, respectively. Apparent cobblestone appearance was observed in 4% of the right-side-up group and 2% of the upside-down group, respectively. Most of the patients were very satisfied with this technique in both groups, and no major systemic or local complications were reported.

Conclusions:

We demonstrated that the SST was effective for stable vitiligo refractory to nonsurgical treatment regardless of the direction of punch grafting. This technique is rapid and convenient with notably minimal rates of adverse events. This technique could not only markedly reduce the time required for surgery, but also substantially reduce the risk of cobblestoning. Given the benefits of short procedure time and excellent outcome, the SST is promising to treat refractory vitiligo on an outpatient basis, particularly in patients with small lesions and in patients who are unlikely to tolerate prolonged surgery.

037

Treatment of Stable Vitiligo Using Both Cultured and Non-Cultured Autologous Melanocytes from Hair Follicle ORS Cell Suspension

Dr. Marwa EL Hawary

Dermatology Department- Cairo University, Cairo, Egypt

Saturday, November 10, 2018, 4:32:00 PM - 4:42:00 PM

TAKE HOME MESSAGE:

A plethora of interventions had been introduced for treating stable vitiligo lesions, however none could guarantee 100% cure. Arguments existed about the safety, efficacy and convenience of cultured melanocytes as compared to non-cultured technique. In 2012, Savkovic and Coworkers developed an improved culture method amplifying human melanocytes from the hair follicles; however, they did not apply this method clinically for treating vitiligo patients.

We assessed the efficacy and safety of modified autologous cultured hair follicle outer root sheath cell suspension transplantation in the treatment of stable vitiligo lesions, in comparison to autologous non-cultured hair follicle cell suspension transplantation within the same patient. The modified cultured method seems to be promising although more expensive and more time consuming than the non-cultured technique.

ABSTRACT:

Background:

Treatment of stable vitiligo is mainly surgical. A plethora of methods are being studied and modified, however none of them guarantee 100% cure up till now. Arguments existed about the safety, efficacy and convenience of cultured melanocytes as compared to non-cultured technique. In 2012, Savkovic and Coworkers developed an improved culture method amplifying human melanocytes from the hair follicles; however, they did not apply this method clinically for treating vitiligo patients.

Aim of the study:

To assess the efficacy and safety of a modified autologous cultured hair follicle outer root sheath cell suspension transplantation in the treatment of stable vitiligo lesions, and to compare it with the results of transplantation of autologous non-cultured hair follicle cell suspension within the same patient.

Patients and methods:

Hair samples were epilated from 24 patients with stable vitiligo (each sample 60-80 anagen hairs), hair follicle ORS was separated by two methods, cultured [we modified the culture method of Savkovic et al. (2012)] and non-cultured methods. Melanocytes characteristics in both methods were determined via measuring cellular melanin content by ELISA and the fold change in pre-melanosome (Pmel-17) gene expression. Patients' response was evaluated clinically for up to one year following treatment.

Results:

Out of 24 patients, 19 patients completed the study, with a total of 40 lesions treated, 21 with cultured and 19 with non-cultured melanocyte cell suspension and continued the follow-up period. Eight (20%) lesions showed excellent response (2 (25%) of them with non- cultured & 6 (75%) with cultured), 10 (25%) good (3 (30%) of them with non-cultured & 7 (70%) with cultured), 7 (17.5%) fair (3 (43%) of them with non- cultured & 4 (57%) with cultured), and 15(37.5%) showed poor response (11(73%) of them with non- cultured & 4 (27%) with cultured). Melanin content and melanocyte viability were more with the modified cultured technique.

Conclusion:

Our provided modified autologous hair follicle ORS melanocytes cultured cell suspension transplantation method is a promising option for treating stable vitiligo lesions, however it is more expensive and time consuming than the non-cultured method.

Scientific Posters



P01

Hypochlorhydria and Leaky Gut Syndrome: Potential Causative Factors Leading to Autoimmunity & Vitiligo

Dr. Ayyaz Shah

Shah Dermatology, Orlando, FL, USA

TAKE HOME MESSAGE:

Vitiligo is considered by most authorities to be an autoimmune disorder which causes white macules on the face or body. Hypochlorhydria is a crucial underlying factor in potentially causing intestinal permeability (leaky gut). If we can improve the hypochlorhydria, we will not get intestinal permeability. If the gut is allowed to heal and remain healthy as it houses 70-80% of the immune system. Most conditions which are considered autoimmune will improve substantially or completely resolve if we pay special attention to the gut.

ABSTRACT:

Vitiligo is a skin disorder which is considered by many scientific authorities to be an autoimmune disease. There are many factors which are implicated in this dermatologic condition. Some of these factors include Genetic defects, nutritional deficiencies, environmental causes, hypochlorhydria (low stomach acid) and intestinal permeability (aka leaky gut syndrome).

This presentation will aim to show the relationship of how an autoimmune condition such as Vitiligo may result from hypochlorhydria which may lead to intestinal permeability and subsequent autoimmunity.

Adequate production and amount of stomach acid (HCl) is required to breakdown and digest the large food particles as they enter the stomach from the esophagus. If there is insufficient stomach acid to breakdown the large carbohydrate and protein molecules, these larger molecules will enter the small intestine as very large particles (since not digested into small particles). Once these large particles are in the large intestine, they become the breeding ground for candida and pathogenic bacteria. Good protective gut bacteria are slowly replaced by pathogenic bad bacteria.

As this process continues to occur, the gut lining becomes inflamed and starts to weaken down. This results in intestinal permeability (leaky). Once the gut lining becomes permeable, these larger undigested particles may enter the blood stream. As these larger undigested proteins enter the blood stream directly from the damaged intestinal lining, the immune system (70-80% in the gut) recognizes these large particles as "foreign" or unrecognizable and will produce antibodies against these so called antigens. This creates an antigen-antibody complex and "activates" the immune system thus creating so called "autoimmunity".

As 70-80% of the immune system is found in the gut, it is crucial to direct our research efforts on the GI tract regarding pathogenesis and potential therapeutic targets for these autoimmune conditions. Conditions which are considered autoimmune in nature such as psoriasis, Celiac Disease, Vitiligo, Hashimoto's thyroiditis and others may potentially be treated or even cured if we focus on some of the underlying Gastrointestinal causes such as hypochlorhydria and intestinal permeability which lead to a hyperactive immune response and autoimmunity ultimately leading to an autoimmune condition such as vitiligo.

P02

Optimizing Nutrition: Important Vitamins & Minerals in Vitiligo

Dr. Ayyaz Shah

Shah Dermatology/UCF College of Medicine, Orlando, FL, USA

TAKE HOME MESSAGE:

Vitiligo has been the subject of multiple studies where it was found that vitiliginous skin was deficient in certain vitamins and minerals. These vitamins and minerals were found to be Vitamin C, Pantothenic Acid, Folic Acid, Vitamin B12 (vitamins); Copper, zinc and iron (minerals).

Optimizing nutrition or a well formulated professional or medical grade "multivitamin" supplement may mitigate and minimize an ailment such as Vitiligo and potentially other skin conditions.

ABSTRACT:

Vitiligo is a skin condition where melanin is not being synthesized in the affected areas of the skin which results in white spots or patches on the skin. There are many theories on what is the actual cause of Vitiligo, Some of the most popular are Genetic alterations, Oxidative stress, poor nutrition, autoimmunity and more.

In this presentation, we will aim to review to show what role nutritional therapy plays in treatment of Vitiligo. The role of vitamins and minerals will be highlighted and shown as per some of the research studies which were conducted.

According to some of the leading researchers on nutritional treatment in Vitiligo, certain specific vitamins and minerals were shown to be deficient in the vitiliginous skin and/or blood. The Vitamins which (when deficient) have been associated with Vitiligo are: Folic Acid (Vitamin B9), Vitamin B12, Vitamin C and Pantothenic Acid (Vitamin B5); The minerals which are most often found to be deficient in Vitiligo are: Copper, Zinc and Iron.

As one looks at the Melanogenesis pathway, one may clearly visualize how it is necessary for some of these vitamins and minerals to be available in adequate amounts for some of the enzymatic reactions to take place. An example of this is the first step in Melanogenesis. The first step of melanin synthesis requires the conversion of the amino acid Phenylalanine to tyrosine via the enzyme phenylalanine monooxygenase; this step requires Folic Acid which has 3 constituents: PABA (paraaminobenzoic acid), Pteridine and L-Glutamic Acid. Phenylalanine requires Pteridine in order to introduce hydrogen and oxygen which are necessary for the conversion of phenylalanine to tyrosine. An additional example is that the conversion of the amino acid tyrosine to DOPA (Dihydroxyphenylalanine) requires the enzyme tyrosinase which requires copper to be activated. If there is an absence or deficiency in the amount of copper available, the reaction does not move forward and the subsequent steps in Melanin synthesis do not occur which results in hypopigmented and/or depigmented skin.

In order for copper to be absorbed, the presence of Pantothenic Acid is necessary. Vitamin C promotes the conversion of Tyrosine to DOPA. As one can see, many of the enzymatic reactions are in need of specific co-factors which would be typically derived from a healthy, well balanced diet. Unfortunately, most patients do not "eat" healthy so they lack many of the necessary building blocks for these co-factors. One may want to consider recommending these people to a nutritionist for healthy nutrition advice or consider using a well formulated professional level "multi vitamin" which contains the necessary nutrients in order patients do not become deficient in the necessary vitamins and minerals and thus less likely to suffer from potential ailments such as Vitiligo.

P03

GVF Universal Protocol for Vitiligo Clinical Studies

Dr. Zainab Abbas

University of Massachusetts Medical School, Dermatology Department, Worcester , MA, USA

TAKE HOME MESSAGE:

A comprehensive, yet adaptable clinical trial template will encourage and facilitate the work of investigators and the pharmaceutical industry and allow for safe and efficacious testing of new therapies. Uniformity in clinical trials will improve the ability to compare various therapies against one another, while enhancing opportunities to develop new therapeutic agents for vitiligo.

ABSTRACT:

Recent advances in basic and translational research studies have significantly improved our understanding of vitiligo disease pathogenesis, opening new horizons and opportunities for the development of targeted therapies. With emerging therapies, there is a need for standardized and validated clinical trials to facilitate safe and efficient testing of new agents.

To address the need for clinical trial optimization, simplification, and promotion of continued clinical trials in vitiligo, the Global Vitiligo Foundation (GVF) has developed and approved a universal protocol which can be used to guide future clinical trials in vitiligo. GVF protocol is a joint effort of clinicians and investigators worldwide who are experienced in treating vitiligo. The universal protocol provides a standardized template for eligibility criteria, safety measures, and outcome assessment tools. The consistency of these criteria will provide a framework through which trials can be easily compared for safety and efficacy.

This universal protocol is primarily designed for pharmaceutically-sponsored phase II and phase III clinical trials evaluating investigational products that have already successfully completed a phase I clinical trial. However, modifications can be made with less stringent efficacy endpoints and fewer patients to support phase I or proof of concept study.

The universal protocol is comprised of a standardized title, inclusion/exclusion criteria, safety assessments, disease outcome assessments, and a standardized statistical methodology to assess results of the clinical trial. Forms, charts, and worksheets are included in the protocol to facilitate study visits and assessments.

P04

The 308-nm Excimer Laser Does not Increase the Risk of Skin Cancer in Patients with Vitiligo: A Population-based Retrospective Cohort Study

Dr. Chong Won Choi

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TAKE HOME MESSAGE:

Xenon chloride excimer laser (EL) has been used to treat patient with localized vitiligo. Meanwhile, there have been concerns for photocarcinogenesis following UV phototherapy. However, data are not available on the association between EL treatment and skin cancers.

We conducted a nationwide population-based retrospective cohort study to evaluate the risk of skin cancers after EL therapy in patients with vitiligo using the Korean National Health Insurance Claims database and found that the risks of skin cancers (actinic keratosis, non-melanoma skin cancer, and melanoma) was not increased after EL therapy in patients with vitiligo compared to the patients who have not experienced EL therapy.

We suggested that EL therapy did not increase the risk of skin cancer lesions in patients with vitiligo. Based on large nationwide population-based study, EL is likely to be a safe treatment option for patients with vitiligo and can be the first choice for localized vitiligo.

ABSTRACT:

Xenon chloride excimer laser (EL), emitting 308-nm monochromatic ray, has been widely used to treat patient with localized vitiligo. Meanwhile, there have been concerns for photocarcinogenesis following long term application of UV phototherapy. However, data are not available on the association between EL treatment and the development of skin cancers.

We conducted a nationwide population-based retrospective cohort study using the Korean National Health Insurance Claims database from January 2007 to December 2016. We defined patients with vitiligo as those who met a physician at least four times with a principal diagnostic code of vitiligo (ICD-10: L80) from 2009 to 2016. we identified patients who were treated with EL therapy for their vitiligo 50 or more sessions between 2009 and 2016 and same number of age-and sex-matched vitiligo patients who had not experienced EL treatment during the study period. Finally, we stratified the enrolled patients into the following 3 groups: group with no EL exposure, 50 to 99 EL treatments, and 100 or more EL treatments. Outcomes of interest were the development of actinic keratosis

(AK), non-melanoma skin cancer (NMSC), and melanoma defined as a physician contact with the corresponding diagnosis (L570 for AK, C44 for NMSC, and C43 for melanoma) after the enrollment.

A total of 5,052 patients were included in this study. Among them 2,526 patients had no exposure to EL treatment, 1,353 patients had 50 to 99 EL treatments, and 1,173 patients had 100 or more EL treatments, respectively. The overall incidence rate of all events was 29.1 per 10,000 person-years in no exposure group, 17.7 in group with 50 to 99 EL treatments, and 33.4 in group with 100 or more EL treatments. The risks of all events did not differ significantly among groups. In addition, the risks of AK, NMSC and melanoma were also not significantly different among groups, respectively.

In conclusion, we suggested that EL therapy did not increase the risk of skin cancers and premalignant lesions in patients with vitiligo. Based on our results, EL is likely to be a safe treatment option for patients with vitiligo and can be the treatment of choice for localized vitiligo. Further prospective studies are needed to corroborate our results.



P05

The Psychosocial Impact of a Social Interaction Skills Training Workshop for Patients with Vitiligo

Andrea Tan

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TAKE HOME MESSAGE:

Clinical measures of anxiety and distress in social situations decrease after the Social Interaction Skills Training workshops. The SIST workshop may be an effective psychosocial intervention for vitiligo patients to improve anxiety and fear of negative evaluation. Further research with this intervention in larger groups of patients should be performed.

ABSTRACT:

Vitiligo can cause detrimental effects on quality of life and self-esteem, especially in the context of social interactions with others. Despite an abundance of research on medical treatments, there is still a lack of interventions that address the psychosocial aspects of vitiligo. To address this need, we developed a Social Interaction Skills Training (SIST) workshop for vitiligo patients, which incorporated techniques such as exploring social dynamics, sharing personal experiences, and role-playing common scenarios to teach communication skills and adaptive coping mechanisms.

Two SIST workshops were held, with 6 participants recruited for the first workshop and 11 participants recruited for the second workshop. Three measurement outcomes (Social Anxiety and Distress (SAD) Scale, Brief Fear of

Negative Evaluation-II (BFNE-II), and open-ended questionnaires with 100-mm Visual Analog Scales) were administered before, immediately after, 3 weeks and 8 weeks after each workshop.

Data from the first workshop showed a mean difference in SAD score of -4.40, a mean difference in BFNE-II score of -3.40, and a mean improvement in two Visual Analogue Scale scores of 8.6 mm and 7.2 mm at 8 weeks after the workshop compared to baseline scores, all significant. Data collection for the second workshop is ongoing.

P06

Validation of a Patient-Reported Global Assessment (PR-GA) Score for Vitiligo Severity, Extent and Impact

Prof. Nanja van Geel

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TAKE HOME MESSAGE:

The results of this study confirmed the reliability and validity of Patients Reported Global Assessment (PR-GA) score for vitiligo extent, severity and impact. These tools can be used for the interpretation/stratification of scores obtained with other Patient Reported Outcome Measures (PROMs) in vitiligo.

ABSTRACT:

Background:

The Self Assessment Vitiligo Extent Score (SA-VES) has recently been introduced as a patients reported outcome measure (PROM) for vitiligo extent. A global score including a broader perception of disease extent, severity and impact from the patient's point of view is still lacking. These Global Assessment tools can be used for the interpretation and stratification into sub-categories of scores obtained by other outcome measures (e.g. SA-VES) in vitiligo.

Objective:

To validate a Patient Reported Global Assessment (PR-GA) score for vitiligo extent (PR-GAe), severity (PR-GAs) and impact (PR-GAi).

Methods:

Patients with vitiligo (non-segmental) were included consecutively and asked to complete a questionnaire including a 5-point global assessment scale for extent and severity. For impact both a 5-point scale (Impact5point) and a score on 10 (ImpactOn10) were tested. To evaluate the test-retest reliability of the PR-GA scores, patients were asked to score their global assessment for vitiligo extent, severity and impact twice with an interval of 2 weeks. Construct validity was evaluated by testing at least 4 predefined hypotheses including correlations with other PROMs (e.g. SAVES).

Results:

In total 639 patients were included. The PR-GA for extent, severity and impact demonstrated all a good to excellent test-retest reliability [intraclass correlation for: extent 0.745 (95% CI: 0.614-0.836); severity 0.861 (95% CI: 0.782-0.913); Impact5point 0.858 (95% CI: 0.777-0.911); ImpactOn10 0.966 (95% CI: 0.930-0.983)]. Evidence for a good validity was provided for all Global Assessment tools as at least 75% of hypotheses were confirmed. Correlations ($p < 0.001$) between the SA-VES and the Global Assessment tools were stronger for extent ($r = 0.622$) and severity ($r = 0.614$) compared to Impact [$r = 0.376$ (Impact5point) and $r = 0.366$ (ImpactOn10)]. On the contrary higher correlation coefficients were obtained between DLQI and the Global Assessment tools for Impact [$r = 0.581$ (Impact5point) and $r = 0.621$ (ImpactOn10)] compared to Severity ($r = 0.440$).

Limitations:

The low number of patients with dark skin types is a limitation. However, an international multicultural setting of this study has been initiated in the meantime.

Conclusion:

The results confirmed the reliability and validity of the PR-GA for extent, severity and impact. These tools can be used for the interpretation/stratification of scores obtained with other Patient Reported Outcome Measures (PROMs) as for instance the SA-VES.

P07**Disease associations with Vitiligo: A Retrospective Study in a Diverse Urban Population**

Dr. Nada Elbuluk

University of Southern California, Keck School of Medicine, Department of Dermatology, Los Angeles, CA, USA

TAKE HOME MESSAGE:

Vitiligo is associated with other diseases, many of which are autoimmune. This study confirms many of these known disease associations, with hypothyroidism being the most common. Furthermore, this study found that vitiligo is significantly associated with multiple sclerosis, idiopathic thrombocytopenic purpura, and lymphoma. These findings can help dermatologists be aware of which conditions to consider when evaluating vitiligo patients.

ABSTRACT:**Background:**

Vitiligo is a disfiguring skin condition characterized by skin depigmentation. It has known associations with certain autoimmune conditions, such as Hashimoto's thyroiditis. However, there have been few studies in the United States investigating the associations between vitiligo and other conditions.

Objective:

To investigate the associations between vitiligo and other diseases in a New York City metropolitan population. Furthermore to evaluate if these associations vary by race or and/or gender.

Methods:

This was a retrospective study that analyzed data collected from the medical records of 1487 vitiligo patients seen at NYU Langone Medical Center. Data collected included age, gender, comorbid diseases, laboratory studies, medications, and family history. This data was compared with available baseline characteristics of the general population.

Results: In total 639 patients were included. The PR-GA for extent, severity and impact demonstrated all good to excellent test-retest reliability [intraclass correlation for: extent 0.745 (95% CI: 0.614-0.836); severity 0.861 (95% CI: 0.782-0.913); Impact5point 0.858 (95% CI: 0.777-0.911); ImpactOn10 0.966 (95% CI: 0.930-0.983)]. Evidence for a good validity was provided for all Global Assessment tools as at least 75% of hypotheses were confirmed. Correlations ($p < 0.001$) between the SA-VES and the Global Assessment tools were stronger for extent ($r = 0.622$) and severity ($r = 0.614$) compared to Impact [$r = 0.376$ (Impact5point) and $r = 0.366$ (ImpactOn10)]. On the contrary higher correlation coefficients were obtained between DLQI and the Global Assessment tools for Impact [$r = 0.581$ (Impact5point) and $r = 0.621$ (ImpactOn10)] compared to Severity ($r = 0.440$).

Limitations: The low number of patients with dark skin types is a limitation. However, an international multicultural setting of this study has been initiated in the meantime.

Conclusion: The results confirmed the reliability and validity of the PR-GA for extent, severity and impact. These tools can be used for the interpretation/stratification of scores obtained with other Patient Reported Outcome Measures (PROMs) as for instance the SA-VES.

**P08****Halo Nevus Excision in Patients of Vitiligo Vulgaris**

Dr. Deepti Ghia

Mulekar Vitiligo Clinic, Mumbai, India

TAKE HOME MESSAGE:

Halo nevi are common in vitiligo patient. This is a marker of cellular autoimmunity against nested melanocytes of the nevi. Excision of the melanocytic nevi is a simple procedure which can improve the outcome of vitiligo therapy.

ABSTRACT:**Background:**

Halo Nevi (Sutton nevi) are characterized by depigmentation surrounding a melanocytic nevus, forming a halo. They are 8-10 times more common in vitiligo patient. This is a marker of cellular autoimmunity against nested melanocytes of the nevi. The individuals having halo nevi have fewer acral and more central involvement.

Objective:

To study the outcome of excision of Halo Nevi followed by standard vitiligo therapy in patients of vitiligo vulgaris on re-pigmentation and disease activity.

Method:

2 patients having extensive vitiligo vulgaris and halo nevi (Patient 1 = 25 % Depigmented Area and Patient 2= 35% BSA Depigmented with Acrofacial Involvement) were treated with Narrow Band UVB (NBUVB) phototherapy for 2 times a week for 3 months with little or no improvement in vitiligo. An excision of the halo nevus was performed and NBUVB phototherapy was continued which showed a rapid rate of re-pigmentation. This was followed by Non-cultured melanocyte-Keratinocyte Transplantation (MKTP) Grafting in the residual areas.

Results:

Patient 1 showed 100% re-pigmentation at all sites at 3 years follow up, Patient 2 showed complete repigmentation in all sites except the finger tips, toes, palmoplantar surface and lip areas at 2 years follow up.

Conclusion:

An excision of halo nevi in patients of vitiligo can improve the outcomes of the vitiligo therapy.

P09**Different Patterns of Acral (Hand) Vitiligo**

Dr. Souzanne Shalaby

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TAKE HOME MESSAGE:

Acral vitiligo is one of the most challenging subtypes of vitiligo. Classification of acral vitiligo could give clues about predicting pathogenesis, spread, prognosis and subsequently treatment plan. Acral vitiligo is not to be considered as one unit, with 5 main distinct clinical types namely: The "knuckle" pattern, "no rule" pattern, "periungual" pattern, "inversed knuckle" pattern and "glove" pattern (6.6%).

ABSTRACT:**Background:**

Vitiligo is an acquired chronic depigmenting disorder with an estimated prevalence of 0.5%. Vitiligo received many classifications over the years, with the acral/non acral being one of the most commonly dealt with.

Aim of work:

Owing to the presumed practical benefits one could achieve from a proper classification, the current study aimed to sub-classify the acral vitiligo, particularly the hands into distinct clinical subtypes.

Patients and methods:

720 vitiligo patients were recruited. Photos were taken for hands of patients with acral vitiligo for both dorsal and palmer surfaces under both visible and wood's light. Photos were later studied by 5 independent dermatologists, and sites of vitiligo affection were marked. Only areas that were found common among at least 3 of them were finally marked as being involved. Hands showing similar affection sites were arranged together, and those found to be repeated in $\geq 5\%$ were considered a pattern.

Results:

The incidence of acral vitiligo was 56.38 %. Among the 406 acral vitiligo patients, 5 types were represented by percentages high enough to be considered a pattern. The "knuckle" pattern (43.84 %) with Kóebner phenomenon suggested as main etiological factor, "no rule" pattern (27%) , "periungual" pattern (14.41%) which carry a bad therapeutic prognosis, "inversed knuckle" pattern (8.1%) with a good prognosis due to presence of hair follicle reservoir and "glove" pattern (6.6%) which can be considered an end stage of other patterns.

Conclusion:

Acral vitiligo is not to be considered as one unit, with 5 main distinct clinical types. Each one has been proposed unique predisposing factors, clinical criteria, prognosis and therapeutic plan. The current study offered a further practical step to better understand how to deal with acral vitiligo and eventually reach better outcomes.

P10**Depression and Quality of Life in Vitiligo Patients Before and After Phototherapy**

Dr. Pezhman Mobasher

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TAKE HOME MESSAGE:

The objective of this study is to establish a correlation between clinical improvement (indicated by lower VASI scores) and depression/quality of life symptoms (indicated by lower VIS-22, CDLQI, PHQ-9, PHQ-A scores) following phototherapy in patients with vitiligo.

We Hypothesize that higher VASI score, or higher body surface area of depigmentation, is correlated with lower quality of life and higher depressive symptoms as indicated by high PHQ-9, PHQ-A, CDLQI, and VIS-22 scores in patients with vitiligo and treatment of vitiligo not only improves cutaneous symptoms, indicated by lower VASI scores, but also improves depression and overall quality of life.

ABSTRACT:

Vitiligo is seen in 0.5-2% of the general population worldwide. Vitiligo is more than a cosmetic disorder as substantiated by numerous studies that demonstrate a profound burden on patients' quality of life. Patients with vitiligo suffer from low self-esteem, negative perception of body image, and social isolation. Additionally, depression is prevalent among vitiligo sufferers; a recent meta-analysis concluded that 33.6% of vitiligo patients

reported depressive symptoms or impaired general health and up to 25% had overt clinical depression. The Vitiligo Impact Scale-22 (VIS-22) has been developed as a vitiligo-specific scoring system to help identify patients who have substantial psychosocial stress by measuring quality of life and can further aid in identifying impact on quality of life. No vitiligo quality of life instrument for adolescents has been developed. However, studies have utilized the Children's Dermatology Life Quality Index (CDLQI) to capture quality of life impairment in children and adolescents with vitiligo.

This study will explore the effect of phototherapy on depression and quality of life in vitiligo patients.

We will include vitiligo patients with depigmentation of the hands and face, or large body surface areas (as defined by VASI 25% or greater) who are currently undergoing or initiating phototherapy. Light therapy can affect circulating levels of Melanocyte Stimulating Hormone (MSH) that has been linked to anti-depressive effects. Therefore, to minimize confounding effect, patients with vitiligo not currently on light therapy will serve as the control group.

Patients will be aged 11 or older, with literacy to complete our scoring surveys. We will utilize the Patient Health Questionnaire-9 (PHQ-9) to quantify the severity of depressive symptoms in patients 18 years and older; and the PHQ-9 modified for Adolescents (PHQ-A) in patients aged 11-17. The Vitiligo Impact Scale-22 (VIS-22), currently the only validated vitiligo-specific quality of life measurement instrument, will be administered to patients 18 years and older in conjunction with the depression survey. A Children's Dermatology Life Quality Index (CDLQI) will be administered in lieu of the VIS-22 for patients aged 11-17.

Correlative statistical tools will be used to establish a baseline correlation between VASI scores, depression, and quality of life instruments. Subjects will undergo phototherapy and receive a PHQ-9, and VIS-22 when appropriate, at each follow-up at an interval of 3 months for the course of 6 months. The first interval, three months, was chosen based on the finding that 62% of vitiligo patients show greater than 25% repigmentation after three months of NB-UVB duration. Clinical improvement based on residual depigmentation (loss of pigment), will be quantified using the VASI score at each follow-up. Changes observed in VASI scores can then be correlated with depressive and quality of life measures, per our instruments.

To our knowledge, this study is the first to establish the psychosocial effects of treating vitiligo. If found beneficial, it may aid in the rationalization of appropriate referrals and insurance coverage for vitiligo patients seeking treatment.

P11

Development and Validation of the Vitiligo Extent Score for a Target Area (VESTA): An International Collaborative Study

Prof. Jung Min Bae

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TAKE HOME MESSAGE:

How can we readily and reliably assess the treatment response of a target lesion with vitiligo in clinical practice? We developed the Vitiligo Extent Score for a Target Area (VESTA) using reference images of both marginal and perifollicular repigmentation to measure the repigmentation rate (%) in a target lesion. In the validation study, the VESTA showed both superior accuracy and inter- and intra-rater reliabilities over the rough estimate. The VESTA afforded intuitive, convenient and reliable assessments of treatment response in a target area. The VESTA would be useful in clinical practice as well as retrospective studies.

ABSTRACT:

Introduction:

Patients with vitiligo are more likely to have limited involvement than widespread one, and localized treatment is as essential as systemic treatment. Therefore, a reliable instrument for target evaluation (single lesion assessment) is needed besides those for whole body evaluation.

Objective:

To validate the accuracy and reliability of the Vitiligo Extent Score for a Target Area (VESTA) for assessing treatment response in a target lesion.

Methods:

A validation study was performed between March and April 2017. A total of 65 dermatologists in 10 institutes, evaluated 17 pairs of vitiligo images (pre- and post-treatment) using both a rough estimate and the VESTA. Two evaluations were conducted 2 weeks apart. Accuracy was evaluated by calculating concordance correlation coefficients (CCCs) between the true values and each measurement. Inter- and intra-rater reliabilities were assessed by deriving intraclass correlation coefficients (ICCs). The smallest detectable change (SDC) was calculated with each coefficient.

Results:

The VESTA (CCC: 0.949, 95% confidence interval [CI] 0.942-0.955) was significantly more accurate than the rough estimate (CCC: 0.896, 95% CI 0.883-0.908). These corresponded to an SDC95 of 1.5% for the VESTA and 4.1% for the rough estimate. Inter-rater reliability showed an ICC of 0.928 (SDC95: 12.8%) for the VESTA and 0.900 (SDC95: 19.6%) for the rough estimate. Intra-rater reliability showed an ICC of 0.944 (SDC95: 1.7%) for the VESTA and 0.943 (SDC95: 1.8%) for the rough estimate.

Conclusion:

The VESTA afforded accurate and reliable assessments of treatment response in a target area. Because the VESTA is quick, convenient, and intuitive, it would be useful in daily clinical practice as well as retrospective studies where the clinical photographs are not properly prepared.

P12

Comparison of 311-nm Titanium:Sapphire Laser and 308-nm Excimer Laser Treatment for Vitiligo: A Non-inferiority Randomized Controlled Trial

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TAKE HOME MESSAGE:

The 308-nm excimer laser (EL) has been widely used to treat localized vitiligo since 2002. Recently, a gain-switched 311-nm Titanium:Sapphire laser (TSL) using a solid medium was developed. In this randomized controlled trial that included 74 paired localized vitiligo lesions, the therapeutic efficacy of the TSL was not inferior to that of the EL when treating patients with localized vitiligo. It follows the strengths of EL, which allows selective treatment of depigmented lesions while preventing unnecessary UV irradiation of uninvolved skin, and can be used to treat young children who cannot tolerate phototherapy units. In addition, maintenance costs would be expected to be low, because the TSL does not require periodic gas charging that is required the EL. The 311-nm TSL is a promising treatment modality for localized vitiligo.

ABSTRACT:

Introduction:

The 308-nm excimer laser (EL) has been widely used to treat localized vitiligo. Recently, a 311-nm Titanium:Sapphire laser (TSL) was developed to this end, but few controlled trials have been reported.

Objective:

To compare the efficacy and safety of the TSL and EL in the treatment of vitiligo.

Methods:

This was a randomized, controlled, non-inferiority split-body trial. All participants were diagnosed with stable vitiligo between June 2016 and May 2017. The vitiligo patients who had not been treated at 6 months prior to enrollment were recruited. Paired symmetrical vitiligo lesions were randomized to either the EL or TSL treatment group. All lesions were treated with a 308-nm EL or a 311-nm TSL twice weekly for a total of 12 weeks. The degree of repigmentation was assessed every 4 weeks (as the percentage of the baseline value), and the non-inferiority margin was set to 10%. We also recorded any adverse events.

Results:

A total of 21 patients aged 21-79 years old were enrolled. Seventy-four paired lesions were assigned to both the EL (n = 37) and TSL groups (n = 37). The mean difference between the two groups (EL data minus TSL data) was -2.862%, and the 95% confidence interval (-6.531 to 0.807%) was lower than the non-inferiority margin. No serious adverse events were noted in either group.

Conclusion:

The 311 nm TSL was as effective as the 308 nm EL when used to treat vitiligo.

P13

Photoprotection in Vitiligo Patients: a New Approach

Dr. Giovanni Leone

San Gallicano Dermatological Institute, Roma, Italy

TAKE HOME MESSAGE:

The common belief is that vitiliginous skin has very little, if any, defensive capacity against solar UV radiation. We have investigated sun exposure, and sunscreen use habits in our patients. We have tried a new approach in photoprotection that allows moderate UV exposure on lesional skin and high protection on normal skin by using a kit dedicated to vitiligo patients with two different sunscreen products. This new approach led to a modification of the sun exposure and sunscreen use habits and a reappraisal of heliotherapy.

ABSTRACT:

Some studies suggest that vitiligo patients have protection mechanisms against the development of actinic damage, basocellular and squamous cell carcinomas, and there are limited reports of vitiligo patients developing these neoplasias. Nevertheless there are many common misconceptions: vitiligo patients should always apply a very high SPF sunscreen on vitiligo patches, avoidance of sun exposure is recommended during the summer period, etc. This is in contrast with the fact that NB UVB phototherapy is considered as the “gold standard” therapy. We believe that excessive photoprotection, in vitiligo patients is a wrong approach; on the contrary we support the idea that controlled and progressive exposure to the sun may be beneficial in vitiligo patients, also when phototherapy is suspended. There is a lack of information on the correct use of sunscreens in vitiligo, and on the positive effect of heliotherapy. For this reason we have evaluated a set of products that may be particularly helpful in vitiligo patients: a medium SPF sunscreen coupled with a very high SPF sunscreen (*). The two sunscreens are available in only one package, with detailed explanations on how to use them: SPF 15 with very high UVA PF is intended for vitiliginous skin and SPF 50+ with very high UVA PF is recommended for application on surrounding pigmented skin.

We have conducted a survey in our patients with vitiligo with the aim to evaluate sun protection habits in these patients and how the use of this new photoprotective strategy in vitiligo could improve habits and outcomes. A questionnaire was used followed by physical examination in patients of the Vitiligo Cell Transplant Unit (VCTU) of San Gallicano Institute in Rome and of the Dermatologic Phototherapy Center in Rome. A total of 134 patients were included and interviewed: 1) sun protection behavior in the past 5 years was evaluated, and 2) then after trying the new photoprotective strategy during the summer season in 2017. The questions covered the following areas: demographic data; clinical characteristics of the vitiligo; sunscreen use (frequency, SPF and duration of use); and habits of sun exposure. After answering the questionnaire, patients had a physical examination to determine the clinical type of vitiligo and phototype.

Results:

The questionnaire led to interesting findings on the sun exposure habits of vitiligo patients. An attitude oriented to excessive sun protection on vitiliginous skin was confirmed. On the other hand, after careful explanation by the dermatologist the patients were more prone to accept controlled sun exposure. The principal drawback was the concern about increase in color contrast with normal skin. The second phase of the survey confirmed that a sunscreen specially dedicated to vitiligo patients is well accepted and considered useful by the patients thus increasing the efficacy of heliotherapy. Observance of instructions and combined use of the two sunscreens (provided in the same package) minimized the ant esthetic effect of sun exposure and encouraged the patients to take advantage of of heliotherapy.

P14**Acculturated South Asian Patients with Vitiligo Have a Lower Burden of Disease Compared to Non-acculturated South Asian Patients with Vitiligo****Jamael Thomas**

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TAKE HOME MESSAGE:

Our results suggest that acculturated South Asian patients with vitiligo have a decreased burden of disease compared to non-acculturated South Asian patients and African American patients with vitiligo.

ABSTRACT:**Background:**

Vitiligo is a disfiguring depigmenting disease affecting about 0.5% of the population. Patients in some racial/ethnic groups also undergo stigmatization and ostracization from society. Some believe that vitiligo causes more detriment in South Asia due to the enhanced cultural and religious significance placed on diseases of the skin. This negative effect on quality of life may improve in South Asians who move to Western countries and become acculturated to their new surroundings. We hypothesized that acculturated individuals from South Asia have a lower burden of disease and better quality of life compared to non-acculturated individuals.

Objectives:

The purpose of our study is to determine if there is a statistically significant difference between the quality of life and burden of disease in South Asians based on acculturation status.

Design:

Prospective survey of South Asian patients

Setting:

Outpatient dermatology clinic at a large tertiary care medical center in Dallas, Texas, USA

Subjects:

South Asian patients with vitiligo 18 years of age or older presenting for dermatologic care to the outpatient dermatology clinic were eligible to participate in the study.

Intervention/Instruments:

All individuals were required to complete the Dermatology Life Quality Index (DLQI) and SF-36 surveys and a Patient Demographic and Vitiligo Assessment Sheet (PDVA). The SF-36 is a survey that measures 8 scales of disease burden contributing to Physical Component Summary (PCS) and another 8 to Mental Component Summary (MCS) scores. South Asian patients were required to complete a validated South Asian acculturation survey in which a score of > 50% meant the individual was acculturated to the United States, thus separating the patients into

acculturated and non-acculturated groups. The Kruskal-Wallis test was used to assess whether any differences in distributions of SF-36, DLQI, and subsection scores existed among acculturated and non-acculturated vitiligo patients. Dunn's test was used to determine the differences in distributions of SF-36, DLQI, and subsection scores among acculturated patients, non-acculturated patients, and African American control patients with vitiligo.

Results:

Our study consisted of 10 acculturated South Asian patients, 18 non-acculturated South Asian patients, and 12 African American control patients. We found that no difference in distributions existed between the DLQI scores and Mental Component Summary scores of the three sample groups. However, there was a statistically significant difference in the distribution of Physical Component Summary scores of the SF-36 in acculturated South Asians with vitiligo (median=60.5) compared to the non-acculturated South Asian patients with vitiligo (median=55.58) and control patients (median=55.03). Further enrollment is ongoing

Conclusions:

A larger PCS score found for acculturated South Asians compared to non-acculturated South Asians corresponds with our hypothesis that acculturated South Asian patients with vitiligo likely have decreased burden of disease compared to non-acculturated South Asian patients. Our results also suggest that African American patients with vitiligo have an increased burden of disease compared to acculturated South Asian patients. Further studies with larger numbers of patients are needed and being conducted at our medical center.

P15

Vitiligo: Observational Study in Children and Possible Association with Celiac Disease

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TAKE HOME MESSAGE:

Vitiligo and celiac disease can be triggered by a common signal within the immune system.

Celiac disease-antibodies are more common in the serum of patients affected by vitiligo, than in healthy individuals, thus suggesting the presence of a common autoimmune and physiopathological mechanism at the base of these diseases.

Further and future studies could lead us to the development of effective treatments both for vitiligo and celiac disease.

ABSTRACT:

Vitiligo typically occurs in otherwise healthy individuals, however well-established associations with autoimmune diseases and circulating autoantibodies have been observed in a minority of patients.

Celiac disease (CD) is a chronic, immune-mediated and gluten-dependent enteropathy that has been associated with several cutaneous manifestations, furthermore antiendomysial, antigliadin and antitransglutaminase antibodies can be found in the serum of patients affected by CD.

The relationship between CD and vitiligo is controversial. Although isolated case reports describe vitiligo in patients with CD, a serological screening for CD by means of antigliadin and antiendomysial antibodies, in large series of consecutive patients with vitiligo, did not show any correlation between these diseases.

Reports of improvement of alopecia areata and psoriatic lesions, after institution of a gluten-free diet in patients with concurrent CD do exist, however repigmentation of vitiligo has rarely been reported.

The aim of our pilot study was to clarify the relationship between CD and vitiligo.

We enrolled 18 children (under 14 years old) affected by vitiligo and 18 healthy children, looking for the presence of antitreoglobulin, antitreoxidase and antitransglutaminase antibodies in their serum.

The results showed that children affected by vitiligo have an higher prevalence of positivity to antitransglutaminase antibodies, found in 3/18 subjects (17%). Conversely, all the healthy subjects turned out negative to the antitransglutaminase antibodies.

Further studies are required to fully explain the mechanisms involved.

P16

Comparing the Efficacy of VL-UVA1 versus NB-UVB on Inducing Repigmentation in Subjects with Generalized Vitiligo

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TAKE HOME MESSAGE:

These findings have potential clinical implications for the treatment of pigmentary disorders including vitiligo. This pilot study aims to compare the efficacy of VL+UVA1 versus NB-UVB phototherapy in subjects with vitiligo.

ABSTRACT:

Vitiligo is an autoimmune depigmenting disorder affecting close to 1% of the population worldwide. Vitiligo can be classified into segmental or non-segmental, the latter of which includes the most common form known as generalized vitiligo. Narrowband (NB) ultraviolet (UV) B (NB-UVB) phototherapy is currently the standard of care for generalized vitiligo, often in combination with topical corticosteroids or immunomodulators. The combination of visible light (VL) with UVA1 (VL+UVA1) has recently been shown to induce skin pigmentation in melanocompetent skin. These findings have potential clinical implications for the treatment of pigmentary disorders including vitiligo. This pilot study aims to compare the efficacy of VL+UVA1 versus NB-UVB phototherapy in subjects with vitiligo. Three patients over the age of 18 with stable, generalized vitiligo involving at least 5% of their total body surface will undergo VL+UVA1 and NB-UVB treatment twice weekly for a total of 24 phototherapy treatments to contralateral sides of the body. Repigmentation will be assessed using colorimetry, diffuse reflectance spectroscopy (DRS), clinical photography, and modified VASI scoring. The study results will be presented and will help to conclude if VL+UVA1 is an optimal waveband for inducing pigmentation in vitiligo patients.

P17**Participation of the Genome TNF-a-308 G/A in Patients with Vitiligo**

Dr. Botir Saatov

Republican Specialized Scientific-Practical Medical Center of Dermatovenerology and Cosmetology, Tashkent, Uzbekistan

TAKE HOME MESSAGE:

Vitiligo is an acquired autoimmune disease of unknown etiology with skin depigmentation due to lack of melanocytes. We studied the association between TNF- α gene -308 G/A polymorphism and types of vitiligo in Uzbek patients.

ABSTRACT:

Vitiligo is an acquired autoimmune disease of unknown etiology with skin depigmentation due to lack of melanocytes. Its prevalence in various populations ranges from 0.1% to 2% with no race, sex or regional differences. Recently, number of patients with vitiligo has intensively increased. Nevertheless, pathogenesis of the disorder remains unestablished, and there are no efficient methods of treatment. TNF- α is a cell signaling protein (cytokine) involved in systemic inflammation playing a significant role in onset and progression of autoimmune diseases, including vitiligo. TNF- α participates in pathogenesis of vitiligo as a paracrine inhibitor of proliferation of human melanocytes and melanogenesis. Role of TNF- α in mechanisms of onset and progression of vitiligo needs to be further elucidated. No studies either on TNF- α gene -308 G/A polymorphism, or its role in ethnic Uzbeks were ever conducted.

Aim.

The work was initiated to study associations between TNF- α gene -308 G/A polymorphism and types of vitiligo in Uzbek patients.

Materials and methods:

We examined 93 patients diagnosed with vitiligo, 50 persons with the general type and 43 subjects with the localized one. 74 healthy donors were included into the control group. Allele-specific polymerase chain reaction (AS-PCR) was run to examine TNF- α gene -308 G/A polymorphism by means of a commercial kit (Research and Production Company Litekh, the Russian Federation). The amplification was performed in a thermocycler "CGI-96" (Corbett Research, (Germany, Australia). The products were examined by means of electrophoresis in 3.5% agarose gel with subsequent staining with ethidium bromide. The data processing was performed by means of "Doctor Stat2013" statistic program.

Results:

Analysis of genotypes by TNF- α gene -308 G/A polymorphism demonstrated that in patients with vitiligo unfavorable A allele of the polymorphism was registered more frequently than in the controls (23.7% versus 10.8%; $X^2 = 9.23$; $P = 0.002$; $OR = 2.56$; 95%CI 1.38-4.75). Frequency of A allele in patients with the localized form of vitiligo was 19.8% versus 10.8% in the controls ($X^2 = 3.60$; $P = 0.06$; $OR = 2.03$; 95%CI 0.97-4.27), its frequency in those with the generalized was 27.0% versus 10.8% ($X^2 = 10.91$; $P = 0.001$; $OR = 3.05$; 95%CI 1.54-6.03). Frequency of G/G, G/A and A/A genotypes in patients with vitiligo was 57.0%, 38.7% and 4.3, respectively, while frequency of these genotypes was 78.4%, 21.6% and 0.0%, respectively.

Conclusions:

A/A polymorphism frequency in Uzbek patients with various types of vitiligo was 8 times than in the controls. For the first time A/A genotype in patients with the generalized type of vitiligo was found to occur 11 times more frequent than in the controls, in patients with the localized type its frequency is 5 times higher than in the controls.

**P18****UV-B Photosensitivity in the Patients with Vitiligo Combined with Various Underlying Conditions and Needs for Dose- Modification in Repigmenting NB-UVB Therapy**

Prof. Ki-Ho Kim

Department of Dermatology, Dong-A University College of Medicine, Busan, South Korea

TAKE HOME MESSAGE:

Ultraviolet radiation (UVR) is a double edged sword in that it can affect photosensitivity as well as it can be an useful treatment modality in various skin disorders. Oxidative stress may play a key role in the pathogenesis of SLE as well as in those of other photosensitive disorders. UVR photosensitivity occurs in 60-100% of SLE patients.

Oxidative stress contributes the Th17/Treg imbalance in SLE patients. Lastly, the combination of synthetic progesterone and estrogen from the corpus luteum may cause photosensitivity reaction.

An excessive exposure to sunlight or exposures to long-term UVB phototherapy and usual UVR doses on the sensitive victims, vitiligo may be initiated or aggravated in association with multiple underlying conditions.

ABSTRACT:

Ultraviolet radiation (UVR) is a double edged sword in that it can affect photosensitivity as well as it can be an useful treatment modality in various skin disorders. Oxidative stress may play a key role in the pathogenesis of SLE as well as in those of other photosensitive disorders. UVR photosensitivity occurs in 60-100% of SLE patients. Oxidative stress contributes the Th17/Treg imbalance in SLE patients. Next, although the pathogenesis of CAD remains unclear, there is evidence of a delayed-type hypersensitivity reaction to a photo-induced cutaneous endogenous antigen and more CD8+ suppressor/cytotoxic T cells infiltrate than other similar disorders. Lastly, the combination of synthetic progesterone and estrogen from the corpus luteum may cause photosensitivity reaction, especially in the patient with vitiligo as a state of decreased photoprotection.

An excessive exposure to sunlight or exposures to long-term UVB phototherapy and usual UVR doses on the sensitive victims, vitiligo may be initiated or aggravated in association with some underlying conditions such as systemic lupus erythematosus(SLE), adrenal adenoma with hyperplasia, inflammatory thyroid disease, alopecia areata, chronic actinic dermatitis(CAD), and progesterone-induced photosensitivity, etc. So we must prepare for the contingency of unexpected exacerbation in vitiligo or unwanted adverse event of photosensitivity including UV burn.

To take the representative examples for vitiligo occurrence through UV photosensitivity in various associated comorbidities: Firstly, 56 year-old Korean woman with multiple autoimmune syndrome (MAS) with 10 years SLE, 4 years' vitiligo and bilateral adrenal hyperplasia, positivity for serum anti-thyroid peroxidase antibody, and recent onset alopecia areata was presented to receive NBUVB repigmenting therapy. Her vitiliginous lesions were located at sun-exposed sites such as face and dorsa of hands. Alopecia areata lesions developed as multiple patchy pattern and became shortly into acute diffuse and total alopecia. As a patient with MAS, she had combination of at least three autoimmune diseases in the same patient. Later phototestings revealed UVB photosensitivity with decreased MED-UVB of 56mJ/cm² and narrowband(NB)UVB treatment started at 360 mJ/cm².

Secondly, 61 year-old Korean high school-principal was scheduled to treat Wood lamp-proven 6 months vitiliginous lesions. After phototesting, MED-NBUVB was revealed a slight low value of 450mJ/cm² as in type III phototype. Dry eczematous skin lesions of 1 year duration were noticed on sun-exposed sites. UVB photosensitivity was revealed by decreased MED-UVB of 56 mJ/cm² and we started NBUVB treatment at 100 mJ/cm² to avoid the possibilities of UV burn in vitiliginous lesions and CAD exacerbation.

Thirdly, 32 year-old Korean woman visited to solve the problem of pruritic erythema lesions developed on the previously treated vitiliginous lesions in centofacial area after Utrogestan administration during IVF-ET. Phototesting revealed a lowered MED-UVB 56 mJ/cm² and MED-UVA 1J/cm² and another round of phototesting after intradermal injection of progesterone 50mg/ml resulted in reproduction of erythema in ranges of at least 20 mJ/cm² UVB, which is lower than non-injected control sites. But, MED-UVA values did not change, compared to the previous phototesting results without progesterone injection.

P19

BMP4-induced Differentiation of Human Hair Follicle NCSCs into Melanocyte Precursors via Downregulated NRG1 & SEMA3C and Upregulated WNT10A in Emigrated Cell Culture and Clinical Importance of Follicular Unit Extraction (FUE) Grafting in the Better and Longer Repigmentation as a Noble Source of Melanocyte Precursors

Prof. Ki-Ho Kim

Department of Dermatology, Dong-A University College of Medicine, Busan, South Korea

TAKE HOME MESSAGE:

Under the various conditions treated with 0, 10, and 50 ng/ml in the emigrated cell cultures, we performed the RNA sequencing with the cultured cell lysates and the heatmap showed downregulated NRG1 (for neural crest cell development) & SEMA3C (for neural crest cell migration) and upregulated WNT10A (for hair follicle specification at early anagen and secondary hair germ) without expression of KIT or KITL. In addition, we investigated whether the cell survival and life span in HF melanocytes by observing the FUE grafting is superior to the epidermal mini-punch grafting in repigmenting therapy for vitiligo.

ABSTRACT:

Vitiligo is the most common acquired depigmenting disorder with a prevalence of 0.5-2.0% in general population. Among various options of treatment, narrowband (NB) UVB phototherapy is the mainstay of repigmenting treatment against vitiligo. The repigmentation grade was significantly lower in 2nd year of NB UVB phototherapy than that in 1st year. In the intractable vitiligo patients, FUE grafting is a more attractive than mini-punch grafting in repigmentation after NB UVB treatment.

The melanocyte stem cells (MSCs) are postulated to exist in the hair follicle (HF). To date, the exact markers for MSCs are not well known, but the neural crest stem cells (NCSCs) express their own markers and exist in the HF bulge also. Although the NCSCs are basically originated from the embryonic stem cells, they can be isolated also from human HF bulge and then migrate and differentiate into the melanocyte precursors via bipotent precursor of Schwann cell and melanocyte. Despite no melanin synthesis, the melanocyte precursors of HF bulge at telogen, equivalent to resting G0 phase, can be activated at the start of anagen.

BMP4 exists constitutively in HF bulge and its treatment can induce MITF expression in the NCSCs. α -MSH is produced and secreted from the adjacent UV irradiated epidermal keratinocytes in the skin and promotes a further differentiation of MITF-expressing cells along the melanocyte lineage.

After the isolation of the NCSCs from human HF bulge and an induction of differentiation along the melanocyte lineage by BMP-4 and α -MSH, we obtained SOX10+ emigrated cells from the HF bulge of adult human scalp; 1) SOX10+ cells proliferation were promoted by bFGF, compared to control. 2) The emigrated HF bulge cells didn't spontaneously differentiate into MITF+ cells, but into SOX2+ Schwann cell progenitors after a prolonged cultivation. 3) A differentiation into MITF+ cells was promoted by BMP-4 and α -MSH treatment.

Under the various conditions treated with 0, 10, and 50 ng/ml in the emigrated cell cultures, we performed the RNA sequencing with the cultured cell lysates and the heatmap showed downregulated NRG1 (for neural crest cell development) & SEMA3C (for neural crest cell migration) and upregulated WNT10A (for hair follicle specification at early anagen and secondary hair germ) without expression of KIT or KITL. In addition, we investigated whether the cell survival and life span in HF melanocytes by observing the FUE grafting is superior to the epidermal mini-punch grafting in repigmenting therapy for vitiligo.

P20

Combination of Cellular and Tissue Grafting Techniques for Patients of Stable Vitiligo Undergoing Repeat Vitiligo Surgery to Improve the Re-pigmentation Rate

Dr. Deepti Ghia

Mulekar Vitiligo Clinic, Mumbai, India

TAKE HOME MESSAGE:

Surgical management of vitiligo can require multiple sessions for complete repigmentation. To improve the repigmentation rates, a combination of cell and tissue transfer technique in the same session can be performed. This is helpful for areas which are difficult to treat like bony areas and also in conditions when patient needs quicker results due to social or personal reasons.

ABSTRACT:

Background:

Melanocyte keratinocyte grafting is a cell transfer technique which is standardized treatment modality for stable vitiligo patches. Suction blister grafting is a tissue grafting technique, which has excellent re-pigmentation rates. A combination of both these techniques on the same stable patch of vitiligo can offer dual advantages to the patient.

Objective:

To improve the re-pigmentation rate in patient of stable limited vitiligo who are undergoing repeat surgery or being treated for difficult to treat areas like acrofacial involvement or patients who have a timeline for treating the patches due to social or personal reasons.

Method:

3 Patients having limited patches of vitiligo less than 15 cm square, undergoing a repeat session were taken up for a combination surgery of MKTP and Suction blister grafting. After taking written informed consent, the donor area blisters were raised using leur-lock syringes of 10 ml and 20 ml volume with three-way knobs. After this the shave biopsy was taken for MKTP. While waiting for blisters to form and trypsin to act on shave skin graft recipient areas were prepared. After that suspension was prepared and roofs of blisters were harvested. The cell suspension was spread evenly on the surface and covered with blister roof. The patients were asked for 48 hours of immobilization.

Results:

All 3 cases were treated with MKTP earlier with partial re-pigmentation and showed complete re-pigmentation with combination therapy .

Conclusion:

Combination therapy is likely to be effective in obtaining complete re-pigmentation.

P21

The Use of Fractional CO² Laser with Topical TCA in Treatment of Recalcitrant Acral and Scalp Vitiligo

Dr. Hasan El-Fakahany

Minia Faculty of Medicine, Minia, Egypt

TAKE HOME MESSAGE:

Fractional CO² and topical TCA may provide a new hope for treatment of acral vitiligo and restoration of hair colour in scalp vitiligo

ABSTRACT:

Introduction:

Although scalp vitiligo is not as difficult as acral vitiligo to treat, the presence of white hair is still a challenge. Palmar vitiliginous patches extending to the sides of the fingers are very difficult to treat even with the advances of surgical treatment of vitiligo.

Patients and methods:

Fractional CO² and topical TCA was used to treat both scalp vitiligo patients and acral vitiliginous patches extending to the sides of hand fingers.

Results:

Successful repigmentation was achieved in acral and scalp vitiligo with scalp hair repigmentation.

Conclusion:

Fractional CO² and topical TCA may provide a new hope for treatment of acral vitiligo and restoration of hair colour in scalp vitiligo

P22

Markedly Reduced Risks of Internal Malignancies in Patients with Vitiligo: A Nationwide Population-based Cohort Study

Dr. Han Mi Jung

Department of Dermatology, College of Medicine, The Catholic University of Korea, Gyeonggi-do, South Korea

TAKE HOME MESSAGE:

Recent studies demonstrated the reduced risks of both melanoma and non-melanoma skin cancers in patients with vitiligo, suggesting that vitiligo-associated autoimmunity may exert the immune surveillance on cancer cells other than melanocytes. What about internal malignancies in patients with vitiligo? In this nationwide population-based cohort study, we found that patients with vitiligo had significantly less overall risk of internal organ malignancy, especially cancer sites in ovary, colon and rectum, and lung. This inverse association between vitiligo and internal malignancy suggests that enhanced immune activity simultaneously cause the development of vitiligo and induce possible preventive effect on cancer cells.

ABSTRACT:

Introduction:

Vitiligo is an autoimmune depigmented skin disorder caused by autoreactive CD8+T cells that lead to destroy melanocytes. Recent studies indicated that the autoimmunity of vitiligo could exert effects on cells other than melanocytes as well, showing the reduced risks of both melanoma and non-melanoma skin cancers in patients with vitiligo. However, the risks of internal malignancies in patients with vitiligo have not been elucidated yet.

Objective:

To investigate the risks of internal malignancies in patients with vitiligo.

Methods:

A population-based retrospective cohort study using Korean National Health Insurance (NHI) Claims database from January 2007 to December 2016. We identified all vitiligo patients aged 20 or older who had at least two physician contacts at which vitiligo was the principal diagnosis from 2009 to 2016 (the vitiligo group). The controls were randomly selected (2 per 1 vitiligo patient) after frequency matching for age and sex with the vitiligo group (the control group) during the same period. The outcome of interest was the development of internal malignancies since the time of enrollment. We compared the incidence rates of overall and organ-specific internal malignancies between the two groups using multivariable Cox proportional hazard models.

Results:

A total of 101,078 patients with vitiligo and 201,156 controls without vitiligo were included in this study. The incidence rates of internal malignancies were per 100,000 person-years were 612.9 and 708.9 in the vitiligo and control groups, respectively. Patients with vitiligo showed notably reduced risk of overall internal malignancies (hazard ratio [HR] 0.86, 95% confidence interval [CI] 0.82-0.89) than the age- and sex-matched controls without vitiligo after adjusting for age, sex, and comorbidities. Among the organs, patients with vitiligo showed remarkably decreased risks of cancer in the colon and rectum (HR 0.62, 95% CI 0.55-0.69), ovaries (HR 0.62, 95% CI 0.46-0.83), and lungs (HR 0.75, 95% CI 0.65-0.86).

Conclusion:

Vitiligo was associated with reduced risks of overall internal malignancies in this study. Our findings suggest that autoimmune disease including vitiligo could have immune surveillance for the development of cancers beyond the targeted organ.

P23**Expression of Janus Kinase 1 in Vitiligo & Psoriasis Before and After Narrow Band UVB:****A Case-control Study****Dr. Maha Fathy Elmasry**

Kasr Alainy, Faculty of Medicine, Cairo University, Cairo, Egypt

TAKE HOME MESSAGE:

JAK1 levels in vitiligo and psoriasis patients were higher than normal controls and these levels were downregulated after treatment. So it is suggested that JAK1 plays a role in the pathogenesis of both vitiligo and psoriasis. This could also support the ideas of targeting JAK1 in both diseases and could open a new era for treatment of vitiligo and psoriasis by anti-JAK modalities.

ABSTRACT:**Background:**

Janus kinases (JAKs) are non-receptor protein tyrosine kinases that are expressed in many tissues. Once the JAKs are activated, a cascade of further signaling events is triggered involving phosphorylation of selected receptor chain tyrosines, binding of signal transducer and activator of transcription (STAT) proteins and phosphorylation of these STATs. Due to their ability to selectively modulate immune function, targeted JAK inhibitors are promising candidates for some skin diseases such as psoriasis and atopic dermatitis.

Objective:

The objective of this study was to assess the level of JAK1 in both vitiligo and psoriasis patients before and after treatment with NB-UVB which is considered a gold standard therapy for both diseases. This study was conducted on 10 patients with psoriasis, 10 patients with vitiligo and 10 controls. JAK1 levels before and after treatment with NB-UVB 311nm (36 sessions) were measured using Western blot assay.

Results:

The level of JAK1 was significantly higher in vitiligo and psoriasis patients than controls. There was a decline in the level of JAK1 after treatment, which was statistically significant. VASI and PASI scores of patients decreased after treatment with NB-UVB. In psoriatic patients, the JAK1 level positively correlated with the female participants, disease duration, and PASI change.

Conclusion:

It was concluded that JAK1 plays a role in the pathogenesis of both vitiligo and psoriasis based on its upregulated level before treatment and downregulated level after treatment. This raises the possibility of using the JAK1 inhibitors as targeted immunotherapy for vitiligo and psoriasis.

P24**Cutaneous Expression of Thymic Stromal Lymphopoietin (TSLP) in Vitiligo Patients; A Case-control Study****Dr. Maha Fathy Elmasry**

Kasr Alainy, Faculty of Medicine, Cairo University, Cairo, Egypt

TAKE HOME MESSAGE:

To the best of our knowledge, this is the first study comparing TSLP tissue level in vitiligo patients versus healthy controls. From our study, we can conclude that TSLP may play an important role in the pathogenesis of vitiligo. In addition, procedures which can increase TSLP level could be a promising treatment option for this disease. On the other hand, exacerbation of vitiligo is expected in atopic dermatitis patients treated with TSLP.

ABSTRACT:**Background:**

Thymic stromal lymphopoietin (TSLP) is a major pro-allergic cytokine promoting T helper-2 responses.

Objective:

This study's objective was to study and verify the hypothesis of the role of TSLP in the pathogenesis of vitiligo.

Methods:

The study was conducted on twenty-five patients with generalized non-segmental vitiligo (recruited from the Dermatology outpatient clinic, Kasr El Ainy, Faculty of Medicine, Cairo University), and twenty-five healthy controls fulfilling the inclusion criteria in a case-controlled study over a period of 7 months (January 2017-July 2017). Patients were subjected to complete medical history, detailed assessment of vitiligo and photography taking. Skin biopsies were taken from vitiliginous skin and from normal skin of controls for which TSLP tissue levels were measured using quantitative real-time polymerase chain reaction technique.

Results:

There was a statistically significant difference between the levels of TSLP in vitiligo patients and normal healthy controls ($P < 0.001$) with lower levels of TSLP in vitiligo patients.

Conclusion:

Based on the fact that TSLP upregulates the T helper-2 inflammatory response and that vitiligo is considered as T helper 1-related disease, results of this study revealed lower TSLP levels in vitiliginous skin versus normal skin suggesting an imminent role of TSLP in the pathogenesis of vitiligo.

P25

UVA light set-up for Vitiligo Photography

Dr. Sanne Uitentuis

Netherlands Institute for Pigment Disorders, Amsterdam UMC, Amsterdam, Netherlands

TAKE HOME MESSAGE:

When comparing four different techniques for administering UV-light for photographing vitiligo the use of a separate high output UV-flash light performed best for both picture quality and ease of use.

ABSTRACT:

Background:

In the field of vitiligo there is consent that the Woods lamp can be used to assess the spreading and staging of vitiligo in selected areas. The method to administer this light for making photographs can vary and it is not clear how to create optimal UV-lightning. Four techniques that can be used are: (i) using hand held Woods lamps; (ii) using soft boxes with UV-lamps; (iii) using a UV-flash light attached to the camera; (iv) using a separate high output UV-flash light.

Objective:

The objective of our study is to compare different techniques of UV light set-ups for photographing vitiligo to find which gives the optimal lightning and is easy to use.

Methods:

Patients with vitiligo aged 18 or older with lesion with borders that could not be clearly defined without the use of UV light were included in this study. Two photographs were made with all 4 different UV-set up techniques per patient, one including a larger area (eg lower legs) and one of a target area closer to the lesion. Photographs were scored separately by three blinded vitiligo experts for 5 criteria: overall quality, clearness of borders, contrast lesional vs non-lesional areas, sharpness and shadows. Furthermore the medical photographers were asked to score the ease of use for each technique.

Results and Conclusion:

Our preliminary data show that the high output-flash light performs best for all criteria for larger areas and target areas. Furthermore this device scored best for ease of use.

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