PIGMENTARY DISORDERS SOCIETY

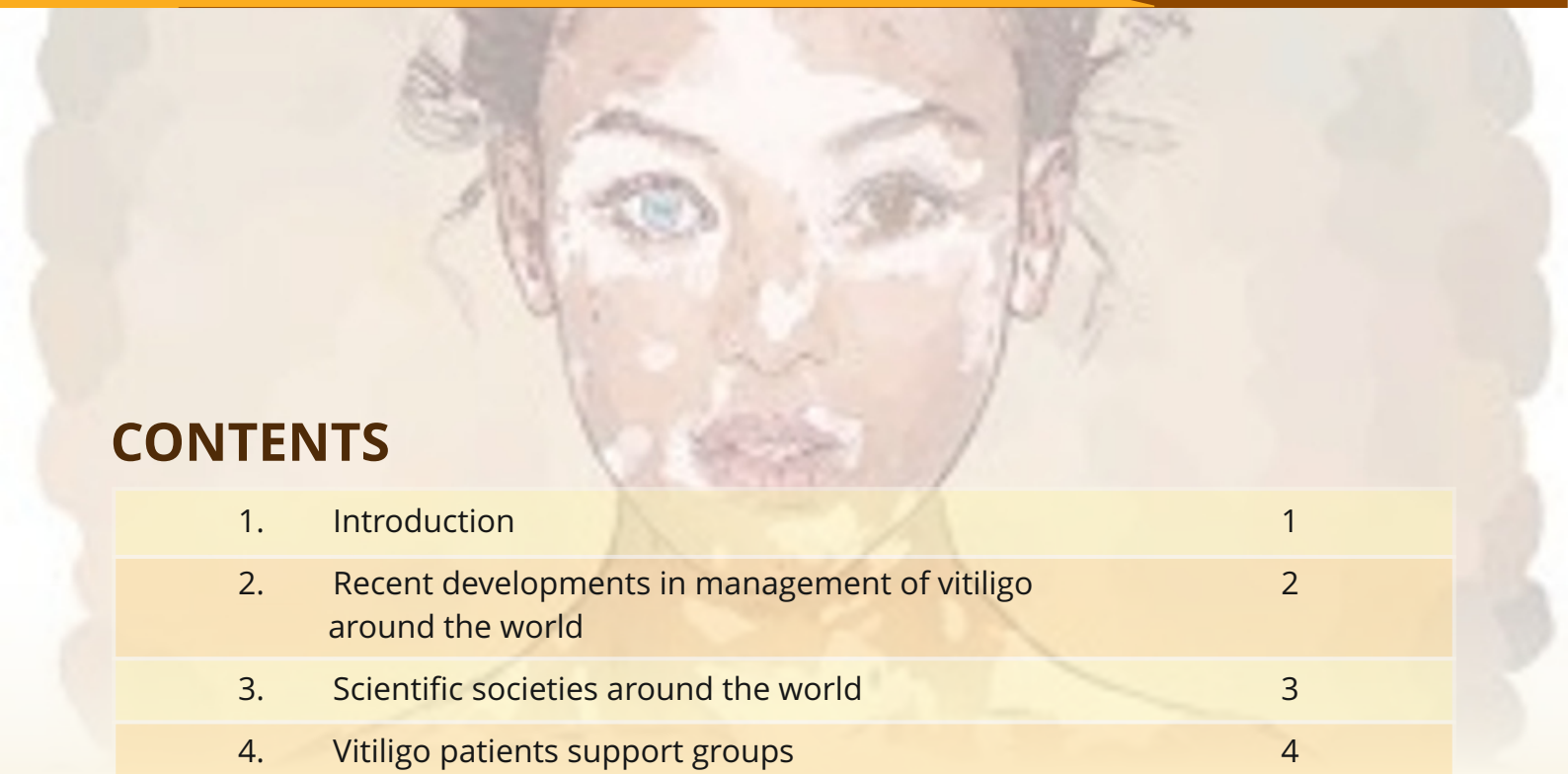
VITILIGO DAY NEWSLETTER

PIGMENTARY DISORDER SOCIETY

WORLD VITILIGO DAY 2021

HELP THEM IN SEEING A BETTER TOMORROW

"SUPPORT AND EMPOWER THE VITILIGO PATIENT"



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INTRODUCTION

On the occasion of the **World vitiligo Day**, the Pigmentary Disorders Society of India (https://pigmentarydisorderssociety.com) is committed to the goals of raising awareness regarding the disease, reducing stigma, disseminating knowledge, enabling research and together give a helping hand in minimizing the suffering of the people affected by the disease.

World vitiligo day is being observed since 2011 on June 25 every year and this year main function is held in Indonesia. It has become a global event, which aims to bring international attention to this neglected disease. From raising awareness, the goals have broadened to include the psychological and social needs of the affected people. The global theme this year is aptly- **"embracing life with vitiligo"**.

The pigmentary disorders society (PDS) from the time of its inception, works for the promotion and advancement of knowledge and practical skills in the management of vitiligo and other pigmentary disorders of skin. The academic wing of the pigmentary disorders society (PDS), the PDS Academy, works specifically to promote research and education in the areas of pigmentary disorders; and vitiligo is a key, focus area. Recently, the PDS academy had offered research grants for its members working on vitiligo and other pigmentary disorders and will be continuing these projects in the coming years.

This newsletter is also an attempt in that direction to bridge the gaps in knowledge and we sincerely hope that this will benefit our colleagues.

Prof. Rashmi Sarkar- Founder Chair & President PDS
Dr Bhavesh Swarnkar - General Secretary PDS

Prof. Sunil Dogra / Dr. Soumya Jagadeesan
Chairperson / Convener - PDS Academy

RECENT DEVELOPMENTS IN MANAGEMENT OF VITILIGO AROUND THE WORLD

A.Medical – Topical Treatment

1. Seneschal J et al. **Efficacy and Safety of Tacrolimus 0.1% for the Treatment of Facial Vitiligo: A Multicenter Randomized, Double-Blinded, Vehicle-Controlled Study.** J Invest Dermatol. 2021 Feb 4:S0022-202X(21)00077-4.

A 24-week multicenter randomized parallel double-blind study with a 24-week post-treatment follow-up extension, was conducted in adult patients with recent facial vitiligo target lesions (<2 years) without changes in pigmentation or size over the previous 3 months. Comparison of 0.1% ointment or vehicle twice daily revealed that 65% of tacrolimus-treated patients had more than 75% repigmentation, while none of vehicle-treated patients did at week 24 (P < 0.0001). There was only 40% of relapse at 48 weeks. Twice-daily tacrolimus 0.1% ointment showed superior efficacy to that of the vehicle through the 24 weeks of intervention and 24 weeks of follow-up in adult patients with facial vitiligo.

2. Esmat SM, et al. **Different methods of enhancing the efficacy of topical tacrolimus in extra-facial vitiligo: A comparative study**. J Cosmet Dermatol. 2021 Feb 24. doi: 10.1111/jocd.14024.

   In this study, 20 adult patients of non-segmental vitiligo, four extra-facial vitiligo lesions were randomly labeled A, B, C, and D and treated with either A: tacrolimus ointment (0.03%) application twice/day; B: microneedling once/week and tacrolimus ointment application directly after microneedling and twice/day the rest of the week;C: microneedling once/week alone; D: tacrolimus ointment application twice/day under occlusion by polyethylene foil. After 6 months of treatment, clinical evaluation revealed responders in B were 45%, and 35% in area C, and 25% in both areas A and D. The difference was however not significant. Combination of microneedling and topical tacrolimus has an edge over monotherapy in vitiligo, and further studies are needed to verify such results.

3. Cárcamo-Martínez Á, et al. **Enhancing intradermal delivery of tofacitinib citrate: Comparison between powder-loaded hollow microneedle arrays and dissolving microneedle arrays**. Int J Pharm. 2021 Jan 25;593:120152.

   In this study, the authors compared the delivery of tofacitinib in neonatal porcine skin using hollow MN arrays (formulated with crosslinked hydrogels containing modifying agents), dissolving MN arrays and the other with Aqueous cream BP. It was seen that hollow MN arrays containing NaCl in the formulation led to slightly higher depositions of tofacitinib in epidermis and dermis of neonatal porcine skin when compared to a control cream, dissolving MN arrays showed superiority in terms of tofacitinib deposition in the dermis. There is an enhanced intradermal drug delivery capacity of MN arrays and their potential for treatment of autoimmune skin diseases.

4. Zhai S, et al. **Successful treatment of vitiligo with cold atmospheric plasma-activated hydrogel**. J Invest Dermatol. 2021 May 21:S0022-202X(21)01237-9.

   The authors assessed the antioxidant and anti-inflammatory properties of Cold atmospheric plasma (CAP) in both mouse model and in patients with active focal vitiligo in a randomised controlled trial. CAP had restored melanocyte distribution and reduced infiltration of chemokines such as

chemokine (C-X-C motif) ligand 10 and cytokine interferon-γ and reduced infiltration of CD11c+ dendritic cells, CD3+ T cells, and CD8+ T cells and enhanced the expression of transcription factor Nrf2. In patients it had achieved partial and complete repigmentation in 80% and 20% of vitiligo lesions, respectively without significant adverse effects. CAP thus offers a promising option for the management of vitiligo.

5. Saleh R, et al. **Efficacy of topical tacrolimus 0.03% monotherapy in the treatment of non-segmental vitiligo: a randomized, controlled trial**. J Cosmet Dermatol. 2021 Mar 3. doi: 10.1111/jocd.14041.

   In a randomised controlled clinical trial, 63 patients were divided into two groups Group A receiving 0.03% tacrolimus ointment (n = 31) and group B receiving 1% hydrocortisone acetate ointment (n = 32). At the end of 24 weeks, VASI was significantly lower than baseline (p = 0.030). In group B, 24-week VASI was not (p = 0.111). Repigmentation was observed in 45.2% of patients in group Abut none in group B (p < 0.001). Of those with repigmentation , it was graded as poor in 6/31 (19.4%), fair in 4/31 (12.9%), good in 1/31 (3.2%), and excellent in 3/31 (9.7%).Tacrolimus-induced repigmentation is more likely in patients with vitiligo vulgaris, head and neck lesions, skin phototype III, and young age.

6. Hu W et al. **Topical epigallocatechin-3-gallate in the treatment of vitiligo**. Australas J Dermatol. 2021 May 28. doi: 10.1111/ajd.13612.

   Patients were randomly given topical application of EGCG on the assigned lesions, with pimecrolimus being used as the control for twice a day over a 6-month treatment period. Though both drugs were found to be effective, there was no statistically significant difference between them. The VASI had diminished from 1.19 ± 0.42 to 0.63 ± 0.38, in the EGCG-treated lesions, while from 1.18 ± 0.43 to 0.61 ± 0.36 in the pimecrolimus-treated lesions (P = 0.755). Similarly, the mean PGA score on the EGCG applied side was 4.39 ± 2.23, while that was 4.43 ± 2.02 on the pimecrolimus applied side (P = 0.886). The difference in the improvement degree between pimecrolimus side and EGCG side was not statistically significant (P = 0.845). Findings of the study indicate that topical EGCG can be effective on treating vitiligo.

7. Yazdani Ashtiani S et al. **Preparation and Safety Evaluation of Topical Simvastatin Loaded NLCs for Vitiligo**. Adv Pharm Bull. 2021 Jan;11(1):104-110.

   The recent observation of Simvastatin induced repigmentation in mouse models of vitiligo spurred the development of Nanostructured Lipid Carriers (NLC) for drug delivery. It was formulated with the aid of Dynamic light scattering, transmission electron microscopy and differential scanning calorimetry with entrapment efficiency of 99.27% and drug-loading capacity of 3.9% Human safety studies did not reveal any alteration in the skin biophysical parameters upon addition of simvastatin to these particles. The preparation method of simNLC developed in this study is a suitable method, and the nanoparticles fabricated were safe with acceptable long-term stability and drug entrapment.

8. Vocetkova K et al, **A Simple Drug Delivery System for Platelet-Derived Bioactive Molecules, to Improve Melanocyte Stimulation in Vitiligo Treatment**. Nanomaterials (Basel). 2020 Sep 10;10(9):1801.

   This was an attempt to prolong effects from bioactive molecules released from platelets. Here, the authors had compared electrospun and centrifugally spun poly-ε-caprolactone (PCL) fibrous scaffolds with

various concentrations of platelets. A two-fold increase in the amount of the released bioactive molecules with a sustained 14-day release was seen with centrifugally spun vs. electrospun scaffolds. There was a strong concentration-dependent response of melanocyte to the bioactive molecules with higher concentrations resulting in an improved metabolic activity and proliferation of melanocytes. This simple system improves melanocyte viability, offers on-site preparation and is suitable for prolonged topical PRP administration.

9. Kanokrungsee S et al. **Clinical outcomes of topical bimatoprost for nonsegmental facial vitiligo: A preliminary study**. J Cosmet Dermatol. 2021 Mar;20(3):812-818.

   In a randomised controlled trial, vitiliginous patches of ten patients were randomized to receive either topical 0.1% tacrolimus ointment or 0.01% bimatoprost ophthalmic solution, applied twice daily for 12 weeks. By week 12, there was a statistically significant decrease in VSA in both groups ($P < .05$) , but there was no intergroup variation. At week 12, 20% of the patients in the bimatoprost group and 10% in the tacrolimus group achieved >50% repigmentation; the difference in the overall grading score between two groups were not statistically significant. Even though patients on bimatoprost reported as itching and burning, they did not have any change in intraocular pressure. Topical bimatoprost solutions were safe and effective for the treatment of nonsegmental facial vitiligo with comparable results to tacrolimus ointment. It can be considered as an alternative treatment for facial vitiligo.

10. Hassan Mumtaz et al. **Efficacy of Tacrolimus Versus Clobetasol in the Treatment of Vitiligo**. Cureus. 2020 Dec 8;12(12):e11985.

    An open randomized control trial conducted in the Department of Dermatology, Nishtar Hospital, Multan, in which they recruited hundred sixty-two patients of vitiligo. Group A was given tacrolimus whereas Group B was given clobetasol. Patients were followed up every four weeks. On the 12th week of treatment, effectiveness was assessed by measuring the Assessment scale proposed by Hossain. In Group A (tacrolimus), 42 patients (51.9%) had effective treatment (on the complete resolution of symptoms) whereas 39 patients (48.1 %) had ineffective treatment. In Group B (clobetasol), 47 patients (58%) had effective treatment, and the rest (34, 42%) had ineffective treatment. There was however no statistically significant difference in both the groups in terms of efficacy or effectiveness of treatment. Given however that tacrolimus has lesser side effects, it may be considered superior to corticosteroids.

B. Medical – Systemic Treatment

1. Fontas E et al. **Oral gliadin-protected superoxide dismutase in addition to phototherapy for treating non-segmental vitiligo: A 24-week prospective randomized placebo-controlled study.** J Eur Acad Dermatol Venereol. 2021. Apr 30. doi: 10.1111/jdv.17331.

   A 24-week monocentric interventional prospective randomized placebo-controlled trial in the tertiary center for vitiligo care in France was conducted. Subjects with non-segmental vitiligo affecting more than 5% of the total body surface were included. The subjects received gliadin-protected SOD (GP-SOD; 1 g/day for 12 weeks followed by 0.5 g/day for 12 weeks) or placebo in combination with twice-weekly sessions of NB-UVB. The primary endpoint was the total repigmentation rate at 24 weeks. A total of

50 patients were included. After 24 weeks, a greater improvement in VES was observed in the GP-SOD group (19.85%; SE 4.63, P < 0.0001) compared with the placebo group (8.83%; SE 4.72, P = 0.0676). It was concluded that use of GP-SOD appears to be a valuable add-on to phototherapy in the treatment of vitiligo patients.

2. Sun Y et al. **Randomized clinical trial of combined therapy with oral α-lipoic acid and NB-UVB for nonsegmental stable vitiligo**. Dermatol Ther. 2021;34:e14610.

   The prospective, multi-center, parallel controlled, double-blind randomized clinical trial was conducted in seven comprehensive tertiary hospitals in China. The patients were randomized into oral ALA group or placebo group at a dose of 300 mg daily for 6 months. All of them received NB-UVB phototherapy three times weekly. The repigmentation rate was evaluated by 4-point grading scale of improvement: >98%, 50-98%, 10-49%, <10%. A total of 133 patients were enrolled in the study, including 72 cases in treatment group and 61 cases in control group. ALA did not show additional benefit to NB-UVB therapy in the treatment of nonsegmental stable vitiligo. More studies should be done to identify other protocols of ALA or other types of antioxidants for stable vitiligo.

3. Wada-Irimada M et al. **Efficacy and safety of i.v. methylprednisolone pulse therapy for vitiligo: A retrospective study of 58 therapy experiences for 33 vitiligo patients**. J Dermatol. 2021.

   The purpose of this study was to validate the efficacy and safety of i.v. methylprednisolone pulse therapy (IVMP) for patients with progressive generalized vitiligo. Among 525 vitiligo patients treated in 10 years, 33 vitiligo patients received IVMP, a single course of daily 500 mg methylprednisolone (8 mg/kg/day for children) for 3 consecutive days. They subsequently observed that 56% achieved stable condition without lesion progression, and 63% had more than 25% repigmentation at 6 months after IVMP. They did not observe any serious adverse events relating to the IVMP procedures. In conclusion, IVMP was found to be a safe and effective treatment for progressive generalized vitiligo.

4. Zhang S et al. **Efficacy and safety of oral simvastatin in the treatment of patients with vitiligo**. J Investig Med. 2021;69:393-396

   The purpose of this study was to analyze the clinical efficacy of simvastatin in the treatment of vitiligo. From December 2016 to October 2019, five vitiligo patients from Peking Union Medical College Hospital were treated with simvastatin and tacrolimus. For simvastatin, the first three patients began to take 40 mg/day, and the latter two patients began to take 20 mg/day. From week 5, patients 1 and 2 received 20 mg simvastatin once a day, 0.1% tacrolimus ointment was used topically. Results were subsequently suggestive of the fact that though oral simvastatin is safe it may not be an effective treatment for vitiligo.

5. Bishnoi A et al. **Oral mycophenolate mofetil as a stabilizing treatment for progressive non-segmental vitiligo: results from a prospective, randomized, investigator-blinded pilot study**. Arch Dermatol Res. 2021;313:357-365.

   In this prospective, randomized, investigator-blinded study, 50 patients of active vitiligo [baseline vitiligo disease activity (VIDA) score 4] were randomized into two groups in 1:1 ratio. Group A received oral dexamethasone (2.5 mg on two successive days a week) and group B received mycophenolate mofetil (up to 2 g) for 180 days with a treatment-free follow-up period of 90 days. It was concluded that both OMP and mycophenolate mofetil halt actively spreading vitiligo, and have diverse adverse effect profiles. These should be offered in progressive vitiligo, especially in

circumstances that do not permit the use of phototherapy. Relapse occurred significantly earlier with mycophenolate and relapse rate was higher (though non-significant) than dexamethasone OMP. The repigmentation potential is minimal for both therapies.

6. Chavez-Alvarez S et al. **Oral mini-pulse therapy in vitiligo: a systematic review**. Int J Dermatol. 2021;60:868-876.

   All randomized controlled trials that compared OMP therapy with any other active treatment or placebo for nonstable vitiligo were included. The duration of treatment was 6 months in all studies. Up to 32% of patients achieved a repigmentation rate of >75% when OMP therapy was administered as monotherapy. No difference was observed between OMP therapy and other treatments in arresting the disease and weight gain was the most frequent adverse effect. Based on the findings of these studies, OMP therapy did not demonstrate additional value compared with other treatments. Hence it was concluded that a pressing need to conduct high-quality clinical trials to evaluate this therapy exists.

7. Phan K et al. **Repigmentation in vitiligo using janus kinase (JAK) inhibitors with phototherapy: systematic review and Meta-analysis**. J Dermatolog Treat. 2020; 2:1-5.

   The study was conducted to determine the expected response of vitiligo to JAK inhibitor therapy and factors which influence response rates. From the 9 eligible studies, individual patient data from 45 cases were pooled. Good response was achieved in 57.8%, partial response in 22.2%, and none or minimal response in 20% of cases. Concurrent phototherapy was significant associated with higher rates of good overall response ($p < .001$) and good facial response ($p < .001$). There is promising low-quality evidence regarding the effectiveness of JAK inhibitors in vitiligo. Concurrent UVB phototherapy appears to improve efficacy of JAK inhibitors for vitiligo.

8. El Ghareeb MI et al. **Combination of oral methotrexate and oral mini-pulse dexamethasone vs either agent alone in vitiligo treatment with follow up by dermoscope**. Dermatol Ther. 2020;33:e13586.

   This study aimed to compare the efficacy and safety of oral methotrexate (MTX) and oral mini-pulse (OMP) dexamethasone alone and in combination in the treatment of vitiligo. A total of 42 patients with vitiligo were included in the study. The patients were treated for three months and randomly assigned into three groups including 14 patients each. It was then concluded that OMP dexamethasone alone or in combination with MTX is better in decreasing the spread of vitiligo. MTX alone or in combination with OMP dexamethasone is better in inducing repigmentation. Oral MTX combined with OMP dexamethasone shows higher efficacy and tolerability and minor side effects and is more effective in treating unstable vitiligo.

C. Laser and Light-Based therapies

1. Gauthier Y,et al. **Tacrolimus (FK506) ointment combined with Nb-UVB could activate both hair follicle (HF) and dermal melanocyte precursors in vitiligo: the first histopathological and clinical study.** Arch Dermatol Res. 2021 Jul;313(5):383-388.

   In this study, the histological findings in twenty patients receiving Nb-UVB were compared with those receiving topical tacrolimus combined with Nb-UVB. Half were selected for the combination therapy and instructed to apply tacrolimus 0.1%

ointment twice daily on the specified lesion of interest. The remaining ten patients did not receive any other topical treatments. Skin biopsy was performed at baseline from the depigmented area and 2-3 months post-treatment from the repigmented area. Clinically, in the combination therapy group, interfollicular repigmentation in addition to the perifollicular and marginal pattern was observed. Histologically, in the combination therapy group, besides the migration of melanocytes from the bulge of the hair follicle seen in the monotherapy group, there was also presence of dermal melanocyte precursors in mid- and superficial dermis. This could pave ways for more effective therapies.

2. Juntongjin P, et al. **Efficacy of the combined excimer light and topical calcipotriol for acral vitiligo: A randomized double-blind comparative study**. Dermatol Ther. 2021 Mar;34(2):e14886.

   A prospective, randomized, double-blind, and intraindividual study was conducted comparing combination treatment (excimer light and topical medication) applied in the first 12 weeks, and monotherapy (topical medication alone) was used in the later 12 weeks. Both hands were irradiated with excimer light three times a week for 12 weeks. Calcipotriol ointment was randomly assigned to one hand, whereas clobetasol ointment was assigned to the other hand. The ointments were applied twice daily for a total of 24 weeks. Of the hands treated with excimer light and calcipotriol, approximately 8% achieved excellent repigmentation at the end of the combination treatment period and 23% achieved good to excellent improvement after 12 weeks of calcipotriol monotherapy. More than 85% and 77% of the hands treated with calcipotriol-based and clobetasol-based regimens showed some repigmentation at the end of the study, respectively ($P < .05$). Nevertheless, no significant difference was found between the treatments. The combination of excimer light and topical calcipotriol followed by topical calcipotriol alone is effective and might be a promising treatment regimen for acral vitiligo.

3. Dincer Rota D. **Comparison of the efficacy of broad-band targeted UVB phototherapy and topical psoralen with targeted UVA phototherapy in localized vitiligo**. Dermatol Ther. 2021 Jan;34(1):e14562.

   In this study 22 cases with symmetrical vitiligo lesions were included. Broad-band targeted UVB was applied on one side and targeted UVA phototherapy with topical psoralen on the other side. After the first month there was success in 25% for targeted broad-band UVB micro phototherapy and 75% for topical psoralen with targeted UVA micro phototherapy. There was a significant difference between groups in terms of treatment response ($P = .017$). At the end of the third month, success rates were 37.5% for targeted broad-band UVB micro phototherapy and 62.5% for topical psoralen with targeted UVA micro phototherapy, however a statistically significant difference was not determined between the two treatments ($P > .05$). In conclusion, both treatments are safe and they provide repigmentation with a limited response.

4. Bakr RM, et al. **A comparative study on the use of fractional CO2 laser with tacrolimus or calcipotriol or narrow band ultraviolet-B in treatment of stable nonsegmental vitiligo**. Dermatol Ther. 2021 Jan;34(1):e14604.

   Thirty patients with stable nonsegmental vitiligo were subjected to three sessions of fractional CO2 laser 1 month apart. Then they were divided into three equal groups. Group (A) treated with tacrolimus ointment twice daily for 3 months, group (B) treated with calcipotriol ointment twice daily for 3 months, and group (C) treated with NB-UVB twice weekly for 3 months. There was a statistically significant decrease in VASI score

after treatment in the three groups. The VASI change and % of regimentation was higher in group (C) treated by laser and NB-UVB and was significantly higher than group (B) treated with laser and calcipotriol. There was no statistically significant difference between other treatment groups. To conclude, the combination of fractional CO2 laser and NB-UVB was found to be more effective.

5. Noborio R, et al. **Efficacy of 308-nm excimer laser treatment for refractory vitiligo: a case series of treatment based on the minimal blistering dose**. J Eur Acad Dermatol Venereol. 2021 Apr;35(4):e287-e289

   In this study of 5 patients with refractory vitiligo were treated with minimal blistering dose of 308nm, once a week for 5 weeks applied in a lattice pattern in two treatment areas per patient. Satisfactory pigment regeneration was achieved by 5 irradiation sessions using the excimer laser based on the MBD, even in refractory cases that were unresponsive to conventional treatments.

6. Sonthalia S. **Topical Band-pass Filter Cream (TBFC)-assisted home-based NB-UVB: A must-know Alternative to artificial phototherapy.** J Cosmet Dermatol. 2021 Jul;20(7):2141-2147

   In this study the use of topical Photocil®, a novel topical band-pass filter cream (TBFC), that selectively filters solar radiation, biasing toward delivery of 311-313 nm (action spectrum of NB-UVB) to the treated lesions was studied. A 12-week protocol of TBFC-assisted NB-UVB showed 75% repigmentation without any remarkable adverse effects was noted with persistent efficacy over the next 12 weeks. The device-free home-based TBFC-assisted NB-UVB delivery using natural sunlight offers a viable, convenient, and cost-effective alternative to artificial phototherapy for successful treatment of vitiligo; with its utility proven even in SV that too in individual(s) with darker SPT.

7. Deshpande AJ. **308nm excimer lamp monotherapy for lip vitiligo-a short case series**. J Cosmet Laser Ther. 2020;22:253-255.

   Vitiligo is a common depigmenting condition that carries a high psychosocial morbidity, especially when it occurs over exposed areas like lips. Many of the current topical and systemic therapies are less effective in lip vitiligo, and surgical modality remains the mainstay of treatment of lip vitiligo. The 308-nm excimer laser in combination with topical calcineurin inhibitors and calcipotriene is effective in the treatment of lip vitiligo. This case series provide further evidence to support effectiveness of 308-nm excimer lamp even as monotherapy in darker individuals with lip vitiligo.

8. Juntongjin P, **Effectiveness of a combined 308-nm excimer lamp and topical mid-potent steroid treatment for facial vitiligo: a preliminary, randomized double-blinded controlled study**. Lasers Med Sci. 2020 Dec;35(9):2023-2029

   In a randomized double blinded controlled study, symmetrical, nonsegmental facial vitiligo subjects were recruited. All facial lesions were irradiated with a 308-nm excimer lamp twice weekly for a total of 24 sessions, following which lesions on each side of the face were randomly allocated to have topical mometasone furoate cream or cream base alone applied once daily for 12 weeks. By the 12th week, 87.5% of the lesions of treated with the combination regimen and 50% of the lesions treated with monotherapy showed good to excellent repigmentation. From the subjects' perspectives, there were significant differences between both treatments at week 4 and week 8 ($p = 0.05$) but not at week 12. No serious adverse effects were reported. A combination of excimer lamp

therapy and once-daily application of topical mometasone cream was effective and could accelerate the treatment outcomes without serious adverse reactions. This may be an alternative regimen for treating facial vitiligo

9. Batchelor JM, et al. **Home-based narrowband UVB, topical corticosteroid or combination for children and adults with vitiligo: HI-Light Vitiligo three-arm RCT**. Health Technol Assess. 2020 Nov;24(64):1-128.

   A pragmatic, three-arm, home based randomised controlled trial with 9 months of treatment and a 12-month follow-up was conducted among adults and children (aged ≥ 5 years) with active non-segmental vitiligo affecting ≤ 10% of their body area. The arms were topical corticosteroids (once a day on alternate weeks) plus dummy narrowband ultraviolet B light; narrowband ultraviolet B light (every other day in escalating doses) with placebo topical corticosteroids or a combination of topical corticosteroids plus narrowband ultraviolet B light. Target patch treatment 'success' was 17% for topical corticosteroids, 22% for narrowband ultraviolet B light and 27% for combination. Combination treatment was superior to topical corticosteroids (p = 0.032). Narrowband ultraviolet B light was not superior to topical corticosteroids (p = 0.290). Quality of life did not differ between the groups. Over 40% of participants had lost treatment response after 1 year with no treatment. There were no serious adverse treatment effects. Whether or not combination treatment is cost-effective depends on how much decision-makers are willing to pay for the benefits observed.

10. Huang C, et al. **Multi-Factors Associated With Efficacy and Adverse Events of Fractional Erbium:YAG Laser-Assisted Delivery of Topical Betamethasone for Stable Vitiligo: A Retrospective Analysis**. Lasers Surg Med. 2020 Sep;52(7):590-596.

    A retrospective study of 1,026 lesions in 684 patients with stable vitiligo who underwent treatment with fractional Er:YAG laser-assisted delivery of topical compound betamethasone solution between January 2014 and December 2017, revealed that 40.3% of the procedures were effective 12 months after the first treatment. Age (<14 years old), disease duration (<1 year), lesion location (on face and neck), hairy lesions, and drug concentration were independent factors associated with effective repigmentation. A common adverse event was hyperpigmentation (14.4%), which was highly correlated with 22% density. Fractional Er:YAG laser-assisted delivery of topical compound betamethasone is a good option for the management of vitiligo. The treatment may be suggested in these situations: younger patients, shorter disease duration, and lesions on the face and neck with hair.

D. Surgical Treatment

1. Ju HJ et al. **Surgical Interventions for Patients With Vitiligo: A Systematic Review and Meta-analysis**. JAMA Dermatol. 2021;157:307-316.

   The study objective was to look into the reported treatment response following different surgical modalities in patients with vitiligo. The rate of repigmentation of greater than 50% after any surgical intervention was 81.01% . In meta-regression analyses, the treatment response was associated with patient age, subtype of vitiligo and anatomical sites. The findings of this systematic review and meta-analysis suggest that surgical intervention can be an effective option for refractory stable vitiligo.

2. Subburaj K et al. **A prospective, randomized clinical study to compare the efficacy of recipient site preparation using dermabrasion, cryoblister, and**

dermaroller in autologous noncultured epidermal cell suspension in stable vitiligo. Dermatol Ther. 2021;34:e14683.

A single-centre, prospective, intra-patient, randomized clinical trial was done to compare the efficacy of recipient site preparation using three methods namely, dermabrasion, cryoblister and dermaroller followed by NCES in stable vitiligo. In this study 36 participants having at least 3 vitiligo patches in same anatomic region with minimum lesional stability of 1 year were randomised 1:1:1 for recipient site preparation using manual dermabrasion, cryoblister and dermaroller followed by NCES. It was concluded that cryoblister as a method of recipient site preparation is equally efficacious as manual dermabrasion in NCES for attaining good to excellent repigmentation, but with risk of hyperpigmentation. However, dermaroller is inferior to both dermabrasion and cryoblister.

3. Doolan BJ et al. **Autologous Non-Cultured Epidermal Cellular Grafting in the Surgical Treatment of Stable Vitiligo: The Skin Hospital Protocol. Dermatology**. 2021;23:1-3

   The authors argue that their study provides modifications to current techniques, including the use of individual Petri dishes to allow for processing larger skin grafts, hyfrecation instead of conventional manual dermabrasion of the recipient site to reduce scar formation as well as better margin delineation, and an intravenous giving set with a filter for improved filtration of the mixed cell population. They state that these modifications facilitated sufficient skin repigmentation in a cost-effective outpatient setting.

4. Dalla A et al. **A prospective study to assess the efficacy of various surgical modalities in treatment of stable vitiligo patches over resistant sites.** Int J Dermatol. 2020;59:837-842.

   The authors aimed at comparing the efficacy of three common methods of grafting in vitiligo in known resistant areas for which a single-center interventional clinical trial involving 30 patients of stable vitiligo located over bony prominences and acral areas were recruited. All patients were treated with noncultured epidermal cell suspension (NCES), suction blister epidermal grafting (SBEG), and mini punch grafting (MPG) on three separate patches. The difference in repigmentation rate between NCES and MPG as well as between SBEG and MPG achieved statistical significance. It was concluded that NCES and SBEG are superior to MPG with reasonably good efficacy and can be offered as a therapeutic modality for stable vitiligo patches over these sites.

5. Abdel-Rahman AT et al. **Clinicopathological evaluation of the donor area following autologous suction blister epithelial grafting vs Thiersch grafting in vitiligo patients: A preliminary study**. Dermatol Ther. 2020;3:e13349.

   Aim of the study was to clinically and histopathologically evaluate donor areas 3 months and 1 year after Thiersch grafting (TG) and suction blister epithelial grafting (SBEG). Forty patients with stable vitiligo were equally divided into two groups before TG and SBEG. In each patient, the donor site was clinically and histopathologically evaluated after 3 months and 1 year. The study concluded that SBEG is a scarless operation and regrafting from the same area can be performed. This is in contrast to TG, which is considered a scarring operation, and wherein the donor site cannot be reused for grafting.

6. Barros JD et al. **Dermoepidermal grafting obtained by shave excision of papule formed post punch grafting in vitiligo: improvement of the cobblestone pattern**. Surg Cosmet Dermatol.2020;12:118-20

   A new technique with a dermoepidermal grafting obtained by shave excision of

papule formed post punch grafting in vitiligo was described in this study. The authors concluded that it could improve the cobblestone pattern in the donor site and the repigmentation in both donor and recipient areas

7. Ashique KT et al. **Ready-to-Use Device for Dermabrasion in Vitiligo Surgery**. J Cutan Aesthet Surg. 2020;13:338-339.

   Adequate dermabrasion of recipient site is a crucial step in vitiligo surgery. The authors suggested the use of a commercially available mechanized abrader as an economical and efficient tool for dermabrasion especially in resource poor settings where more sophisticated methods may not be available.

8. El Hawary M et al. **Recipient site preparation by cryoblebbing in melanocyte keratinocyte transplantation procedure over the fingers in vitiligo: A pilot study**. Dermatol Ther. 2020;33:e14199.

   In this intra-patient comparative study, 12 patients with stable non-segmental vitiligo (NSV) affecting the middle three fingers of one hand were included. Three variations were used in treatment of finger vitiligo lesions: minipuch grafting, melanocytes keratinocyte transplantation procedure (MKTP) preceded by cryoblebbing or full CO2 laser resurfacing of the recipient site. About 4/18 lesions treated by cryoblebbing followed by MKTP showed ≥75% repigmentation while only 1/17 lesions treated by laser resurfacing + MKTP and 1/17 lesions treated by minipunch grafting showed 30% and 10% repigmentation, respectively. No complications occurred in MKTP treated lesions. Hence it was concluded that cryoblebbing of the recipient site seems to improve the outcome of MKTP in lesions over the fingers in stable NSV.

9. Bae JM et al. **Micropunch grafting as an adjuvant for noncultured melanocyte-keratinocyte transplantation for refractory vitiligo**. J Am Acad Dermatol. 2020;82:1548-1550.

   This was a retrospective study that reviewed the medical charts and photographs of vitiligo patients who did not achieve complete repigmentation after 1 session of MKTP, followed by excimer laser treatment for at least 3 months, and subsequently underwent motorized 0.8-mm micropunch grafting to fill the remaining areas. It was seen that the motorized micropunch grafting can be performed as an adjuvant to noncultured MKTP, when the surgical outcome of MKTP alone is not sufficient. When the remaining depigmented area is small, repeated application of MKTP can be cumbersome for both patients and physicians.

E. Platelet Rich Plasma Based Treatments

1. Salem SAM, et al. **Effect of platelet-rich plasma on the outcome of mini-punch grafting procedure in localized stable vitiligo: Clinical evaluation and relation to lesional basic fibroblast growth factor**. Dermatol Ther. 2021 Mar;34(2):e14738.

   In a intra patient-controlled study, thirty-four vitiliginous patches, two per each patient with stable vitiligo, were treated with autologous MPG and subsequent exposure to phototherapy with and without enhancement via PRP procedure at the time of the procedure, and monthly for the subsequent 3 months. PRP assistance to MPG/phototherapy treatment resulted in earlier re-pigmentation at week 8. However, this enhancement effect vanished at the study end (week 20) as ideal re-pigmentation (>75% re-pigmentation) was encountered in 10 patches (58.8%) treated with MPG/phototherapy modality, and in 12

patches (70.6%) treated with PRP-assisted method without significant difference between them. Lesional bFGF increased after both treatments with a higher expression with PRP assistance but without clinical reflection on the final outcome. PRP can speed the re-pigmentation response for MPG/phototherapy procedure without any significant effect on the final outcome.

2. Raizada A, et al. **Fractional Carbon Dioxide Laser versus Fractional Carbon Dioxide Laser with Autologous Intralesional Platelet-rich Plasma in the Treatment of Stable, Non-segmental Vitiligo: A Randomized Comparative Study**. J Cutan Aesthet Surg. 2021 Jan-Mar;14(1):55-63.

   A prospective, randomized, comparative, open-label interventional study of 66 patients with stable non segmental vitiligo was undertaken in a tertiary care hospital. Group A received treatment with FCO2 laser with intralesional PRP, whereas Group B was treated with FCO2 laser alone. They were followed up monthly for a period of 3 months. All the patients received topical psoralen with ultraviolet A (UVA) PUVA-sol treatment. VASI score reduction was significantly more in the Group A with (mean ± standard deviation [SD]) 9.5 ± 0.22, 5.8 ± 1.12, and 3.6 ± 1.81 as compared to Group B 11.9 ± 2.83, 9.9 ± 3.11, and 8.9 ± 3.46 at each subsequent follow-up visits, respectively. Also the intensity and duration of side effects was also shorter in group A. Combination of FCO2 laser and autologous intralesional PRP has a synergetic effect in treating patients with vitiligo as an adjuvant therapy with minimal adverse effects.

3. Deng Y, **308-nm Excimer Laser Plus Platelet-Rich Plasma for Treatment of Stable Vitiligo: A Prospective, Randomized Case-Control Study**. Clin Cosmet Investig Dermatol. 2020 Jul 23;13:461-467.

   A prospective , randomised case control study among 60 patients with localized stable vitiligo who had received treatment at Beijing Friendship Hospital and Xi'an Vitiligo Specialist Hospital between May 2019 and January 2020 was conducted. 60 patients with localized stable vitiligo were equally randomized into three groups: intradermal PRP injection (group I), 308-nm excimer laser alone (group II), and 308-nm excimer laser plus PRP injection (group III). All treatments lasted for 3 months. The VAS scores showed significant differences among the three groups (P<0.001), with the highest score in group III, followed by group II and then group I. Repigmentation responses also showed significant differences among the groups (P<0.001), and the best effect was observed in group III. No side effects were reported in any of the groups. The effect of PRP combined with 308-nm excimer laser on stable vitiligo is significantly better than that of PRP and 308-nm excimer laser alone. It is safe and satisfactorily tolerant.

4. Afify AA, et al. **Fractional CO2 laser, platelet rich plasma and narrow band ultraviolet B in the treatment of Vitiligo (A randomized clinical trial)**. Lasers Med Sci. 2020 Nov 25.

   A self-controlled randomized clinical trial included 20 patients with at least 6 patches of vitiligo (VIDA score 1 and 0) was conducted and each patient received either, fractional CO2 laser, PRP, combined fractional CO2 with PRP, combined fractional CO2 with NB-UVB, combined fractional CO2 with PRP and NB-UVB or left as a control. There was a statistically significant improvement in all treatment groups on comparing the surface area of vitiligo patches before and after treatment. However, on comparing the percentage of reduction in surface area in different treatment groups, there was no statistically significant difference (P = 0.122). Fr: CO2 laser and PRP may be adjuvant therapeutic options to NB-UVB especially in the treatment of refractory cases of non-segmental vitiligo.

5. Mercuri SR, et al. **The Usefulness of Platelet-Rich Plasma (PRP) for the Treatment of Vitiligo: State of the Art and Review**. Drug Des Devel Ther. 2020;14:1749-1755.

   In a systematic review of Electronic databases of MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) from inception to November 2019 ha using different combinations of terms: "platelet-rich plasma", "platelet gel", "platelet-rich fibrin", "PRP" and "vitiligo". There were 6 clinical studies included, with a total of 253 patients. In all reports, all treated patients showed a stable vitiligo, and a significantly higher improvement in the PRP groups was always observed compared to control groups. Regarding the side effects, PRP in vitiligo patients is useful and without important side effects.

6. Khattab FM, et al **Evaluation of combined excimer laser and platelet-rich plasma for the treatment of nonsegmental vitiligo: A prospective comparative study**. J Cosmet Dermatol. 2020 Apr;19(4):869-877.

   In a comparative study 52 patients with stable non segmental vitiligo were divided equally into two groups. Group I: treated by intradermal PRP injection and the excimer laser, while group II: treated with the excimer laser only. The PRP injection was repeated every 3 weeks for 4 months and excimer laser two times a week and for 16 weeks till complete response. At the end of 3 months follow up, there was a higher statistically significant treatment response in group I compared with group II. There was also a statistically significant correlation between the treatment response and the lesion site in group I ($P < .000$) and a significant difference in VAS between both groups ($P < .000$). The combination of PRP and excimer laser phototherapy is an efficient vitiligo treatment as PRP increases the excimer laser impact and also improves the result.

7. Garg S, et al. **Laser Ablation of the Recipient Area With Platelet-Rich Plasma-Enriched Epidermal Suspension Transplant in Vitiligo Surgery: A Pilot Study**. Dermatol Surg. 2019 Jan;45(1):83-89.

   A pilot study was conducted, studying the extent of repigmentation with noncultured trypsinized fragmented epidermal suspension using platelet-rich plasma (PRP) as a suspending agent and pixel erbium yttrium aluminium garnet laser for ablation of recipient area in 10 patients with stable vitiligo. It was seen that, repigmentation was observed as early as 2 weeks after the treatment. Of 20 lesions, 12 (60%) showed excellent response; of which 10 lesions (50%) showed complete repigmentation in 8 weeks only. There were no milia or keloid formation, donor-site scarring, stuck on appearance at recipient site or infection. This study indicates that PRP-enriched epidermal suspension transplant (LA-PEEST) has the potential to improve the rate of healing and repigmentation in vitiligo patches. Further investigations and larger controlled trials are required to establish this technique as a rapid surgical method to restore pigmentation.

8. Yin L, et al. **Platelet-rich plasma, a promising adjunctive treatment for vitiligo: A case report. JAAD Case Reports**. 2020 Dec;6(12):1320.

   A 39-year-old male with a 26-year history of nonsegmental vitiligo began vitiligo treatment 2 months prior with narrowband ultraviolet B (NB-UVB) phototherapy 3 times per week and the application of 1% pimecrolimus cream twice daily on his face. He also had NB-UVB treatment The treatments were well tolerated and resulted in repigmentation on his bilateral upper extremities. However, he had minimal changes to his head and neck after 17 treatments. The patient received a total of 6 mL of PRP, with approximately 3 mL injected along the frontal and temporal regions of the

scalp in the areas of depigmented patches. Concomitant treatment with PRP injections (monthly, total 3 treatments) and NB-UVB (3 times a week) was continued for 2 months, resulting in >50% improvement over baseline (good response). Thus PRP may be used as a therapy in refractory cases of vitiligo.

9. Kale MS, et al. **To compare the safety & efficacy of platelet rich plasma therapy plus narrowband ultravoilet B (NBUVB) therapy versus narrowband ultravoilet B therapy alone in the treatment of vitiligo–a double blind, randomised controlled study**. J Med Sci Clin Res. 2019;7(3):314-21.

   A prospective, open-labeled, comparative study done in 20 patients with stable nonsegmental vitiligo, each with three vitiligo patches of similar shape and size. All the patients received PUVASOL as standard treatment modality. PRP or PPP was injected into two separate study patches as an adjuvant treatment with PUVASOL; however, the third patch acted as a control and was treated by PUVASOL alone. These patients were followed up for 4 weeks after the end of four treatment sessions. Compared with control areas (exposed to PUVASOL only), statistically significant more repigmentation was seen in areas treated with a platelet preparation (either PRP or PPP) along with PUVASOL. However, there was no significant difference between PRP and PPP arm (P=0.824) as per qualitative and quantitative assessment. Hence, the addition of PRP may improve the efficacy of PRP.

10. Saify K, et al. **Treatment of vitiligo by PRP and umbilical cord blood: a prospective study in 120 cases**. IOSR J Dent Med Sci. 2019;18(5):1-5.

    120 patients from all over India, suffering from Vitiligo were enrolled in this open prospective study. One unit Buffy coat platelet/ single donor platelet/Cord blood was utilized either as local application, intralesional injection or transfusion in every session. Approximately 400 treatments were given overall during the study period (Min 1 to max 6 in each patient) with treatment cycle every 30 days. Follow up was done every 15 days up to 3 months. Good response i.e 2/3 rd re-pigmentation in affected area in cases of vitiligo was observed in 48.4% of patients out of which maximum response was observed in patients who received combines local PRP + UCB transfusion. No side effects of UCB transfusion and local application of PRP and micro-needling was observed. PRP and UCB Transfusions are beneficial in the initiation of re-pigmentation in old, chronic and non-responding patients.

Acknowledgement: We appreciate contribution of Dr Vignesh Narayan & Dr Apoorva Sharma (Junior Residents, Department of Dermatology, PGIMER, Chandigarh) in compiling this recent literature on the treatment of vitiligo.

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