Treatment of Vitiligo Associated Eyebrow and Eyelash Leukotrichia - A Systematic Review of Existing Information

Abstract

Background: Vitiligo in hair bearing areas, especially segmental vitiligo, is frequently associated with leukotrichia. Leukotrichia, in general, is considered a predictor of unsatisfactory response to conventional treatment methods like phototherapy. This review aims to systematically review various available treatment options in patients with eyebrow and eyelash leukotrichia and assess the response to these therapeutic modalities. Materials and Methods: Articles were searched using the keywords "eyelid", "eyelash", "leukotrichia", either singly or combined. The databases searched include Pubmed, Cochrane Library, Embase, and Science Direct. The strategy was to include studies in which any therapeutic modalities were undertaken for treatment of eyelash or eyebrow leukotrichia. Results: After applying the inclusion and exclusion criteria, this review included 15 studies. There was a positive response to the surgical treatment options for eyebrow and eyelash leukotrichia. Topical tofacitinib has emerged as a promising new therapeutic option, but further studies are needed to establish its efficacy. Conclusion: In conclusion, there are several treatment options for eyebrow and eyelash leukotrichia. However, further studies are needed to better understand their efficacy and optimal applications.

Keywords: Eyelash, eyelid, leukotrichia, vitiligo

Introduction

Vitiligo, dermatological condition a characterized by depigmented macules, has a global prevalence of 1%-2%.[1] Vitiligo in hair-bearing areas, especially segmental vitiligo, is frequently associated with leukotrichia and its occurrence is said to range from 9% to 48.4% in vitiligo patients.[2-5] The hair follicle bulge stem cells are thought to be the source of melanocytes for skin repigmentation in vitiligo and this deficient melanocyte reservoir in leukotrichia is considered to represent a poor response to treatment.^[6] Leukotrichia is thus considered a predictor of unsatisfactory response to conventional treatment methods like phototherapy.^[7,8] This accompanied by the psychological impact, especially in easily visible areas like the eyebrows and eyelashes, makes it a challenging proposition to treat for the dermatologist and a frustrating experience the patient. Surgical treatment modalities such as mini punch grafting and keratinocyte melanocyte cell suspension have been found to result in repigmentation

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of leukotrichia in many cases.^[4] In general, eyebrow leukotrichia has been observed to repigment with various surgical therapies, whereas eyelash leukotrichia has been found to be resistant to treatment.^[9]

This study aims to systematically review various available treatment options for patients with eyebrow and eyelash leukotrichia and assess the response to these therapeutic modalities.

Materials and Methods

Search strategy

The search strategy included following keywords: "eyelid", "eyelash", "leukotrichia", either singly or combined. The databases searched include Pubmed, Cochrane Library, Embase, and Science Direct. The search strategy was to include studies in which any therapeutic modalities were undertaken for the treatment of eyelash or eyebrow leukotrichia. Temporary treatment options such as eyebrow/eyelash dyeing were not included in the study. This review included case reports, case series, prospective, retrospective, and experimental

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studies because of the scarcity of literature regarding the present topic.

Inclusion and exclusion criteria

Studies were included if they fulfilled the following criteria:

- 1. Studies involving eyebrow leukotrichia
- 2. Studies involving eyelash leukotrichia
- 3. Studies involving both eyebrow and eyelash leukotrichia
- 4. Studies in which there were subjects with eyelid and eyelash leukotrichia and effects of treatments at these sites were documented
- 5. Studies in which English full text could be obtained

Studies were excluded if they involved patients with leukotrichia at sites other than eyebrow or eyelash, employed temporary treatment measures, or were in languages for which a translated version could not be obtained.

Results

The search results for 'leukotrichia' from the various databases generated a total of 115 results. Of these, after applying the inclusion and exclusion criteria, 15 studies were included. [Table 1] Case studies, case series, experimental, prospective, and retrospective studies were included in the review [Figure 1]. The studies had 98 participants with either eyebrow vitiligo or eyelash vitiligo or having both. Out of the 15 articles, 11 were about eyelid vitiligo, 2 were eyelash vitiligo, and remaining 2 had both. [Table 1].

Discussion

The treatment strategy in most of the studies were mainly surgical in nature. The various surgical options for eyebrow leukotrichia included dermabrasion with split skin graft, suction blister transplantation, and follicular unit extraction and transplantation^[5,10-14] The first two procedures showed excellent repigmentation of leukotrichous hairs, and authors felt that the epidermal melanocytes probably served as a source of repigmentation in both. Although the hair follicle melanocytes have traditionally been thought to be the reservoir of melanocytes, excellent results of skin grafting suggest that melanocytes from the epidermis may replenish deficient melanocytes in leukotrichous areas.^[6]

Three studies focusing on follicular unit extraction and transplantation in the affected area were included in this research. [12-14] Out of them, two case studies with excellent pigmentation (98%–100%) and even repigmentation of adjacent vitiligo patch were reported. [12-14] This again points to the probable fluidic nature of melanocytes whether they are follicular or epidermal and one source can serve to replenish the other, when deficient. There was an experimental study conducted on 15 patients with vitiligo and eyebrow and eyelash leukotrichia, in which single

follicle hair transplantation was done post-electrolysis of leukotrichia hair. The average survival of the transplanted hairs was found to be almost 72% and most of the depigmented hairs were found to be repigmented. Na *et al.* Ioo also performed single hair transplantation on patients with eyebrow vitiligo using post procedure PUVA or steroid therapy and moderate to excellent repigmentation was noted in 50% lesions. Both the authors concluded that single hair transplant, although being labor intensive and time consuming, was an excellent method to treat eyebrow and eyelash leukotrichia.

Non-cultured cellular grafting, using split skin grafts harvested and applied to the laser ablated or dermabraded recipient sites, was the therapeutic modality examined in two studies.^[1,4] Both retrospective studies showed excellent results, and the authors claim that it could be an alternative to single tedious and time-consuming hair transplantation method. Another advantage was the simultaneous repigmentation of both the vitiliginous skin and depigmented hairs, although repigmentation of hairs generally required more time compared to the skin. The recipient area that could be treated was much larger compared to the area of the donor skin. Thus, it represents a safe, effective, economical, albeit time-consuming, therapeutic modality for leukotrichia. The authors postulated that repigmentation may result from the retrograde migration of transplanted melanocytes or epidermal stem cells, as well as cytokine production which stimulates melanogenesis in hair follicles.[4] This could also explain the longer time taken for repigmentation of leukotrichia compared to the skin, as the melanocytes must migrate to the hair bulb, multiply and then melanise the

Autologous melanocyte transplantation and autologous melanocyte-keratinocyte transplantation was done in a case report and a prospective study, respectively, both showing excellent results.^[17,18] However, more than one session was needed to achieve repigmentation, especially in case of eyelash leukotrichia, where three sessions were required.^[18]

Eyelash leukotrichia in general has a poorer prognosis compared to eyebrow leukotrichia. Some authors have suggested that, the single hair grafting may be more effective in this scenario. [19] Chatterjee *et al.*[9] conducted a prospective study on 15 patients with eyelash vitiligo, where eyelash transplantation was done. [9] Single hair follicles were prepared from the temporal area and were transplanted into chambers created by involved eyelash removal. Majority of the patients needed two sessions and 13 out of the 15 patients had good to excellent response to the treatment. However, the procedure is time consuming and has a steep learning curve.

Arguably the most exciting among all the above options, partly due to its non- invasive nature is a case report of

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Name of study	Type of study	Sample size	Population	Treatment done	Result	Conclusion
Agrawal K et al.[10]	Case series	8 patients	Patients with stable vitiligo and leukotrichia of 3-12 years duration, 4 patients had eyebrow leukotrichia	Dermabrasion and thin split skin grafting was done	There was early and excellent repigmentation of the eyebrow leukotrichia (70-95%)	Surgical treatment of leukotrichia represents an excellent management option and migration of melanocytes from repigmentated epidermis to the hair follicle probably results in repigmentation of leukotrichia
Hann SK et al.[11]	Case report	3 patients	Patients with vitiligo and leukotrichia of the eyebrow	Patients underwent epidermal grafting and received weekly psolaren plus UV-A (PUVA) treatment vs PUVA alone. Half the eyebrows had the first treatment and the other half the second.	Repigmentation appeared on the surrounding skin, but black hairs appeared only after 8 cycles of PUVA. Subsequently almost complete repigmentation of leukotrichia was noted.	The authors hypothesize that epidermal melanocytes activated in response to PUVA treatment migrate to the hair follicles as the grafter site showed repigmentation only in response to subsequent PUVA therapy.
Oh SJ et al. ^[5]	Case study	2 patients	11 years old boy with segmental vitiligo (SV) and leukotrichia of eyebrow. 16 year old girl with SV of eyelid and leukotrichia of eyebrow and eyelid	Suction blister epidermal grafting after hair plucking	Recipient areas almost completely repigmented and leukotrichia significantly improved after 1 to 2 years of follow up	This option seems effective for treatment of leukotrichia in SV
Sacchidanand S et al.[12]	Case study	1 patient	12 year old female with stable vitiligo patch and leukotrichia of eyebrow	Follicular unit extraction was done with donor hairs from the post auricular region and transplanted in the depigmented macules. Patient was started on post-operative tacrolimus 2 weeks after the procedure.	Complete pigmentation of vitiligo patch was seen at 12 weeks and resolution of leukotrichia after 6 months	This seems to be an effective procedure for treatment of localized vitiligo lesions with leukotrichia although the skill and time required for the surgery are more compared to routine grafts
Pangti R et al.[13]	Case study	1 patient	25 year old woman with segmental vitiligo and leukotrichia of eyebrows	Follicular unit extraction of leukotrichia, followed by transplantation of 30-40 hair follicular units from the occipital scalp into the created pockets	Around 98% repigmentation of leukotrichia was noted over a follow up period of 2 years	The procedure gives encouraging results in management of leukotrichia. There is also an added advantage of repigmentation of the underlying vitiligo patch from the melanocytes of the transplanted hair follicles.
Kumar A V et al. ^[14]	Case study	3 (1 eyebrow leukotrichia)	24 year old patient with eyebrow leukotrichia	Follicular unit extraction and grafting was done after removal of few eyebrow hairs	Almost complete repigmentation was observed after 7 weeks	The authors feels that this is an effective method for treating leukotrichia

Table 1: Contd							
Name of study	Type of study	Sample size	Population	Treatment done	Result	Conclusion	
Wu Y et al. ^[15]	Experimental study	15 patients	Patients with vitiligo associated eyebrow and eyelash leukotrichia	Patients were treated with a trichiasis electrolyzer followed by single follicle hair transplantation	The average survival rate of the transplanted hair follicles was noted to be 71.6% and the average regeneration rate of the depigmented hair was 11.6%	This methods appears to be a safe and effective method to treat eyebrow and eyelash leukotrichia associated with vitiligo	
Na GY et al.[16]	Experimental	21 patients (age 5 years to 53 years)	14 patients with eyebrow vitiligo were included	Single hair transplantation was performed and this was followed by post procedure PUVA or corticosteroid therapy	Out of the 14 lesions, 7 showed moderate to excellent repigmentation during the 12 month follow up	Single hair graft appears to be an effective method to treat eyebrow leukotrichia.	
Gan EY et al. ^[4]	Retrospective study of electronic medical record data	84 vitiligo patients, of which 10 patients had eyebrow leukotrichia	Patients who underwent non cultured cellular grafting in areas of leukotrichia were assessed for repigmentation of white hairs	13 patients with leukotrichia and vitiligo (including 10 with eyebrow leukotrichia) underwent non cultured cellular grafting and were followed up for repigmentation of white hairs by clinical assessment and standard digital photography	Leukotrichia of the eyebrows showed excellent repigmentation in 8 out of 9 patients (almost 89%) at 9-12 month follow up.	Good to excellent repigmentation of leukotrichia was obtained by non- cultured cellular grafts, thereby eliminating the need for hair transplantation.	
Holla AP et al. ^[1]	Retrospective study using photographic analysis of patient lesions.	31 patients	16 patients with facial (eyelid) leukotrichia	Autologous non cultured epidermal suspension was prepared from split skin graft and was then transplanted onto the dermabraded recipient site. Post procedure methylcobalamine and sun exposure was advised.	14 out of 16 facial (including eyebrow) leukotrichia patients showed improvement.	This is the first study with this methodology which showed a good result to the treatment followed.	
Yao L et al.[17]	Case report	1 patient (22 year old female)	Patient had a white patch on periocular area, eyebrow and temporal region	Cultured autologous melanocytes were transplanted to the recipient area after plucking the eyebrow hair with forceps and transplantation was done at a density of 6×10 ⁴ cells/mm ²	repigmentation was observed except the eyelashes and palpebral margin. The eyebrow however achieved pigmentation.	The procedure appears to be an effective treatment for eyebrow vitiligo	
Al Jasser MI et al. ^[18]	Prospective	4 patients	There were 4 patients with vitiligo, out of	Patients were treated with autologous non –	There was excellent repigmentation in	This treatment modality of eyelid leukotrichia seems	

Contd...

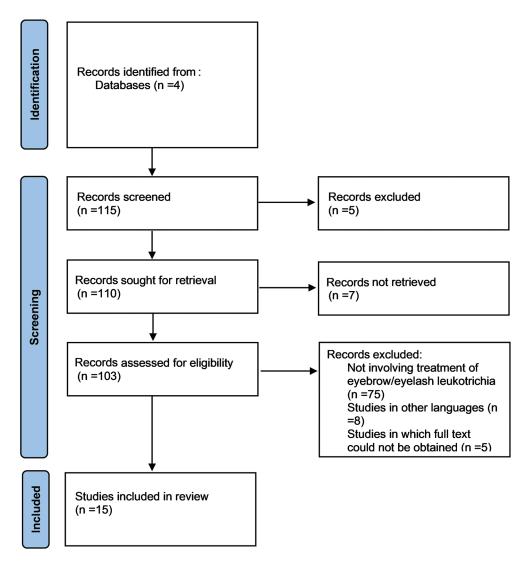
Table 1: Contd						
Name of study	Type of study	Sample size	Population	Treatment done	Result	Conclusion
Tvame of study	Type of study	Sample size	whom 3 had eyelid vitiligo with leukotrichia	cultured melanocyte	eyebrow leukotrichia in 2 patients at 3 month follow up. One patient needed 2 sessions for repigmentation of eyebrow leukotrichia and one patient needed 3 sessions for eyelash leukotrichia with	encouraging but more studies are needed to generalize the result
Chatterjee M et al. ^[9]	Prospective	15 patients	Patients with eyelash vitiligo	Eyelash transplantation was done (transplantation of pigmented follicular units from the scalp)	good results. 86.6% patients achieved good to excellent result at 6 months post procedure	This procedure is a safe and effective treatment option for patients with eyelash vitiligo
Kim SR et al. ^[6]	Case report	1 patient	17 year old girl with 4 month history of vitiligo of both upper lids with eyelash vitiligo	Tofacitinib 2% cream was applied twice daily	Partial repigmentation of eyelids and eyelashes was seen after 2 months and 5 months later, almost complete repigmentation was noted	This is the first study documenting effectiveness of Janus kinase inhibitors on eyelash leukotrichia. The authors feel that early intervention probably contributed to the excellent patient response.
Jha AK et al. ^[20]	Case report	1 patient	28 year old female with depigmented macule above both eyebrows along with leukotrichia	The patient was treated with 0.03% bimatoprost ophthalmic solution and followed up at monthly intervals	After 3 months of treatment, there was partial repigmentation of the vitiliginous area with some improvement of leukotrichia	Partial repigmentation and some improvement of leukotrichia with topical bimatoprost is promising but more studies are needed to evaluate efficacy for leukotrichia

a patient with eyelid vitiligo and associated eyelash leukotrichia who was treated with topical tofacitinib 2% twice daily. The patient showed almost complete repigmentation after 5 months of treatment. [6] This patient's early consultation with the physician probably contributed to the excellent treatment response. The authors also postulate that exposure to ambient sunlight for this patient also contributed to the positive response. The Janus kinase inhibitor is believed to stimulate the proliferation of whatever few existing melanocytes are present in the leukotrichous hair bulb, or to promote the migration of epidermal melanocytes into the hair follicles. Further studies are needed to bolster the status of topical tofacitinib as a reliable and effective treatment modality in the armamentarium for vitiligo. Another promising topical preparation that has been studied is bimatoprost 0.03% used in a case of eyebrow leukotrichia. [20] There was some

improvement of leukotrichia and partial pigmentation of the adjacent skin with the topical preparation. However, more extensive studies are needed to establish the suitability for routine use in management of leukotrichia.

Conclusion

Leukotrichia in general, and eyebrow and eyelash leukotrichia in particular, represents extremely stressful situations for both the physician doing the treatment and the patient and family. Some of the studies discussed above show good outcomes, especially the surgical modalities. Treatment of leukotrichia remains essentially surgical. However, advent of agents like tofacitinib and bimatoprost raises hopes of effective medical treatment options, especially in patients reluctant to undergo or unfit for surgery. Further research and studies with larger subject



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Figure 1: PRISMA flow chart

groups involving these newer treatment options could significantly advance the availability of satisfactory and cost effective options for managing eyebrow and eyelash leukotrichia.

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Conflicts of interest

There are no conflicts of interest.

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