DERMATO-SURGERY

CHEMICAL PEELING WITH PHENOL: FOR THE TREATMENT OF STABLE VITILIGO AND ALOPECIA AREATA

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Chemical peeling with 88% phenol was carried out on 142 sites of stable vitiligo (hairy-126, non hairy-16) and on 69 sites of alopecia areata (AA). After cleansing and defatting,phenol was applied on affected areas till a uniform frost appeared. On healing,all the lesions of vitiligo showed perifollicular pigmentation in hairy areas and perilesional repigmentation in non hairy areas. These were further treated with PUVA/PUVASOL. After the healing,82.5% of hairy sites and 81.3% of non hairy sites showed repigmentation. In cases of AA, patients developed vellus hair. In AA, 72.5% had good regrowth and 27.5% had poor response. Side effects seen were hypopigmentation (58 AA), hyperpigmentation (11 AA), persistent erythema (42 vitiligo,28 AA), demarcation lines (4 AA), secondary bacterial infection (2 vitiligo,5AA) and superficial scarring (2 vitiligo,7AA). The wounding action of phenol is useful to repigment the vitiligo patches and for induction of regrowth of hair in alopecia areata.

Key Words: Phenol, Chemical peeling, Vitiligo, Alopecia areata

Introduction

Some patients of vitiligo are either refractory or respond very slowly to the medical line of therapy. Such cases can then be treated by surgical modalities provided that their disease is stable for at least 2 years. Various surgical methods that are being practiced are thin Thiersch's skin grafting,therapeutic spot dermabrasion, excision and closure,melanocyte culture, needling,spot chemical wounding with TCA etc.[1,2]

Alopecia areata (AA) is a common autoimmune condition characterised by patchy loss of hair without atrophy and is sometimes refractory to treatment. The treatment modalities that have been tried in alopecia areata include intralesional and systemic steroids, cyclosporin, isoprinosine,thymopentin,topical nitrogen mustard, phototherapy with UVB and PUVA, hair follicle stimulant like minoxidil, topical sensitizers like dinitrochlorobenzene (DNCB), squaric acid dibutyl ester (SADBE) and diphencyprone (DCP), cryotherapy with liquid nitrogen, hair replacement options like prostheses and tattooing and irritants like anthralin, phenol,cantharidine, croton oil etc.

Phenol or carbolic acid is one of the oldest antiseptic and antipruritic agents. It also acts as a local anaesthetic. It is extremely irritating to the exposed tissues and can cause necrosis.[4] Liquified phenol (88% U.S.P.) has been used for medium depth chemical peeling facial rejuvenation,[5] and as a cauterant in lateral nail matrix phenolisation, epidermal cysts, molluscum contagiosum, etc. In the present study, it has been successfully used as

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a medium depth chemical peelant which causes wounding, to treat stable vitiligenous areas and patches of alopecia areata.

Materials and Methods

The study group for vitiligo comprised of 54 patients (36 females and 18 males; aged 14-65 years). Their disease had been stable for atleast 2 years. A total of 142 sites were treated as follows :- lower extremities-70, upper extremities-32, back-18, chest and abdomen-12 and nape of neck-10. Out of the 142 sites selected,126 were hairy and contained atleast 70% of black hair. The rest 16 areas were non-hairy and were situated on ankle, feet etc. The size of the lesions measured between 1-8 inches. Their shape varied from round, oval,linear or followed any geographical pattern. Most of the cases had received local or oral steroids or PUVA/PUVASOL prior to the therapy with limited or no improvement.

The study group for alopecia areata consisted of 32 patients (20 females and 12 males; aged 6-44 years). A total of 69 sites on the scalp were treated as follows:- frontal area-28, parietal areas-36, occipital area-5. The lesion size varied between 1/2 inche-6 inches. The patches were either round, oval, irregular in shape or in a band-like fashion in the ophiasis region. Eleven of the patients had received treatment with local and intralesional steroids,but had not responded to treatment. Six subjects had used minoxidil without any improvement. Fifteen patients were being treated for the first time with phenol and had not received any modality of therapy in the past.

The prepeel protocol, method of peeling and post peel care were similar in both the study groups. Only intact skin was selected. A routine urine examination, and tests for serum creatinine, blood urea nitrogen, SGOT and SGPT were carried out on all patients prior to the peel. BCG scars or old scars were examined for keloidal tendency. An informed consent was obtained and their blood pressure, heart rate and pulse rate were monitored. The area to be treated was defatted by scrubbing with savlon, followed by spirit and acetone. In a small glass container, 1/2 to 1 ml. phenol was taken. A thin cotton tipped applicator was dipped in it. This was then applied gently with uniform smooth strokes so as to cover the entire lesion till an ivory white uniform frosting appeared. Feathering of the borders was done by painting phenol from the periphery of the lesion into the surrounding normal skin. No neutralisation was done in any of the patients as it is not required in phenol peels. All patients were monitored after half an hour for pulse rate and heart rate. They were asked to apply **Mupirocin** ointment twice in a day till the lesions healed. All of them were advised to consume plenty of water over the next 2 hours to promote diuresis to avoid toxicity. After 10-15 days (on completion of wound healing),all patients of vitiligo were started on PUVA/PUVASOL. The procedure was repeated once in a month if required. Forty sites of vitiligo (32 hairy and 8 non hairy) who had either repigmented partially or had not responded to first application,were subjected to second application of phenol taking care to apply it only on the depigmented zone and not to paint the already repigmented area.

In case of alopecia areata, out of the 69 sites, 66 were treated with 2 and 28 with 3 applications of phenol respectively on those areas where the hair growth was not observed.

All patients in both the groups were followed up at weekly intervals for 2 months,15 days intervals for the next 4 months and at monthly intervals for one year. Fifty eight patients (38 vitiligo, 20 AA) were followed up for 1 year and 34 (22 vitiligo,12 AA) for 1½ years.

Results

The frosting that occurred during application disappeared in 15-30 minutes. All patients immediately

experienced a mild to moderate burning sensation for 15-30 seconds. They were symptom free for the next 20-30 minutes after which they experienced a low intensity burning and discomfort that lasted for 1-4 hours. The next day skin became dark brown to black in colour and started peeling at places along with crusting. Most of the crust fell off in 10-15 days when re-epithelialisation occurred revealing a shiny, erythematous, hypo-depigmented skin.

Of the 126 hairy sites of vitiligo, 109 showed pin point perifollicular pigmentation on repithelialisation. Of the 16 non hairy sites,8 showed total and 4 showed partial repigmentation only along the margins of the lesions. However, the remaining 4 sites showed no change. After the crust fell off, all patients were given PUVA/PUVASOL treatment for the next 2-3 months. Gradually the perifollicular hyperpigmentation started enlarging in size and coalesced together to cover the entire patch. In cases of non hairy sites,the pigment spread slowly from the border of the lesions for a small distance towards the centre. The rate of spread of pigment was sluggish in non hairy areas compared to the hairy areas. Forty sites of vitiligo (32 hairy and 8 non hairy) which had either sluggishly responded or not responded were treated with second application of phenol. Ten out of the 32 hairy areas repigmented further to cover up the entire vitiligo lesion in the next 2-3 months. However, 22 hairy sites either did not further repigment or repigmented only partially. Among the 8 non hairy sites, 5 showed repigmentaion all along the border. Remaining 3 did not show any pigmentation.

In cases of alopecia areata, small light-coloured vellus hairs were seen on the phenol painted areas after the initial peeling, crusting and re-epithelialisation (10-15 days). The vellus hair gradually started growing in size and became thicker in diameter and darker in colour. Out of 69 sites, 3 developed excellent (60-80%) regrowth of hair, 30 developed good (40-60%) and 36 sites had poor (40 or less percentage) growth. Those sites which responded only upto 60% were treated for a second time with phenol after 4 weeks. Only partially responsive or areas which had not responded were painted with the solution. Out of such 66 sites, 38 sites showd 60-80% regrowth. However 28 had to be treated for the third time. Of these, 9 showed excellent, 5 showed poor and 9 did not show any hairgrowth. Remaining 5 sites had initial hair growth but had lost the hair after 3-4 months.

Side effects and complications seen in both the studies were hypopigmentation which remained for 3-4 weeks in 58 AA sites, hyperpigmentation which lasted for 8 weeks in 11AA sites,persistent erythema which remained for 4-6 weeks (42 vitiligo,28AA), demarcation lines due to improper feathering (4 AA), secondary bacterial infection (2 vitiligo,5AA) due to improper wound care and superficial scarring (2 vitiligo,7AA).

Discussion

Liquified phenol consists of 88% solution of phenol in water and causes kerato coagulation by precipitating the surface proteins.[5] At this concentration, phenol causes medium depth wounding which creates changes through necrosis of the epidermis and part or all of the papillary dermis with an inflammatory reaction in the upper reticular dermis.[5] Re-epithelialisation starts from the 3rd day and is continued till 10th-15th day. The initial event in this process is the migration of keratinocytes from the residual adnexal epithelium at the base of the wound (pilosebaceous follicles and eccrine glands) and also from the wound margin.[6]

In vitiligo, among the hairy sites 82.5% showed total repigmentation and 17.5% had only partial pigmentation. In the non-hariy sites, 81.3% repigmented perilesionally and 18.7% showed no response. In alopecia

areata 72.5% had good-excellent growth and the rest 7.2% showed initial partial response but later on the disease relapsed.

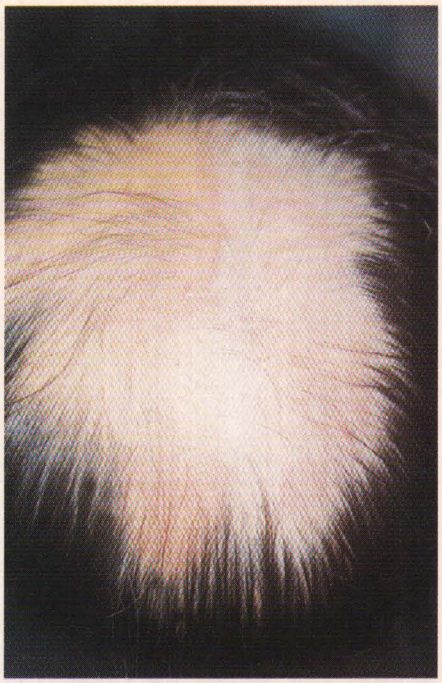
The commonest major side effect seen was hypopigmentation which remained for 3-4 weeks in 58 AA sites. It is known after facial phenol peels that the melanin synthesis is impaired temporarily and this results in hypopigmentation.[7] Eleven AA patients developed hyperpigmentation. It is a known phenomenon that skin diseases induce post inflammatory hyperpigmentation. The inciting inflammatory process causes an increase in both melanogenesis and the transferring of melanin granules to the surrounding keratinocytes.[8] Demarcation lines were seen between normal and treated hypopigmented skin in 4 patients of AA due to abrupt ending of peel at the periphery. This could have been avoided if proper feathering was done during the application. Forty-two vitiligo and 28 AA sites showed persistent erythema which cleared in 4-6 weeks. Post peel erythema represents angiogenesis in response to re-epithelialisation and occurs during would healing initially.[6] Secondary bacterial infection occured as a complication in 2 vitiligo and 5 AA sites due to improper wound care on the part of the patients. All of them reported early and their smear examination revelaed *Staphylococcus aureus* which responded to cephalosporins. Superficial scarring was seen at 9 sites (vitiligo,7 AA). Seven of these 9 sites were those which had developed secondary bacterial infection. Two more AA sites also developed scarring, and was because the phenol could have seeped in deeper.

Phenol when used for facial rejuvenation, is known to cause cardiac arrythmias, if the quantum of phenol exceeds 3 ml, the duratioon of application is less than 60 min [9] or when applied to large cutaneous surface areas.[5] This was not seen in any of our patients since precautions were taken not to exceed 1/2- 1 ml in one session. Phenol is also known to be hepatotoxic and nephrotoxic.[9] Diuresis is known to promote metabolism and excretion of phenol. Hence in this study all patients were asked to take plenty of water after the peel.

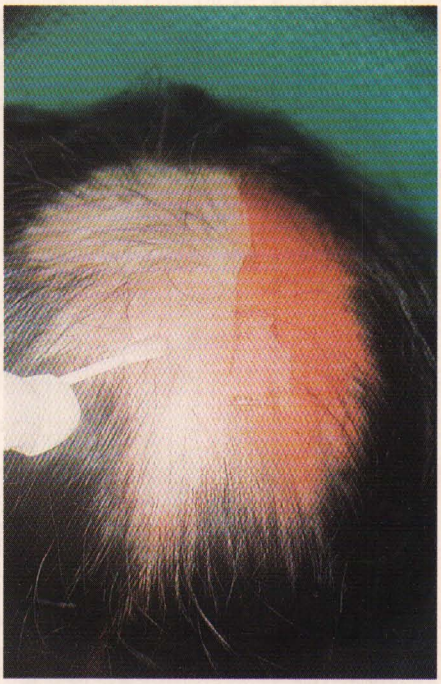
In cases of vitiligo, spot or regional dermabrasion has been used to repigment the hairy areas.[1] It is also known that sometimes topical psoralens with UVA gives rise to blister formation resulting in post inflammatory pigmentation[1], Phenol in this study has been used for repigmentation on the same principles of wounding. During wounding,there is acute inflammation which is known to induce melanogenesis. During the re-epithelialisation process, melanocytes migrate from the remnants of hair follicles, eccrine glands and also from the surrounding normal skin. In the hair follicles, the inactive melanocytes in the middle and/or lower parts of the outer root sheath divide, proliferate and migrate upwards to near by epidermis. The melanocytes continue to migrate radially to form the pigmented island which is seen as perifollicular pigmentation.[10] Also, the melanocytes from the perilesional normal epidermis migrate towards the centre of the lesions along the border in both hairy and non-hairy areas thus causing perilesional pigmentation.[1] These findings of pigmenting perifollicularlly and perilesionally was observed in our study also. During wound healing, various growth factors are released like endothelial growth factors and fibroblast growth factors which are mitogenic for the melanocytes.[1] Moreover the inflammatory mediators like leukotriene C4 and D4 stimulate the melanocyte proliferation.[11] It is possible that these factors could also have stimulated the pigmentation after a phenol peel wound.

Combining the wounding procedure with medical lines of treatment is known to enhance the rate of pigmentation. Tsuji t and Hamada combined dermabrasion of vitiligo lesions with post operative application of 5-fluorouracil cream under occlusion to successfully repigment stable vitiligo patients.[1] In earlier studies also,

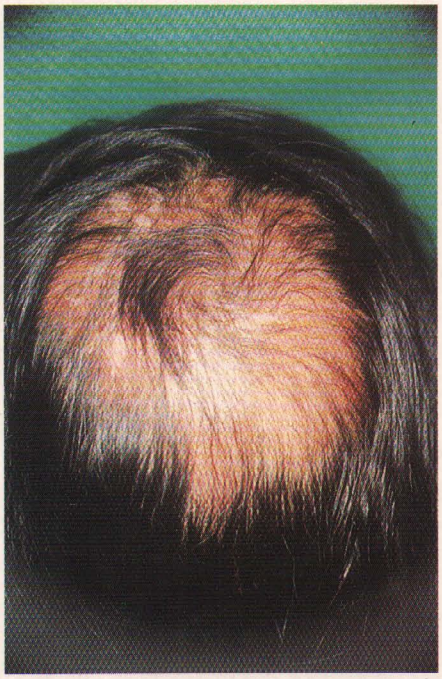
PHENOLIZATION : ALOPECIA AREATA



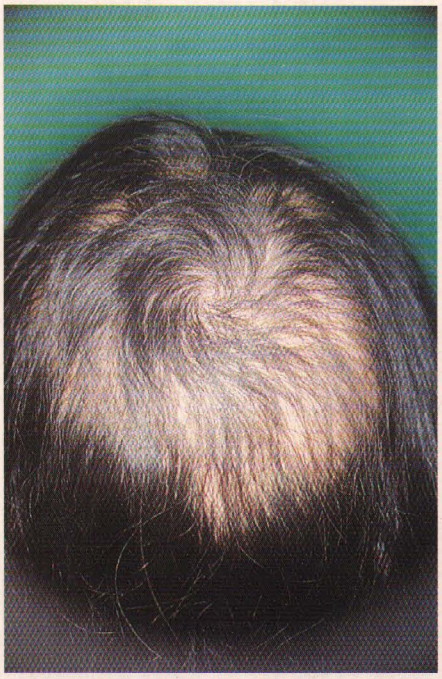
FROSTING AFTER APPLICATION OF PHENOL - RIGHT HALF



APPLICATION OF PHENOL WITH FROSTING - LEFT HALF

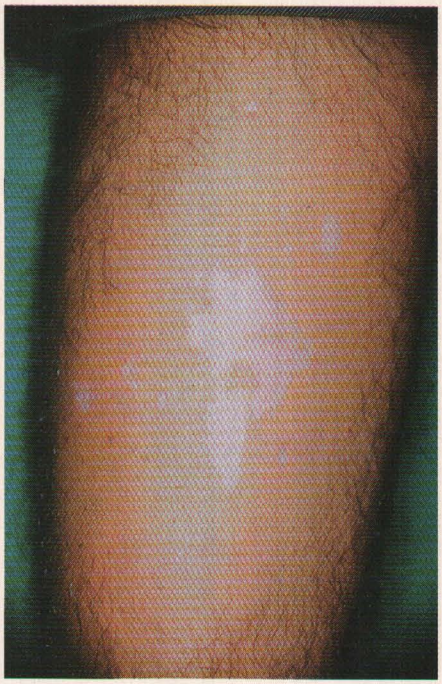


CRUSTING AND HYPERPIGMENTATION WITH EARLY HAIR GROWTH

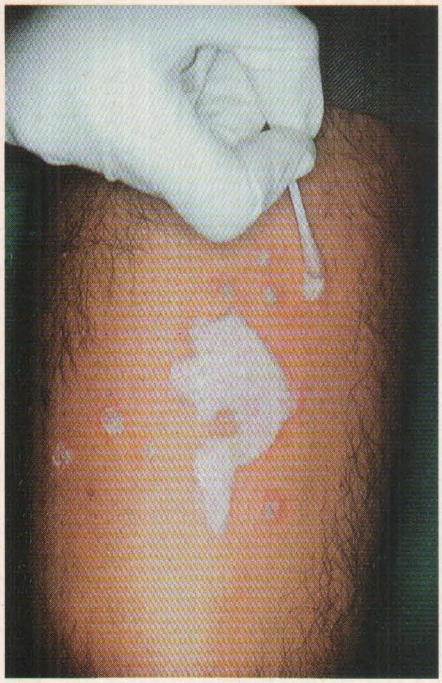


FURTHER GROWTH OF HAIR

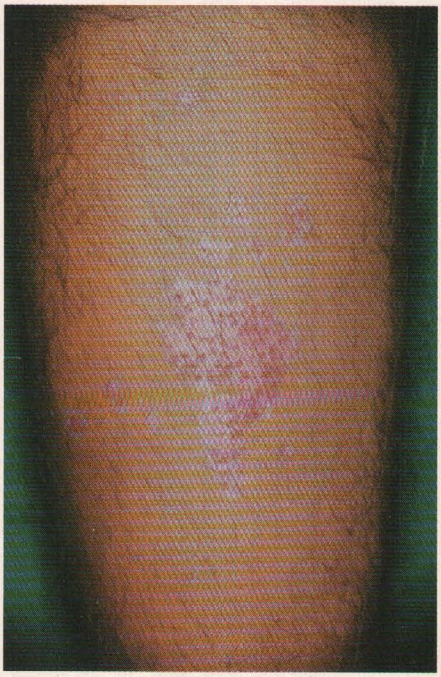
PHENOLIZATION : STABLE VITILIGO (HAIRY AREA)



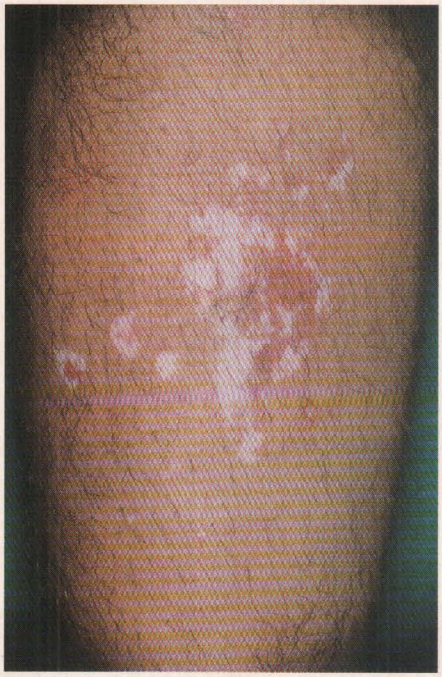
BEFORE



FROSTING ON APPLICATION OF PHENOL



HEALING WITH PERIFOLLICULAR PIGMENTATION



PIGMENTING LESION

it was seen that a combination of PUVA/PUVASOL after spot dermabrasions in stable vitiligo yielded better results. One of these studies showed that the success rate of repigmentation and 81.3% of non hairy areas had perilesional pigmentation.

Alopecia areata is an autoimmune disorder characterised by non scarry patchy hair loss and is mediated by lymphocytic infiltrates and granulomatous inflammation in and around the hair bulbs. Most of these hairs are in the telogen phase. In AA, peribulbar area consists of inflammatory cells, CD4 lymphocytes, Langerhan's cells and mononuclear cells. T-cells when attracted to follicular keratinocytes react with it and release additional cytokines as well as celllular components, some of which are potential antigens.[3]

The mechanism of action of various irritants (anthralin, phenol, croton oil etc.) and topical sensitizers in alopecia areata is unclear. Immunomodulation is considered to be the main mechanism of action of these drugs. With contact sensitizers, a counteracting cytokine pattern that is induced by the therapeutic contact dermatitis mediates hair growth.[12] Rosenberg and Drake have hypothesized that the lymphocytic cells that aggregate during contact allergy eliminates the antigenic stimulus.[13] Happle has proposed the concept of antigenic competition.[14] According to Hoffmann et al after DCP applicaion, the basal keratinocytes secrete bioactive IL-10 resulting in an inhibitory effect on lesional lymphocytes.[15] Phenol in very low concentration was tried in the earlier studies as an irritant to cause noninflammatory, nonallergic dermatitis and was found to be ineffective.[16] In this study, 88% phenol was used successfully in AA through its wounding action. It could have possibly acted through the following mechanisms:-

(1) During wound repair process , several growth factors are released which could be stimulating the affected follicle.

(2) Various cytokines are released during wound healing which might neutralise the peribulbar lymphocytic infiltrates causing regrowth of hair through immunomodulation.

(3) Most of the follicles in AA are in the telogen phase and thus lie high in the dermis. It is possible that phenol may be passing through the follicular opening and directly stimulating the germinal centre.

However, for confirmation of these mechanisms, further studies need to be performed.

Phenol peel, as seen in this study is a simple office procedure with no complicated surgery or anaesthesia involved and also needs no expertised training. Discomfort and pain are minimum and hospitalisation or dressings are not required. It can be considered as one of the alternate method to repigment stable vitiligo specially on hairy areas where atleast 50-70% black hair is present and can also be used on non-hairy sites to induce perilesional pigmentation. Repeat peels can be done on these areas if required. One can cover large areas in multiple sittings. In AA also phenol can induce hair growth. Large areas can be treated with multiple sessions. Repeat peels can be undertaken on partially responded or not responded sites. It has been found to be very useful especially in children who fear the intralesional injections.

Thus the wounding action of 88% phenol has been used in this study to repigment vitiligo lesions and induce regrowth of hair in patches of alopecia areata and to the best of our knowledge this has not been previously reported in the literature.

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