Therapeutic wounding - 88% phenol in idiopathic guttate hypomelanosis

Shilpashree P. Ravikiran, S. Sacchidanand, B. Leelavathy

Department of Dermatology, Sexually Transmitted Diseases and Leprosy, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

ABSTRACT

Context: Therapeutic wounding includes wounding the skin to induce pigmentation of the depigmented skin patches that was earlier used for repigmenting small patches of stable vitiligo. In this study, we have used the same principle to induce pigmentation in idiopathic guttate hypomelanosis (IGH) by spot peel with 88% phenol.

Aims: To study the efficacy of phenol in causing repigmentation in IGH and its adverse effect profile.

Settings and Design: Open prospective study.

Materials and Methods: Twenty patients with 139 IGH macules were subjected to spot peel. Eighty-eight percent phenol was applied with an ear bud once a month for two sittings. Patients were assessed both subjectively and objectively after every session and at the end of 3 months of initiation of therapy.

Results: Repigmentation was noted in 64% of IGH macules. More than 75% improvement was seen in 45% of the total IGH macules, while 41.5% showed 50-75% improvement at the end of three months. Persistent scabbing was the common adverse effect noted in 17.26% of lesions.

Conclusion: Spot peel with 88% phenol is a safe, simple, cost-effective, outpatient procedure for IGH, which can be combined with other medical therapies.

Key words: 88% phenol, idiopathic guttate hypomelanosis, therapeutic wounding

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Address for correspondence:
Dr. Shilpashree P. Ravikiran,
Department of Dermatology, Sexually Transmitted Diseases and Leprosy, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India.
E-mail: drshilpark@gmail.com

INTRODUCTION

Idiopathic guttate hypomelanosis (IGH) is an acquired leukoderma, characterized by discrete, round to oval porcelain-white macules of approximately 2-5 mm diameter, which increase in number with aging.[1] This disorder is characterized by multiple small pure white macules distributed on sun exposed surfaces of the forearms and the legs, usually in association with other skin changes of chronological aging and photodamage. The denominations of solar leukoderma or actinic punctate leukoderma have been proposed for this disorder.[2] IGH appears after the third decade; the macules tend to increase in number with time.[3] The histological findings associated with IGH are hyperkeratosis, an atrophic epidermis, and flattened rete ridges. In addition, a decreased melanin content and reduced numbers of melanocytes are reported features.[4] A variety of therapies with variable success are described, including cryotherapy, superficial abrasion, topical steroids and topical retinoids.[1] Recently, successful treatment of this condition with pimecrolimus 1% cream has been reported.[5]

Therapeutic wounding of the lesion stimulates melanocytes from the periphery and surrounding hair follicles to proliferate, migrate, and repigment the lesion, e.g., therapeutic dermabrasion, laser ablation, cryosurgery (liquid nitrogen spray), needling, and local application of phenol or trichloroacetic acid.[6] Starico reported the mechanism of migration of melanocytes from the hair follicles into the epidermis following dermabrasion.[7] Savant and Shenoy have reported spot chemical wounding with 88% phenol for repigmentation of stable vitiligo.[8]

Phenol or carbolic acid is one of the oldest antiseptic and antipruritic agents. It also acts as local anesthetic.[9] Full strength phenol (88%) is used as a medium depth chemical peelant for facial rejuvenation and as a spot peelant for treating stable vitiligo and alopecia areata. This is another novel treatment method for IGH that is based on post inflammatory hyperpigmentation induced by chemical wounding with 88% phenol.[8]

The aim of this study was to assess the efficacy and safety of spot peel with 88% phenol for repigmentation of IGH macules.

MATERIALS AND METHODS

A total of 20 patients (12 females, 8 males; age group: 20-85 years) with 139 IGH macules were included in the study. Patients with active infection, keloidal tendencies, bleeding disorders, active vitiligo, and atrophic lesions were excluded from the study. The study was conducted over a period of one year from January to December 2010. Informed consent was taken from all the patients. Pretreatment photographs were taken. The area was first cleaned with spirit. In a glass container, 0.5 ml of phenol was taken and applied with a cotton tipped applicator so as to cover the entire lesion. Feathering of the border was done to cover 1 mm of peripheral normal skin. Uniform white frost appeared in 30 sec. Pulse and blood pressures of the patients were monitored before and after application, as phenol is known for its cardiac toxicity. All the patients were advised to apply topical 2% mupirocin cream, twice daily for 7 to 10 days. Patients were asked to expose daily to sunlight (for 5 min) after the lesions healed. After application, all the patients complained of immediate mild burning sensation lasting for 1-2 min. This was followed by severe burning sensation lasting for 4-6 hours after 30 min. The uniform frost disappeared in 30 min, followed by erythema, dark brown to black discoloration of the lesions with crusting in 24 hours. The skin peels off in next 15 days leaving behind erythema. The procedure was repeated after 1 month. All the patients were reassessed at the end of 3 months, both subjectively and objectively. Repigmentation was noted in all the patients between 4 and 6 weeks. (Figures 1-3) The repigmentation was interpreted according to five point grading system ranging from G0 to G4, G0-No pigmentation, G1-Up to 25% pigmentation, G2-25-50% pigmentation, G3-50-75% pigmentation, and G4-75% or more pigmentation. Side effects such as burning sensation, persistent scabbing [Figure 4], postinflammatory hyperpigmentation [Figure 5], secondary infection, and ulceration [Figure 6] were recorded.

Descriptive statistics was analyzed on the parameters of range, mean ± S.D., frequencies (number of cases), relative frequencies, ratio or percentages, whichever was appropriate. For analytical statistics, the numeric data (continuous variables) were analyzed by using unpaired *t*-test and the categorical data were analyzed by using Fisher's exact test or Chi-square test (as applicable). Statistical software Medcalc® version 10.2.0.0 for Windows vista (http://www.medcalc.be) was used for statistical analysis and *P* value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 20 patients with mean age of 46.7 ± 14.14 years (range: 23-82 years) were included in this prospective

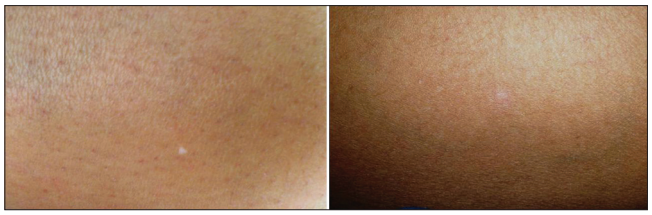

Figure 1: Complete pigmentation of the IGH macule at the end of three months

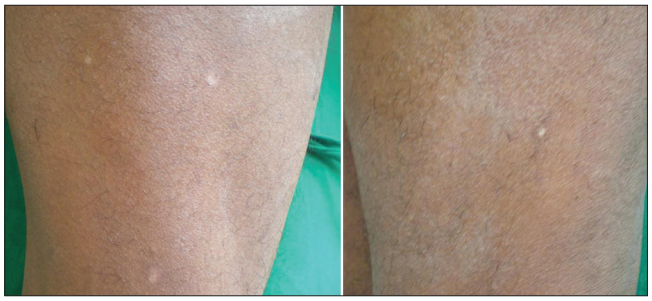

Figure 2: Two of the three IGH macules have pigmented at the end of three months

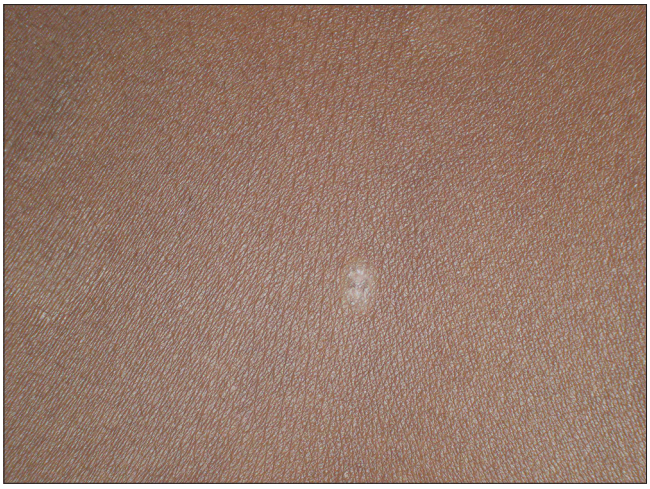

Figure 3: Perilesional spread of pigmentation

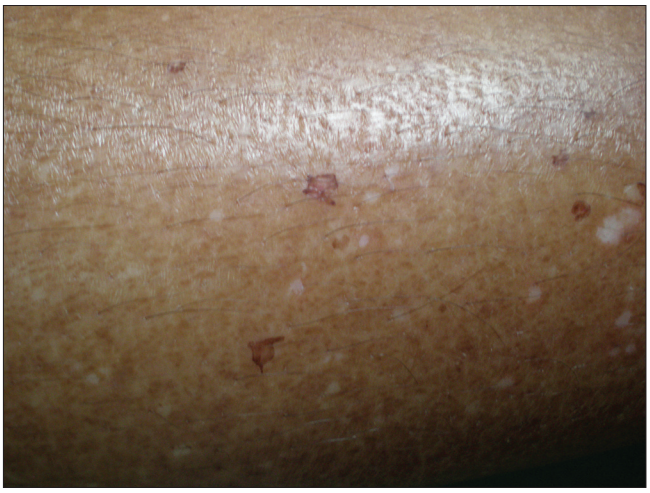

Figure 4: Side effects: Persistent scabbing

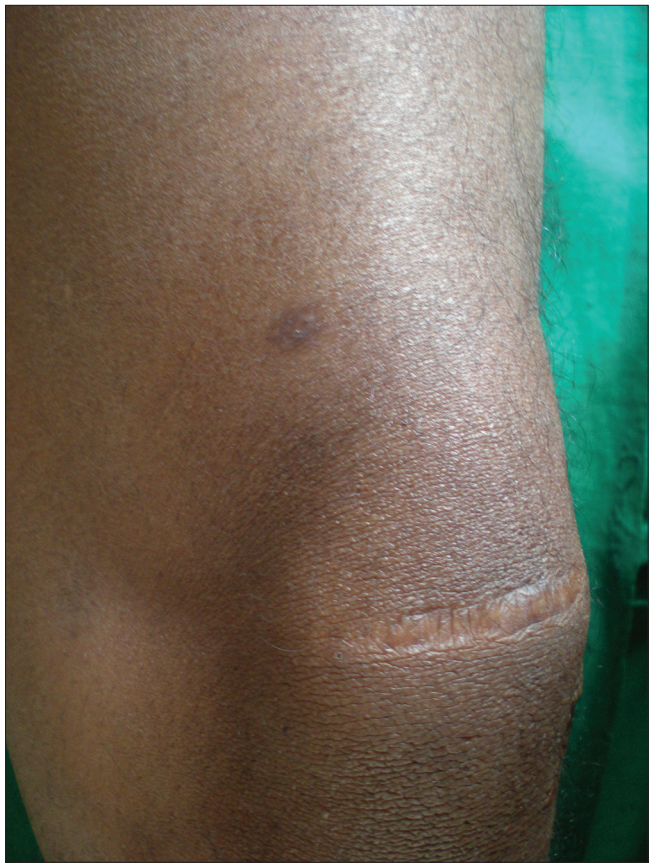

Figure 5: Side effects: Post inflammatory hyper pigmentation

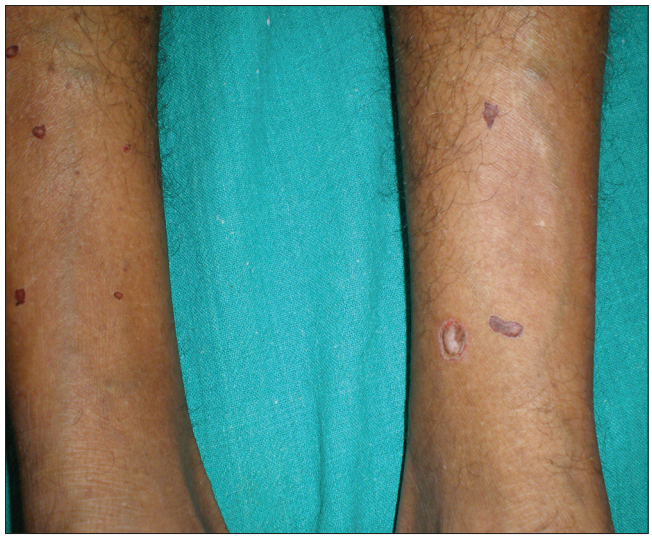

Figure 6: Side effects: Ulceration

study. Of the 20 patients included in the study, 12 (60%) were females and eight (40%) were males. Male to female ratio was 1:1.5. Seven patients were of Fitzpatrick type IV and remaining 13 was of Fitzpatrick type V. The sum of total number of lesions in all the patients was 139 IGH macules. The maximum number of lesions was in the age group of 51 to 60 years as shown in Table 1. IGH macules were found to have some preferential location on shins (20%) followed by forearms (14%) compared to other sites as depicted in Table 2 ($P < 0.05$). Most of the individuals had more than two sites of involvement.

Of the 139 IGH macules, 89 (64%) showed repigmentation at the end of 3 months and 50 (35.9%) had no response. On comparing the depigmented macules before application of phenol and the depigmented macules remaining after application of phenol, the *P* value obtained was statistically significant (paired '*t*' test), this indicates that the application of phenol on IGH macules was effective in repigmenting them [Table 3]. Forty-five percent of the repigmented lesion ($n = 89$) showed more than 75% improvement, 41.5% showed 50-75% improvement, and 13.4% of lesions showed 25-50% response [Table 4]. All the grades of pigmentation attained at the end of three months were divided finally into two groups. Group A includes poor responders comprising of macules showing G0, G1, and G2 repigmentation, while Group B includes better responders comprising of macules showing G3 and G4 repigmentation. On comparing these two groups, there was no statistically significant (Chi-square test) difference in the grade of the pigmentation attained by every IGH macule on application of phenol [Table 5]. Hence, every IGH macule responds independently in getting repigmented. Response of the lesions with respect to various age groups and site is shown in Tables 1 and 2. However, there was no significant relationship of the outcome attained with respect to age groups ($P = 0.125$) and site ($P = 0.165$) (Chi-square test).

Side effects noted were persistent scabbing for more than 15 days in 17.2% of IGH macules. Other side effects were ulceration, secondary infection and scarring [Table 6]. These were common in elderly patients. Post inflammatory hyperpigmentation was seen in 11.5% of pigmented lesions. The patient's subjective response correlated well with the investigators response. Though phenol is known to cause depigmentation, this was not observed in our case.

DISCUSSION

The exact mechanism of depigmentation in IGH is not known. As absence of melanocytes is not an essential feature in this condition, it is possible that a functional abnormality of melanocytes, perhaps due to factors prevailing on the lesional melanocytes in the immediate milieu of the lesion (neighboring keratinocytes, ultraviolet (UV) injury, cytokines) may be a cause.[10]

In therapeutic wounding, re-epithelialization takes place from the remnants of dermal appendages like sebaceous glands, hair follicles, and sweat glands. During the wound healing process, the inflammatory reactions and the re-epithelialization phase stimulate the follicular and perilesional melanocytes

Table 1: Age-wise distribution of IGH macules and its response to treatment

Age group (years)	Number of patients	Number of lesions (*n*) (%)	Number of lesions showing response/ (percentage)
21-30	3	11 (8)	9/(81.8) *n*=11
31-40	4	29 (20.8)	20/(68.9) *n*=29
41-50	5	38 (27.3)	24/(63.1) *n*=38
51-60	7	54 (38.9)	33/(61.1) *n*=54
>60	1	7 (5)	3/(42.8) *n*=7

IGH: Idiopathic guttate hypomelanosis

Table 2: Distribution and response of the lesions to the treatment with respect to site

Site	Number of lesions (*n*) (%)	Number of lesions showing response/(percentage)
Shins	39 (20)	29/(74.3) *n*=39
Fore arms	20 (14)	14/(70) *n*=20
Abdomen	17 (12)	12/(70.5) *n*=17
Arms	16 (12)	10/(62.5) *n*=16
Back	15 (11)	8/(53.3) *n*=15
Gluteal region	12 (9)	7/(58.3) *n*=12
Thighs	12 (9)	7/(58.3) *n*=12
Chest	8 (6)	2/(25%) *n*=8

Table 3: Comparison of means of depigmented lesions before and after application of phenol (paired '*t*' test)

	No. of depigmented lesions before phenol use (n1=139)	No. of depigmented lesions after phenol use (n2=50)
Mean	6.95	2.50
SD	2.5	1.877

(DF:19; *P*<0.0001). SD: Standard deviation

through liberation of cytokines like leukotriene C4 and D4, Transforming growth factor-alpha (TGF-α), interleukin-1 and endothelin-1 to induce perifollicular and perilesional pigmentation. Topical 88% phenol has been previously used on same principles of therapeutic wounding for repigmenting the stable vitiligo macules successfully.[9]

At concentrations less than 80%, phenol acts as keratolytic agent promoting its further penetration into dermis, while at concentration greater than 80%, phenol acts as keratocoagulant, causing coagulation of epidermal proteins. This blocks the further penetration of phenol into dermis. Hence, at 88% phenol causes medium depth chemical wound, which creates changes through necrosis of epidermis and part or all of the papillary dermis with an inflammation in upper reticular dermis. Phenol when used for facial rejuvenation, is known to cause cardiac arrhythmias, if the quantum of phenol exceeds 3 ml and the duration of application is more than 60 min or when applied

Table 4: Assessment of pigmentation: (*n*=number of lesions showing pigmentation=89)

Pigmentation (%)	Percentage of lesions
Upto 25 repigmentation (G1)	0 (0)
25-50 repigmentation (G2)	13.4 (12)
50-75 repigmentation (G3)	41.5 (37)
75 or more repigmentation (G4)	45 (40)

Table 5: Comparison between the poor and better responders: (Chi square test)

Value	Group A (poor responders)	Group B (better responders)
Observed	62	77
Expected	46	46

(DF=1; *P*>0.5029s)

Table 6: Side effects: *n*=139 (No. of lesions treated)

Side effects	Percentage
Persistent scabbing	24 (17.26)
Post inflammatory hyperpigmentation	16 (11.5)
Ulceration	11 (7.9)
Secondary infection	12 (8.6)
Scarring	8 (5.6)

Rest of the lesions shows no side effects, except for immediate burning sensation in all the lesions

to large cutaneous surface areas.[8] This was not seen in any of our patients since precautions were taken not to exceed 1/2-1 ml in one session.

The exact mechanism of repigmentation following cryotherapy in IGH is still being debated. Unlike in vitiligo, spontaneous repigmentation does not occur in any IGH lesions. Some authors postulate that, IGH results from an active process of depigmentation including active inhibition of repigmentation.[10,11] Freezing may inactivate an inhibitory enzyme or chemokines allowing repigmentation to occur. Another possibility is that cryotherapy may be beneficial as it destroys the overlying keratinocytes which may be exerting some destructive effect on the melanocytes or exerting some negative effect on melanogenesis/melanosome transfer to the keratinocytes. However, these possible explanations will need to be further clarified and substantiated with ultra-structural and molecular biological studies.[11] Similar mechanism may be involved in repigmentation of the IGH macules after 88% phenol application. To the best of our knowledge, this is the first study that has dealt with use of topical 88% phenol for repigmentation of IGH macules.

The results of our study conclude that 88% phenol is an inexpensive, safe, simple office procedure with no specialized training or equipment required. Burning sensation, scabbing,

and post inflammatory hyperpigmentation were the side effects noted during the study.

The only draw back of the study is the small sample size. Comparison with control and further follow up may add more information about its use.

What's known?

Idiopathic guttate hypomelanosis is an acquired leukoderma, in which various therapies are described. Cryotherapy and superficial abrasion is one of them. Both are based on the principle of therapeutic wounding, which stimulates the perilesional melanocytes to produce pigment in vitiligo.

What's new?

In this study, we have presented a new cost-effective treatment modality for repigmentation of IGH macules, based on the principle of therapeutic wounding, using 88% phenol.

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