

Efficacy and safety of 88% phenol application versus cryotherapy in repigmentation of idiopathic guttate hypomelanosis: A comparative study

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Abstract

Background Idiopathic guttate hypomelanosis (IGH) is a common, acquired dermatosis characterized by multiple, round or oval, hypopigmented to depigmented macules. A variety of therapies with variable success are described, despite that, the treatment remains still unsatisfactory and therapeutic challenge for dermatologists.

Objective The objective of this study is to compare the safety & efficacy of 88% phenol application & cryotherapy in repigmentation of IGH macules.

Materials and Methods A total of 30 patients with more than 10 IGH macules were selected. For each enrolled patient 88% phenol was applied to 5 IGH macules and single cryotherapy for 3-5 seconds was applied for another 5 IGH macules once in a month till the repigmentation for maximum of 3 applications. Patients were assessed monthly for 3 months for the side effects and improvement in pigmentation. The degree of improvement in pigmentation was assessed using a grading system, <25% - no response (grade-1), 26-50% minimal (grade-2), 51-75% good (grade-3) and >75% excellent response (grade-4).

Results A total of 25 patients completed the study. At the end of the treatment period, out of 125 macules treated with short contact cryotherapy 75(60%) macules showed excellent response & 20(16%) macules showed good response. In phenol group, out of 125 macules 37(29.6%) & 29(23.2%) macules showed excellent & good improvement in pigmentation respectively, with p-value<0.05. Side effects like persistent scabbing, ulceration were more common with 88% phenol application compared to cryotherapy.

Conclusion Short contact cryotherapy of 3-5 seconds was found to be more efficacious and safe compared to therapeutic wounding with 88% phenol in inducing pigmentation of IGH macules.

Key words

Idiopathic guttate hypomelanosis, 88% phenol, cryotherapy.

Introduction

Idiopathic guttate hypomelanosis (IGH) is a common, acquired and benign dermatosis characterized by multiple, round or oval,

hypopigmented to depigmented macules which mainly appear in upper and lower extremities.¹ The macules appear in descending order of frequency in upper and lower extremities, trunk and face. Usually the total number increases with time, whereas the size remains unchanged.²

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Sunlight has been long incriminated in the pathogenesis of IGH because lesions are mainly located at sun exposed body areas.¹ 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.³

A variety of therapies with variable success are described, including cryotherapy, superficial abrasion, topical steroids, therapeutic wounding with 88% phenol, topical retinoids & topical pimecrolimus.⁴ Despite several therapeutic modalities, the treatment of IGH still remains unsatisfactory and therapeutic challenge for dermatologists.

The aim of our study is to compare the safety & efficacy of cryotherapy versus 88% phenol application for repigmentation of IGH macules.

Materials and Methods

A comparative study was conducted in our institute after obtaining the ethical committee clearance for the duration of 1 year between June 2017 to May 2018. Patients were enrolled for the study after obtaining the written informed consent. Detailed history and clinical examination were carried out to know the type, distribution and number of lesions. A total of 30 patients with Fitzpatrick skin type IV & V between the age group of 18-70 years, with more than 10 IGH macules were included in the study. Patients who were severely ill and debilitated, with known cardiac problems, active infections, keloidal tendencies, active vitiligo, cold intolerance, pregnant and lactating women were excluded from the study. For each enrolled patient 88% phenol was applied with cotton tip applicator to 5 IGH macules once in a month till the repigmentation for maximum of 3 applications and single cryotherapy for 3-5 seconds, using liquid nitrogen spray gun was applied for another 5 IGH macules once in a month till the repigmentation for maximum 3

application. A total of 250 macules (125 in each group) were assessed. The Phenol (<0.5ml at each sitting) was applied with a cotton tip applicator to cover the entire macule and feathering of the border done to cover 1mm of surrounding normal skin. Pulse and blood pressures of the patients were monitored before and after application of phenol because of its cardiac toxicity. All the patients were advised to apply topical 2% mupirocin ointment, twice daily for 1 week. Patients were assessed monthly and followed up for 3 months for the side effects and improvement in pigmentation.

The degree of improvement in pigmentation was assessed in each macule using a grading system, <25%- no response, 26-50%- minimal, 51-75%- good & >75%- excellent response.

The data were entered and analyzed using descriptive and analytical statistical tests. P-value of <0.05 was considered statistically significant.

Results

A total of 30 patients (18 males, 12 females M:F: 1:0.6) with mean age of 56.5±12.87 years (range: 30-70years) were included in this comparative study. 25 patients completed the study. 10 macules in each patient, a total of 250 macules were assessed. 88% phenol was applied for 125 macules (5 in each patient) and short contact cryotherapy was applied for remaining 125 macules (5 in each patient). Common site of distribution of IGH macules in our study was shin (70%), followed by forearm (46.6%) and trunk (26.6%). Most of the individuals had more than 2 sites involvement.

Among the phenol applied 125 macules, 96(76.8%) macules showed improvement in pigmentation, 29(23.2%) macules had no response. Of the 125 macules treated with

Table 1

Grade of improvement	Cryotherapy n=125	Phenol n=125
No response	15(12%)	29(23.2%)
Minimal	15(12%)	30(24%)
Good	20(16%)	29(23.2%)
Excellent	75(60%)	37(29.6%)

Table 2

Side effects	Cryotherapy group	Phenol group
Persistent scabbing	3(2.4%)	41(32.8%)
Post inflammatory hyperpigmentation(PIH)	5(4%)	18(14.4%)
Scarring	0	16(12.8%)
Ulceration	0	0



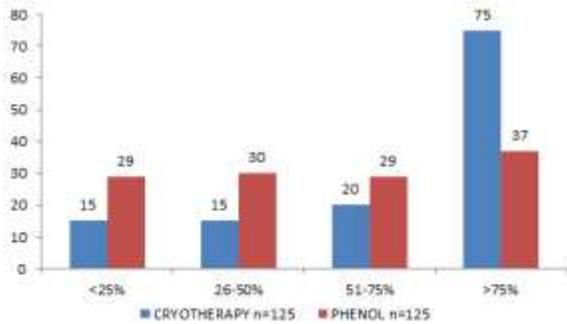
1a before treatment **1b** after treatment

Figure 1 Excellent response(>75%) with 88% phenol application:



2a before treatment **2b** after treatment

Figure 2 Excellent response (>75%) with short contact cryotherapy



Graph I Assessment of efficacy

cryotherapy, 110(88%) macules showed signs of repigmentation, 15 (12%) macules showed no repigmentation. In phenol group, out of 125 macules 37(29.6%) & 29 (23.2%) macules showed excellent (**Figure 1a&1b**) & good improvement in pigmentation respectively. In cryotherapy applied group, 75(60%) macules showed excellent improvement (**Figure 2a & 2b**) & 20(16%) macules showed good improvement in pigmentation. p-value<0.05 which is statistically significant (**Table 1 & Graph 1**). Individual variation in the treatment response was observed in each macule (**Figure**

3a&3b). Signs of repigmentation noted in each macule at the end of 4 weeks in phenol group and 6-8weeks in cryotherapy group. 5 patients in phenol group and 8 patients in cryotherapy group required 2nd application. None of the macules in both the groups showed reappearance in depigmentation at the end of 3months follow up.

Side effects like persistent scabbing (scab which persisted for > 15days) (**Figure 4**), scarring (**Figure 5**) and post-inflammatory hyperpigmentation (**Figure 6**) were common with phenol applied macules (**Table 2**). In our study short contact 3-5seconds cryotherapy was found to be safe compared to 88% phenol application.

Discussion

Idiopathic guttate hypomelanosis (IGH) is a benign dermatosis of skin, first described in 1951 by Costa as “symmetric progressive

Table 3 Studies on treatment of IGH

Reference	Number of lesions	Treatment	Method	Results
Falabella <i>et al.</i> ¹²	15	Intralesional corticosteroids along with skin grafting	Once a month for 3 months	Almost 50% patients showed satisfactory repigmentation
Ravikiran <i>et al.</i> ¹⁰	139	88% phenol peeling	Spot peeling with cotton tipped application, monthly for 2 sessions	64% of the lesions showed satisfactory repigmentation
Ploysangam <i>et al.</i> ¹¹	87	10 s cryotherapy	Single application of a 10-s cryoprobe	Almost 90% of lesions showed repigmentation after 6–8 weeks
Kumarasinghe ⁸	15	3–5-s cryotherapy	Single application of a 3–5-s cryogen	All treated lesions showed good repigmentation
Shin <i>et al.</i> ¹³	40	Fractional CO2 laser	Single session	47.9% patients showed >75% repigmentation



3a before treatment **3b** after treatment
Figure 3 Excellent response and no response in same individual with phenol application



Figure 4 Persistent scabbing with phenol **Figure 5** Scarring with phenol



Figure 6 Postinflammatory hyperpigmentation following phenol application

leukopathy of the extremities”⁵ Cummings and Cattel introduced the term IGH in clinical practice in 1966 & confirmed its incidence in

large group of population.⁶ The exact etio-pathogenesis of IGH is still unknown. Various factors like hereditary, environmental had been implicated in the pathogenesis. Occurrence of IGH macules in post renal transplant patients associated positively with HLA-DQ3.⁷ Sunlight had been incriminated in the pathogenesis because the IGH macules predominantly distributed in the sun exposed areas.¹ Repeated trauma also acts as a precipitating factor for development of IGH.¹ The exact mechanism of depigmentation in IGH is not known, possible mechanism is the functional abnormalities in the lesional melanocytes.

There are three morphological variants of IGH. The typical lesion is a hypopigmented macule

(or multiple macules) in a background of sun-damaged skin, in an exposed area. The second type is an ivory white, stellate, well demarcated, sclerotic macule unrelated to sun exposure. The third type is a hypopigmented, well demarcated small lesion with a keratotic flat crust; this type often has a scalloped border.⁸ The dermoscopic study of IGH lesions reveals the existence of normally pigmented specks scattered within the macules and perimetric pigmentary extensions. IGH may be developed according to four patterns, which are nebuloïd, petaloïd, amoeboid and feathery.⁹

Various treatment modalities are available for management of IGH; including cryotherapy, superficial abrasion, topical steroids, therapeutic wounding with 88% phenol, topical retinoids, topical calcineurin inhibitors & fractional CO₂ LASERS.

The postulated mechanism of repigmentation following therapeutic wounding with 88% phenol is that, during the process of wound healing inflammatory process stimulates follicular and perilesional melanocytes through liberation of cytokines to induce pigmentation.¹⁰ Exact mechanism of repigmentation following cryotherapy is still unknown.

Postulated factors includes, freezing inactivates inhibitory enzymes and chemokines to allow the repigmentation to occur. Second possibility is that destruction of overlying keratinocytes inhibit the negative effect of keratinocytes on melanocytes. Thirdly, following cryotherapy post inflammatory hyperpigmentation may be responsible for repigmentation.⁸

Ravikiran SP¹⁰ *et al.*, in their study reported 64% of the IGH macules showed repigmentation with 88% phenol spot peel compared to our study 76.8% macules showed repigmentation.

Ploysangam T¹¹ *et al.*, in their study reported 90.8% of the treated lesions were repigmented 6-8 weeks after being gently frozen with liquid nitrogen, which was applied with a cryoprobe for 10 seconds. Kumarasinghe SP,⁸ in his study reported 100% improvement in pigmentation of the macules using a liquid nitrogen spray gun for 3-5 seconds. In our study, 88% macules showed signs of repigmentation with short contact cryotherapy using liquid nitrogen spray gun (**Table 3**). Further studies with longer duration of follow up required to confirm our results.

To the best of our knowledge, this is the first comparative study between cryotherapy and phenol application in repigmentation of IGH macules.

Conclusion

Disorders of pigmentation affect a large proportion of the population, causing great concern not only for human health, but also for the induced social implications. Short contact 3-5 seconds cryotherapy with liquid nitrogen spray is simple, more efficacious and safe compare to 88% phenol application.

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