Comparative Study of Cryotherapy & Anthralin in Alopecia Areata

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Introduction: Alopecia Areata (AA) is a non–scarring inflammatory hair loss disease that can affect men, women and children. Though multiple modalities of treatment are available, topical therapy is preferable in view of fewer side effects. Hence this study was carried out to see the responses of two topical modalities of therapy.

Materials And Methods: Patients presenting with AA, to our dermatology department during the period Jan 2017 were recruited. The two topical modalities were tried and results were analysed at the end of 3 month study period. (March, April, May-2017)

Results And Conclusion:- Acceptable regrowth of hair was seen in patients treated with Liquid Nitrogen than with Anthralin.

I. Introduction

ALOPECIA AREATA (AA) (Abbreviation: AA-Alopecia areata) is a non scarring, inflammatory hair loss disease that can affect men, woman and children. It produces marked cosmetic disability and extensive psychological morbidity. Though multiple modalities of treatment are available, topical therapy is preferable in view of fewer side effects. Hence this study was carried out to see the responses of few topical modalities of therapy. AA accounts for about 2% of new dermatological outpatient attendance. Various theories such as infectious, genetic, stress, trauma (physical), immunologic, endocrine dysfunction and focal sepsis have been postulated.

Prognosis
The prognosis is good in the common simple form of AA in which the hair loss is confined to the scalp and has got a high natural remission rate.

Treatment
Early recognition, intervention involving topical and or intralesional therapy and education can provide patient with comforting reassurance about eventual recovery.

Topical Therapies Include
1 Non specific irritants- Phenol, Salicylic acid, Sulphur, Dithranol, Liquid Nitrogen, cantharidines etc.
2 Contact sensitisers – Dinitrochlorobenzene, squaric acid dibutyl ester (SADBE) and diphenacyprone.
3 Topical steroids.
4 Other topical modalities include- Topical PUVA, Topical Minoxidil, Topical Tacrolimus, Imiquimod.

Systemic Therapy Includes
1 Systemic steroids.
2 Immunomodulators like cyclosporine, systemic psoralen, inosiplx (Isoprinosine), etc.

Miscellaneous Modalities Include
1 Intraliesional steroids
2 Irradiation
3 Psychotherapy
4 Wig.

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II. AIMS OF STUDY

The aims of the present study was
1. To study the efficacy of two modalities of topical treatment and to compare them with one another.
2. To study the adverse effects of the topical modalities used.
3. The topical therapies used in the present study were
   (i) Cryotherapy with liquid Nitrogen.
   (ii) Topical 5% Anthralin.

III. MATERIALS AND METHODS

Patients presenting with AA to the dermatology department of our hospital during the Month of Jan, Feb 2017 were recruited for the study. A thorough history was elicited with regards to the duration of symptoms, progression of the disease, history of past episodes, history of any treatment both topical and systemic therapy, history suggestive of any psychiatric disturbances and septic foci. A personal and family history of atopy, other dermatoses, diabetes mellitus and hypertension and history suggestive of any other autoimmune disease were also elicited. A meticulous general and systemic examination was performed. A Dental and ENT opinion was sought to rule out septic foci. A complete hemogram was carried out in all the patients and a random blood sugar in adults was done. The individuals with history of exposure to the risk of STD were subjected to a blood VDRL examination. After completing the examinations, 20 patients were taken for the study. Patients having only scalp involvement, Patients who had no treatment either topical or systemic in the past 3 months. Before starting the therapy appropriate treatment of focal sepsis if any were given to patients. The patients were divided into 2 groups comprising 10 in each group and the following therapy was instituted. The study period was 3 months (March, April, May).

Group I: Patients Submitted For Liquid Nitrogen Therapy

Ten patients comprising the first group were treated with liquid nitrogen. It was applied over the patches of AA with a cotton wool liquid applicator producing 2-3 freeze thaw cycles at an interval of 2-3 seconds until an erythema developed over the patches. This treatment was repeated very week, until acceptable hair growth occurred or till the end of the study period that is 3 months.

Group II: Patient Treated With 0.5 Topical Anthralin

Ten patients were treated with 0.5% anthralin. A short contact therapy was used. The patients were advised to apply a small quantity of 0.5% anthralin initially for 10 minutes and subsequently the contact period was increased to 30 minutes. After 30 minutes the ointment was removed with a cotton swab. Patients were cautioned to wash hands after applying anthralin, to protect treated skin against sun exposure and to beware of staining clothes and linen.

The patients were reviewed once in 15 days for 3 months. During follow up the following changes were noted and recorded.
1. Increase in size of the lesions.
2. Appearance of new lesions.
3. Response to therapy was noted as follows
   a. No growth of hair
   b. Appearance of vellus hair
   c. Growth of pigmented normal hair
   d. Extent of regrowth.
4. Complication of therapy like
   a. Burning and irritation
   b. Erythema
   c. Vesculation
   d. Pigmentary changes
   e. Folliculitis
   f. Atrophy etc. were recorded

IV. Observations

An analysis of the clinical profile of the patients recruited for the therapeutic responses revealed the following data. There were 13 females and 7 males in the study groups. The age of the patients ranged from 7 years to 52 years, the average age being 25.2 years. The duration of the disease ranged from 1 week to 3 years, the average duration being 4.8 months. Two patients had a family history of atopy in the form of asthma. There
was a personal history of atopy in 4 patients in form of allergic rhinitis (1), urticaria (2), pityriasis alba (1). One patient had a family h/o atopy in the form of asthma and also had pityriasis alba on the face at the time of examination. All patients had single episode except for one patient who had five episodes previously. The number of patches varied from 1 to 8, the average being 1.8. The region wise distribution of the patches were Temporal (3), Parietal (8), Occipital (4) and Frontal (5). The region wise distribution of the patches were Temporal (3), Parietal (8), Occipital (4) and Frontal (9). The nail changes noticed among the patients were pitting of the nails in 5, punctuate leukonychia in 4, linear grooves in 2 and melanolychia striata in 1 patient. Two patients had hyperpigmentation of the oral mucosa.

**Group I: results obtained in patients who underwent cryotherapy with liquid nitrogen were as follows.**

Acceptable regrowth occurred in 9 out of 10 patients of whom excellent response was seen in 6 patients, good response in 1 and moderate response in 2 patients. Very poor response was noted only in 1 patient. In patients with excellent response regrowth of hair started after 2 weeks in one, and after four weeks in 4 and after 6 weeks in one patient. In the patient with very poor response the regrowth of hair was noticed only at 8 weeks but the density of the regrowth continued to be very poor during the entire study period. The untoward effects noticed by the patients were stinging and burning sensation at the time of application of liquid nitrogen. In 3 of the patients the regrowth of hair was in the form of depigmented hair, which showed very slow repigmentation.

**Group II: Results Obtained By The Short Contact 0.5 Anthralin Therapy**

Acceptable regrowth of hair occurred in 4 out of 10 patients in this group, excellent response was seen in 2 patients, good response in 1, moderate response in 1, poor response in 1 and very poor response in 5.

In the patient showing excellent response, the hair regrowth started at 4 to 6 weeks, with gradual increase in thickness and density of hair. The patient with good response, showed similar response as in patients with excellent response but during the therapy patient developed 3 new patches, in which there was only a moderate hair growth. In the patient with poor response the hair started regrowth only at 6 weeks and it was vellus initially, pigmented hair appeared only at 10 weeks. In patients with very poor response there was no regrowth of hair which included one patient with oophiasic pattern. In this group the regrowth of hair was vellus type in 3 of the patients including in one of the patients with excellent response. The adverse effects noticed were staining of the area of alopecia in one patient and stinging sensation in another. The stinging sensation was tolerable and this patient was willing to continue therapy.

<table>
<thead>
<tr>
<th>Table 1: Table Showing Responses To Topical Therapies</th>
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<tbody>
<tr>
<td>Response</td>
</tr>
<tr>
<td>Liquid Nitrogen</td>
</tr>
<tr>
<td>Anthralin</td>
</tr>
</tbody>
</table>

Response of single and multiple patches to various modalities of topical therapy is given below

<table>
<thead>
<tr>
<th>Table 2: Response Of Single And Multiple Patches To Topical Therapy</th>
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<tbody>
<tr>
<td>Single Patch</td>
</tr>
<tr>
<td>Liquid Nitrogen</td>
</tr>
<tr>
<td>Anthralin</td>
</tr>
<tr>
<td>Multiple Patch</td>
</tr>
<tr>
<td>Liquid Nitrogen</td>
</tr>
<tr>
<td>Anthralin</td>
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</tbody>
</table>

Therapeutic responses in patients with personal and family history to atopy compared to other normal individuals is given in the table below.

<table>
<thead>
<tr>
<th>Table 3: Therapeutic Response In Atopics Vs. Non Atopics</th>
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<tbody>
<tr>
<td>Atopic</td>
</tr>
<tr>
<td>Single Patch</td>
</tr>
<tr>
<td>Multiple Patch</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Non Atopic</td>
</tr>
<tr>
<td>Single Patch</td>
</tr>
</tbody>
</table>
3 of the 4 (75%) patients with atopy showed acceptable regrowth of hair and 33 of the 40 (60%) patients without personal or family history of atopy showed acceptable regrowth of hair.

V. Discussion

Group I : Patients Treated Using Liquid Nitrogen

Cosmetically acceptable regrowth of hair was noticed in nine out of ten patients in the present study group which is comparable to 97.2% noticed in the earlier studies. Out of nine patients six of them had excellent and three of them had moderate and good response. Regrowth of hair was first noticed between four to six weeks in all but one of them to whom regrowth started at two weeks. This is in contrast to the earlier study where regrowth started at two weeks. This is in contrast to the earlier study where regrowth was reported by one to two weeks.43

Three persons in the excellent response group had single patch and three of them multiple patches and in the patients with moderate and good response there was one patient with single patch and two of them had multiple patches. Thus no correlation could be made in the response patterns of this group among the patients with single and multiple patches. In the patients with excellent response, none of them had a personal or family history of atopy, diabetes mellitus, hypertension or thyroid disease and only one of them had dental caries, which was treated. Similarly in the patients with good and moderate response none of them had a personal or family history of atopy, diabetes mellitus, hypertension or thyroid disease, but for one with a past history of recurrent AA and gingivitis. In this group two patient developed new patches while on therapy and in addition one of them developed and increase in size of the patches.

In this study one patient had very poor response in whom there was no personal or family history of atopy, diabetes mellitus, hypertension or thyroid disease, but the patient had dental caries and gingivitis which were treated. The size of the patch in this patient was the largest noticed in this group. Duration of disease in this patient was six months, although three other patients with an excellent response, also had AA of six months duration. Therefore it may be presumed that the duration of disease probably does not influence the outcome of therapy, but larger area of involvement could probably be the reason for poor response. Persistent depigmentation of hair was noticed in two of the patients which may be probably due to destruction of melanocytes and this patient is being followed. This could be avoided by reducing the duration of freezing, during application of Liquid Nitrogen. From the above it can be concluded that Liquid Nitrogen is a cheap, effective mode of therapy for AA.

Patients Treated With 0.5% Anthralin

Acceptable regrowth of hair was noticed in only four of ten patients i.e. 40% of patients, this is a little higher when compared to a response rate of 20 to 25% reported in the earlier study. In this group two patients had excellent response. Both the patient with excellent response had single patch of simple type of AA. Thyroid disease in the form of multinodular goitre manifesting as hypothyroidism and foci of dental sepsis were noticed in both of them. The duration of the disease was three and six months. However there was no family history of thyroid disease or personal or family history of diabetes mellitus, hypertension of atopy. In this group two patients showed good and moderate response. Both the patient had single patch and duration of disease was twelve and one and half months. There was no personal or family history of atopy, diabetes mellitus, hypertension or thyroid disease nor was there any foci of dental sepsis.

Acceptable regrowth of hair was noticed by ten weeks in three patients and eight weeks in one of the patients, this is in contrast to 24 weeks reported in the earlier studies. One of the patient with good response developed three new patches and one of them showed an increase in size during therapy. In this group six patients showed poor and very poor response to therapy. Two of the patients had multiple patches. The duration of disease ranged from 15 days to 36 months. Patients with single patch of AA as well as multiple patches showed poor response thus showing no correlation between the number of patches and response. In this group none of them had a personal or family history of atopy, diabetes mellitus, hypertension or thyroid disease, but there of them had foci of dental sepsis, which was treated. The untoward effect noticed was irritation that has been reported earlier, scaling and folliculitis noticed in the other studies were not observed in our patients. The other feature noticed in patients treated with anthralin was the appearance of vellus type of hair initially. This was noticed in four patients.

A longer period of follow-up is probably essential to assess the optimal efficacy of anthralin in other patients and these patients are being followed. A larger study may be necessary to assess the exact response to topical anthralin.
To sum up it is observed that excellent coupled with moderate and good responses was seen in 9/10 patients treated with liquid nitrogen and 4/10 in patients treated with 0.5% anthralin. Poor responses were seen mostly in patients treated with 0.5% anthralin (6). Excellent coupled with good and moderate responses were seen in 9/10 patients with single patches treated with liquid nitrogen. Even atopic persons showed excellent along with good and moderate response(6/8) thus showing, personal or family history of atopy does not appear to be a fact in the therapeutic response.

CONCLUSION
1. Atopy in the form of personal and family history was the only significant association found in the present study group.
2. Acceptable regrowth of hair was seen in patients treated with Liquid Nitrogen than Anthralin.
3. Liquid Nitrogen is a cheap and effective mode of therapy.
4. Atopy does not appear to be a significant factor in the response to therapy in patients with alopecia areata.

REFERENCES