RANDOMIZED THERAPEUTIC TRIAL FOR PATIENTS WITH ALOPECIA AREATA

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CERTIFICATE

Certified that this dissertation entitled ***"RANDOMIZED THERAPEUTIC TRIAL FOR PATIENTS WITH ALOPECIA AREATA"*** is a bonafide work done by **DR. G. MEERA,** Post Graduate Student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 600 003, during the academic year 2007 – 2010. This work has not previously formed the basis for the award of any degree.

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CONTENTS

Sl.No.	Title	Page No.
1.	INTRODUCTION	1
2.	REVIEW OF LITERATURE	2
3.	AIM OF THE STUDY	35
4.	MATERIALS AND METHODS	36
5.	OBSERVATIONS	43
6.	DISCUSSION	61
7.	CONCLUSION	73
	ANNEXURES	
	REFERENCE	
	PROFORMA	
	MASTER CHARTS	

INTRODUCTION

In humans, hair's main purpose revolves around its profound role in social interactions. Oliver Herford said “A hair in the head is worth two in the brush”. Given their prominence in daily dermatologic practice, hardly any dermatologist can escape having to manage patients with hair growth disorders.

ALOPECIA AREATA (Abbreviation : AA) is a chronic, organ-specific autoimmune disease, probably mediated by autoreactive T cells, which affects hair follicles and sometimes the nails. Although not life threatening, the cosmetic disfigurement that leads on to significant psychological and emotional distress supports a multibillion-dollar effort to reverse this condition.

Though various modalities are available for the treatment of alopecia areata, assessment of the efficacy of a treatment must be considered with care because the condition is highly unpredictable in presentation, evolution, and response to treatment. Little data exist regarding the natural evolution of the condition. Hence with this in mind the following study was carried out to see the treatment response for various modalities and chances of spontaneous resolution for this benign condition.

REVIEW OF LITERATURE

INTRODUCTION

Hair is a cutaneous appendage typical of mammalian skin[1]. It has lost its functional value in humans except probably over the scalp. With the exception of the palms, soles, dorsa of terminal phalanges of digits[1], glans penis and mucocutaneous junctions, the entire skin surface is populated by hair follicles. The follicular density (number of hair follicles/cm2) decreases with age.

HAIR CYCLE

Hair grows in cycles of various phases:[2] **anagen** is the growth phase(2 – 10 yrs); **catagen** is the involuting or regressing phase(1 - 3 wks); followed by **telogen**, the resting or quiescent phase (3 months). Prior to the start of cycling is a phase of follicular morphogenesis (formation of the follicle). There is also a shedding phase, or **exogen**, that is independent of anagen and telogen in which one of several hairs that might arise from a single follicle exits. Normally up to 90% of the hair follicles are in anagen phase while, 10–14% are in telogen and 1–2% in catagen. The cycle's length varies on different parts of the body. Growth cycles are controlled by a chemical signal like epidermal growth factor.

ALOPECIA AREATA (AA) – DEFINITION

Alopecia Areata is defined as a sudden or gradual complete loss of hair in sharply defined round or oval patches without accompanying atrophy or inflammation resulting in non scarring smooth patch of baldness. Hippocrates first used the term alopecia (literally translated as “Fox’s disease”). Alopecia areata was first described by Cornelius celsus in 30AD & Sauvages used the term alopecia areata.

SYNONYMS[3]

Alopecia Celsi, Porrigo Decalvans, Alopecia Circumscripta, Cazenave's Vitiligo, Celsus' Vitiligo, Vitiligo capitis, Alopecia cicatrisata, Fox’s disease, Jonston's Alopecia, Area celsi , Area tonstonii, Pelade of the French, Tinea decalvans & Ophiasis of the Greek.

SUBTERMS OF ALOPECIA AREATA[4]

Alopecia areata : Most commonly used term covering all forms of the disease.

Alopecia partialis: Name given to specific patchy hair loss.

Alopecia Totalis: Complete loss of terminal hair on the scalp.

Alopecia Universalis: Total loss of all terminal hair on the scalp and body.

Oophiasis : Band-like pattern of hair loss at the periphery of the scalp. Usually affecting the occipital and temporal region. Oophiasis comes from the latin word ‘Snake’ and in Greek means serpent due to the winding turban or snake like pattern of hair loss on the periphery of the scalp.

Sisaipho AA: It is defined as entire loss of scalp hair except for a narrow ring of hair around the periphery. This term is used by a clinical group in Seville, Spain (Munoz1996)

Alopecia Areata Barbae: Alopecia affecting the hair of the beard region.

Reticular Alopecia Areata: Hair loss occurs in irregular patterns in a net like fashion. In the scalp, there are regions of hair loss interspersed with areas of normal hair growth.

Diffuse type of Alopecia Areata: In this case, there is a premature cessation of anagen growth, which causes partial hair loss throughout the scalp. No distinct patches are evident.

Perinevoid Alopecia Areata: A very rare form of AA where patches of hair loss occurs around naevi.

Triangular AA: Another very rare form where the hair loss presents in a triangular shape.

AETIOLOGY

At any given time 0.2% have alopecia areata and approximately 1.7% experience an episode of a AA during their lifetime. Various theories have been put forth but these couldn’t stand the test of time. They are the parasitic theory (infectious etiology), trophoneurotic theory (AA

was produced in cats following denervation associated with stress), genetic, trauma, tick bites, immunologic, focal sepsis and endocrine theory (associated with thyroid disorders)[5,6].

The etiopathogenesis of AA will be discussed under the following headings:

- Genetic factors
- Immunological factors
- Atopy
- Stress
- Infections

GENETIC FACTORS

Many factors favor a genetic predisposition for alopecia areata. The frequency of positive family history for alopecia areata in affected patients has been estimated to be 10-20%[7]. The mode of inheritance is ought to be autosomal dominant with variable penetrance. One study showed that the concordance rate of 55% for alopecia amongst monozygotic twins. Two studies demonstrated that

human leukocyte antigen DQ3 (DQB1*03) was found in more than 80% of patients with alopecia areata, which suggests that it can be a marker for general susceptibility to alopecia areata. The studies also found that human leukocyte antigen DQ7 (DQB1*0301) and human leukocyte antigen DR4 (DRB1*0401) were present significantly more in patients with alopecia totalis and alopecia universalis[8,9,10]

Other possible associations that were found are HLA – A1, HLA –B62, HLA – DR4, HLA DQ – 1, HLA – DQ3, HLA- DR11. Juvenile onset and severe involvement were related with CW7 and DR1. HLA – DR5 is linked to early onset form of AA and more extensive hair loss. HLA DR16 was significantly less commonly found in patients and this allele probably has a protective role for AA[11,12.] Another gene, the interleukin 1 receptor antagonist gene, may correlate with disease severity. TNF – alpha gene polymorphism has been found to be associated with autoimmune/ inflammatory diseases including

Systemic lupus erythematosus, Rheumatoid arthritis, Dermatitis herpetiformis and celiac diseases. Finally, there is upto 8.8% increased frequency of AA in patients with Down's syndrome. The increased frequency of down's syndrome and polyglandular syndrome type 1 is due to mutation of autoimmune regulator gene on chromosome 21.

IMMUNOLOGICAL FACTORS

Much evidence supports the hypothesis that alopecia areata is an autoimmune condition[13]. Increased incidence of circulating organ-specific antibodies against thyroid, gastric parietal cell, adrenal tissue, smooth muscle, testes and the ovaries have been reported[14,15]. A statistically significant association between AA and hashimoto's thyroiditis, addison's disease, and pernicious anemia has been reported[16]. Other autoimmune diseases that have occurred with AA include vitiligo (4%), lichen planus, morphea, lichen sclerosus et atrophicus, pemphigus

foliaceus, lupus erythematosus, Sjogren's syndrome, ulcerative colitis, myasthenia gravis, autoimmune hemolytic anemia, diabetes mellitus, autoimmune testicular and ovarian disease and chronic mucocutaneous candidiasis with endocrinopathy[17]

HUMORAL IMMUNITY[18]

Antibodies directed to multiple hair follicle structures have been found with increased frequency in alopecia areata patients compared with control subjects by Toban et al using immunofluorescence. The outer root sheath is the structure targeted most frequently, followed by the inner root sheath, the matrix, and the hair shaft. Anti hair follicle antigen (IgG) expressed in alopecia areata is also expressed by hair follicle melanocyte and keratinocytes in vitro supporting that melanocyte and keratinocyte are also possibly targeted in AA.

CELL MEDIATED IMMUNITY

The following studies supports the cell- mediated immunity theory. Messenger et al found that hair bulb keratinocytes aberrantly expressed HLA-DR antigen, indicating immunological cell injury. Total numbers of

circulating T lymphocytes have been reported at both decreased and normal levels. Studies have shown that hair regrows when affected scalp is transplanted onto SCID (severe combined immunodeficiency) mice that are devoid of immune cells[19.] Response of AA to a variety of immunomodulators such as cyclosporine, Isoprinosine, thymopentin, contact sensitizers, PUVA, and steroids also supports the immunologic hypothesis[20,21]. Target cells implicated in immune response in AA have been identified as keratinocytes, melanocytes, and follicular papillary fibrocytes. Loss of "immune privilege" has been hypothesized to be causative of AA.

CYTOKINES

Recent studies have suggested that cytokines play a critical role in the pathophysiology of alopecia areata. Interleukin 1 and tumor necrosis factor were shown to be potent inhibitors of hair growth in vitro. Serum levels of cytokines, including interferon γ (IFN-γ), tumor necrosis factor α, interleukin 1α (IL-1α), IL-2, IL-4, and IL-6, were measured using radioimmunoassay or enzyme-linked immunosorbent assay techniques in patients with the localized form and the extensive form (alopecia universalis). The serum levels of IL-1α and IL-4 were significantly elevated in patients with the localized form. In contrast, the serum levels

of IFN-γ and IL-2 were significantly elevated in patients with the extensive form. These results indicate that immune responses in the localized form and the extensive form of alopecia areata are regulated by Th2 cytokines and Th1 cytokines, respectively[22].

ATOPY

The association between a history of atopy and AA is not well established. A study analysis revealed that a history of atopy and autoimmune disease was associated with an increased risk of AA and that the results were consistent for both the severe subtype of AA and the localized subtype (ie, AA persistent)[23]. In Ikeda's classification the 2nd type is called atopic type and accounts for 10% of AA patients.

STRESS

Psychosocial stress has been reported to play a role in the onset and/or exacerbation of alopecia areata via psychoneuroimmunological pathways[24]. A study analysis revealed that patients whose alopecia is stress-reactive may suffer from depressive illness, a potentially important consideration in the overall management of such patients[25].

INFECTIONS

Alopecia areata was believed to possibly have an infectious origin, but no microbial agent has been isolated consistently in these patients. Many efforts have been made to isolate cytomegalovirus, but most studies have been negative.[13] Focal sepsis particularly dental disease has been reported as precipitating factor for AA[26.]

INNERVATION AND VASCULATURE[13]

Another area of interest concerns the fact that patients with alopecia areata occasionally report itching or pain on affected areas raises the possibility of alterations in the peripheral nervous system. Circulating levels of the neuropeptide calcitonin gene-related peptide (CGRP) were decreased in patients with alopecia areata. CGRP has multiple effects on the immune system, including chemotaxis and inhibition of Langerhans cell antigen presentation and inhibition of mitogen-stimulated T-lymphocyte proliferation. CGRP also increases vasodilatation and endothelial proliferation. More studies are needed to shed light on the significance of these findings.

HISTOPATHOLOGY[27,28]

The diagnostic pathologic feature is peribulbar lymphocytic inflammation (swarm of bees) affecting anagen follicles or follicles in early catagen. The inflammatory assault on anagen follicles induces a premature conversion to catagen. Consequently, the number of catagen and telogen follicles found to be approaching 100%. Follicles may enter a persistent phase of telogen in which the hair shaft has already been shed, manifested by the telogen germinal unit. As follicles enter catagen, peribulbar inflammation frequently disappears, but the lymphocytic infiltrate in late catagen may be present around the epithelial remnant of the receding follicle, and also within and surrounding the collapsed follicular sheaths. Telogen hairs show little to no perifollicular inflammation. Lymphocytes may also be seen sparsely infiltrating the matrix epithelium of anagen follicles, inducing damage to the matrical cells that includes intra- and

intercellular edema, cellular necrosis, and microvesicle formation.

As a result of injury to bulbar melanocytes and keratinocytes, pigment casts, which are clumps of melanin pigment, may be found within the dermal papilla, the sheath of miniaturizing or regressing follicles, or in the follicular epithelium. Abnormal follicles called nanogen hairs are a distinctive finding in long-standing cases. As telogen follicles re-enter anagen, the follicles miniaturize and are situated more superficially, with their bulbs situated in the mid to lower dermis. Miniaturization and conversion to catagen and telogen leave many collapsed fibrous root sheaths in the subcutis.

Whiting found that transversely sectioned scalp biopsies showed the diagnostic features of alopecia areata more often than vertically sectioned biopsies. He emphasized the use of follicular counts to aid in the diagnosis of AA

when the characteristic peribulbar inflammation is missing. Eosinophils have been demonstrated around the bulb and within fibrous tracts. Some plasma cells may also be present[28]. In long-standing AA, the inflammatory infiltrates appear to diminish.

HISTOPATHOLOGICAL DIFFERENTIAL DIAGNOSIS[29]

Alopecia syphilitica may include lymphocytes situated near the isthmus, the presence of plasma cells, an endothelial reaction, interface dermatitis, or neutrophils in the stratum corneum closely mimic active AA. Androgenic alopecia shows diminution of follicular size, dermal infiltrates that are present in this condition are usually superficial, perivascular, and peri-infundibular. In telogen effluvium normal number of hair follicles with no miniaturization of follicles and a slight decrease in the anagen to the telogen ratio may be noted[30]

ELECTRON MICROSCOPIC CHANGES AND IMMUNOHISTOCHEMISTRY [30,31,32]

Electron microscopic changes in the perivascular zone of both unaffected and affected skin showed rich infiltrate of CD4+ cells and CD1a+ cells, in the progressive phase of AA. In the stabilized phase the infiltrate was scanty, both in unaffected and affected skin and limited to the peribulbar area.

Receptors of adhesion molecules (ICAM-2, ELAM-I, LFA-1) were strongly expressed, mainly at the microvascular level in both unaffected and affected skin in the progressive phase, but were only weakly or not at all expressed in the stabilized phase, these adhesion molecules can mediate the adherence of leucocytes to endothelial cells and their subsequent trafficking into the dermis which probably is one of the first immunologic events. Ilaria ghersetich et al. concluded that an immunologic

process, apparently carried out by CD4+ lymphocytes and by dendritic CD1a+ and CD36+ cells, may play a key role at least in the early phase of the disease involving primarily microvessels and later on the bulbar area.

CLINICAL FEATURES [4, 33]

Alopecia areata is responsible for 0.7- 3% of patients seen by dermatologists. All races are affected, one study showed equal sex incidence[34.] AA can occur at any age from birth to the late decades of life. Congenital cases have been reported. Peak incidence appears to occur from age 15-29 years.

Alopecia areata most often is asymptomatic, but some patients (14%) experience a burning sensation or pruritus in the affected area. The characteristic lesion of AA is commonly a round or oval; totally bald, smooth patch. The condition usually is localized when it first appears. Alopecia areata most often affects the scalp however, it can affect any hair-bearing area. More than one area can be affected at once.

The following forms are commonly seen

- ***Patchy AA*** – Most common type, characterised by round or oval patches of hair loss.
- ***Reticular AA*** – Reticulated pattern of patchy hair loss.
- ***Oophiasis band like AA*** – Hair loss in the parietal temporal – occipital scalp.
- ***Oophiasis inversus (Sisapho)-*** a rare band like pattern of hair loss in the frontal parietotemporal scalp (the exact opposite of oophiasis).
- ***Diffuse AA*** – A diffuse decrease in hair density over the entire scalp.

By the extent of involvement, the following types may be seen.

- ***Alopecia areata*** – Partial loss of scalp hair
- ***Alopecia totalis*** – 100% loss of scalp hair
- ***Alopecia universalis*** – 100% loss of hair on scalp and body.

Ikedas' has categorized AA into 4 types[31] as follows

- ***Type 1*** – The common type. Accounts for 83% of patients, mainly between age of 20 and 40 yrs. The condition usually lasts less than 3 yrs. Individual patches tend to regrow in less

than 6 months and only about 6% of patients progressed to alopecia totalis.

- ***Type 2*** – The atopic type. Accounts for 10% of patients. The onset is usually in childhood and the disease runs a lengthy course were individual patches tends to persist a year and alopecia totalis developed in 75%.

- ***Type 3*** – The prehypertensive type: Accounts for 4% of patients, occurs mainly in young adults. The disease runs a rapid course with an alopecia totalis in 39% of patients.

- ***Type 4*** – The combined type (5%) occurred mainly in patients over 40 years of age. The disease runs a prolonged course with alopecia totalis developing in about 10% of patients only.

A frequent feature of an AA patch is “exclamation mark” that may be present at its margin[3]. The presence of exclamation point hairs /easily extractable short broken hairs (ie. hairs tapered near proximal end) is pathognomonic but is not always found. A positive result from the hair pull test at the periphery of a patch usually indicates that the disease is active, and further hair loss can be expected.

A hand lens shows that at the margin, the free ends are splayed, giving a frayed appearance. Even the apparently normal terminal hair, found within the patches, may show one or more constrictions in their shaft. Shuster has described the coudability sign (to differentiate diffuse AA from other diffuse alopecia), in AA, a normal looking hair kinks at angle of 45 degree when forced inwards, the kink being situated 5 – 10 mms above the surface[35.]

COURSE OF ALOPECIA AREATA

AA runs a highly unpredictable course. The initial patch may regrow within a few months, or further patches may appear after an interval of 3 to 6 weeks and further patches may appear in a cyclical fashion at varying intervals. A succession of discrete patches may rapidly become confluent by the diffuse loss of remaining hair. Diffuse hair loss also may occur over a part or whole of the scalp without the development of bald patches. Patients with sudden diffuse onset of AA would appear to "go white" over the course of a few days. Re- growth is often at first, fine and unpigmented but usually the hair gradually resume its normal caliber and colour. Persistent depigmented hair regrowth from the site of AA has also been reported[36..]

ASSOCIATED CLINICAL SIGNS[4,13,30]

NAIL CHANGES

One of the clinical features of alopecia areata is aberrant nail formation. This feature is found in almost 10% to 66% of people affected by this disease. Nail changes usually coincide with hair loss but may occur earlier or later than the hair shedding, by months or years. Finger nails are commonly involved. The commonest nail aberration is nail pitting – superficial, uniform minute pits arranged regularly along and across the nail giving a “Scotch Plaid” effect or coalescing into ripples. The disease causes irregular keratinization on the nails. These irregular keratins fall off from the nails leaving behind depressions or pits.

Other changes include thinning or thickening, onychorrhexis (brittle nails having vertical ridges, which sometimes split vertically and peel off), onychomadesis (proximal part of the nail separates from the nail bed, leading on to shedding), onycholysis, koilonychia punctuate or transverse leuconychia and red spotted lunula. Some others speculate the possibility of “twenty nail dystrophy sine alopecia”

HISTOLOGY OF NAIL CHANGES[4,13,30]

Both, light and electron microscopy show that the disease affects the upper or the proximal part of the nail plate in a major way, the lower or distal part in a minor way while the subungal or the nail bed is largely spared which suggests a deep disorder of the matrix keratinization.

EYE CHANGES[37,38]

Keratoconus, cataract are the most common eye changes reported in association with AA. Other reported eye anomalies include Horner's syndrome, ectopia of the pupil, iris atrophy or tortuosity of the fundal vessels.

DIAGNOSIS

Diagnosis usually can be made on clinical grounds. Examination of hair from the margins reveal "exclamation mark hair", coudability sign helps in the diagnosis. A scalp biopsy seldom is needed, histology can be used to corroborate the diagnosis. Trichogram reveals a mixed telogen dystrophic pattern. Telogen hair predominates in slowly progressive patches and dystrophic anagen hairs form the majority in rapidly progressing disease. In alopecia areata, dermoscopy of active disease

shows yellow dots, dystrophic hairs, as well as cadaverized (black dots) and exclamation mark hairs. The presence of numerous yellow dots is a specific feature of alopecia areata, occurring in 95% of patients in all stages of the disease[39,40.]

Complete hemogram, motion examination, ear, nose, throat and dental examinations are done to rule out any foci of sepsis. Potassium hydroxide wet mount of hair root is examined to rule out tinea capitis and serological test is done to rule out syphilis. Random blood sugar and serum levels of thyroid hormones may be of use and may be done in suspected cases[1,30,37.]

DIFFERENTIAL DIAGNOSIS[1,30,37]

AA has to be differentiated from the following conditions.

Trichotillomania -Alopecic patches have broken hairs seen at varying levels; no inflammation or epidermal change occurs. A scalp biopsy can be helpful if the diagnosis is difficult clinically.

Tinea capitis - The diagnosis is suggested by crusting, erythema rarely and interspersed areas of broken stubs of hair and scaling with dry

lustreless hair together giving appearance of grey patch and black dot locally on the scalp. Hair root examination in KOH wet mount helps in ruling out the condition.

Telogen effluvium - believed to be associated with high fever, severe emotional stress, sudden starvation, certain medications and predominantly consist of telogen hairs. Other conditions associated with diffuse alopecia (to be ruled out in diffuse AA) include acrodermatitis enteropathica, arsenicism and thallium poisoning, though these conditions usually have systemic symptoms[41].

Secondary syphilis - It is a moth eaten alopecia with positive serological test.

Androgenetic alopecia – Hair loss is patterned and usually is slowly progressive rather than acute.

Congenital triangular alopecia – characterized by a triangular area overlying the frontotemporal suture just inside the anterior hair line with its base directed forward which is completely bald or covered by sparse vellus hair[42].

Alopecia neoplastica - a rare form of alopecia, is associated most commonly with breast cancer; it may resemble localized alopecia areata, a biopsy usually clinches the diagnosis[43,44]

Scarring alopecia and post traumatic alopecia: These can be differentiated by the absence of follicular ostia or some degree of atrophy. Systemic lupus erythematosus may also at times resemble alopecia areata.

PROGNOSIS

Alopecia areata prognosis will vary from person to person. The prognosis is good in case of common simple form of AA in which the hair loss is confined to the scalp and has got a high natural remission rate.

The following are indicators of poor prognosis - Child with atopy, patients with Down's syndrome, alopecia totalis or alopecia universalis, involvement of more than 50% of the scalp, oophiasis and reticular pattern, bilateral

loss of eyebrow and eyelashes, severe nail changes and when associated with autoimmune disorders.

TREATMENT[1,37]

Treatment is not mandatory because the condition is benign, and spontaneous remissions and recurrences are common. Treatments used are believed to stimulate hair growth, but no evidence indicates they can influence the ultimate natural course of alopecia areata. Treatment modalities are usually considered according to the extent of hair loss and the patient's age. An unpredictable course and heterogenity of the disease leads to varying results being obtained with the same therapy. The various modalities can be classified as follows,

1. Topical therapy
2. Systemic therapy
3. Others

TOPICAL THERAPY includes

1. ***Immunosuppressants***[37,45] – corticosteroids: with or without occlusion, intralesional steroids, nitrogen mustard.
2. ***Contact sensitizers*** – SADBE, DNCB, Diphencyprone
3. ***Irritants*** – Anthralin, phenol, salicyclic acid, sulfur, oil of cade, cantharidin, croton oil, tretinoin
4. ***Photochemotherapy*** – topical PUVA, turban PUVA
5. ***Cryotherapy*** – liquid nitrogen
6. ***Laser therapy*** – Excimer laser (308nm), pulsed infrared diode laser(904nm)
7. ***Other topical modalities*** – topical tacrolimus, imiquimod, topical minoxidil.

SYSTEMIC THERAPY

1. ***Immunosuppressants*** - corticosteroids, cyclosporine

2. ***Immunomodulators*** – Alefacept, Isoprinosine (inosiplex), systemic psoralen etc.

3. ***Photochemotherapy*** – whole body PUVA

4. ***Miscellaneous*** – sulfasalazine, IV Ig

OTHERS

1. ***Psychotherapy*** – hypnotherapy, systematic desensitization

2. ***Supportive therapy*** – Dermatography (tattooing), wigs

3. ***Investigational therapy*** – Recombinant human bone morphogenetic protein, intralesional candida antigen[46].

TOPICAL THERAPY

The mode of action and effects are as follows.

Immunosuppressants - Topical steroids of class 1 to 5 are effective in alopecia areata, but takes several months for elicitation of hair growth. They can be either used with or without occlusive dressing. Most of the studies have used flucinolone and halcinonide. Side effects include folliculitis, hypertrichosis, acneiform eruptions, local atrophy or chronic dilatation of capillaries leading to red blotchy patches. Before being used in the periocular region, a preliminary eye examination or regular follow up examinations must be done for glaucoma and cataract. Children requiring high doses of class I or class II topical corticosteroids need to be monitored to control systemic side effects.

Intralesional steroids[47,48,49] - Depot corticosteroid injected intralesionally stimulates hair regrowth

at the site of injection. Hydrocortisone acetate (25 mg mL[-1]) and triamcinolone acetonide (5-10 mg mL[-1]) are commonly used. Corticosteroid is injected just beneath the dermis in the upper subcutis. A 0.05-0.1 mL injection will produce a tuft of hair growth about 0.5 cm in diameter. Treatment is repeated every 4 – 6 weeks. Intralesional steroids are administered with a needleless device (dermajet)/ tuberculin syringe or insulin syringe. Repeated injection at the same site or the use of higher concentrations can lead to reversible local, perilesional, or perilymphatic atrophy or systemic toxicity. Risk of cataract and raised intraocular pressure is high if intralesional corticosteroids are used close to the eye. Rarely anaphylaxis and amaurosis have been reported. Intralesional corticosteroids is of little practical value if hair loss is extensive.

CONTACT SENSITIZERS [4,37,50,51,52,53]

Topical immunotherapy is the most effective and accepted modality in the treatment of AA. The mechanism of action of local sensitizers is by immunomodulation. There is a decrease in the peribulbar CD4+/CD8+ lymphocyte ratio, a shift in the position of T lymphocytes away from perifollicular areas to the inter follicular areas and dermis. The following are the two concepts of local immunomodulation, they are that effector T cells are attracted in that area. There is probably a localized antigen competition occurring and that repeated application activates nonspecific suppressor responsible for AA. Three contact sensitizers used are squaric acid dibutyl ester(SADBE), dinitrocholorbenzene (DNCB) and diphenylcyclopropanone (DPCP). SADBE or DPCP are widely used immunogen though DNCB has be reconsidered as its been used for treatment of chronic resistant cases of AA. SADBE is not found in the natural environment, doesn't cross react with other chemicals and is not mutagenic. The disadvantage is that it is not stable.

Diphenylcyclopropenone[53] (DPCP) is also an accepted modality for treatment of severe AA. One study demonstrated a 70% response rate in DPCP-treated patients with severe alopecia areata affecting more than

40% of the scalp. Pruritus, dermatitis, urticaria, face and scalp edema and the development of vitiligo are known side effects of DPCP use.

DNCB[50,52] powder is dissolved in acetone and diluted in appropriate concentrations of 0.001%, 0.01%, 0.05%, 0.1%, 0.5%, 1%, 1.5% and 2% solutions. Solution is stored in dark bottles until use in room temperature. DNCB is applied using cotton buds. Sensitization done by applying 2% DNCB over 4 x 4 cm area on back during the first visit. After 2 weeks, weekly applications of DNCB is continued starting with lowest concentration (0.001%) to the affected area of hair loss. Patients are advised to avoid washing the area and to protect it from sunlight for 48 hours. Applications of DNCB are repeated weekly with increasing concentrations. The aim of the treatment is to maintain a low grade tolerable erythema and pruritus on the treated side for 24 to 36 hrs after application. Mild to moderate eczema was maintained by titrating the DNCB concentrations. Untoward effects includes eczematous reactions with or without blistering or extension of allergic contact dermatitis to other areas, itching and oedema of the face and scalp, regional lymphadenopathy and post inflammatory hyperpigmentaion or hypopigmentatiton. Contact urticaria, vitiligo and erythema multiforme have also been reported. Contact sensitizers are contraindicated during

pregnancy. Once hair growth is established on one side the next side is treated. If there was no sensitivity even after 12 weeks, it was considered as treatment failure and the patient can be withdrawn.

IRRITANTS

Anthralin[30,54] – Anthralin has been used in treatment of AA in concentration of 0.25 to 1.0%. It may have a non- specific immunomodulating effect in eliciting hair growth. Short contact therapy is effective and cosmetically acceptable regrowth has been reported to vary from 20 to 25%. Anthralin 0.5% to 1% cream may be applied overnight or as a short contact therapy initially for 30 mins and gradually increased to one hour with 1% anthralin cream. When therapy is effective new hair growth is seen usually within 3 months. It may take 24 or more weeks for cosmetically acceptable response. Anthralin is a good choice for children. Adverse effects include irritation, scaling, folliculitis and regional lymphadenopathy. Patients should be advised to protect treated area from sunlight, avoid getting anthralin into the eye and be warned about staining of the treated skin and clothes that come in contact with anthralin.

Onion Juice[55] – Sharquie KE et al showed in a study that the use of crude onion juice gave significantly higher results with regard to hair re-growth than did tap water and that it can be an effective topical therapy for patchy alopecia areata. In his study patients were advised to apply the crude onion juice twice daily for two months. Re-growth of terminal coarse hairs started after two weeks of treatment. High amounts of sulphur in onions make them particularly effective in regenerating hair follicles and stimulating hair regrowth. In addition, naturally-concentrated sulphur compounds have been proven to show additional hair-restoring function.

Tretinoin[56,57] – Retinoids are normally used in the treatment of acne vulgaris, however has more recently been used in the treatment of both Alopecia areata and Androgenetic alopecia. Topical tretinoin appeared to enhance the hair growth producing effect of the intralesional

triamcinolone. Tretinoin helps to normalize cell differentiation, and the familiar retinoid dermatitis may contribute to the stimulation of hair growth by creating an immune response. It also acts through inhibition of toll like receptors -2 and hence reduces the inflammation. Usually retinoids in a gel form is rubbed on the area of hair loss. The gel works best when used in combination with topical Minoxidil. It is suggested that Minoxidil be applied in the morning and retinoids in the evening due to the fact that retinoids increase the skin's sensitivity to sunlight.

PHOTOCHEMOTHERAPY

Topical Puva Therapy [58,59] – Orally administered PUVA therapy has been one among the numerous available modalities in the treatment of alopecia areata. The use of oral PUVA is often limited by systemic side effects. Hence PUVA has been used topically. It has also been used in the form of turban, where towels soaked in 0.0001% of 8 methoxy

psoralen are wrapped around the patients head in a turban fashion, for a period of 20 mins and then it was followed by UVA irradiation.

PUVA therapy results for alopecia areata are highly varied – the major problem with PUVA is the high relapse rate. Circumscribed lesions respond better than total alopecia and total body PUVA is probably more effective than local irradiation. Follow up studies of large group of patients have shown that PUVA in general is not an effective treatment options.

CRYOTHERAPY

Liquid Nitrogen[60] – Liquid nitrogen is an efficient, simple, cheap modality of therapy without any troublesome side effects which relies on the induction and maintenance of skin inflammation by repeated application of an irritant. Lei et al used a cotton swab dipped in liquid nitrogen to the patches of AA, for 2 freeze thaw cycles of 2 to 3 seconds at an interval of 2 to 3 seconds. This treatment was repeated once weekly for 4 to 6 weeks and new hair growth was noticed in over 60% of the areas involved. Mechanism of action of liquid nitrogen may be due to improved blood circulation to the hair follicles thus promoting nutrition and acceleration of hair growth. The adverse effects noted were

insignificant and included mild swelling, hyperesthesia and mild itching in the treatment area for a few hours following treatment.

OTHERS

Topical Tacrolimus[61,62] –Initial trials of tacrolimus were promising and has induced anagen phase of hair growth.

Topical Minoxidil[63,64,65,66] – (2– 4 Diamino 6 piperidino pyrimidine 3 oxide) minoxidil is a powerful vasodilator. It causes direct relaxation of arteriolar smooth muscle with little effect on venous capacitance. Its effect on alopecia areata is by stimulation of DNA synthesis in hair follicles. It has direct effect on the proliferation and differentiation of keratinocytes invitro and regulates hair physiology independently of blood flow influences. Cosmetically acceptable hair growth has been reported in 20 to 45% of the patients. It is probably not effective in alopecia universalis and totalis. Side effects are rare and include local irritation, allergic contact dermatitis and facial hair growth.

Encouraging results have been obtained with xenon chloride excimer laser (308 nm) and pulsed infrared diode laser (904nm)[1]

SYSTEMIC THERAPY[1,30,37,67]

Systemic Steroids – Probably have a role in controlling the spread of the disease. They are very effective but its use is reduced due to its adverse effects. Pulse therapy have been used in the treatment of AA. Systemic steroids have been used in the following regimens:

1. Methyl prednisolone – (i.v) 500mg/day for 3 consecutive days or 5 mg/kg body weight b.i.d for 3 days every 4 weeks

2. Prednisolone 40 – 60 mgm and to taper by 5 mgm every week/ some recommend oral monthly pulse of 300mg[68]

3. Oral minipulse therapy – Dexamethasone 5 mg twice weekly on two consecutive days for 3 to 6 months, 2.5 – 3.5 mgm for children less 12 years.

PUVA[69]

Oral PUVA has been used in the treatment of alopecia areata. Claudy et al proposed that PUVA acts through systemic immunomodulation they also suggested that oral methoxsalen and whole body PUVA were more useful than local PUVA therapy. However over

the long term use PUVA produced cosmetically acceptable results only in 10% of the cases.

OTHER SYSTEMIC MODALITIES

Sulfasalazine – [70] It acts through inhibition of chemotaxis and synthesis of various cytokines and antibodies. Ellis et al found it to be efficacious and proposed that it should be started at 500mg/day and gradually increased by 500mg weekly to reach a daily dose of 3 g to be continued for atleast four months. Others include cyclosporine, inosiplex and intravenous immunoglobulin[71] for AA treatment.

In conclusion, the future therapeutic options include recombinant human bone morphogenetic protein as the latter is involved in hair morphogenesis and certain biologicals like efalizumab, humanized monoclonal anti- CD11a antibody also show promising future.

AIMS OF STUDY

The aims of the present study was

1. To study the efficacy of various modalities of treatment & to compare them with one another.

2. To study the adverse effects of the various modalities used.

The various modalities of treatment used in the present study were

i. Topical tacrolimus (0.03%)

ii. Topical tretinoin (0.025%)

iii. Topical minoxidil (2%)

iv. Topical anthralin (0.5%)

v. Intralesional steroids

vi. Topical crude onion juice

vii. Topical DNCB

viii. Topical steroid 0.1% betamethasone ointment

ix. Cryotherapy with liquid nitrogen.

x. Control group

MATERIALS & METHODS

Patients presenting with AA to the Dermatology Department of our hospital during the study period August 2007 to September 2009 were recruited for the study. A diagnosis of AA was made on clinical grounds, based on the following criteria.

Asymptomatic, well circumscribed, smooth, non scaly, non scarring patch of hair loss on the scalp. Mycology opinion & fungal scraping from the patch was done to rule out tinea capitis in doubtful cases. A thorough history was elicited with regards to the duration of symptoms, disease progression, history of past episodes, history of any topical/ systemic treatment, history suggestive of any psychiatric disturbances & septic foci, a personal & family history of atopy, other dermatoses, diabetes mellitus, hypertension and history suggestive of any other autoimmune disease were also elicited.

A meticulous general & systemic examination was performed. Complete dermatological examination was performed taking care to note any other dermatosis in the patient. Nail changes and mucosal changes were noted.

The location of the patches of AA, with reference to the size, presence of hair in the patches was also made. The presence of exclamation hair mark, coudability sign & pluckability of hair at the margins was also recorded. Presence of erythema & scaling if present at the margins of the patch were noted.

A complete hemogram, ENT & dental opinion to rule out septic foci was carried out in all the patients & RBS in adults was done. The individual with history of exposure to the risk of STD were subjected to a blood VDRL examination.

After completing the examinations & making the necessary exclusions (children < 12 years, pregnancy) 100 patients were taken in the

therapeutic study & were allocated treatment randomly. Before starting the therapy appropriate treatment of focal sepsis if any were given to patients. The patients were divided into ten groups comprising 10 in each group & the following therapy was instituted.

GROUP 1: PATIENTS SUBMITTED FOR TOPICAL TACROLIMUS 0.03%

Ten patients comprising the 1st group were treated with topical tacrolimus 0.03%, patients were advised to apply it daily every night over the AA patches. Patients were asked to continue the treatment until acceptable hair growth occurred or till the end of the study period that is 3 months.

GROUP 2: PATIENTS TREATED WITH TOPICAL TRETINOIN 0.025%

Ten patients were treated with topical tretinoin (0.025%). Patients were asked to apply

it topically over AA patch only during night and were followed up till the end of study period.

GROUP 3: PATIENTS TREATED WITH 2% MINOXIDIL

10 patients were treated with 2 % topical minoxidil, the patients were advised to apply few drops evenly over the patches not exceeding by 1ml/day twice daily and followed up till the end of the study period.

GROUP 4: PATIENTS TREATED WITH 0.5% TOPICAL ANTHRALIN

10 patients were treated with 0.5% topical anthralin. A short contact therapy was used. Patients were advised to apply a small quantity of 0.5% anthralin initially for 10 mins & subsequently the contact period was increased to 30 mins. After 30 mins the ointment was removed with a cotton swab followed by hair wash. Patients were cautioned to wash hands after applying anthralin, to protect the treated skin

against sun exposure and to be aware of staining clothes and linen.

GROUP 5: PATIENTS TREATED WITH INTRALESIONAL STEROID

10 patients were treated with monthly injection of steroid intralesionally in the AA patch. Patients were reviewed monthly before the next injection for any side effects and injection was given till acceptable hair growth occurred during the study period.

GROUP 6: PATIENTS TREATED WITH CRUDE ONION JUICE

10 patients were treated with onion juice. Patients were applied with extract of crude onion juice over the AA patch till the period of study.

GROUP 7: PATIENTS TREATED WITH TOPICAL DNCB

Ten patients were treated with topical DNCB. Initially 2% concentration of DNCB in acetone solution was applied to a small area and was

advised for photoprotection for 48 hrs & to wash it off after that. Two weeks later the scalp is painted with a weak solution of DNCB, starting at 0.001% and this is repeated at weekly intervals. The concentration is increased at each treatment until a mild dermatitis reaction is obtained. The frequency of treatment is reduced after the growth has been obtained and discontinued after 6 months if no positive response occurs.

GROUP 8: PATIENTS TREATED WITH TOPICAL 0.1% BETAMETHASONE OINTMENT

Ten patients were treated with topical steroid ointment containing betamethasone & were advised to apply it at night until acceptable hair growth occurred or until end of the study.

GROUP 9: PATIENTS SUBMITTED FOR LIQUID NITROGEN THERAPY

Ten patients 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 every week, until acceptable hair growth occurred or till the end of the study period that is 3 months.

GROUP 10: PATIENTS SUBMITTED FOR PLACEBO

Ten patients were not given any specific treatment (only multivitamins).

Al the patients were reviewed once in 15 days for 3 months and were graded as follows.

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) Complications of therapy like

a. burning and irritation

b. erythema

c. vesiculation

d. pigmentary changes

e. folliculitis

f. atrophy etc. were also recorded.

Response grading to therapy was in the following manner.

0 – 25%	A	Hair regrowth covering < 25% of the patch. Vellus regrowth was not taken into account. Very poor response
25 – 50%	B	Hair regrowth occurs, but is not cosmetically acceptable to the patients. Poor response
50 – 75%	C	The hair regrowth is cosmetically acceptable and cover 3/4th of the patch. Moderate response
75 – 90%	D	The hair regrowth covered almost all of the patch, but the hair was not of similar density to the surrounding hair. Good response
90	E	Complete regrowth of hair, which is

-100%		indistinguishable from the surrounding area. Excellent response

For the purpose of statistical analysis, comparison & interpretation patients with excellent, good & moderate response were considered to be improved and those patients with very poor and poor response were considered to be not improved. Also a mean score for each response were allotted as follows: (Table No:12)

A – 1, B – 2, C – 3, D – 4 & E – 5.

OBSERVATIONS

An analysis of the clinical profile of the patients recruited for the therapeutic response revealed the following data.

There were 40 females & 60 males in the study groups.

The age of the patient ranged from 13 to 50 years and the average age is 27.72 years.

The duration of the disease ranged from one week to 4 years, average duration being 4.7 months.

5 patients had a family history of atopy. There was a personal history of atopy in 20 patients in the form of allergic rhinitis, urticaria (11), pitryiasis alba in one patient.

A thorough history and examination revealed rheumatic mitral stenosis in one patient and valvotomy was done for this patient, one had

hyperthyroidism with PCOD, one patient had history of TB and another one had oral submucosal fibrosis. Almost all the patients had single episode except for 12 patients who had >1 episode. In addition to the family history of atopy recorded earlier 12 & 5 patients had family history of DM and hypertension.

Examination of the patches of AA revealed the following:

The number of patches varied from 1 to 8, the average being 1.8. The size of the smallest patch was 0.5cm and the size of the largest patch was 6 X 6 cm. The coudability sign and exclamation mark hair were positive only in 3 patients.

The regionwise distribution of the patches were occipital (34), parietal (24), frontal (29) and temporal (20). The nail changes noticed were pitting in 13 patients, leuconychia in 10, linear grooves in 5, melanonychia in 3 patients. Two patients had hyperpigmentation of oral mucosa.

Other associated dermatological manifestations were tinea corporis, pityriasis versicolor, psoriasis, lichen planus and seborrheic dermatitis in 3 patients. Clinical examination of focal sepsis revealed chronic gingivitis in 22 patients, dental caries in 24 and pharyngitis in 2 patients.

OBSERVATION OF THERAPEUTIC RESPONSES

GROUP I: RESULTS OBTAINED WITH TOPICAL TACROLIMUS 0.03%.

Among the 10 patients treated with tacrolimus, 3 patients showed excellent response & 2 patients each showed good & moderate response. Poor response was seen in 2 patients and very poor response in one patient (Table no:1) Regrowth of hair started after 2 weeks in one, after 4 weeks in 3 patients with excellent response. Patients with very poor response showed no growth at all except for vellus growth of hair which was poor during the entire study period. One patient with excellent response had developed

new patches elsewhere.

Gp I: (TABLE NO: 1) CLINICAL PROFILE OF PATIENTS ON TOPICAL TACROLIMUS (n=10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	24	14	33	41	19	34	13	31	27	15
Sex	M	F	M	M	M	M	F	M	M	F
No. of patches	3	2	1	2	1	1	1	1	1	1
Dur. (months)	5	12	1	6	8	7	1wk	2	6	4
Cum. resp.	E	E	D	E	D	C	C	B	B	A

The untoward effect noticed by the patient were transient burning sensation, others include mild erythema & headache, but this resolved later after continued application.

GROUP II: RESULTS OBTAINED WITH TOPICAL TRETINOIN (0.025%)

Moderate regrowth of hair occurred in three out of 10 patients in this group. Excellent and good response were seen in one patient each. Two patients showed very poor response and three patients showed a poor response (Table no: 2). In

patients with excellent response, regrowth started after 2 weeks & was complete by 14 weeks. In patients with good and moderate response regrowth started at 4 weeks. In patients with poor and very poor response regrowth started at 10 wks. Only one patient showed extension of the existing lesion during the study period.

Gp II: (TABLE NO:2) CLINICAL PROFILE OF PATIENTS ON TOPICAL TRETINOIN (n=10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	13	30	50	21	27	42	32	35	30	26
Sex	F	F	F	M	M	M	F	F	F	F
No.of patches	2	3	2	1	2	1	2	1	1	2
Dur. (months)	6	5	12	8	3	1	1	2	5	2
Cum. Res.	B	A	E	C	D	C	C	B	A	A

Four patients reported mild burning sensation in the patches on sun exposure alone & these patients were advised sun protection.

GROUP III: RESULTS OBTAINED WITH 2% MINOXIDIL

Acceptable regrowth of hair occurred in 9 out of 10 patients in this group. Excellent response was seen in four patients, good response in three, moderate response in two patients and very poor response in one (Table no: 3)

Gp III: (TABLE NO:3) CLINICAL PROFILE OF PATIENTS ON 2% MINOXIDIL (n=10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	26	26	24	38	28	22	12	45	40	20
Sex	M	M	M	F	M	F	F	M	F	F
No. of patches	1	1	2	1	1	1	1	1	1	1
Dur. (months)	5	2	5	6	3	2	0.5	3	2	3
Cum. Res.	E	D	E	E	D	D	E	C	C	A

Regrowth of hair occurred at the end of 2 weeks in two patients with excellent response & after 4 weeks in two patients. All the patients showed complete hair regrowth at the end of 12 weeks. Patients with good response showed hair regrowth after 4 weeks. In one of the patient with moderate response, though the patch showed

complete hair growth, the patches continued to increase in size at the margins, in the other 2 patients with moderate response regrowth was noticed at 8 wks. The patient with very poor response did not show any evidence of hair regrowth & the patch was in beard region.

None of the patients complained of any adverse effects to the medication nor were any signs of irritation noticed during the follow up period.

GROUP IV: RESULTS OBTAINED WITH 0.5% ANTHRALIN:

Acceptable regrowth of hair occurred in four out of ten patients in this group, excellent response was seen in two patients, good response in one, moderate and poor response one each and very poor response was seen in five patients (Table no: 4).

Gp IV: (TABLE N0:4) CLINICAL PROFILE OF PATIENTS ON 0.05% ANTHRALIN (n = 10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	12	32	36	25	35	25	15	52	14	28
Sex	F	M	F	M	F	F	M	F	M	M
No.of patches	8	1	2	1	3	1	1	1	1	1
Dur. (months)	12	3	6	0.5	4	1	1.5	3	12	1
Cum. Res.	A	A	E	A	A	B	D	E	C	A

In the patient showing excellent response, hair regrowth started at 4 to 6 weeks with gradual increase in thickness of the hair. Patient with good response showed hair regrowth after 4 weeks. In the patient with poor response the hair started regrowing only at 6 weeks & it was vellus hair that growed initially. Patients with very poor response showed no regrowth at all.

The main adverse effect noticed was staining of the area of alopecia & stinging sensation. One patient developed folliculitis & patch edema.

GROUP V: RESULTS OBTAINED WITH INTRALESIONAL STEROIDS

Acceptable regrowth was seen in nine out of ten patients. In this group 5 patients showed excellent response; four showed good response; rest each one patient showed moderate & poor response (Table no:5)

Gp V: (TABLE NO:5) CLINICAL PROFILE OF PATIENTS ON INTRALESIONAL STEROIDS (n=10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	45	17	10	25	26	35	16	32	33	16
Sex	M	M	M	M	M	M	F	F	M	F
No.of patches	1	2	2	1	1	1	3	2	1	2
Dur. (months)	2	6	2	2	5	3	3	4	2	2
Cum. Res.	E	E	D	B	E	E	D	D	E	D

All the five patients with excellent response & one patient with moderate response showed hair regrowth after 4 weeks. Out of four patients with good response two patients showed appearance of new patch when on treatment.

Patient with a poor response developed local atrophy at the injection site following a single session. Most of the patients showed hair regrowth after single injection of intralesional steroid but cosmetically acceptable results were obtained after two sessions.

GROUP VI: RESULTS OBTAINED WITH ONION JUICE:

Among the 10 patients treated with onion juice one patient showed excellent response, three showed good response, two showed moderate response and two of each patient showed poor and very poor response (Table no: 6). In patient with excellent regrowth the hair growth started at 4 weeks. Acceptable regrowth was seen in five patients with growth starting after 2 weeks.

Patients with poor and very poor response showed fine vellus hair at the end of the study period. The main adverse effect that was noted is contact dermatitis, two patients showed erythema and scaling. One showed few areas of hypopigmentation within the patch.

Gp VI: (TABLE NO: 6) CLINICAL PROFILE OF PATIENTS ON CRUDE ONION JUICE (n=10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	41	30	21	28	35	30	32	25	42	18
Sex	M	M	M	F	M	M	F	M	M	M
No. of patches	1	1	1	2	2	1	2	1	1	1
Dur. (months)	2	3	2	4	3	1	5	2	3	4
Cum. Res.	D	C	B	D	D	B	A	C	A	E

GROUP VII: RESULTS OBTAINED WITH TOPICAL DNCB

Out of ten patients excellent response was seen in two patients, two patients each showed good and moderate response and three patients showed poor response and one showed very poor

response (Table no: 7). Patients with excellent response showed regrowth after 4 weeks, and the effect was sustained till the patient was followed up in the study period. One patient with good response had occurrence of new lesion elsewhere on the scalp during the course of treatment. One patient with oophiatic pattern showed no growth at all. Patients with poor response showed few fine vellus hair regrowth.

GpVII: (TABLE NO:7) CLINICAL PROFILE OF PATIENTS ON DNCB (n=10)

Case no.	1	2	3	4	5	6	7	8	9	10
Age	38	30	40	35	28	16	26	32	45	37
Sex	M	M	M	M	M	M	M	F	F	F
No.of patches	AU	O	2	2	8	1	2	3	2	1
Dur. (months)	24	84	6	4	2	3	0.5	2	2	1
Cum. Res.	B	A	D	C	B	D	E	B	E	C

The commonest side effect encountered was burning sensation. Two patients had mild erythema at the site of application. Lymphadenopathy was seen in one patient.

GROUP VIII: RESULTS OBTAINED WITH TOPICAL 0.1% BETAMETHASONE OINTMENT

Acceptable regrowth of hair occurred in six out of ten patients in this group. Three patients showed excellent response, two showed good response and one showed moderate response, poor and very poor response was seen in one patient each (Table no:8)

Gp VIII: (TABLE NO:8) CLINICAL PROFILE OF PATIENTS ON 0.1% BETAMETHASONE

Case no.	1	2	3	4	5	6	7	8	9	10
Age	14	30	29	30	18	13	31	18	18	12
Sex	F	M	M	M	F	F	F	F	F	F
No. of patches	2	1	2	3	1	2	3	2	3	1
Dur. (months)	24	1	3	3	3	12	2	3	3	3
Cum. Res.	B	C	E	A	E	B	D	B	E	A

In all the three patients with excellent response, regrowth started after 2 weeks and in one of them it was complete by 12 weeks. In patients with good and moderate response regrowth started at 4 weeks. In patients with poor and very poor response, regrowth started only at 8 weeks. One patient with diffuse type of AA the response was very poor.

No adverse effects of the therapy were noticed on observation or reported by the patient during the study period.

GROUP IX: RESULTS OBTAINED WITH CRYOTHERAPY

Acceptable regrowth occurred in nine out of 10 patients of whom excellent response was seen in five patients, good response in one patient and moderate response in two patients. Each of one patient showed poor and very poor response (Table no:9)

Gp IX: (TABLE NO: 9) CLINICAL PROFILE OF PATIENTS ON CRYOTHERAPY (n=10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	33	28	25	15	30	10	40	28	40	35
Sex	M	M	F	F	F	F	M	M	M	M
No. of patches	1	1	3	4	2	3	1	1	5	1
Dur. (months)	3	6	0.5	6	1	0.75	6	6	3	2
Cum. Res.	D	E	E	E	E	C	A	E	C	B

In patients with excellent response regrowth of hair started after 2 weeks in one, and after 4 weeks in three. In the patient with very poor response the regrowth was noticed only at 8

weeks. Patient with good response showed increase in size of the patch initially. New patch was noticed in patient with moderate response.

The side effect commonly reported by the patients were burning, stinging sensation at the time of LN application. One of the patient developed depigmentation at the site of application. Patient with a poor response showed sparse vellus hair.

GROUP X: RESULTS OBTAINED WITH CONTROL GROUP

Out of the ten patients two patients showed acceptable regrowth. One patient each showed moderate response. Most of the patients showed no hair regrowth at all even after completion of the study period (Table no:10). Two patients showed fine vellus hair regrowth. One patient with moderate response showed hair regrowth only after 6 weeks. One patient of this group complained of itching at the site of the patch.

Gp X: (TABLE NO:10) CLINICAL PROFILE OF PATIENTS ON PLACEBO (n = 10)

Case no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Age	35	21	18	36	31	31	29	30	18	25
Sex	M	F	F	M	M	M	F	F	F	M
No of patches	2	1	4	2	1	2	2	1	1	1
Dur. (months)	6	2	6	12	12	5	3	3.5	2	3
Cum. Res.	B	B	A	A	A	C	A	C	B	A

TABLE NO: 11 COMPARISON OF PROPORTION OF IMPROVEMENT AMONG DIFFERENT STUDY GROUPS

Group	Improved		Not improved		Overall P-Value*	Significant groups at 5% level[$]
	No	%	No	%		
I	7	70	3	30	0.03 (Sig.) [$X^2 = 18.51$, d. f. = 9]	III vs. X V vs. X IX vs. X
II	5	50	5	50		
III	9	90	1	10		
IV	4	40	6	60		
V	9	90	1	10		
VI	6	60	4	40		
VII	6	60	4	40		
VIII	6	60	4	40		
IX	8	80	2	20		
X	2	20	8	80		

*Chi-square test was used to calculate the P-Value

[$]Chi-square with Yates' Continuity Correction or Fisher's Exact (2-tailed) was employed to identify the significant groups at 5% level.

TABLE NO: 12 RESPONSE OF HAIR REGROWTH IN TEN GROUPS WITH MEAN SCORE

Group	A=1	B=2	C=3	D=4	E=5
I	1	2	2	2	3
II	3	2	3	1	1
III	1	0	2	3	4
IV	5	1	1	1	2
V	0	1	0	4	5
VI	2	2	2	3	1
VII	1	3	2	2	2
VIII	2	2	2	1	3
IX	1	1	2	1	5
X	5	3	2	0	0

A = Very poor, B = Poor, C = Moderate, D = Good, E = Excellent

TABLE NO: 13 COMPARISON OF MEAN SCORE AMONG DIFFERENT STUDY GROUPS

Group	Mean ± S.D	Overall P value*	Sig.groups at 5% level$
I	3.4 ± 1.4	0.004 (Sig.)	III vs. X V vs. X
II	2.5 ± 1.4		
III	3.9 ± 1.3		
IV	2.4 ± 1.7		
V	4.3 ± 0.9		
VI	2.9 ± 1.4		
VII	3.1 ± 1.4		
VIII	3.1 ± 1.6		
IX	3.8 ± 1.5		
X	1.7 ± 0.8		

*Kruskal Wallis One Way ANOVA was used to calculate the P-value.

$ Mann-Whitney U – Test followed by Bonferroni Correction method was employed to identify the significant groups at 5% level.

TABLE NO: 14 COMPARISON OF PROPORTION OF

IMPROVEMENT AMONG DIFFERENT STUDY GROUPS – SINGLE

PATCH

Groups	SINGLE PATCH				P value*
	Improved		Not improved		
	No.	%	No.	%	
I	4	57.1	3	42.9	0.26 (N.S) [X^2 = 11.18, d. f. = 9]
II	2	50.0	2	50.0	
III	8	88.9	1	11.1	
IV	3	42.9	4	57.1	
V	5	83.3	1	16.7	
VI	4	80.0	3	42.9	
VII	2	66.7	1	33.3	
VIII	2	66.7	1	33.3	
IX	4	80.0	1	20.0	
X	1	20.0	4	80.0	

*Chi-square test was used to calculate the P-Value

TABLE NO: 15 COMPARISON OF PROPORTION OF IMPROVEMENT AMONG DIFFERENT STUDY GROUPS – MULTIPLE PATCH

Groups	MULTIPLE PATCHES				P value*
	Improved		Not improved		
	No.	%	No.	%	
I	3	100.0	0	0.0	
II	3	50.0	3	50.0	
III	1	100.0	0	0.0	
IV	1	33.3	2	66.7	0.26 (N.S.)
V	4	100.0	0	0.0	
VI	4	66.7	2	33.3	[X^2 = 11.30, d. f. = 9]
VII	4	57.1	3	42.9	
VIII	4	57.1	3	42.9	
IX	4	80.0	1	20.0	
X	1	20.0	4	80.0	

*Chi-square test was used to calculate the P-Value

TABLE NO: 16 COMPARISON OF PROPORTION OF IMPROVEMENT AMONG SINGLE PATCH AND MULTIPLE PATCH - ATOPICS

Patch	Improved		Not improved		P value*
	No.	%	No.	%	
Single	7	58.3	5	41.7	1.00 (N.S.)
Multiple	4	50.0	4	50.0	

*Fisher's Exact test (2-tailed) was used to calculate the P-Value

TABLE NO: 17 COMPARISON OF PROPORTION OF IMPROVEMENT AMONG SINGLE PATCH AND MULTIPLE PATCH – NON-ATOPICS

Patch	Improved		Not improved		P value**
	No.	%	No.	%	
Single	25	59.5	17	40.5	0.92 (N.S)
Multiple	24	63.2	14	36.8	

** Chi-square test with Yates' continuity correction was used to calculate the P value.

TABLE NO: 18 COMPARISON OF PROPORTION OF IMPROVEMENT BETWEEN ATOPICS AND NON ATOPICS

Patch	Improved		Not improved		P value***
	No.	%	No.	%	
Single	11	55	9	45	0.80 (N.S)
Multiple	49	61.2	31	38.5	

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***Chi-square test with Yates' continuity correction was used to calculate the P value.

TABLE NO: 19 COMPARISON OF MEAN AGE AMONG DIFFERENT STUDY GROUPS

Group	Mean ± S.D	Overall P value*	Sig. groups at 5% Level$
I	25.1 ± 9.7	0.31 (N.S.)	NIL
II	30.6 ± 10.4		
III	28.1 ± 10.1		
IV	27.4 ± 12.2		
V	25.5 ± 10.9		
VI	30.2 ± 7.8		
VII	32.7 ± 8.2		
VIII	21.3 ± 7.8		
IX	28.9 ± 8.8		
X	27.4 ± 6.6		

* One way ANOVA was used to calculate the P- value
$ Tukey – HSD procedure was employed t identify the significant groups at 5% level.

TABLE NO: 20 COMPARISON OF GENDER AMONG DIFFERENT STUDY GROUPS

Groups	Male		Female		Overall P value*
	No.	**%**	**No.**	**%**	
I	7	70	3	30	0.30 (N.S.) [X^2 = 10.71, d. f. = 9]
II	3	30	7	70	
III	5	50	5	50	
IV	5	50	5	50	
V	7	70	3	30	
VI	8	80	2	20	
VII	7	70	3	30	
VIII	3	30	7	70	
IX	6	60	4	40	
X	5	50	5	50	

*Chi-square test was used to calculate the P-Value

DISCUSSION OF THE THERAPEUTIC RESPONSES

GROUP I: PATIENTS TREATED WITH TOPICAL TACROLIMUS

Cosmetically acceptable regrowth of hair in otherwords improvement was noticed in seven out of ten patients in the present study. Out of 7 patients, three showed excellent response & two each showed good and moderate response.

A study[61,62] conducted by Vera and Price et al in Minneapolis where eleven patients treated with 0.01% tacrolimus showed no terminal hair growth even after 24 weeks. This is in contrast to our study where regrowth of hair was noticed after 6 weeks in six patients whereas 4 patients showed regrowth at 6 weeks.

All the three patients with excellent response had multiple patches & all the patients with good and moderate response had single

patches. Rest of the three patients with single patches, two showed poor response & one showed very poor response. This shows that patients improved with both single and multiple patches and hence no significance was noted with regard to number of patches. Patients with good, moderate, poor and very poor response had no personal or family history of atopy. One patient with excellent response developed new patches else where. This showed that though treatment was initiated it did not alter the course of the disease progression. One patient with moderate response had family history of hypertension and two patients with good response had chronic gingivitis and dental caries which was treated.

One patient with poor response had a minimum disease duration of one week & another patient with excellent response had a maximum duration of one year hence the disease duration doesn’t influence the outcome of the therapy.

With seven patients showing good improvement without any adverse effects it can be concluded that tacrolimus could be considered to be one of the treatment modality.

GROUP II: PATIENTS TREATED WITH TOPICAL TRETINOIN

Five out of ten patients improved in this group. Out of which one each showed excellent and good response & three showed moderate response. Hence 50% showed improvement and rest 50% did not show any improvement. Hass & Arndt[57] et al showed the beneficial treatment outcome using topical tretinoin with other combinations for hair growth disorders unlike our study where tretinoin alone was used. In this group 50% of the patients with single and multiple patch improved & 50% of the same did not show any improvement. Therefore the response outcome was not determined by number of patches. Two patients had a personal history of atopy & they showed poor and moderate response.

One patient with a family history of atopy showed a good response and he also had history of urticaria. Hence it can be presumed that atopy doesn’t influence the response outcome. One patient with poor and very poor response had family history of diabetes mellitus and hypertension respectively. In this group all the three patients with very poor response had dental caries and the two patients with poor response had chronic gingivitis. Further studies are needed to confirm the efficacy of this modality when used alone.

GROUP III: PATIENTS TREATED WITH 2% MINOXIDIL

90% of the patients in this study group showed improvement. This is in contrast to a regrowth of 20 – 45% reported in an earlier study[30]. Fiedler Weiss et[64] al have shown a response of 81% with 5% minoxidil solution versus a 38% response with 1 % solution. Except one patient all the patients had single patch

involvement in contrast to other studies where multiple patches were more. In patients with improvement four had excellent response and two had moderate and three had good response. In four patients with excellent response one had history of atopy and others did not have any personal/ family history of atopy, diabetes mellitus or thyroid disease. Two patients with personal history of atopy had good response which shows that atopy doesn’t influence the response outcome. One patient with a good response had hyperthyroidism with polycystic ovarian disease and was managed accordingly in the corresponding speciality department. One patient with moderate and good response each had family history of diabetes mellitus. Two patients each with moderate and excellent response had evidence of dental sepsis which was treated. One patient with a poor response had family history of hypertension and she had chronic gingivitis also. The disease duration ranged from 15 days to

maximum of 6 months & all the patients with excellent response had a duration ranging from 15 days to 6 months proving disease duration doesn’t modify the response outcome.

Our study did not show any adverse effects in contrast to other studies[3].Hence with 90% of the patients showing improvement minoxidil appears to be very promising treatment modality.

GROUP IV: PATIENTS TREATED WITH 0.05% ANTHRALIN

Four out of ten patient showed improvement. Two patients showing excellent response, one patient each with good response and moderate response in others. Six out of ten patients did not show any improvement. This is little higher when compared to a response rate of 20 to 25% reported in the earlier study[54].

Two patients with good and excellent response had personal history of atopy alone. One patient

with poor response had personal history of hypertension. One patient each with good, moderate and very poor response had family history of diabetes mellitus. Acceptable regrowth of hair was noticed by ten weeks in three patients and 8 weeks in one of the patient, this is in contrast to 24 weeks reported in the earlier studies[64].Three patients with very poor response had chronic gingivitis and one patient with poor and very poor response had dental sepsis which could be the possible cause for poor response to treatment. One patient with a good response had follicular pharyngitis which was treated. Two patients with excellent response had both single and multiple patches. 42.9% of the patients with single patch improved whereas 33.3% of the patient with multiple patches showed improvement, rest of them did not improve. Thus no significance could be established with regard to number of patches. Also atopy did not appear to play any role like in previous modalities.

Scaling, folliculitis and staining of the clothes were observed like in other studies. A large study may be necessary for the exact assessement of topical anthralin.

GROUP V: PATIENTS TREATED WITH INTRALESIONAL STEROIDS

90% of the patients showed considerable improvement in this group. 5 patients showed excellent response, four showed good response and one showed poor response. Chang, Kyung Hee[49]et al showed in his study that six out of ten patients showed considerable improvement in contrast to our study where 90% improvement occurred. About 83.3% of cases with single patch improved and 100% improvement occurred in patients with multiple patches, unlike in other studies where extensive AA is of little improvement[47,48] which shows number of patches having no influence in the response outcome. One patient each with poor and good response had personal history of atopy.

Patient with poor response also had family history of atopy, with atopy being the probable cause of poor response. Two patients with good response had family history of diabetes mellitus. Two patients with excellent and good response had chronic gingivitis and dental sepsis which was treated. Out of ten patients treated, only one patient had atrophy at the site of injection.

Intralesional triamcinolone acetonide is a safe and effective treatment for patients with extensive alopecia areata. Larger sample size and long term follow up are needed to assess the long term outcome of this treatment modality.

GROUP VI: PATIENTS TREATED WITH CRUDE ONION JUICE

Six patients showed improvement out of which one had excellent response, three showed good response and two showed moderate response. One patient each showed poor and very poor response.

Sharquie[55] et al showed in his study that out of 23 patients, 20 patients (86.9%) showed significant hair growth with crude onion juice. Males showed terminal hair regrowth than females similar to our study. Two patients with moderate response had personal history of atopy and both had single patches responding after 6 weeks of treatment. 57.1% improvement was noticed in patients with single patch and 66.7% improved in multiple patches with no significance in number of patches and treatment outcome. One patient with poor response had oral submucosal fibrosis. One patient with good response had family history of hypertension and diabetes. Two patients with good response and one with poor response had dental caries and chronic gingivitis which was treated. One patient had irritant contact dermatitis as a side effect. Further studies are needed to assess the long term outcome of this therapy.

GROUP VII: PATIENTS TREATED WITH TOPICAL DNCB

Six out of ten patients showed improvement. Two patients had excellent response and two patients each showed good and moderate response. KH Mohan[50,52] et al in his study concluded that out of 22 patients 36.36% of the patients showed complete response which is much less when compared to the response in our study. One patient with poor response had personal history of atopy and had alopecia universalis. Hence atopy could have been the cause for this poor response. One patient with good response had family history of diabetes mellitus, rest of the patients did not have any personal or family history of diabetes or hypertension. 66.7% of the patients with single patch and 57.1% of the patients with multiple patches showed improvement showing that number of patches doesn’t alter the response outcome. Two patients with moderate response and one patient with excellent response had chronic gingivitis, also two patients with

poor response and one patient with good response had dental sepsis which was treated. The only disadvantage of DNCB is its mutagenicity by Ames test. However, drugs like norfloxacin, isoniazid and psoralen with ultraviolet A (PUVA) treatment, textile dyes and fumes of oils have also been found mutagenic by Ames test. DNCB requires a relook as an option in alopecia areata rather than other contact sensitizers that are available only with difficulty and are expensive.

GROUP VIII: PATIENTS TREATED WITH 0.1% BETAMETHASONE OINTMENT

Six out of ten patients showed improvement. Three patients showed excellent response, two patients showed moderate response and one showed good response. Two patients each showed poor and very poor response. Unlike most of the studies[4] conducted with 0.05% betamethasone diproprionate, our study was done with 0.1% betamethasone valerate which had shown improvement similar to

other studies after continuous application for three months with regrowth of terminal hair. Two patients with moderate response and one patient with very poor response had personal history of atopy and one patient with excellent response had family history of atopy. Therefore it can be concluded that atopy doesn’t significantly influence the response outcome. 66.7% of patients with single patch and 57.1% of the patients with multiple patches showed improvement. Patient with excellent response had family history of diabetes mellitus. Two patients with moderate response and one patient with good response had chronic gingivitis and two patients with very poor response had dental sepsis which was treated. The poor response in the latter group might be due to the focal dental sepsis.

From this study it can be concluded that topical steroid remains a promising treatment modality for alopecia areata.

GROUP IX: PATIENTS TREATED WITH CRYOTHERAPY

Eight out of ten patients showed improvement and remaining 20% did not show any improvement. Five patients showed excellent response, two showed moderate response and one showed good response. One patient each showed poor and very poor response. Lei[60] et al in his study showed that hair regrowth occurred in greater than 60% of affected areas in 70 of 72 patient, which is in contrast to our study wherein 80% of the patients showed improvement. Patients with moderate response and one patient with good response had chronic gingivitis. Two patients with excellent response and one patient with very poor response had dental caries. Hence in this group focal sepsis doesn’t seem to influence the response outcome. 80.0% of the patients with single and multiple patches showed improvement which shows that there is no significance in the number of patches in the response outcome.

From the above it can be concluded that liquid nitrogen seems to be one of the cheap, cost effective therapy that could be tried in the treatment of alopecia areata.

GROUP X: PATIENTS TREATED WITH PLACEBO/ CONTROL GROUP

Out of ten patients two showed moderate response, five showed very poor response and three showed poor response. Antonella Tosti[72] et al in his study showed in his placebo controlled trial that intervention with treatment doesn't possibly influence the response outcome, which is in contrast to our study. Out of five patients with very poor response, one had family history of diabetes mellitus and three had chronic gingivitis. One patient with poor response had history of tuberculosis and he had finished his anti tuberculous treatment. Out of three patients with personal history of atopy, two had poor response and one had moderate response. Hence the response was not dependant on the presence of

atopy. All the latter three patients also had dental caries which was treated. Only 20% of the patients with single and multiple patches had improvement showing that number of patches were not significant in response outcome. Hence from this it can be concluded that there is only 20% chance of spontaneous resolution in cases of alopecia areata and that therapeutic intervention significantly modifies the course and response outcome of the disease.

To sum up, comparison of proportion of improvement among different study groups showed that only groups treated with intralesional steroids(90%), topical minoxidil (90%) and cryotherapy(90%) showed statistically significant improvement (Table No:11,12,13/ Fig No:1) than the control group(20%) ($P<0.05$). However, no other contrasts are statistically significant ($P>0.05$).

Comparison of mean score among different study groups further confirms our conclusion.

Also there is no significant difference in the proportion of improvement among various groups (Table no:14,15/ Fig No:2,3) for single patch (P=0.26) and multiple patches (P=0.26).

Comparison of proportion of improvement among single and multiple patches among atopics (P=1.00) (Table No:16/ Fig No: 4) and among the non atopics (P=0.92) (Table No:17/ Fig No: 5) showed no significant difference. Also there was no significant difference in improvement among atopics and non atopics (P=0.08) (Table No:18). Statistically, there is no significant difference in mean age (P=0.31) (table no: 19) and gender distribution (Table No:20) among different study groups (P=0.31).

CONCLUSION

1. Significant improvement occurred in patients treated with topical minoxidil(90%), intralesional steroids(90%) and cryotherapy with liquid nitrogen(90%) than the control group(20%) treated with placebo.

2. All the three significant treatment modalities produced only transient adverse effects which did not interfere with the patient compliance.

3. Other contrasts (study groups) are not statistically significant since each group comprised of ten patients only (n=10) and this remains the limitation of our study. Therefore studies in larger groups are needed are needed for further evaluation of other groups in our study.

4. The number of patches (single/ multiple) among different study groups doesn’t

influence the response outcome (P=0.26).

5. Proportion of improvement in number of patches (single/ multiple) among atopics and the non atopics was statistically insignificant and hence there is no correlation between atopy and the number of patches and its response outcome.

6. Atopy does not appear to be a significant factor in the response to therapy in patients with alopecia areata.

7. Atopy in the form of personal and family history was the only significant association found in the present study group (20%).

8. There was no significant difference in the mean age and gender distribution among different study groups.

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PROFORMA FOR THERAPEUTIC TRAIL FOR ALOPECIA AREATA

Case No.
OP NO:
Name
Address
Age/Sex
Occupation

Complaints

i. Loss of hair – Duration
ii. Pruritus
iii. Others (specify)

Treatment taken in the past

a) Topical application

Duration

Clinical response
1) Steroids preparation
2) Others (specify)
3) Native medicine

b) Systemic therapy
1) Oral steroids
2) Others (specify)

c) Other modes of treatment (specify)

Family history

Diabetes mellitus
Hypertension
Atopy (specify the features)
Endocrine disorders
Autoimmune disorders

Personal history

Hypertension
Diabetes mellitus
Migrane
Urticaria
Childhood eczema
Thyroid disease
Septic foci – ENT/DENTAL/OTHERS (specify)

Past history of the same disease

Site
Duration
No. of episodes
Duration of treatment
Response of treatment

General examination

Pallor
Icterus
Lymphadenopathy
BP

Systemic examination

Cardiovascular system
Respiratory system
ENT
DENTAL
Other finding if any

Dermatological examination
No of patches

Site	Size	Shape	Presence of white hair

Coudability sign
Exclamation hair mark
Nail changes – Pitting, others (specify)

Associated changes – Vitiligo, Other dermatosis (specify)
Oral mucosa
Palms and soles
Eyes

Investigations
Blood sugar
Other investigation (specify)

THERAPY - GIVEN
Duration of therapy

Post therapeutic follow up

Clinical response	2nd week	4th week	6th week	8th week	10th week	12th week	14th week	16th week
Patch size								
Hair growth								
Pigmentation								
Length of hair								

Adverse effects	2nd week	4th week	6th week	8th week	10th week	12th week	14th week	16th week
Pigmentation								
Irritant reaction								
Burning								
Itching								
Folliculitis								

Others (specify)								

Result:
Pre treatment and post treatment photographs

LEGENDS

AA – Alopecia areata

B – Beard

DC – Dental caries

EB – Eyebrows

F – Frontal

G – Chronic gingivitis

HPO – Hyperpigmentation of oral mucosa

HT – Hyperthyroidism

Lt – Left

L – Leuconychia

LP – Lichen planus

LS – Longitudinal striations

M – Melanonychia

O – Oophiasis

OSF – Oral submucosal fibrosis

P – Parietal

PCOD – Polycystic ovarian disease

RHD – Rheumatic heart disease

R – Right

Seb.derm – Seborrheic dermatitis

TC – Tinea cruris/ Tinea corporis

V – Vertex

VVC – Vulvovaginal candidosis