"A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER WITH TOPICAL TRIAMCINOLONE ACETONIDE VERSUS INTRALESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF ALOPECIA AREATA"

BY

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DISSERTATION SUBMITTED TO

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA,

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

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IN

DERMATOLOGY, VENEREOLOGY AND LEPROSY

UNDER THE GUIDANCE OF

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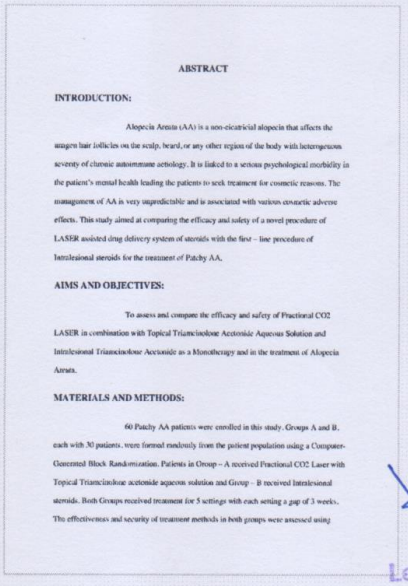

ABSTRACT

INTRODUCTION:

Alopecia Areata (AA) is a non-cicatricial alopecia that affects the anagen hair follicles on the scalp, beard, or any other region of the body with heterogeneous severity of chronic autoimmune aetiology. It is linked to a serious psychological morbidity in the patient's mental health leading the patients to seek treatment for cosmetic reasons. The management of AA is very unpredictable and is associated with various cosmetic adverse effects. This study aimed at comparing the efficacy and safety of a novel procedure of LASER assisted drug delivery system of steroids with the first – line procedure of Intralesional steroids for the treatment of Patchy AA.

AIMS AND OBJECTIVES:

To assess and compare the efficacy and safety of Fractional CO2 LASER in combination with Topical Triamcinolone Acetonide Aqueous Solution and Intralesional Triamcinolone Acetonide as a Monotherapy and in the treatment of Alopecia Areata.

MATERIALS AND METHODS:

60 Patchy AA patients were enrolled in this study. Groups A and B, each with 30 patients, were formed randomly from the patient population using a Computer-Generated Block Randomization. Patients in Group – A received Fractional CO2 Laser with Topical Triamcinolone acetonide aqueous solution and Group – B received Intralesional steroids. Both Groups received treatment for 5 settings with each setting a gap of 3 weeks. The effectiveness and security of treatment methods in both groups were assessed using

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LIST OF ABBREVIATIONS

S.NO	ABBREVIATIONS	FULL FORMS
1	AA	Alopecia Areata
2	LASER	Light Amplification by Stimulated Emission of Radiation
3	CO2	Carbon dioxide
4	GPA	Global Photograph Assessment
5	LAD Score	Lesional Area Density Score
6	LAD Score Improvement %	Lesional Area Density Score Percentage of Improvement
7	VDS	Visual Discomfort scale
8	VAS	Visual Analogue Scale
9	AST	Alopecia Sub Totalis
10	AT	Alopecia Totalis
11	AU	Alopecia Universalis
12	ADATAF	Acute Diffuse And Total Alopecia of the Female Scalp
13	ILS	Intra Lesional Steroids
14	DLQI	Dermatology Life Quality Index
15	GWAS	Genome Wide Association Studies
16	IFN	Interferon
17	ROS	Reactive Oxygen Species

18	MHC	Major Histocompatibility Complex
19	JAK – STAT PATHWAY	Janus Kinase Signal Transducers and Activators of Transcription Pathway
20	CD	Clusters of Differentiation
21	HLA	Human Leukocyte Antigen
22	AGA	Andro Genetic Alopecia
23	SLE	Systemic Lupus Erythematosus
24	KOH	Potassium Hydroxide
25	OCT	Optical Coherence Tomography
26	SALT SCORE	Severity of Alopecia Tool Score
27	AAPI	Alopecia Areata Progression Index
28	OMP	Oral Mini Pulse
29	DNCB	Di Nitro Chloro Benzene
30	SADBE	Squaric Acid Di Butyl Ester
31	DPCP	DiPhenCyProne
32	JAKis	Janus Kinase Inhibitors
33	IL	Inter Leukin
34	MAB	Monoclonal Anti Body
35	PUVA	Psoralen plus UltraViolet – A
36	NBUVB	Narrow Band UltraViolet – B
37	PRP	Platelet Rich Plasma

38	Er	Erbium
39	RCT	Randomized Controlled Trial
40	MASER	Microwave Amplification by Stimulated Emission of Radiation
41	Nd- YAG	Neodymium Doped Yttrium Aluminum Garnet
42	SPT	Selective Photo Thermolysis
43	CM	Centi Meter
44	MAC	Micro Ablative Column
45	IEC	Institutional Ethical Clearance

ABSTRACT

INTRODUCTION:

Alopecia Areata (AA) is a non-cicatricial alopecia that affects the anagen hair follicles on the scalp, beard, or any other region of the body with heterogenous severity of chronic autoimmune aetiology. It is linked to a serious psychological morbidity in the patient's mental health leading the patients to seek treatment for cosmetic reasons. The management of AA is very unpredictable and is associated with various cosmetic adverse effects. This study aimed at comparing the efficacy and safety of a novel procedure of LASER assisted drug delivery system of steroids with the first – line procedure of Intralesional steroids for the treatment of Patchy AA.

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Photograph Assessment (GPA) – Scale, Lesional Area Density Score Percentage of Improvement (LAD Score Improvement %), Visual Discomfort scale (VDS), Visual Analogue Scale (VAS), and documentation of adverse effects in each setting.

RESULTS:

Efficacy of treatment modality – assessed using means score of GPA – Scale and LAD Score Improvement % suggests quicker results to patients in Group - B in initial settings but drastic improvement happens to patients in Group – A in subsequent settings. At the end of 5^{th} setting, GPA – Scale and LAD Score Improvement % suggests maximum efficacy in patients in Group – A and they are statistically significant (P – Value < 0.001). The mean VDS in both groups suggests maximum discomfort in Group – A yet the patient satisfaction at the end of 5^{th} setting was maximum with patients in Group – A and they are statistically significant (P – Value < 0.001). Cosmetic notable adverse effect of atrophy of skin was documented in 30 % of patients in Group – B.

CONCLUSION:

This study showed that Fractional CO2 LASER with Topical Triamcinolone Acetonide is a better treatment modality than the Intralesional Triamcinolone Acetonide for the treatment of Alopecia Areata with respect to efficacy, safety, and adverse events.

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INTRODUCTION

INTRODUCTION:

Alopecia Areata (AA) is a non-cicatricial alopecia that affects the anagen hair follicles on the scalp, beard, or any other region of the body with heterogenous severity of chronic autoimmune aetiology. Among the whole world population, two percentage of population suffers from AA. The most widely recognized idea regarding the etiopathogenesis of AA is that the immune privilege of the hair follicle is compromised by an erratic immunological process. Their etiopathogenesis is influenced by a variety of genetic and environmental factors.[1]

Significant differences exist in AA's clinical characteristics. The most common presentation is a smooth, circular, complete patchy loss of hair that has occurred over weeks. This is called Patchy AA and it ranges from single to multifocal patchy loss of hair. Special variants of AA include 1) Ophiasis, 2) Sisaipho, 3) Alopecia Reticularis, 4) Alopecia Subtotalis, 5) Alopecia Totalis (AT), 6) Alopecia Universalis (AU), 7) Perinevoid Alopecia, 8) Linear Alopecia, 9) ADATAF ("Acute Diffuse and Total Alopecia of the Female scalp" and 10) AA Incognito.[2,3]

The clinical course of AA shows unpredictable episodes of relapsing and remission. The undivinable response of the patients to various treatment modalities increases the mental struggle and hence association of anxiety and depression in AA is more than the general population.[4]

AA patients seek treatment exclusively for cosmetic reasons. Till now, innumerable local and systemic treatment options are accessible, and their efficacies are varied. Hence the clinical presentation should be assessed before deciding the therapy. Intralesional steroids (ILS) is a proven first-line treatment modality for Patchy AA. Patients

undergoing ILS should be observed for the notable side effect of atrophy of the skin which is not cosmetically appealing.[5]

Hence there is a hunt for an alternate treatment modality with less side effects and cosmetic concern. Fractional CO2 LASER is one among the "LASER-assisted drug delivery system". "Fractional CO2 LASER assisted drug delivery of steroids" for AA is a novel treatment discipline with paucity of research and literature regarding their efficacy and safety. [6, 7, 8]

Thus, this study was proposed to assess and compare the efficacy and safety of Fractional CO2 Laser in combination with Topical Triamcinolone Acetonide Aqueous solution and Intralesional Triamcinolone Acetonide as a Monotherapy in the treatment of Alopecia Areata.

AIMS & OBJECTIVES

AIMS OF THE STUDY:

- To assess and compare the efficacy and safety of Fractional CO2 LASER in combination with Topical Triamcinolone Acetonide Aqueous Solution and Intralesional Triamcinolone Acetonide as a Monotherapy in AA.

OBJECTIVES OF THE STUDY:

- To assess and compare the efficacy of Fractional CO2 LASER in combination with Topical Triamcinolone Acetonide Aqueous Solution and Intralesional Triamcinolone Acetonide as a Monotherapy in AA.
- To assess and compare the safety of Fractional CO2 LASER in combination with Topical Triamcinolone Acetonide Aqueous Solution and Intralesional Triamcinolone Acetonide as a Monotherapy in AA.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

SYNONYMS:

- PELADE
- AREA CELSI

DEFINITION:

AA is defined as "A non-cicatricial alopecia that affects the anagen hair follicles on the scalp, beard, or any other region of the body with heterogenous severity of chronic autoimmune aetiology." [9,10]

HISTORY:

Cornelius Celsus, first described the disease 2000 years ago as "AREAE". Sauvages de Lacroix first used the term "Alopecia Areata" in 1763. [10,11] Alopecia Areata originates from the combination of a Greek word "ALOPEX" and a Latin word "AREATA". Detailed clinical description of the disease was given by Bateman, Kaposi and Hebra. Physicians of early 19th century considered it to be a parasitic disease but the failure to inoculate the causative organism has disproved this hypothesis. Although the histopathological studies have narrowed down the etiology to be an autoimmune disease in 1958. Genome studies in recent years have discovered the gene UL16-binding protein, which is responsible for attracting cytotoxic cells to the follicles of hair. [12,13]

EPIDEMIOLOGY:

AA accounts for 2% of the global general population.[9] Hospital based studies show 0.7% and 2.11% of Dermatology OPD clinics of India and USA respectively.[11,14,15] Among Alopecia cases, 25% of cases are Alopecia Areata. Among Alopecia cases in children, AA is the most common.[16] Second to Fourth decade is the commonest age of onset.[17,18] No predilection with respect to race or sexual orientation but in few studies men show early onset.[18,19] Few AA patients, due to cosmetic impact over their body end up in severe depression. Dermatology Life Quality Index (DLQI) is severely affected in this patient. In children, their parents' Quality of life is severely affected. Hence AA is classified as "Secondary Psychiatric Disorders" by Koo and Lee in the classification of Psychodermatological Disorders.[20,21,22]

ETIOPATHOGENESIS:

Historically various etiological factors have been enumerated.[13,23] In the Last decade, "C3H/HeJ Mouse" model studies by Genome Wide Association Studies (GWAS) has shown AA to be an autoimmune chronic disease targeting hair follicles triggered in genetically susceptible individuals by environmental factors resulting in hair cycle dynamics impairment.[24,25]

GENETIC FACTORS:

4-28% of AA patients have a positive familial predilection.[26] Studies show 55 percent of monozygotic twins are concordant while dizygotic twins are not concordant.[27] Various genes have shown to be in association with AA mainly MHC Class II alleles – HLADRB1*1104 and HLA-DQB1*0301.[13,28] Recent studies by GWAS show association of AA with UL16 Binding protein, SH2B3(LNK)/ATXN2 genes signaling JAK, ACOXL/BCL2L11 and Syntaxin-17 genes.[29,30,31]

ENVIRONMENTAL FACTORS:

Various Environmental factors are triggers for AA.[10] Psychological stress has been postulated to be one of the most important trigger factors for AA because stress causes reduced corticosteroid production.[32,33,34,35]

Infections such as Hepatitis-B, Cytomegalovirus and Swine Flu virus triggers AA by stimulation of IFN-Gamma and CXCL10.[36,37] Association of Helicobacter pylori infection is highly controversial.[38,39]

Vitamin D deficiency is presumed to affect the severity of AA.[40,41,42,43] Few studies show Iron, Zinc and Manganese deficiency also leads to AA.[10,44,45] However contradictory findings in few studies suggest increase in Iron, Mercury, Cadmium, Cobalt, Lead and Nickel leads to AA.[45] It is mainly attributed to the increased production of Reactive Oxygen Species (ROS).[46]

AUTOIMMUNITY:

A number of autoimmune disorders including such as Lichen Planus, Vitiligo, Hashimoto's Thyroiditis and Pernicious Anemia have been linked to AA. These disorders have supportive evidence for autoantibodies directed against Keratin – 16 and Trichohyalin in hair follicle.[20,30,10,47]

FOLLICULAR IMMUNE PRIVILEGE AND ITS COLLAPSE IN AA:

In a normal individual, the lower part of hair follicle has MHC Class – I proteins which are constantly downregulated to prevent autoantibody formation against Keratin 16 and Trichohyalin in the hair follicle.[47,48]

Environmental factors in a genetically susceptible AA individuals stimulate the production of inflammatory signals like Interleukin-15 and IFN – Gamma.[49,50] This activates $CD8^+$ T-Cells via JAK – STAT Pathway (Janus Kinase Signal Transducers and Activators of Transcription Pathway).[48] This causes the MHC proteins (Class – I, II) to get upregulated. This in turn activates the infiltration of lymphohistiocytes near the lower ends of hair follicle resembling "Swarm of Bees".[30,48] This causes apoptosis of matrix cells in hair leading to "Anagen Arrest".[48] This Anagen arrest leads to abrupt cessation of shaft of hair formation contributing to the appearance of "Exclamation mark". Thus, the Anagen phase gets shortened leading to the formation of dystrophic thin hairs. Hence Alopecia Areata is formed.[48,49,50,51,52]

Isthmus and Hair bulge is sparred from these inflammatory infiltrates sparring the Stem cells in hair follicle. Thus, AA is a non cicatrical alopecias.[51,52]

CLINICAL FEATURES:

A non-scarring alopecia of sudden onset with single to multiple, round or oval with patchy loss of hair over a smooth surface.[10,53] Most of the cases are asymptomatic while few are associated with mild itching and erythema.[54,55]

Scalp (90% cases) is the most involved area while it also involves eyebrows, moustache, beard, eyelashes and body hair. Beard is usually initially involved in men before the onset of scalp lesions.[10,48]

AA has characteristic hair changes. They are as follows:

1. "Broken Hair" – within the patch the hair shaft just breaks above the scalp surface.[56,57]
2. "Cadaver Hair" or "Black Dots" – Hair breaks just before the emerging surface area.[56,57]
3. "Tapering Hair" or "Exclamation mark (!) Hair" – Due to anagen arrest, the hair shaft is narrow at the scalp end while it is wider in the free ends. They are common in the peripheral borders of the patch, but it may involve the central areas also.[56,57]

"Coudability Sign" – a kink of about 5-10 mm in the normal appearing hair above the surface when it is forced inward. This helps to differentiate from other alopecias which are diffuse in nature.[58]

White hairs are spared because the target for autoantibodies are hair bulb melanocytes. "Going white overnight" phenomenon – phenomenon in which white hairs are alone spared in a rapidly deteriorating case of alopecia areata in a very acute onset. This is also called Antoinette syndrome or Canities Subita.[10,59]

AA is noticed suddenly, and the size varies.[10] They may be small ranging from few millimeters to large ranging from few centimeters.[25,53] They may resolve spontaneously after the onset in few months. Acquired poliosis over the lesions also can occur.[53] New patches can occur as pre-existing lesions resolve.[55]

CLINICAL CLASSIFICATION/VARIANTS OF AA:

Patchy Alopecia Areata is also called as Alopecia Localis. The prognosis of Patchy AA is good and they respond very well to the various treatment modalities. There are certain special variants of AA. They are associated with poorer prognosis.[10,60] These variants are classified based on several criteria such as distribution, extent and pattern.

TABLE – 1: CLINICAL CLASSIFICATION / VARIANTS OF ALOPECIA AREATA [10,60]

CLINICAL CLASSIFICATION / VARIANTS OF ALOPECIA AREATA[10,60]		
Based on Extent	Based on pattern	Miscellaneous variants
Patchy AA Alopecia Subtotalis Alopecia Totalis Alopecia Universalis	Reticular Ophiasis Sisaipho (Ophiasis Inversus) Linear Perinevoid	Acute, diffuse, and total AA AA Incognito (AAI)

ALOPECIA SUBTOTALIS – multiple patchy loss of hairs coalescing together to involve major areas of the scalp almost 70 % but not complete involvement of scalp.[61]

ALOPECIA TOTALIS (AT) – complete loss of scalp hairs and it has poor prognosis. 10-20% AA end up in AT.[25]

ALOPECIA UNIVERSALIS (AU) – loss of hairs all over the body.[10,25] Individuals with atopic history and Down syndrome are more prone for AU and it has a poor prognosis.[10,18] 5% AA ends up in AU.[25]

ALOPECIA RETICULARIS – characterized by tiny numerous recurrent patchy AA scattered all over the scalp with poor response to treatment.[13,62]

OPHIASIS – characterized by a peculiar involvement of temporal and occipital borders of the scalp resembling a "Snake – like" band. It is most common among atopic children with a poor prognosis.[25,63]

SISAIPHO (OPHIASIS INVERSUS) – characteristically resembling Androgenetic Alopecia with central involvement over vertex sparing the temporal and occipital margins with a poor prognosis.[10,25,64]

LINEAR – rare presentation with band-like patches.[10]

PERINEVOID – rare presentation with AA around a pigmented nevus.[30,65]

ACUTE, DIFFUSE, AND TOTAL ALOPECIA –

characterized by acute diffuse extensive alopecia predominantly involving the females resembling Acute Telogen Effluvium. It ultimately leads to involve the complete scalp. After three to six months, hair regrows quickly and completely.[10,30,66]

AA INCOGNITO – characterized by acute diffuse alopecia in AGA prone areas and presentation resembles telogen effluvium. Females are predominantly affected.[30,67]

IKEDA'S CLASSIFICATION OF AA:[62,68]

AA was classified by Ikeda based on the course and association of the disease in to four main types:[62,68]

TABLE – 2: IKEDA'S CLASSIFICATION OF AA[62,68]

TYPES OF AA
• ATOPIC TYPE • AUTOIMMUNE TYPE • PREHYPERTENSIVE TYPE • COMMON TYPE

1. ATOPIC TYPE: (10% OF CASES)

It accounts for 10 % of AA cases. It is associated with atopy. It is more of childhood or adolescent in onset. Reticular and ophiasis are the most common patterns. 30-75% of Atopic AA progress to Alopecia Totalis.[62,68]

2. AUTOIMMUNE TYPE: (5% OF CASES)

The association of autoimmune disorders, peptic ulcer diseases and diabetes mellitus are most common. It is more of middle age onset. 10-50 % of cases progress to Alopecia Totalis.[62,68]

3. PRE – HYPERTENSIVE TYPE: (4% OF CASES)

There is higher familial incidence of hypertension. It is of early adulthood in onset. Reticular type is the common entity. 40% of these cases end up in Alopecia Totalis.[62,68]

4. COMMON TYPE: (81% OF CASES)

The second to fourth decade of life is when symptoms typically first appear. Patients present with a sudden onset classical patchy alopecia over any part of the body, and it may last for more or less 6 months. It can completely resolve in 3 years. 5-15% of this type AA progress to Alopecia Totalis.[62,68]

NAIL CHANGES:

Inflammation of nail matrix causes nail changes in AA. About 10-66% of AA cases have changes in nail. It correlates with the disease severity. Males and children are more likely to experience nail alterations.[69,70]

The characteristic nail changes in AA are enumerated as follows:[69,70,71,72,73]

- Pitting – multiple, uniform, tiny, regular, shallow pits in the nail plate ("Scotch Plaid" Appearance)[71]
- Thinning of nails
- Prominence of ridging in nails
- Sand Paper nails or Trachyonychia
- Onycholysis
- Beau's Lines
- Atrophic onychodystrophy
- Onychomadesis
- Acute severe AA manifest as Red lunula or mottled lunula
- Punctate Leukonychia or Geometric Leukonychia ("Grill" Pattern)

TWENTY NAIL ALOPECIA SINE ALOPECIA:

Usually, hair changes precede nail changes in AA. But in a few cases nail changes present first. This phenomenon is called Twenty Nail Alopecia Sine Alopecia.[74]

EYE CHANGES:

Ocular changes in AA are as follows:[13,75]

- Lens opacities
- Cataract
- Fundus abnormalities

DIFFERENTIAL DIAGNOSIS OF AA:

Various congenital conditions and acquired conditions that have the similar presentation of patchy loss of hair must be kept in mind when AA is diagnosed. Differential diagnosis of AA is listed as below:[13,48,76,77,78]

- Congenital Triangular Alopecia
- Ectodermal dysplasia
- Congenital atrichia
- Tinea Capitis
- Loose Anagen Syndrome
- Trichotillomania
- Friction Alopecia
- Pressure Alopecia
- Traction Alopecia
- Alopecia neoplastica especially seen in cases of breast carcinoma
- Secondary Syphilis presenting as moth eaten alopecia
- Androgenetic Alopecia (AGA)
- Anagen Effluvium
- Telogen Effluvium

- Systemic Lupus Erythematosus (SLE) presenting as “Lupus Hair”

ASSOCIATIONS OF AA:

AA is associated with the following disorders:[20,79,80]

- Atopy
- Lichen Planus
- Psoriasis
- Vitiligo
- SLE
- Morphea
- Celiac disease
- Pernicious anemia
- Addison’s disease
- Ulcerative colitis
- Multiple sclerosis
- Nuchal Nevus Flammeus
- Multiple sclerosis

A study by Chu et al in Taiwan reported that there is age wise association of AA with various autoimmune disorders. The first decade of life is when SLE and Atopy are associated with AA, the second decade is when rheumatoid arthritis or psoriasis is, and the sixth decade is when thyroid diseases are.[81,82]

COURSE AND PROGNOSIS:

There is no permanent damage to the stem cells in hair bulge area.[10] Hence almost 50-80% of patchy AA attain spontaneous remission within a

year.[10] However clinical remission is very unpredictable while some have persistent clinical disease.[14,83] Almost 25% of the cases can progress to AT or AU which undergo complete remission in 10-17% of cases.[83] Muller et al observed poor prognosis in children.[84]

The factors that determine the poor prognosis in AA are enumerated as follows:[25,83,84,85]

- Early age of onset
- Positive Familial history
- Atopy
- Association of Systemic diseases such as connective tissue disorders, hypertension
- Association of genetic diseases such as Down's syndrome
- AA with extensive involvement of scalp (>50%)
- Special variants of AA – Alopecia Subtotalis, Alopecia Totalis , Alopecia Universalis
- Atypical patterns of AA – Ophiasis, Sisaipho, Reticular
- Eyebrow and Eyelashes involvement
- Clinical presentation more than 1 year
- Frequent recurrences
- Presence of terminal hairs which are regrown and scattered with in a patch
- New patches started appearing despite on treatment
- Positive Nail changes
- Abnormal Trichogram over uninvolved areas of scalp
- Trichoscopic signs that indicate poor prognosis

DIAGNOSIS:

For the majority of patients, AA can be directly diagnosed through clinical assessment.[10] Laboratory tests for diagnosis of AA are usually not required. However, if the clinical presentation is severe and unresponsive to treatment, routine screening studies are carried out to determine the relationship between AA and thyroid conditions and other autoimmune illnesses.[86] But to rule out the differentials, patient can be evaluated for syphilis serology, KOH mount, Lupus serology, Hair pull test, Fungal culture, skin biopsy, Hair pull test, trichoscopy, trichogram and optical coherence tomography (OCT).[25,86]

HAIR PULL TEST:

Along the periphery of a patchy AA, gentle traction over a grasped hair is applied and if more than 10% of hairs is shedding then positive Hair Pull Test is recorded.[8,13]

TRICHOGRAM:

Completely Plucked hair from the periphery of Patchy AA in a microscopy illustrates “Mixed Telogen and Dystrophic Anagen Pattern”. In slowly progressing AA, more telogen hairs are observed. In rapidly progressing AA, more dystrophic anagen hairs are recorded.[13,87,88]

HISTOPATHOLOGY:

Biopsy is done only when clinical diagnosis is very inconclusive.[86] Two deep biopsy specimens are essential along the periphery of Patchy AA using a 4 mm punch. One specimen to be used for vertical sectioning and another for horizontal sectioning. In acute cases, inflammatory changes are very evident and hence Vertical sections are done. Whereas horizontal sections are done in chronic cases to appreciate the diameter and density of hair follicles and proportion of various stages of hair, thus helping in not only diagnosis but also indicating possible regrowth. If mean hair follicle count is less than one, then it indicates poor prognosis.[10,30,89,90]

The characteristic histopathological features are as follows:

- **ACUTE CASES –** Intra bulbar and peribulbar lymphohistiocytic infiltrate (mainly CD4+ T-Cells) around anagen hair follicles resembling "Swarm of Bees".[30,86]
- **CHRONIC CASES –** Minimal infiltrate around telogen hair follicles.[30]
- **SUBACUTE CASES –** Infiltrate around hair follicles in catagen and telogen phase.[87]
- **OTHER POSSIBLE FEATURES:** Pigmented casts are found along peribulbar area and along vascular stellae, Trichomalacia, Lympho-eosinophilic infiltrate with increased vascular stellae and dilated openings in the hair follicles.[91]

DERMOSCOPY/TRICHOSCOPY:

A noninvasive, simple and easy technique which helps in the accurate diagnosis of AA in challenging cases.[92,93] The characteristic features of AA in Trichoscopy are as follows:[10,57,92,93,94]

- Exclamation Mark (!) Hair – also called as Tapering Hair
- Black Dots – also called as Cadaver Hair
- Broken Hair
- Yellow Dots (indicates dystrophy of follicular epithelium and sebaceous glands) – increased more than in Androgenetic Alopecia.
- Coudability sign can be appreciated even clearly as the trichoscope is placed over the terminal hairs.
- Increased number of yellow dots and black dots indicates the disease severity.
- Ratio of terminal to vellus hair is 1:1 indicating severe miniaturization exclusively in chronic cases.
- "i Hair" – in resolving lesions.

OPTICAL COHERENCE TOMOGRAPHY (OCT):

A noninvasive diagnostic technique to assess the diameter of hair shaft or any other abnormalities. The diameter of hair shaft is very much less in areas of Patchy AA compared with the normal area. It helps to differentiate from Trichotillomania where the diameter of hair shaft is unaffected.[13,95]

SIGNS OF ACTIVITY OF AA PATCH:

The various signs that indicate active disease in a patchy AA are enlisted as follows:[18,55,93]

- Exclamation Mark (!) Hair present around the lesion's edge
- Hair Pull Test positive
- Daily hair count of more that 100 hairs shedding
- Hair Pluck Test indicates more telogen hairs
- Trichoscopic findings of AA – Black dots, Exclamation Mark hair, Broken hair and Coudability sign.

SEVERITY SCORING:

SEVERITY OF ALOPECIA TOOL (SALT) SCORE:[10,30,96]

It is a quantitative scoring approach that is frequently used to assess the severity of the disease in AA and the effectiveness of the treatment. The entire scalp is subdivided in to four parts namely Top, Posterior, Right side and Left side and a fixed constant is assigned for each part depending on the body surface area. Top area, Posterior, Right side, and Left side has a body surface area of 40%, 24%, 18% and 18% respectively. Hence the constant assigned to these areas are 0.4, 0.24, 0.18 and 0.18 respectively.

Severity of Alopecia Tool (SALT) Score is given by the following formula:

SALT Score = (Percentage of hair loss over the top of scalp X 0.4) + (Percentage of hair loss over posterior aspect of scalp X 0.24) + (Percentage of hair loss over right side of scalp X 0.18) + (Percentage of hair loss over left side of scalp X 0.18)

Limitation with this SALT Score is that it cannot be used to evaluate the severity of AA over any other part of the body. SALT Score is limited to only AA involving the scalp. However, it is extremely useful, as scalp is the most common site involved.[10,30,96]

AA PROGRESSION INDEX (AAPI):[97]

It is an updated version of SALT Score where the degree of disease activity is taken into consideration. The hair pull test and trichoscopic results over the affected and unaffected areas of the scalp were used to gauge the disease's activity level.

Alopecia Areata Progression Index (AAPI) is calculated by the determination of two separate entities in each compartment of the scalp such as Top(T), Back(B), Right(R), Left(L):

1. The percentage of Alopecia Areata (% AA) – calculated as the percentage of AA in each compartment of scalp (T – Top, B – Back, R – Right, L – Left)

2. Score of hair Loss activity (SL) – calculated as the total of Hair Pull Test results in each compartment (Score 2 = > 20% hair shedding, Score 1 = 10-20% hair shedding, Score 0 = < 10% hair shedding) and positive abnormal trichoscopic findings in each compartment (Score 4 = ≥ 50% involvement of scalp, Score 2 = < 50% involvement of scalp, Score 0 = scalp not involved 0%).

AAPI Score is given by the following formula:

AAPI = [%AA x SL x 0.40] (Top of scalp) + [%AA x SL x 0.24] (Back of scalp) + [%AA x SL x 0.18] (Right side of scalp) + [%AA x SL x 0.18] (Left side of scalp)[97]

LESIONAL AREA AND DENSITY (LAD) SCORE PERCENTAGE OF IMPROVEMENT:[98]

It is a quantitative scoring method that may be utilised to evaluate the severity of AA and its therapy response in any area of the body during follow-up examinations.

Initially, Lesional Area and Density (LAD) score was calculated by the formula.

LAD Score = Area of alopecia areata site x Density of hair loss in percentage

The therapeutic response of AA in subsequent follow-up from their initial presentation can be assessed by LAD Score Percentage of Improvement.

LAD Score Percentage of Improvement was calculated by the formula:

$$\text{LAD Score Percentage of Improvement} = \frac{\text{LAD Score at initial presentation} - \text{LAD score at a given presentation}}{\text{LAD Score at initial Presentation}} \times 100$$

The advantage of this scoring system is that it can be utilized for Patchy AA not only for scalp but also for Patchy AA involving any part of the body.[98]

MANAGEMENT:

After careful clinical evaluation, diagnosis of AA can be made. AA patients seek treatment exclusively for cosmetic reasons. Till now, innumerable local and systemic treatment options are accessible, and their efficacies are varied. Hence the clinical presentation should be assessed before deciding the therapy. Special variants of AA are highly resistant to various treatment options and their course of the disease is highly unpredictable.[99]

COUNSELING:

Patients of AA must be counselled in detail regarding the benign nature, unpredictable clinical course, spontaneous resolution, varied response to treatment options. Counseling from Clinical psychologist, Child psychiatrist and educational psychologist may be needed in some cases as AA can cause significant psychological impact over the patient. Hence AA is classified under Secondary Psychiatric Disorder.[86]

TREATMENT:

Depending on the patient's clinical presentation, a variety of therapy approaches, such as topical application, intralesional treatment, and systemic medication, have been recommended for the treatment of AA.[10]

TOPICAL CORTICOSTEROIDS:

In a small, patchy AA, topical corticosteroids are used extensively. They are available in various formulations such as creams, ointment, and lotions. Superpotent steroids (Class – I and Class – II steroids) are advocated for patchy AA in adults while Midpotent steroids are given for children with patchy AA. The most common adverse effects include atrophy of skin, folliculitis and telangiectasia.[86,101,102,103]

INTRALESIONAL CORTICOSTEROIDS:

Intralesional corticosteroids are usually used for AA patients where less than 50 percent of scalp is involved. It can be used for facial lesions such as beard, moustache and eyebrows. It is not recommended in cases where AA is actively progressive or if it is extensive.

The agents that are given intralesional for AA are Triamcinolone Acetonide and Hydrocortisone Acetate. Major drawbacks with intralesional therapy include patient discomfort during painful injections and atrophy of the skin. Cataract and glaucoma can be caused over periorbital injections of steroids.[86,100,104,105]

SYSTEMIC CORTICOSTEROIDS:

Systemic corticosteroids are advocated for rapidly progressive AA and extensive patchy AA with more than 50 % involvement of scalp. Oral steroids such as Prednisolone, Dexamethasone are usually given daily over a period of 3-6 months with monthly follow-ups but steroids daily dosages over a prolonged time are not advised for children due to adverse effects. Short term daily dosage steroids are usually given in cases where extensive AA. Various pulse therapies have been tried for AA to minimize the adverse effects of steroids. There have been tried and successful monthly pulse regimens, such as intravenous dexamethasone 100 mg for three days, intravenous methylprednisolone 500 mg for three days, and intramuscular triamcinolone acetonide 40 mg once a month. For severe, extensive AA and specific AA variations, oral mini pulse (OMP) therapy with betamethasone (0.1 mg/kg/body weight) has been explored.[106,107,108]

MINOXIDIL:

Topical Minoxidil apart from their vasodilatory action, stimulates differentiation of cells above dermal papilla and proliferation of cells over the hair bulb area. Topical Minoxidil is available in concentrations ranging from 1 percent to 5 percent. Topical Minoxidil can be applied twice a day. Topical Minoxidil as a monotherapy does not show much improvement whereas it can be used as an adjuvant with oral steroids or intralesional steroids or anthralin. The adverse effects of topical minoxidil include unwanted facial hair, eczematization, pruritus and aggravation of seborrheic dermatitis.[109,110]

ANTHRALIN: (DITHRANOL)

Anthralin is a topical irritant that is applied to the scalp and inhibits the Th1 immune activity at the hair follicle in order to have a non-specific immunomodulatory effect. It is offered in topical cream and ointment formulations ranging from 0.5 to 1.0 percent. It is first applied over the affected area for 20 to 30 minutes over the first two weeks, increasing gradually to 45 minutes over the following two weeks, and then leaving the contact time at around one hour daily or until the onset of moderate erythema for the following three to six months. It is usually used in treatment resistant cases of AA, extensive and special variants of AA. The adverse effects include irritation, irritant contact dermatitis, regional lymphadenopathy, folliculitis, and it stains the clothes brown. It is avoided over the face to prevent prolonged UV – rays exposure.[10,103]

TOPICAL IMMUNOTHERAPY:

Topical Immunotherapy with allergic contact sensitizers are utilized for extensive AA recalcitrant to treatment and special variants of AA. The principle behind the topical immunotherapy is the induction of an allergic contact dermatitis over the affected lesional area by their immunomodulatory action of reducing the peribulbar CD4+ lymphocytes and the contact allergen over the affected lesional area acts like a competitive antigen over the surface. This phenomenon is called Principle of Antigenic competition. The potent contact sensitizers used are Dinitrochlorobenzene (DNCB), Squaric Acid Dibutylester (SADBE), Diphencyprone(DPCP) and Diphenylcyclopropenone. DNCB is avoided because of its mutagenic property. DPCP is usually preferred over the other agents because they

are cost effective and have a better efficacy and safety than the other contact sensitizers.[9,111]

PROSTAGLANDIN ANALOGS:

Prostaglandin – F2α Analogs such as Bimatoprost and Latanoprost used for the treatment of open angle glaucoma were incidentally found to cause eyelashes hypertrichosis. Hence, they are utilized for the treatment of AA. However conflicting results have been documented regarding their efficacy.[10,86]

IMMUNOSUPPRESSIVE DRUGS:

Various immunosuppressive drugs are used for the treatment of severe extensive AA which are enlisted below:

CYCLOSPORINE:

Cyclosporine inactivates the T-Cell activation and suppresses Interferon – Gamma. It is given orally at a dose of 6 mg/kg/day. Their use is limited because they have high relapse rates and serious side effects.[10,112]

AZATHIOPRINE:

Azathioprine has actions on Langerhan's cells and CD4/CD8 lymphocytes by their immunosuppressive and immunomodulator effect. The daily dosage of Azathioprine is 2mg/kg/day for 6 months is usually recommended.[10]

METHOTREXATE:

Methotrexate (2.5 mg/week to 25 mg/week) is being used for the treatment for AA either as monotherapy or as an adjuvant with oral steroids or intralesional steroids for severe recalcitrant AA.[113]

JANUS KINASE INHIBITORS(JAKis):

The JAK-STAT signalling pathway, which enhances CD8+ T-cell activity, is crucial to the pathophysiology of AA. Janus Kinase Inhibitors inhibit this rate limiting JAK-STAT signaling pathway thus inducing regrowth of hair in cases of AA.[114]

First generation JAKis are Tofactitinib, Baricitinib and Ruxolitinib.[114,115]

TOFACITINIB:

It causes selective inhibition of JAK – 1 AND 3 dependent JAK – STAT signaling pathway, thus causing the reduced production of IL – 2,4,7,15,21 and IFN-gamma. For six months, Tofacitinib must be taken twice daily at a dose of 5 mg. Tofacitinib is also available as a topical formulation although their efficacy is not as such as oral tofacitinib. Oral formulations are associated with side effects such as myelosuppression. Topical Formulation is associated with mild itching in very few cases.[116,117]

RUXOLITINIB:

It causes selective inhibition of JAK – 1 and 2 dependent JAK – STAT signaling pathway. Typically, oral formulations should be taken twice day at a dosage of 20 mg for a period of six months. Topical formulations of Ruxolitinib are also found to be efficacious.[118]

BARICITINIB:

It has non-specific activity on JAK-3 and is a powerful, selective inhibitor of JAKs 1 and 2. It is very efficacious as a daily dosage of 7 mg and 4 mg in morning and evening respectively for a period of 9 months.[118]

SECOND GENERATION JAKis:

The second generation JAKis include Filgotinib and Decernotinib which are selective inhibitors of JAK – 1 and 3.[118]

All JAKis have given encouraging results for AA and hence they can be incorporated as a treatment option for recalcitrant cases and extensive cases of AA.[119]

BIOLOGICS:

The promising biologics that are utilized as a treatment option for AA are Abatacept, Dupilumab and Anti – IL15RB MABs. They block the activation of cytotoxic CD8 T- lymphocytes.[120]

SULFASALAZINE:

Sulfasalazine is used for AA because of their immunomodulatory function and immunosuppressive action. 0.5 mg to 1.5 mg are administered twice day for three months.[10,121]

RETINOIDS:

Topical Baxoretene 1 percent gel is effective for AA because of their immunomodulatory action.[10,122]

ANTIHISTAMINES:

Few antihistamines like Ebastine and Fexofenadine can be used for Atopic AA patients.[10]

PHOTOTHERAPY/PHOTOCHEMOTHERAPY:

Phototherapy can be given for AA cases which are very extensive and recalcitrant. Oral Psoralen and Topical PUVA therapy has shown significant results with severe variants of AA such as AT and AU. Turban PUVA can be used for patients who are resistant to treatment. Depletion of antigen-presenting cells like Langerhan's cells and inflammatory cells like T lymphocytes is how PUVA works. Although numerous research have indicated that NBUVB is ineffective.[123,124]

308 nm EXCIMER LASER:

It is a non-invasive alternative therapy method that has produced positive outcomes when applied over the afflicted spot twice a week for a period of 12 weeks. However, it cannot be used for extensive recalcitrant cases of AA.[125]

MESOTHERAPY:

Intralesional injections of pentoxiphylline and multivitamins as multiple injections in the affected areas have shown excellent results.[126]

PLATELET – RICH PLASMA:

Platelet – Rich Plasma (PRP) has almost more than twenty growth factors which help as a nutritious source for the stem cells to proliferate. A number of studies must be conducted in order to understand the effectiveness of PRP in the treatment of AA due to the inconsistent findings of earlier studies.[127]

HAIR TRANSPLANTATION:

Hair transplantation is usually not recommended for AA. Few case reports have been done for recalcitrant cases of AA where the results were good with a disease-free period for about 8 months.[128]

OTHER TOPICAL EFFECTIVE THERAPIES:

Few nonspecific topicals which have given excellent results with AA are enrolled as follows:[129,130]

- Tincture Iodine
- Topical Azelaic Acid
- Capsaicin Gel
- Tretinoin 0.025 %,0.05 % cream and 0.1 % gel
- Inosiplex
- Calcipotriol
- Leflunomide with anthralin
- Cryotherapy with liquid nitrogen
- Fractional Er:Glass LASER

PSYCHIATRIC THERAPY:

AA being a secondary psychiatric disorder has shown significant results with therapies that alter their anxiety and depression. Few RCT studies have shown significant results with Aroma therapy, Hypnotherapy, and cognitive behavior therapy.[130]

CAMOUFLAGE/WIGS:

Patients of AA seek treatment exclusively for their cosmetic reasons because AA severely affects the quality of life. The clinical progression of AA is always unpredictable and the response to various treatment modalities is always uncertain. Hence Camouflage or appropriate Wigs can be given for patients and their quality of life has improved significantly, according to research.[131]

TREATMENT ALGORITHM:

Since treatment options are innumerable for AA with varied efficacy and limited usage depending on the types and variants of AA, a special treatment algorithm is being suggested for AA.[10] The algorithm for AA is as follows:[132,133]

TABLE – 3: ALOPECIA AREATA TREATMENT ALGORITHM < 10 YEARS[132]

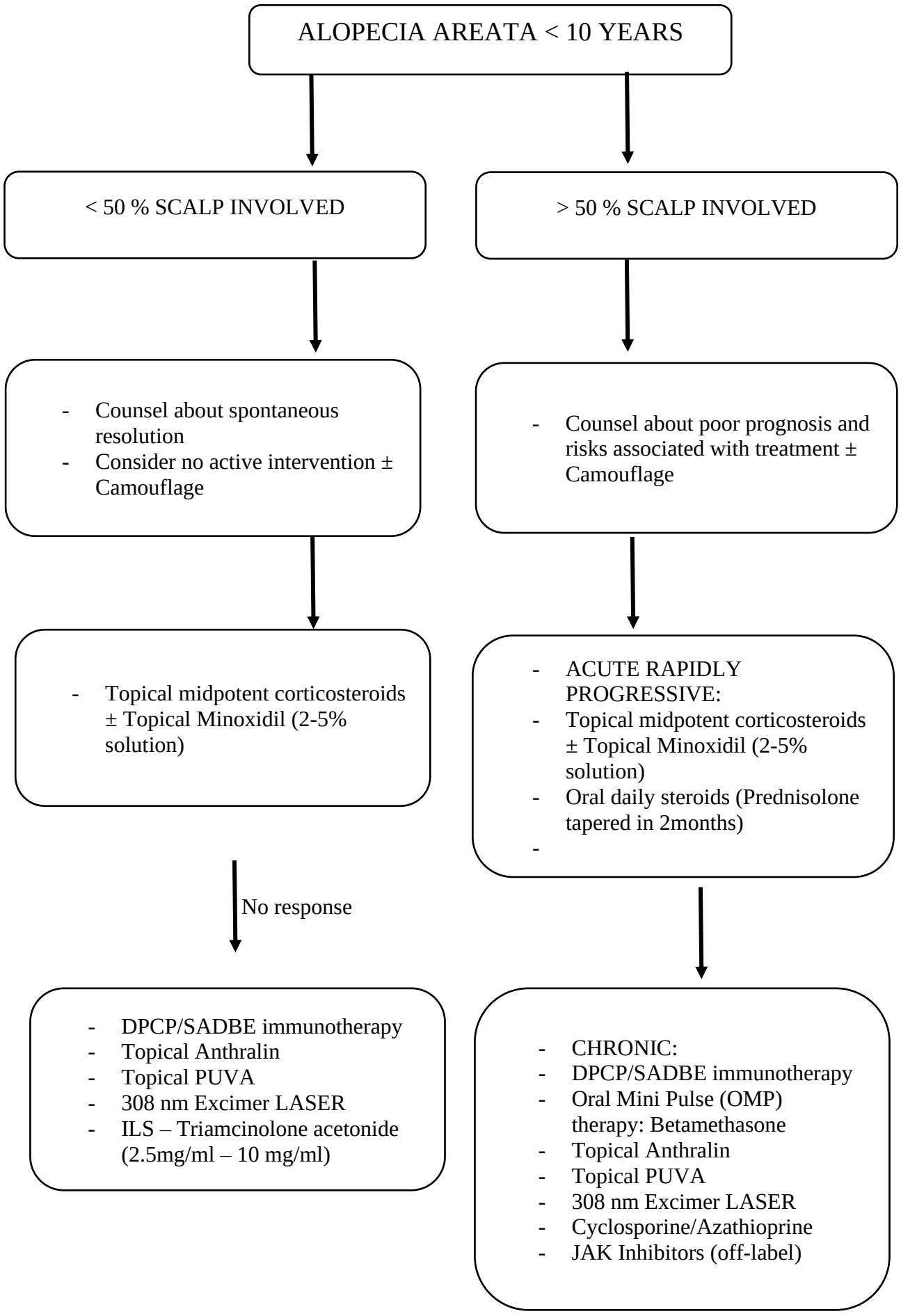
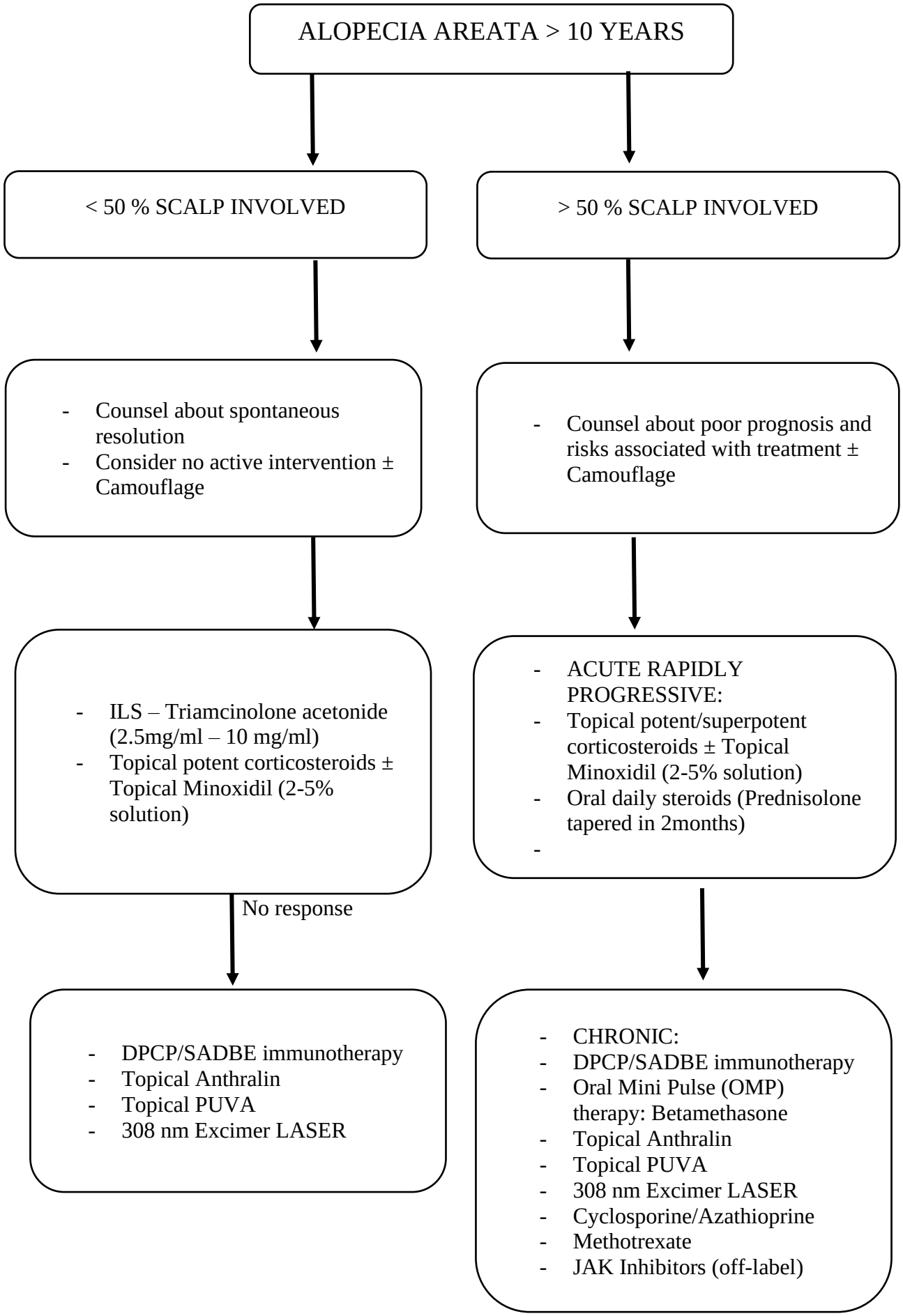


TABLE – 4: ALOPECIA AREATA TREATMENT ALGORITHM > 10 YEARS[133]



LASER

HISTORY:

The groundwork for LASER production traces back to the "On the Quantum Theory of Radiation" by Einstein in 1916.[134] MASER is the predecessor to LASER with integrated production of microwaves. It was invented by Gordon in 1955.[135] The physical operating principles behind LASER production was laid by Schwalow and Townes in Bell Laboratories.[136] In 1960, LASERS were first produced by Maiman using a Ruby crystal with a flash pump that emits intense pulses of light.[137]

LASER medicine's founder is Leon Goldman. In the year 1960, he was the first person to employ LASER therapeutically in the field of medicine. He utilized Ruby LASER for pigmented lesions which are benign in nature.[138,139] Mixture of helium and neon gas was the first LASER which is of gas medium was introduced in the year 1961.[140] The red colour from this LASER formed the basis for prime targeting in Carbon dioxide LASER (CO2 LASER).[141]

In subsequent years, Nd-YAG LASER and Argon LASER were introduced into the market in 1961 and 1962 respectively.[141] In 1962, Goldman used Ruby LASER to treat pigmented tattoos. In 1964 Patel developed CO2 LASER at Bell Laboratories.[143]

1983 marked the revolution of LASERs in the field of medicine by the ideology and principles of "Selective Photo Thermolysis (SPT)" by Anderson and Parish.[144]

LASER – "LIGHT AMPLIFICATION BY STIMULATED EMISSION OF RADIATION" [144]

BASICS OF LASER:

LASER is based on the principle of photoelectric effect. Bohr's model states that in an atom, there is a central mass called nucleus which contains neutrons and positively charged particles namely protons. Negatively charged Electrons that have a fixed orbit around the nucleus is shown in (a) of Figure – 1.[144,145]

The electron orbiting the nucleus in a orbit closer to nucleus has lower energy than the electron in farther orbit. When the electron absorbs a light energy (Photon), the electrons get activated and move on to higher energy level orbit. Thus, the electron has moved from a resting state to an excited state in an atom by the absorption of photons as shown in (b) of Figure – 1.[144,145]

Electrons are in a unstable state when they are in excited state. Hence, The release of light energy in the form of photons causes them to revert to their resting state, which happens spontaneously and erratically in all directions as illustrated in (c) of Figure - 1. This is called "SPONTANEOUS EMISSION OF RADIATION". This forms the basis for sunlight and any other naturally observed light.[144,145]

If the electrons in an excited state, absorbs one more photon of same energy levels then when the electrons come back to the resting state, it releases two photons of same energy levels, wavelength, phase and unidirectional of the absorbed photon as shown in (d) and (e) of Figure – 1. This phenomenon is called "STIMULATED EMISSION OF RADIATION".[144,145]

The energy required to produce stimulated emission of radiation in a LASER machine is by an external energy power source. Each time this process of stimulated emission of radiation happens, the number of photons keeps increasing in the LASER cavity. When most of the electrons are in a high energy state by the absorption of photons, the electrons are said to be in a state of "Population Inversion". So, when the electrons fall back to the lower energy level, a very powerful coherent eruption of stimulated emission of radiation happens. This chain reaction produces LASER.[144,145]

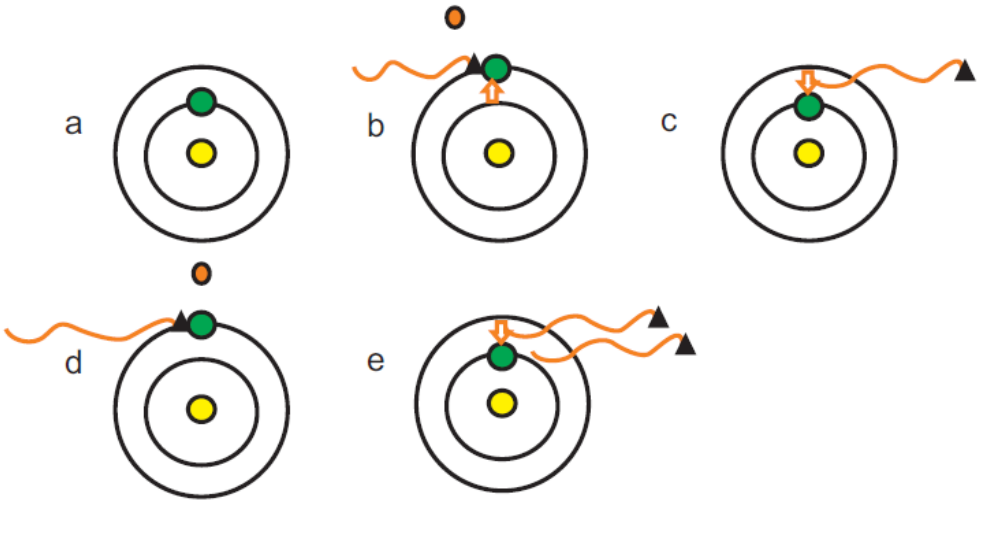


FIGURE – 1: BASICS OF LASER[144,145]

PROPERTIES OF LASER LIGHT:

The characteristic features of LASER light are as follows:[146,147]

- **MONOCHROMATIC:** All waves emitted from LASER have same wavelength and when it is passed through prism it shows one color only. (Mono – one, Chromatic – color).
- **COHERENT:** In terms of space and time, all waves in a laser medium are in phase with one another.
- **COLLIMATED:** All waves in LASER travel parallel to each other and they don't have divergence.
- **HIGH INTENSITY:** They emit light of magnitude with high intensity.[146,147]

EFFECT OF LASER ON TISSUES:

LASER can cause biological changes in skin only if the chromophore in the skin absorbs the light and is converted in to thermal energy. The temperature reached in the targeted chromophore and the time spent at that temperature determine the biological effect of laser on skin.[148,149]

Biological reactions observed due to LASER include the following:

- Photothermal reaction – coagulation of tissues
- Photomechanical reaction – vibratory effect on tissues
- Photochemical reaction – photooxidative effect on tissues[148,149,150]

SELECTIVE PHOTOTHERMOLYSIS:

Anderson and Parish at Harvard Medical School initiated the concept of "Selective Photo thermolysis" in 1983 that revolutionized the utilization of LASERS in the field of medicine.[151]

Factors that determine selective photothermolysis are enlisted as follows:

- Wavelength
- Fluence or energy density
- Pulse width/duration[151,152]

CHROMOPHORES IN SKIN:

Chromophores are the substances that absorb specific wavelength of a particular light depending on the absorbing gradient. The skin has three chromophores. They are water, haemoglobin, and melanin. Each chromophore has a unique peak absorption and absorption spectrum.[153]

LASER PARAMETERS:

The LASER parameters that are utilized for administration of LASER for therapeutic purposes are enumerated as follows: [146,152,153]

- **ENERGY:**

It is the quantity of photons sent in a single pulse. The unit of measurement for Energy of LASER light is Joules. [146,152,153]

ENERGY (JOULES) = POWER (WATT) X DURATION (SECONDS)

- **POWER:**

It is described as the quantity of LASER energy released in a certain amount of time. It is measured in Watts.[146,152,153]

- **POWER DENSITY:**

Power density refers to the amount of energy given per unit area in an affected tissue area. It is otherwise called Irradiance. It is measured as Watt/ cm^2.[146,152,153]

- **FLUENCE:**

The total measure of energy that is delivered is called Fluence. It is calculated by the following formula: [146,152,153]

FLUENCE (JOULES/CM^2) = POWER DENSITY x EXPOSURE TIME

- **WAVELENGTH:**

The distance between two troughs or two crests in a LASER wave is called wavelength. It is measured for LASER in nanometers. [146,152,153]

- **SPOT-SIZE:**

The term "spot size" refers to the diameter of the laser beam. It is measured in millimeters. [146,152,153]

- **FREQUENCY:**

The number of crest or trough in a LASER wave for a second is called Frequency. It is measured in Hertz (Pulses/second). [146,152,153]

CLASSIFICATION OF LASERS:

LASERS are classified based on the LASER medium constituents and the pulse characteristics. Hence the classification of LASERS are as follows:[150,152,153]

TABLE – 5: CLASSIFICATION OF LASERS[150,152,153]

CLASSIFICATION OF LASERS

BASED ON LASER MEDIUM CONSTITUENTS

1.GAS LASERS:

- ARGON LASER
- CO2 LASER
- EXCIMER LASER

2. LIQUID LASERS:

- PULSED DYE LASER

3. SOLID LASERS:

- DIODE LASER, ERBIUM YAG LASER, Nd:YAG LASER, RUBY LASER, and ALEXANDRITE LASER

4.SOLID STATE LASER:

- RUBY LASER

BASED ON PULSE CHARACTERISTICS

1. CONTINUOUS LASERS

2. PULSED LASERS:

- SUPER PULSE LASERS
- ULTRA – PULSE LASERS

3. Q – SWITCHED LASERS:

- QUALITY SWITCH LASERS

FRACTIONAL CO2 LASER

Fractional CO2 LASER is one of the ideally used surgical LASER in day today practice. The wavelength of a fractional CO2 laser is approximately 10,600 nm. The water that serves as a chromophore in dermal collagen and keratinocytes is its main target in the skin. Fractional CO2 LASER is widely used for various surgical interventions because of their high-water absorption. They work on the waveband of invisible Infrared rays. The biological effect that is caused by Fractional CO2 LASER are incision, excision, vaporization, and coagulation of tissues.[154,155]

MECHANISM OF ACTION:

The boiling point of water is 100 degrees Celsius. Water is present in 70 % of soft tissues in skin. The chromophore for fractional CO2 laser is water. When the CO2 LASER light incidents over these tissues, the water content in this tissue attain a temperature rise of 100 degrees Celsius due to the photothermal effect of LASERS. This causes water vapor formation and gasification changes that coagulates the tissues which then gets removed by fragmentation and ablation. Thermocoagulation occurs in the region of impact of LASER over the area due to protein degradation and protein denaturation.[154,155,156]

MODES OF FRACTIONAL CO2 LASER:

Various modes in a Fractional CO2 LASER includes the following:[154,156,157]

- Continuous Wave (CW)
- GATED Continuous Wave (GATED – CW)
- QUASI – Continuous Wave (QUASI – CW)
- "ULTRA PULSED" OR SUPER PULSED" Continuous Wave[154,156,157]

MICRO ABLATIVE COLUMN (MAC):

Micro Ablative Column (MAC) is created when Fractional CO2 LASER is administered over skin. Micro Ablative Column (MAC) extends into epidermis and dermis. The extent of MAC depends on the power and duration over the lesion area.[154,156]

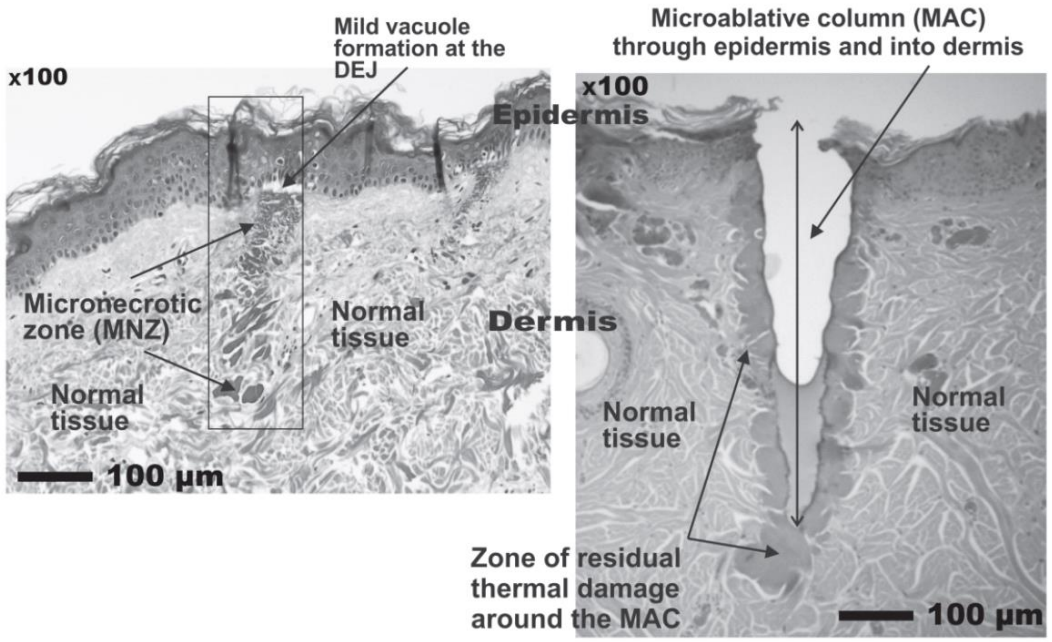


FIGURE – 2: MICRO ABLATIVE COLUMN (MAC)[154,156]

Once MAC is created, the epidermis is ablated and in dermis, collagenesis is induced followed by remodeling of collagen bundle occurs. Moreover, MAC acts as a transdermal passage for various drugs to get percolated over the diseased site. So, for a variety of dermatoses, Fractional CO2 LASER can be employed as a "Transdermal Drug Delivery System."[154,158]

SAFETY WITH FRACTIONAL CO2 LASER:

Fractional CO2 LASER is a destructive LASER procedure and hence safety for patients is an essential task to be considered. Patients must be given protective eye shields as the corneal reflex and conjunctival reflex cannot protect the eyes from LASER.[154,156,157]

Since targeted therapy is done using Fractional CO2 LASER, it is always advisable to drape the normal skin using a damp cloth and focus the targeted lesion for administering LASER over the area.[154,155]

Potentially harmful viable viral particles can be created by the LASER plume and hence Smoke Evacuator must be switched on during the procedure.[154,155,156]

INDICATIONS:

Fractional CO2 LASERS are considered as Surgical LASERS by the late professor Kaplan who quotes that Fractional CO2 LASERS can be used for any surgical procedures because of their precise targeted actions. Hence various indications of Fractional CO2 LASERS are enumerated below:[154,155,156,157]

- **SKIN LESIONS:**

  The clinical indications of Fractional CO2 LASER for various skin ailments are due to their targeted incision, vaporization of targeted areas and coagulation thus attaining better homeostasis than the cold scalpel. Usually, Fractional CO2 LASER is avoided in cases of malignancy

because of their tendency to metastasis. Fractional CO2 LASERS are widely used in the following clinical dermatological cases:

- **NEVI** – All types of nevi can be excised using Fractional CO2 LASER after successful topical anesthesia is achieved. Nevi which have a tendency for malignant transformation are avoided. The advantage with Fractional CO2 LASER than the other treatment modalities is because of their cosmetic superiority.
- **SEBORRHEIC KERATOSIS**
- **ACROCHORDONS** (also known as skin tags)
- **DERMATOSIS PAPULOSA NIGRA**
- **SYRINGOMAS**
- **XANTHALESMA PALPEBRUM**
- **CERTAIN MALIGNANT CONDITIONS:** It can be used for Basal Cell Epithelioma because of their little or rare tendency for malignant transformation.
- **WARTS:** Verruca vulgaris, Palmoplantar warts, Anogenital warts and Condyloma acuminatum can be removed with minimal charring using Fractional CO2 LASER. Precautions must be taken because viable viral DNA particles are observed in the LASER plume. Hence, it is better to operate with a smoke evacuator switched on for warts.
- **TOENAIL DISEASE:** Onychodystrophy and Ingrowing toe nail can be therapeutically removed using Fractional CO2 LASER. In cases of Onychodystrophy, nail bed is irradiated. In cases of Ingrown toe nail, wedge resection of toe nail is done using ablative setting of Fractional CO2 LASER.

It has a very good cosmetic and therapeutic appeal than the conventional surgical methods.

- **ANTI – AGING:** After successful topical anesthesia over face, facial rejuvenation can be achieved over face by administration of a low power Fraction CO2 LASER fluence over full face. This procedure is also called LASER Peel.
- **MILD WRINKLES:** Fractional CO2 LASER helps to revise the mild wrinkles over face in multiple settings.
- **STRIAE / STRETCH MARKS:** Stretch marks get revised by the fluence of Fractional CO2 LASER in subsequent settings.
- **ACNE SCARS:** The superficial epidermis is ablated by Fractional CO2 LASER, which also causes collagen synthesis and dermal remodelling, aiding in the correction of acne scars.
- **KELOIDS/HYPERTROPHIC SCARS**
- **LASER ASSISTED DRUG DELIVERY SYSTEM FOR VARIOUS DERMATOSES**[154,155,156,157,158]

FRACTIONAL CO2 LASER ASSISTED DRUG DELIVERY SYSTEM:

It creates micro ablative column pores over the skin, thus enabling a means to reach the active pathological site. Thus, the LASER administration followed by topical application of therapeutic agents can cause better percolation of the agents thus enabling increased bioavailability and enhanced delivery of drug. It has been proved that Fractional CO2 LASER assisted drug delivery has more efficacy than other topical or intralesional medications for various dermatoses. Various dermatoses where Fractional CO2 LASER assisted drug delivery can be incorporated as follows:[154,157,158]

- **NON – MELANOMA SKIN CANCERS:**
    1. **ACTINIC KERATOSES:** Ablative LASER over the area with Topical application of 5 – Fluorouracil and Imiquimod has shown better results.
    2. **BOWEN'S DISEASE:** Ablative LASER over the premalignant lesion with Topical application of 5 - Fluorouracil under occlusion can be used as a treatment modality for Bowen's disease.
    3. **ACTINIC CHEILITIS:** Fractional CO2 LASER assisted Photo Dynamic Therapy is a novel treatment modality for actinic cheilitis.
    4. **BASAL CELL CARCINOMA:** Ablative LASER followed by Photo Dynamic Therapy has shown good results for Basal cell carcinoma.

- **PIGMENTARY DISORDERS:**
    1. **VITILIGO:** (Ablative LASER followed by NBUVB)
    2. **MELASMA:** (Ablative LASER followed by Tranexamic acid)

- **LOCAL ANESTHESIA AND ANALGESIA:** (Ablative LASER followed by topical anesthesia and topical analgesics like diclofenac)
- **KELOIDS/HYPERTROPHIED SCARS:** (Ablative LASER followed by potent steroids like Topical Triamcinolone Acetonide Solution)
- **HEMANGIOMA:** (Ablative LASER followed by Topical Timolol can be used for the treatment for infantile hemangiomas)
- **ALOPECIA:**
    1. **ANDROGENETIC ALOPECIA – MALE PATTERN:** (Ablative LASERS followed by Topical Finasteride – 0.05 %, Ablative LASERS followed by Topical Minoxidil – 5 %, Ablative LASERS followed by Topical Growth factors or platelet rich plasma)
    2. **ALOPEICA AREATA:** Ablative LASERS followed by Potent steroids application is a novel treatment for AA.
- **ONYCHOMYCOSIS:** (Ablative LASERS followed by Topical Amorolfine)

- **COSMETIC ANTI – AGEING PROCEDURES:** (Ablative LASER followed by topical botulinum toxin have given good results for wrinkles)[154,156,157,158]

FRACTIONAL CO2 LASER SETTINGS:

The recommended settings of Fractional CO2 LASER for various dermatoses indications are as follows:[154,155,158]

TABLE – 6: FRACTIONAL CO2 LASER SETTINGS[154,155,158]

INDICATIONS	POWER	DURATION	DISTANCE	POINT ENERGY J/cm2	REPEAT	TIMES	MODE
Skin Rejuvenation / Lightening Laser peel	10-15	1	0.8	10-15	Single	1	Normal Random
Mild Wrinkle/ Wrinkle removal	20-30 30-40	1	1.0-1.2	20-30 30-40	Single	1 or 2 Deep Scar	Normal
Stretch marks/ Accident Scar	30-45	1-1.5	0.8	30-60	Single	2-3	Normal Random
Acne Scar	30-45	1-1.5	0.8	30-60	Single	2-3	Normal Random
Keloid	40-50	2-3	1.2 & above	90-120	Single	2-3	Normal

The above recommended settings are derived based on the depth of Micro Ablative Columns created by the Fractional CO2 LASER in a given setting. The energy required to reach the targeted areas in skin are as follows:[154,157,158]

TABLE – 7: FRACTIONAL CO2 LASER POINT ENERGY FOR TARGETED DAMAGE[154,157,158]

DEPTH OF DAMAGE	POINT ENERGY = POWER X DURATION
Epidermis	10-15 mJ
Dermo Epi Junction	15-20 mJ
Upper Dermis	20-30 mJ
Mid Dermis	30-45 mJ
Acne scar (Box Car Scar or Deep Scar)	45-60 mJ
Keloid or Hypertrophic Scar	90-120 mJ

COMPLICATIONS:

Fractional CO2 LASERS due to their coagulation and ablation properties can cause various complications which are categorized as follows:[159,160]

- **GENERAL COMPLICATIONS:[159,160]**
    1. **OCULAR INJURY:** Cornea, Conjunctiva, Vascular choroid structures, and Retinal injury can happen if eye shields are not used to protect the eyes during Fractional CO2 LASER procedure.
    2. **FIRE HAZARD:** Flammable substances should not be present during Fractional CO2 LASER procedure. Hence during procedures,

cleaning the targeted area with alcohol should never be done. Only a wet gauze with water is encouraged to clean the area prior procedure because water is the targeted chromophore for Fractional CO2.

3. **ELECTRIC HAZARD:** Regular maintenance and services by trained professionals are essential to prevent the hazards of electrocution.
4. **PLUME HAZARD:** Plume or surgical smoke is produced when the cauterization and coagulation of tissues occur during Fractional CO2 LASER. Plume has mutagenic properties and viable viral particles. Hence, during Fractional CO2 LASER procedures, it is always advisable to switch on the smoke evacuator.
5. **TEETH HAZARD:** Enamel in teeth can undergo irreversible melting and resolidification at higher fluences and can result in charring, flaking, and cracking of teeth. In lower fluences, it can cause discoloration of teeth. Hence during procedures, mouth is kept closed and damp wet gauze is placed over the mouth.

- **EPIDERMAL COMPLICATIONS:**[159,160]

1. **HYPERPIGMENTATION:** Post inflammatory hyperpigmentation is a common entity following any coagulative procedures. It is more among individuals with darker skin tone. It may last for three to four months and responds well to topical depigmenting agents.

2. **HYPOPIGMENTATION:** Post inflammatory hypopigmentation is very common if melanocytes are destroyed during procedure. They usually resolve insidiously.
3. **BLISTER FORMATION:** Thermal injury caused by the Fractional CO2 LASER can cause blisters in epidermis and dermis. It can be prevented by prior usage of sunscreens before the LASER procedure.
4. **MILIA:** Milia commonly occurs after the Fractional CO2 LASER resurfacing of skin.
5. **POST OPERATIVE CRUSTING:** Crusting is common after Fractional CO2 LASER procedures.

- **DERMAL COMPLICATIONS:**[159,160]

1. Wound infection
2. Scarring
3. Hypertrophied Scars
4. Atrophic Scars
5. Irritant Contact Dermatitis to post LASER topical medications
6. Post procedural Erythema
7. Purpura
8. Chrysiasis after LASER procedures
9. Allergic lichenoid, granulomatous and photoallergic reactions can occur over the LASER administered area.

FRACTIONAL CO2 LASERS FOR AA:

In addition to working as a transdermal drug delivery mechanism for powerful steroids in the treatment of AA, fractional CO2 lasers have a variety of therapeutic effects on the scalp. It is believed that fractional CO2 lasers cause T cells to undergo apoptosis, stop hair follicles in the telogen stage, and stimulate the anagen stage. In hair follicles, it also induces de novo neogenesis and stem cell differentiation. Additionally, fractional CO2 laser stimulates the Anagen phase of the hair cycle in mouse model studies via Wnt/-catenin signalling pathways. In the meantime, the heat impact that lasers have on the papillary dermis promotes hair development.[6,156,157,158]

The use of fractional CO2 LASER as a transdermal medication delivery system for steroids in the management of alopecia areata is scarcely documented in the literature. Hence the efficacy and safety profile are limited to few studies which have shown excellent results in recalcitrant cases and adverse effects are very minimal.[157,158]

METHODOLOGY

MATERIALS AND METHODS

SOURCE OF DATA:

This hospital-based interventional study was conducted in the outpatient clinic of Department of Dermatology Venereology and Leprosy in R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar from January 2021 to July 2022 after the Institutional Ethical Clearance (IEC). An informed consent was procured from AA patients about the participation in the study, disease nature and the necessity to follow-up.

STUDY DESIGN: Randomized Controlled Trial [RCT]

INCLUSION CRITERIA:

1. Patchy AA.
2. Patients who had not received any medical care in the previous three months.

EXCLUSION CRITERIA:

1. Patients with special variants of AA and atypical patterns.
2. Patients with cardiac, renal, and hepatic diseases as well as other systemic illnesses
3. Immunocompromised patients
4. Pregnant patients

SAMPLE SIZE CALCULATION:

Sample Size was estimated based on the complete improvement proportion seen in the recent research article – "Comparative Study between Fractional Carbon Dioxide Laser versus Intralesional Steroid injection in Treatment of Alopecia Areata" by Husseiny, et al. The complete improvement proportion in the treatment of Alopecia Areata seen with Fr CO2 Laser and Topical Steroids was 25% while the complete improvement proportion seen with Intralesional Steroid injection was 1%. So, with 95% Confidence interval, Alpha error 5% and Power value of 80% - the estimated total sample size for the study is 60 and the sample size per group is 30.

TABLE – 8: SAMPLE SIZE CALCULATION	
Proportion in Group I	25%
Proportion in Group II	1%
Risk Difference	24%
Power (%)	80%
Alpha Error (%)	5%
Required sample size for each group	30
Total Sample size	60

$$N_1 = \left\{ z_{1-\alpha/2} * \sqrt{\bar{p} * \bar{q} * (1 + \frac{1}{k})} + z_{1-\beta} * \sqrt{p_1 * q_1 + (\frac{p_2 * q_2}{k})} \right\}^2 / \Delta^2$$

$$q_1 = 1 - p_1$$

$$q_2 = 1 - p_2$$

$$\bar{p} = \frac{p_1 + k p_2}{1 + K}$$

$$\bar{q} = 1 - \bar{p}$$

$$N_1 = \left\{ 1.96 * \sqrt{0.13 * 0.87 * (1 + \frac{1}{1})} + 0.84 * \sqrt{0.25 * 0.75 + (\frac{0.01 * 0.99}{1})} \right\}^2 / 0.24^2$$

$$N_1 = 30$$

$$N_2 = K * N_1 = 30$$

---

p_1, p_2 = proportion (incidence) of groups #1 and #2
$\Delta = |p_2 - p_1|$ = absolute difference between two proportions
n_1 = sample size for group #1
n_2 = sample size for group #2
α = probability of type I error (usually 0.05)
β = probability of type II error (usually 0.2)
z = critical Z value for a given α or β
K = ratio of sample size for group #2 to group #1

The study's total sample size is 60. 60 cases had been evaluated and followed-up on throughout the study's time frame (January 2021 to July 2022). A and B were the two groups formed from the 60 cases.

Thirty patients in Group A had five settings of fractional CO2 laser therapy with topical triamcinolone acetonide aqueous solution, with three weeks between each setting.

Intralesional triamcinolone acetonide was administered intravenously to 30 patients in Group B five times, with three weeks between each administration.

RANDOMIZATION:

Total sample size for the study is 60 and the sample size per each group (Group A and Group B) is 30. To avoid the SELECTION BIAS in the study, randomization of the sample selection is essential. Hence randomization is done by using COMPUTER GENERATED BLOCK RANDOMIZATION.

COMPUTER GENERATED BLOCK RANDOMIZATION PLAN is generated from www.randomization.com. To create the randomization list, following parameters are set:

- Seed: 28397
- Treatment groups: Group – A, Group – B
- Block Size: 4
- List Length: 60

A Randomization Plan

from

http://www.randomization.com

1. B
2. B
3. B
4. B
5. A
6. B
7. A
8. A
9. A
10. A
11. B
12. B
13. B
14. A
15. A
16. A
17. A
18. B
19. B
20. B
21. A
22. B
23. B
24. A
25. B
26. B
27. B
28. A
29. A
30. B

31.	A
32.	A
33.	B
34.	B
35.	A
36.	A
37.	B
38.	B
39.	B
40.	A
41.	A
42.	B
43.	B
44.	B
45.	A

46.	A
47.	A
48.	B
49.	A
50.	A
51.	A
52.	B
53.	B
54.	A
55.	A
56.	A
57.	A
58.	B
59.	A
60.	B

60 subjects randomized into 1 block
To reproduce this plan, use the seed 28397
Randomization plan created on 10/11/2020, 14:38:58

METHODOLOGY:

<u>GROUP – A:</u> (FRACTIONAL CO2 LASER WITH TOPICAL TRIAMCINOLONE ACETONIDE)

On the treatment region, a topical anaesthetic cream was administered for 45 minutes. It contained a combination of TETRACAINE - 7.0 percent w/w and LIDOCAINE - 7.0 percent w/w. A gauze dipped in distilled water was used to wipe the treatment region when a suitable level of topical anaesthesia was attained. Eyes was protected with eye shields.

Fractional CO2 LASER was then delivered to the Alopecia Areata site at the following setting:

FIGURE – 3: FRACTIONAL CO2 LASER

TABLE – 9: SETTINGS

1.	Power	30 W
2.	Duration	1.5 ms
3.	Distance	0.8 cm
4.	Point Energy	45 mJ/cm2
5.	Repeat	Single
6.	Times	2
7.	Mode	Normal

Then within 2 minutes of LASER procedure, Topical Triamcinolone Acetonide Aqueous solution (2.5 mg/ml to 10 mg/ml) was applied depending on the site. (10 mg/ml – Scalp, 5 mg/ml – Beard/Moustache, 2.5 mg/ml – Eyebrow).

Patients in Group A received Fractional CO2 Laser with Topical Triamcinolone acetonide aqueous solution for 5 settings with each setting a gap of 3 weeks.

GROUP – B: (**INTRALESIONAL TRIAMCINOLONE ACETONIDE**)

Multiple 0.1ml injections (4 Units) of triamcinolone acetonide were administered intradermally using an insulin syringe at 1 cm intervals. (10 mg/ml – Scalp, 5 mg/ml – Beard/Moustache, 2.5 mg/ml – Eyebrow).

Intralesional triamcinolone acetonide was administered intradermally to patients in Group – B five times, with a three-week interval between each setting.

Assessment of efficacy and safety profile in both groups were done by using the following scales:

1. Global Photograph Assessment (GPA) Scale
2. Lesional Area and Density (LAD) Score Percentage of Improvement
3. Visual Discomfort Scale (VDS)
4. Visual Analogue Scale (VAS)
5. Documentation of adverse effects

Using the following scales, the effectiveness of the treatment in both groups was determined:

1) **GLOBAL PHOTOGRAPH ASSESSMENT (GPA) SCALE:**

Patients of this study had undergone serial photography of the lesions at baseline and at subsequent settings. Lighting and Positioning were kept identical for all serial photographs.

The serial photographs were assessed independently by a Blinded Third Observer. The Blinded Third Observer gave the grading of the efficacy of the treatment modality based on the Global Photograph Assessment (GPA) scale. GPA – Scale was calculated for all the patients of the study at the baseline presentation and at subsequent follow up settings.

The Blinded Third Observer assigned a score of 0, 1, 2, or 3 depending on whether the response was less than 25%, between 25% and 50%, between 51 and 75 percent, or greater than 75 percent.

2) **LESIONAL AREA AND DENSITY (LAD) SCORE PERCENTAGE OF IMPROVEMENT:**

Lesional Area and Density (LAD) score Percentage of Improvement was used to determine the efficacy of the treatment modalities in each group.

LAD score was calculated by the formula:

LAD Score = Area of alopecia areata site x Density of hair loss in percentage

LAD Score was calculated for all the patients of the study at the baseline presentation and at subsequent follow up settings.

The LAD Score Percentage of Improvement was assessed at each setting with the baseline presentation.

LAD Score Percentage of Improvement was calculated by the formula:

$$\text{LAD Score Percentage of Improvement} = \frac{\text{LAD Score at baseline presentation} - \text{LAD score at given setting}}{\text{LAD Score at Baseline Presentation}} \text{ X } 100$$

The safety of both treatment modalities was assessed using the following:

1) **VISUAL DISCOMFORT SCALE (VDS):**

The Visual Discomfort Scale (VDS) (Score ranges from a scale of 0 to 10) was used to record the subjective discomforts of the patients during the procedure such as pain, burning sensation and any other non-specific discomforts.

2) **VISUAL ANALOGUE SCALE (VAS):**

The visual analogue scale (VAS) (Score ranges from a scale of 0 to 10) was used to record the satisfaction of the treatment modality as perceived by patients at the end of 5 settings.

3) **ADVERSE EFFECTS:**

Post procedural adverse effects were also documented to assess the safety of both the treatment modalities.

STATISTICAL ANALYSIS:

Data from the study was recorded into an Excel data sheet of Microsoft Windows. After that, it was examined and analysed using SPSS 22 software.

$\sum$ (average) was calculated for GPA and LAD Improvement % at the end of all settings and VDS and VAS at the end of 5^{th} setting.

Data that was categorical was displayed as frequencies and proportions. For qualitative data, the Chi-Square Test or Fischer's Exact Test was employed as the Test of Significance. Mean and Standard Deviation were used to represent continuous data. To determine the mean difference between two quantitative variables, the independent t test was applied as a measure of significance.

After taking into account all the guidelines for statistical tests, P Value less than 0.05 was deemed statistically significant.

RESULTS

RESULTS:

TABLE – 10: DISTRIBUTION OF CASES ACCORDING TO SEX

SEX	GROUP – A	GROUP – B	TOTAL
MALE	24	22	46
	80 %	73.3 %	77 %
FEMALE	6	8	14
	20 %	26.6 %	23 %
TOTAL	30	30	60
	100 %	100 %	100 %

Amongst the study population, 77% of cases were men (46 cases) and 23% of cases were women (14 cases). 43.3% in our study (26 cases) had a strong familial history of AA. 23.3% (14 cases) had a past history of Patchy AA who were treated with various treatment modalities in the past.

GRAPH – 1: GRAPH SHOWING DISTRIBUTION OF CASES ACCORDING TO SEX

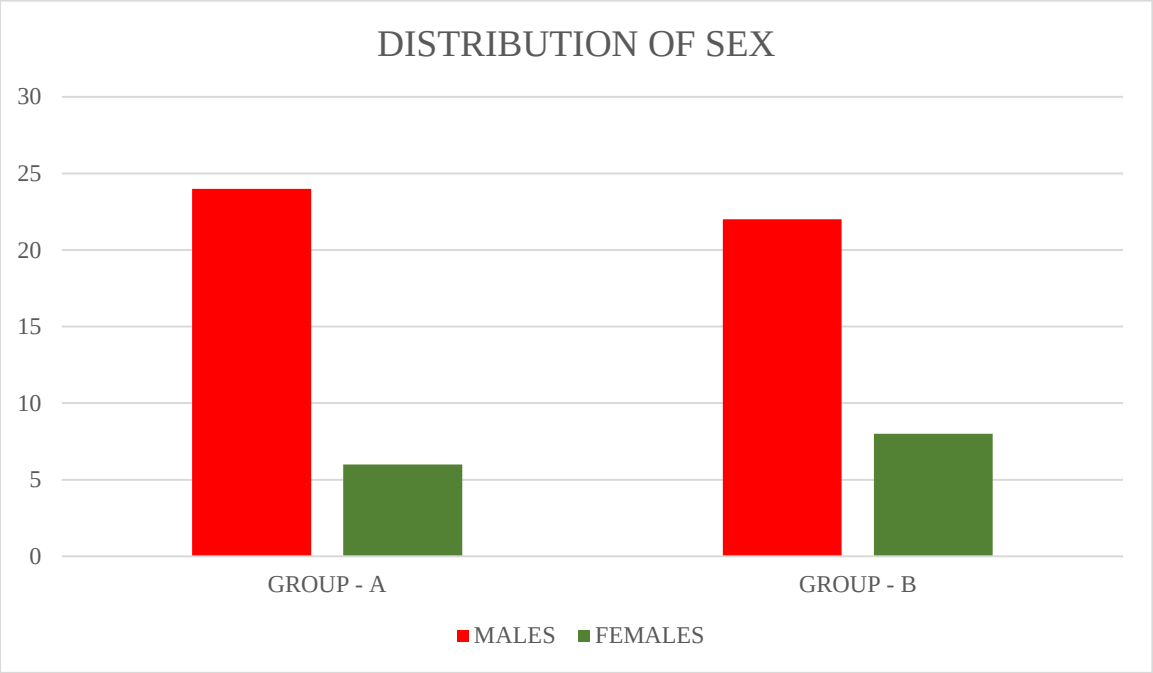


TABLE – 11: DISTRIBUTION OF CASES ACCORDING TO AGE GROUPS

AGE	GROUP – A	GROUP – B	TOTAL
< 18 YEARS	2	4	6
	6.67 %	13.3 %	10 %
18 – 30 YEARS	13	12	25
	43.3 %	40 %	41.6 %
30 – 40 YEARS	12	11	23
	40 %	36.6 %	38.3 %
40 – 50 YEARS	1	2	3
	3.3 %	6.6 %	5 %
> 50 YEARS	2	1	3
	6.6 %	3.3 %	5 %
TOTAL	30	30	60
	100 %	100 %	100 %

In our study, most of them are of 18-30 years (41.6% - 25 cases) of age followed by 30-40 years of age (38.3% - 23 cases).

GRAPH – 2: GRAPH SHOWING DISTRIBUTION OF CASES ACCORDING TO AGE GROUPS

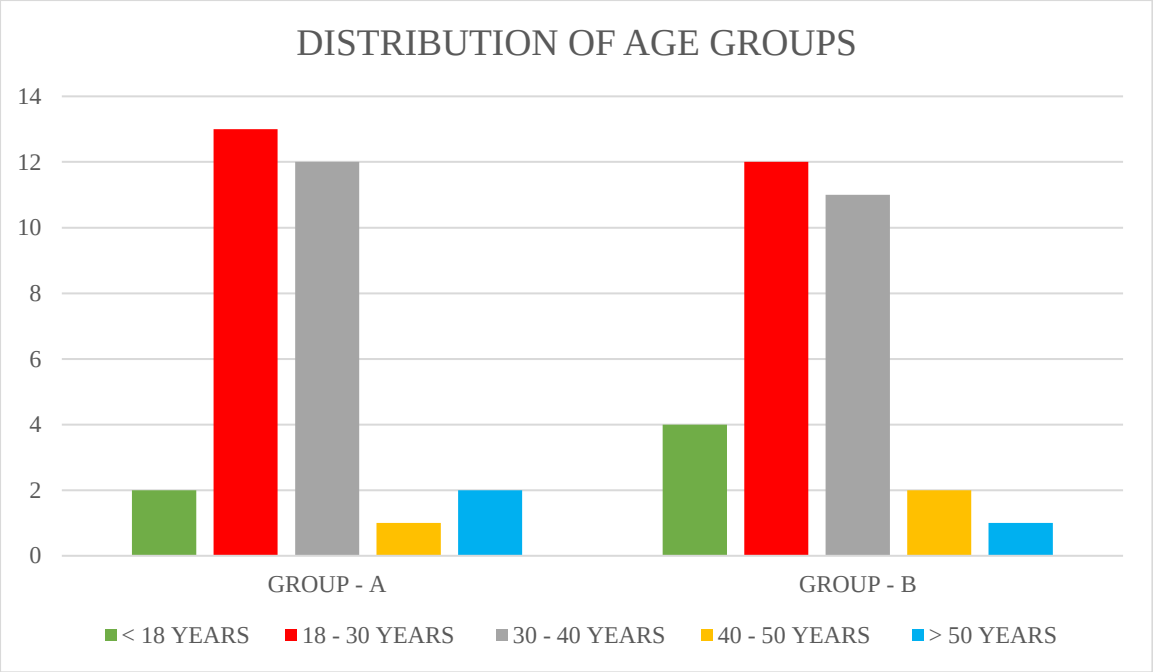
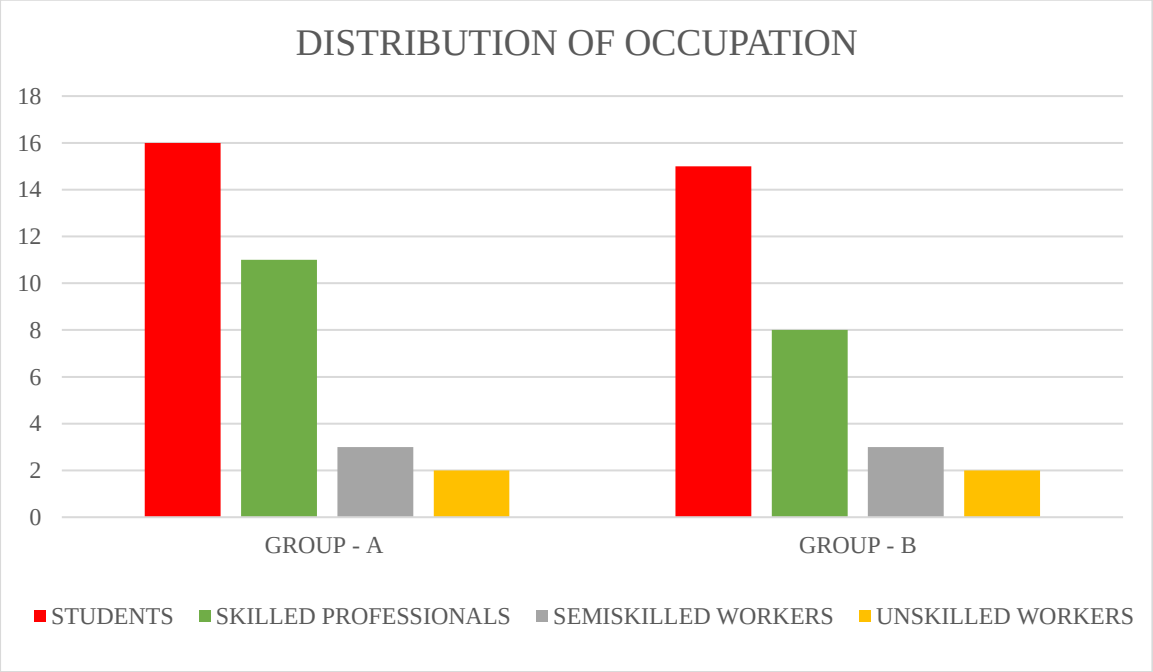


TABLE – 12: DISTRIBUTION OF CASES ACCORDING TO OCCUPATION

OCCUPATION	GROUP – A	GROUP – B	TOTAL
STUDENT	16	15	31
	53.3 %	50 %	51.6 %
SKILLED PROFESSIONALS	11	8	19
	36.6 %	26.6 %	31.6 %
SEMISKILLED WORKERS	3	3	6
	10 %	10 %	10 %
UNSKILLED WORKERS	2	2	4
	6.6 %	6.6 %	6.6 %
TOTAL	30	30	60
	100 %	100 %	100 %

In our study, 51.6% (31 cases) of the patients were Students (School/College going students), 31.6% (19 cases) were Skilled Professionals (which includes IT Professionals, Doctors, Bankers, Policemen), 10% (6 cases) were semi-skilled workers and 6.6% (4 cases) were unskilled workers.

GRAPH – 3: GRAPH SHOWING DISTRIBUTION OF OCCUPATION



78.3% (47 cases) of them had constant stress in their day-to-today activities.

TABLE – 13: DISTRIBUTION OF CASES DEPENDING ON THE NUMBER OF PATCHES

NUMBER OF AA PATCHES	GROUP – A	GROUP – B	TOTAL
SINGLE PATCH	7	9	16
	23.3 %	30 %	26.6 %
MULTIPLE PATCHES	23	21	44
	76.67 %	70 %	73.3 %

At the baseline presentation, 26.6% (16 cases) of the patients were having a single Patchy AA and 73.3% (44 cases) of the patients were having more than one patchy AA.

GRAPH – 4: GRAPH SHOWING DISTRIBUTION OF CASES BASED ON THE NUMBER OF PATCHES

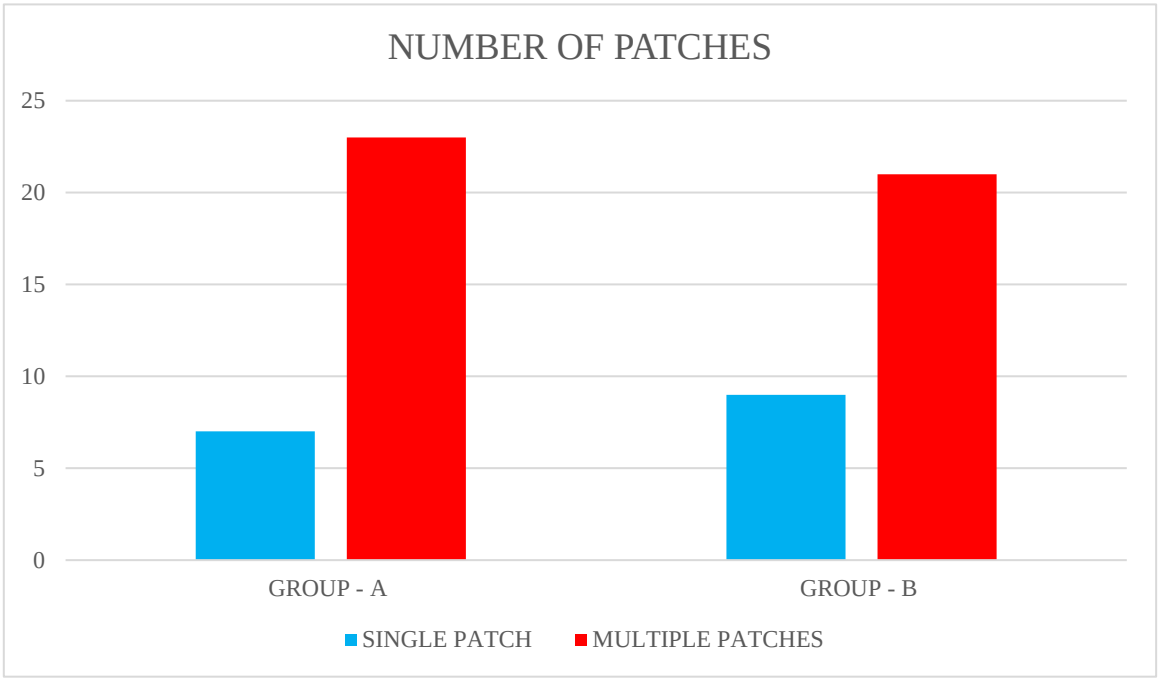


TABLE – 14: DISTRIBUTION OF CASES BASED ON THE SITE OF AA PATCHES

SITE OF AA PATCHES	GROUP – A	GROUP – B	TOTAL
SCALP	24	28	52
	80 %	93.3 %	86.6 %
BEARD	5	1	6
	16.6 %	3.3 %	10 %
MOUSTACHE	1	1	2
	3.3 %	3.3 %	3.3 %
EYEBROW / ANY OTHER PART OF BODY	-	-	-
	-	-	-

Regarding the site of Patchy AA in our study, 86.6% cases (52 cases) had Scalp involvement, 10% cases (6 cases) had Beard involvement and 3.3% cases (2 cases) had Moustache involvement. Nil cases were enrolled with eyebrow involvement or any other part of the body.

GRAPH – 5: GRAPH SHOWING DISTRIBUTION OF SITES OF AA PATCHES

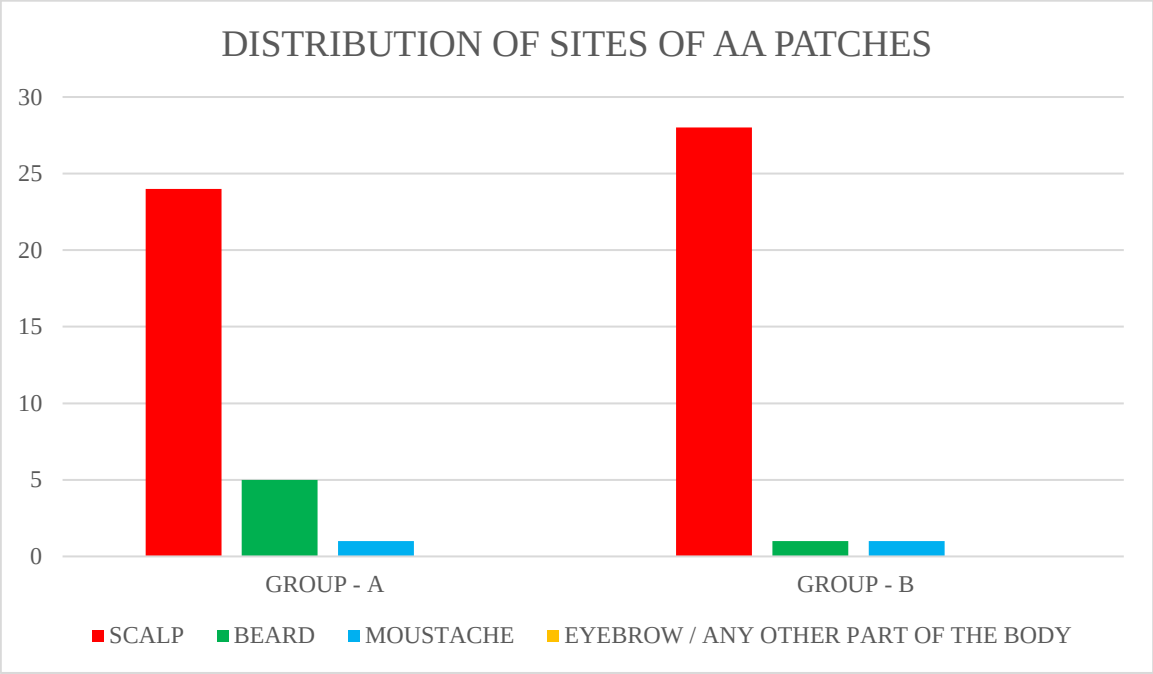


TABLE – 15: DISTRIBUTION OF CASES BASED ON THE AREA OF AA PATCHES

AREA OF AA PATCH	GROUP – A	GROUP – B	TOTAL
> 50 CM^2	15	18	33
	50 %	60 %	55 %
30 – 50 CM^2	10	6	16
	33.3 %	20 %	26.6 %
< 30 CM^2	5	6	11
	16.6 %	20 %	18.3 %

Among the Patchy AA patients in our study, 55% (33 cases) of cases had AA area > 50 cm^2 , 26.6% (16 cases) of cases had AA area 30 – 50 cm^2 and 18.3% (11 cases) of cases had AA area < 30 cm^2.

GRAPH – 6: GRAPH SHOWING DISTRIBUTION OF AREA OF AA PATCHES

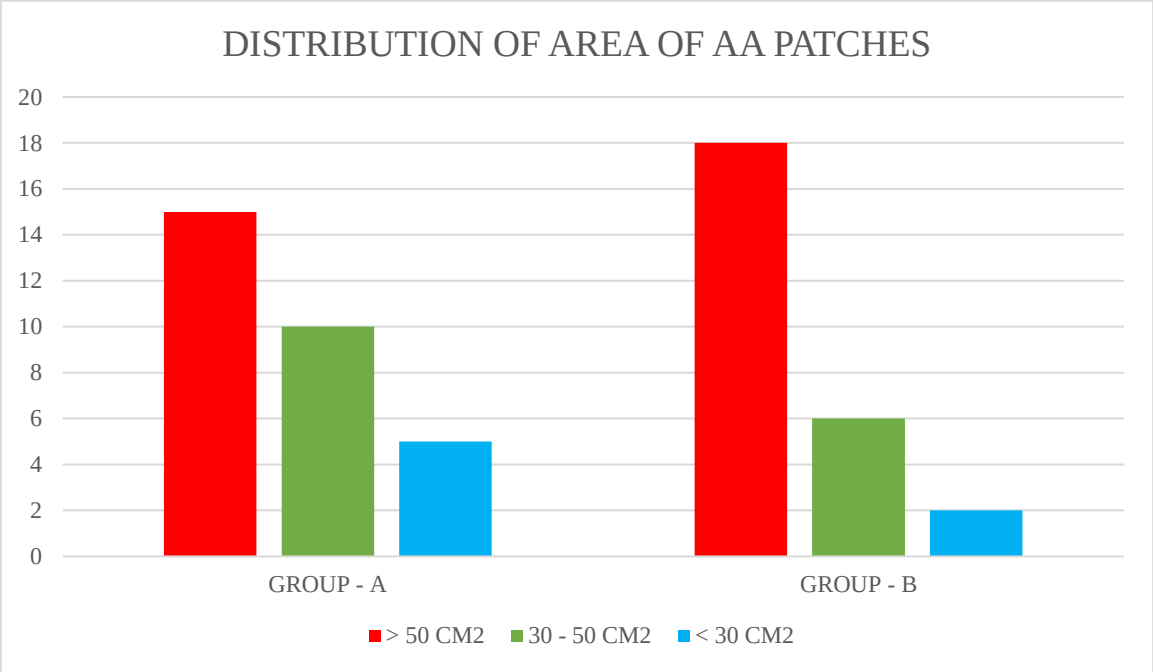


TABLE – 16: DISTRIBUTION OF CASES BASED ON ASSOCIATED SYMPTOMS

ASSOCIATED SYMPTOMS	GROUP – A	GROUP – B	TOTAL
ASYMPTOMATIC	28	29	57
	93.3 %	96.6 %	95 %
ITCHING	2	1	3
	6.6 %	3.3 %	5 %

Majority were asymptomatic (95% - 57 cases). 5% (3 cases) of the patients were associated with itching.

GRAPH – 7: GRAPH SHOWING DISTRIBUTION OF CASES BASED ON ASSOCIATED SYMPTOMS

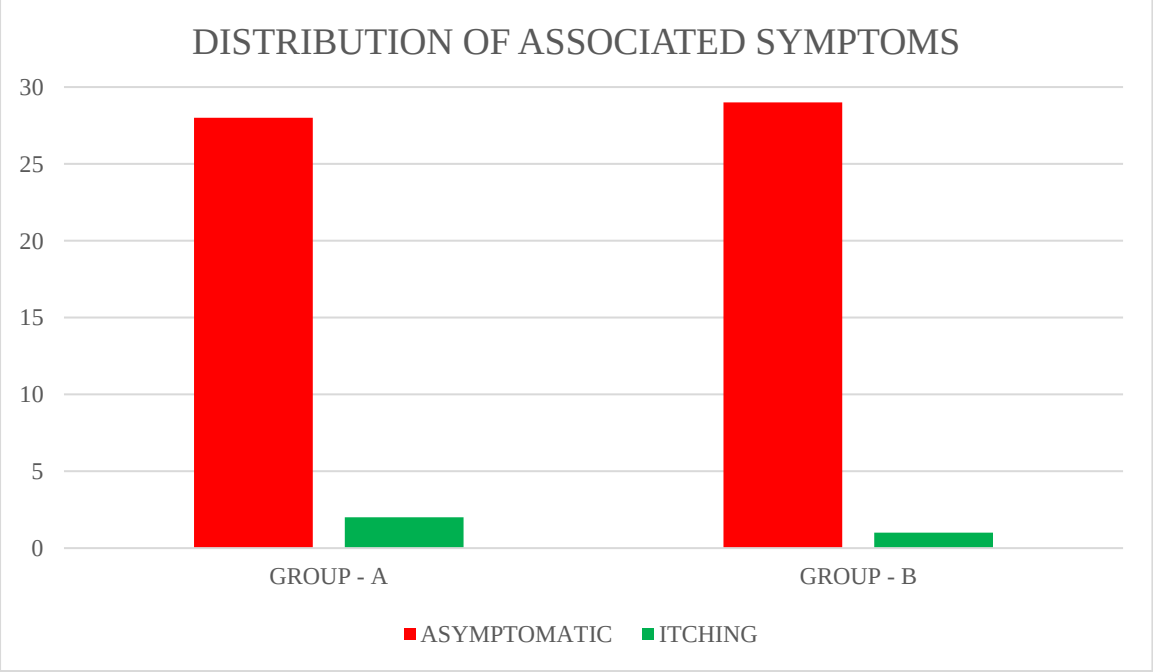


TABLE – 17: DISTRIBUTION OF CASES BASED ON REASONS FOR TREATMENT

REASON FOR TREATMENT	GROUP – A	GROUP – B	TOTAL
COSMETIC REASONS	22	24	46
	73.3 %	80 %	76.6 %
THERAPEUTIC BENEFIT	8	6	14
	26.6 %	20 %	23.3 %

Almost 76.6% (46 cases) of the cases in our study resorted treatment for cosmetic non appealing nature of AA. 23.3% (14 cases) of the cases in our study resorted treatment for therapeutic benefit.

GRAPH – 8: GRAPH SHOWING DISTRIBUTION OF CASES BASED ON REASONS FOR TREATMENT

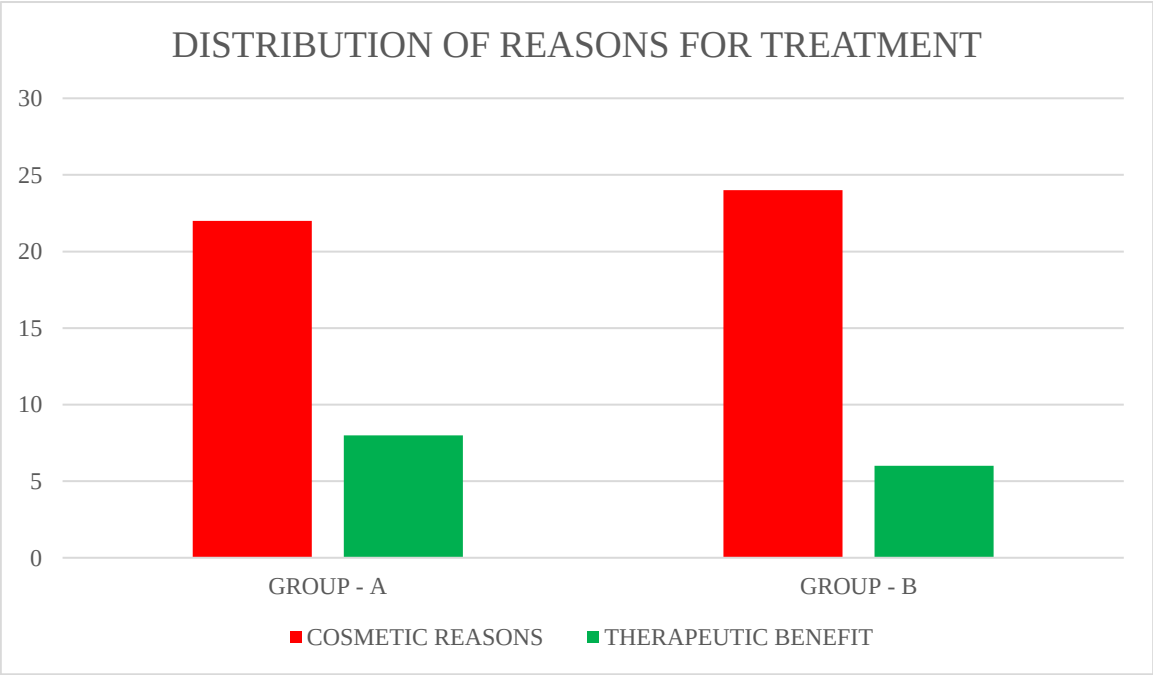


TABLE – 18: EFFICACY ASSESSED USING GPA – SCALE

GROUPS	MEAN SCORE (∑)					Percentage of cases with GPA -3 at the end of 5th setting
	1	2	3	4	5	
GROUP – A	0.33	1.13	2.13	3	3	100 %
GROUP – B	0.93	1.76	2	2	2.16	16.6 %
P-VALUE	< 0.001	< 0.001	0.112	< 0.001	< 0.001	

The Blinded Third Observer assessed the efficacy of the treatment modalities using GPA – Scale. At the end of 5th Setting, the Blinded Third Observer gave a score of 3 (> 75% improvement) to all cases in Group – A (100% - 30 cases) and 16.6% of cases in Group – B (5 cases). The Blinded Third Observer gave a score of 2 (50-75% improvement) to 83.3% of cases in Group – B (25 cases).

At the end of the first, second, third, fourth, and fifth settings in Group A, the mean GPA-Scale score was 0.33, 1.13, 2.13, 3 and 3, respectively. At the end of the first, second, third, fourth, and fifth settings in Group B, the mean GPA-Scale score was 0.93, 1.76, 2, 2, and 2.16, respectively.

GRAPH – 9: GRAPH SHOWING EFFICACY ASSESSED USING GPA – SCALE

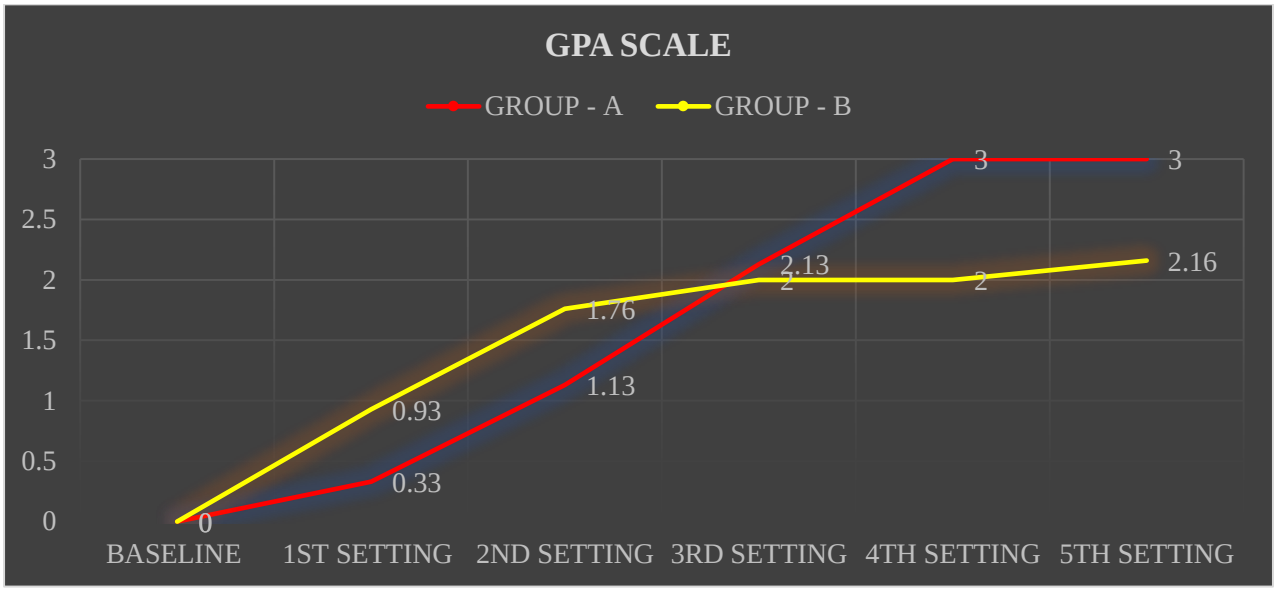


TABLE – 19: EFFICACY ASSESSED USING LAD – SCORE AND LAD SCORE PERCENTAGE OF IMPROVEMENT

GROUPS	MEAN SCORE (∑)					Percentage of cases with LAD Score Percentage of Improvement > 90% at the end of 5th setting
	1	2	3	4	5	
GROUP – A	14.84	26.39	54.09	74.84	91.85	66.6 %
GROUP – B	24.05	36.76	48.17	60.82	80.92	10 %
P-VALUE	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	

The effectiveness of treatment modalities in both groups was evaluated using the LAD Score Percentage of Improvement. > 90% LAD Score Improvement % was seen in 66.6% of cases in Group – A (20 cases) and 10% of cases in Group – B (3 cases). 33.3 percent of cases in Group A (10 cases) and 90 percent of cases in Group B showed a 70 to 90 percent LAD Score Improvement percent (27 cases).

The mean LAD Score Improvement percent in Group A was 14.84 percent, 26.39 percent, 54.09 percent, 74.84 percent, and 91.85 percent, respectively, at the conclusion of the first, second, third, fourth, and fifth settings. The mean LAD Score Improvement percent in Group B was 24.05 percent, 36.76 percent, 48.17 percent, 60.82 percent, and 80.92 percent, respectively, at the conclusion of the first, second, third, fourth, and fifth settings.

GRAPH – 10: GRAPH SHOWING EFFICACY ASSESSED USING LAD SCORE

PERCENTAGE OF IMPROVEMENT

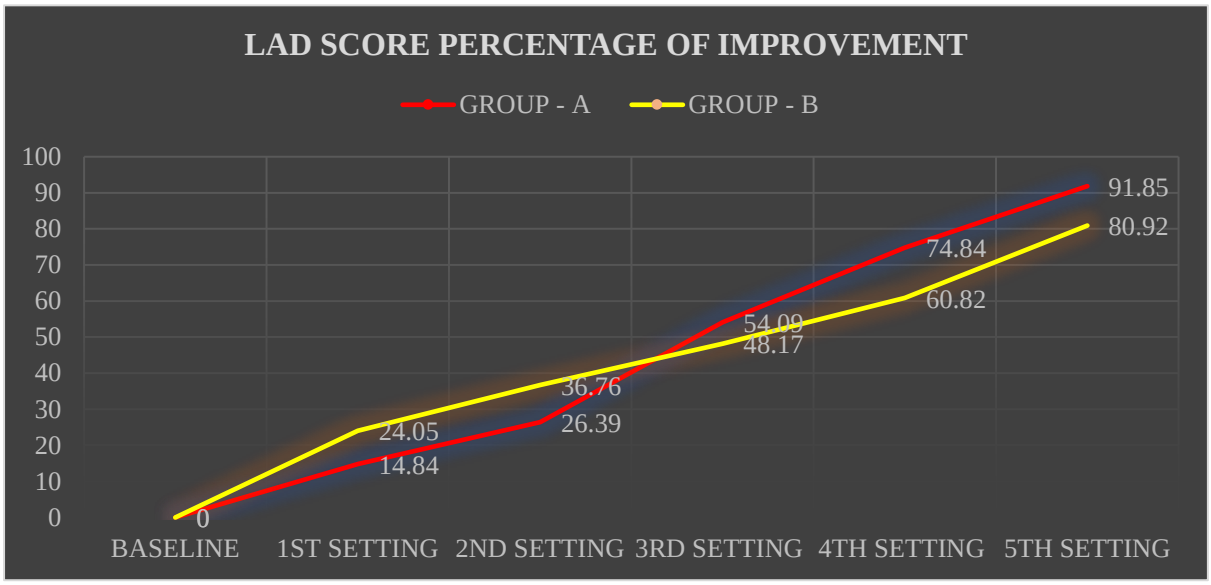


TABLE – 20: SAFETY ASSESSED USING VDS AND VAS SCALES

GROUPS	VDS [MEAN SCORE (∑)] (out of 10)	VAS [MEAN SCORE (∑)] (out of 10)	VDS >5 (out of 10)	VAS ≥ 8 (out of 10)
GROUP – A	6.1	8.8	83.3 %	100 %
GROUP – B	4.3	7.43	6.6 %	50 %

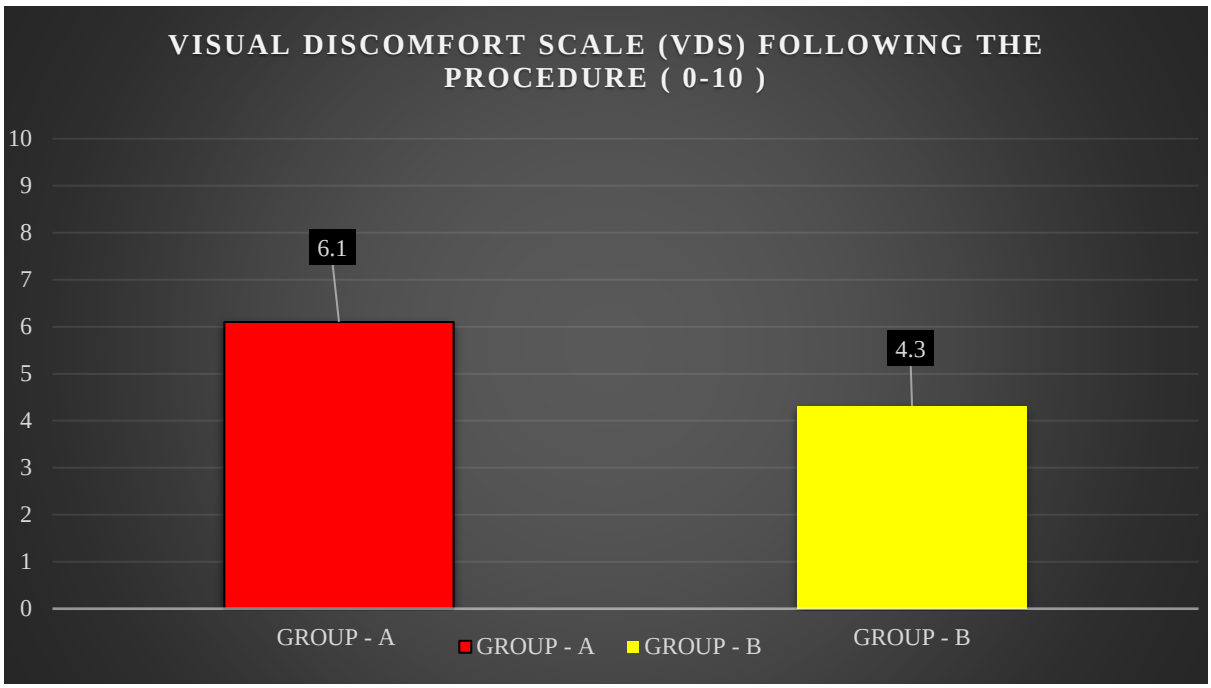
Visual Discomfort Scale (VDS) documented the discomfort of the patients during the procedure. 83.3% of cases in Group – A had VDS > 5 despite anesthesia over the patch. 6.6% of cases in Group – B had VDS >5.

Visual Analogue Scale (VAS) documented the satisfaction of the patients at the end of the 5^{th} setting. All cases in Group – A (100% cases) had VAS ≥ 8 and 50 % of cases in Group – B had VAS ≥ 8.

The average VDS in Groups A and B was 6.1 and 4.3, respectively, demonstrating that the LASER procedure caused the most discomfort.

The mean VAS in Group A and Group B were 8.8 and 7.43, respectively, indicating that Group A patients were the most satisfied with their chosen treatment technique.

GRAPH – 11: GRAPH SHOWING SAFETY ASSESSED USING VDS SCALE



GRAPH – 12: GRAPH SHOWING SAFETY ASSESSED USING VAS SCALE

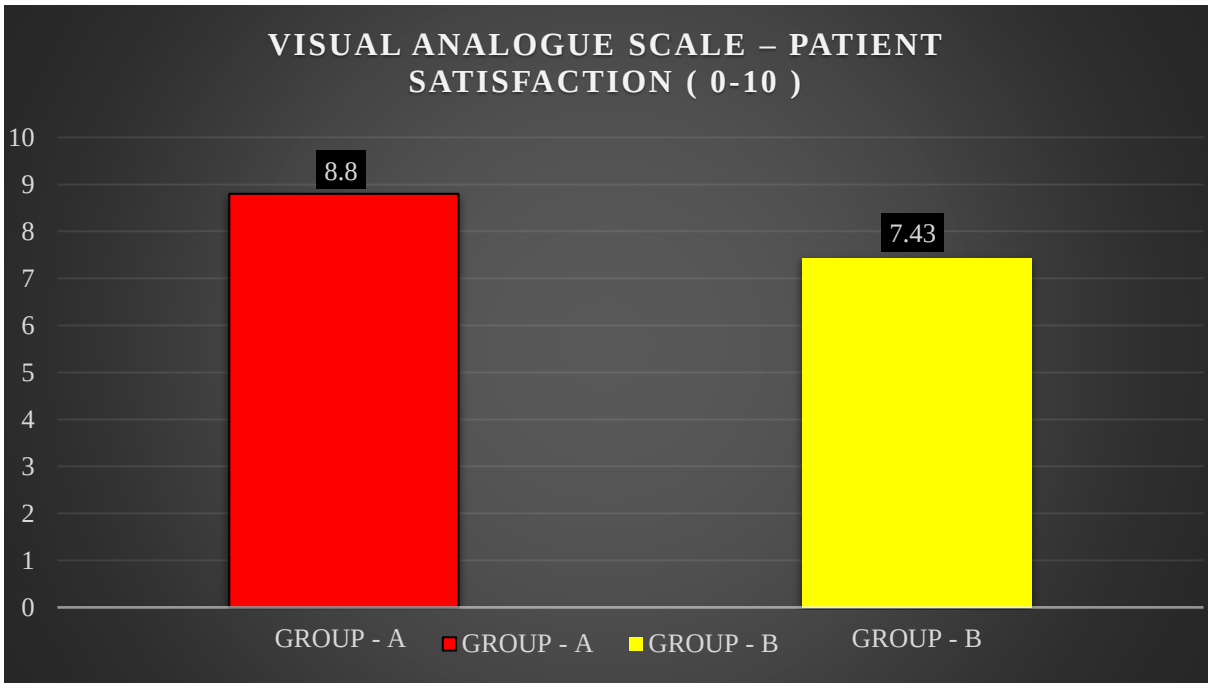
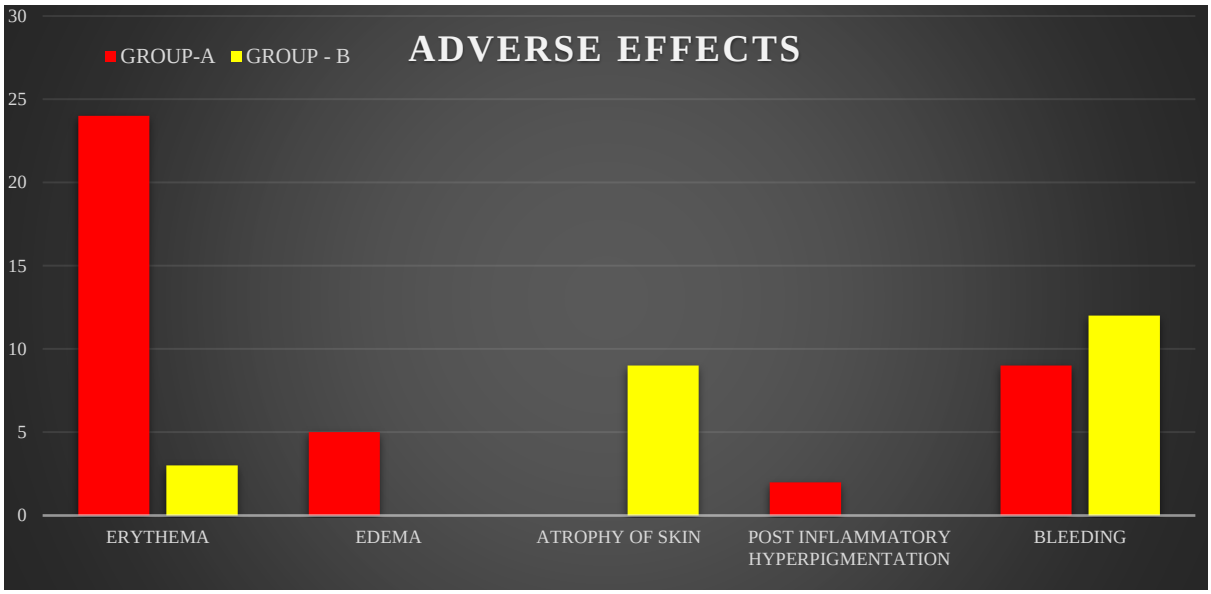


TABLE – 21: ADVERSE EFFECTS

GROUPS	ERYTHEMA	EDEMA	ATROPHY OF SKIN	POST INFLAMMATORY HYPERPIGMENTATION	BLEEDING
GROUP – A (OUT OF 30 CASES)	24 (80%)	5 (16.6%)	0	8 (26.6%)	9 (30%)
GROUP – B (OUT OF 30 CASES)	3 (10%)	0	9 (30%)	0	12 (40%)

The most common adverse effect observed in Group – A was Erythema (80% cases – 24 cases) during post LASER procedure. In our study, 30% of individuals (9 cases) in Group B had skin atrophy documented, while there were no cases in Group A. Skin atrophy is the most frequent significant cosmetic adverse effect of steroids. The other adverse effects documented in both groups include edema, post inflammatory hyperpigmentation and bleeding.

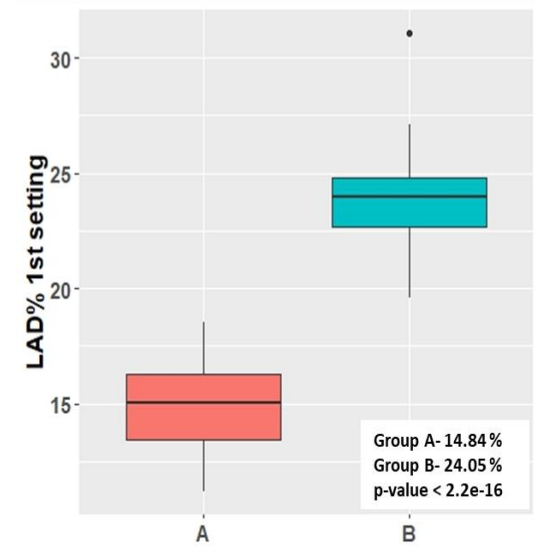
GRAPH – 13: ADVERSE EFFECTS

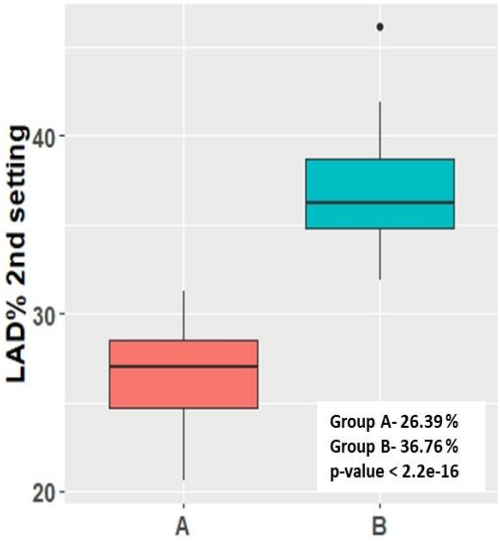


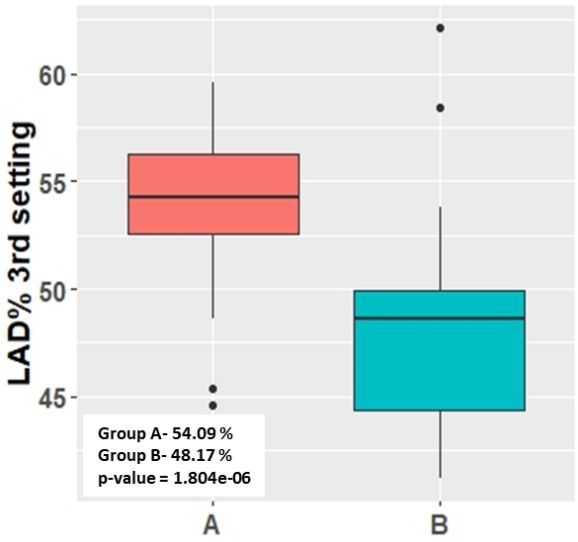
Efficacy of treatment modality – assessed using means score of GPA – Scale and LAD Score Improvement % suggests quicker results to patients treated with intralesional steroids in initial settings but drastic improvement in GPA – Scale and LAD Score Improvement % happens to patients treated with LASER assisted drug delivery of steroids in subsequent settings. The GPA Scale and the LAD Score percentage of Improvement at the conclusion of the fifth setting indicate that patients receiving LASER assisted medication administration of steroids experienced the highest level of efficacy.

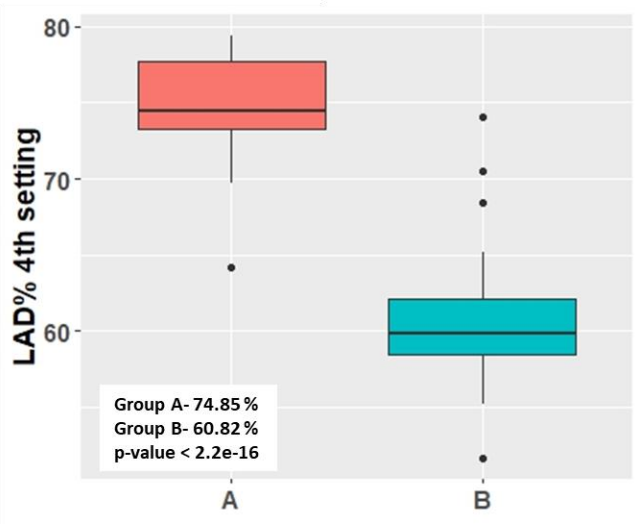
The mean VDS in both groups suggests maximum discomfort during LASER procedure with Topical Steroids yet the patient satisfaction at the end of 5^{th} setting was maximum in patients undergoing LASER procedure with Topical Steroids.

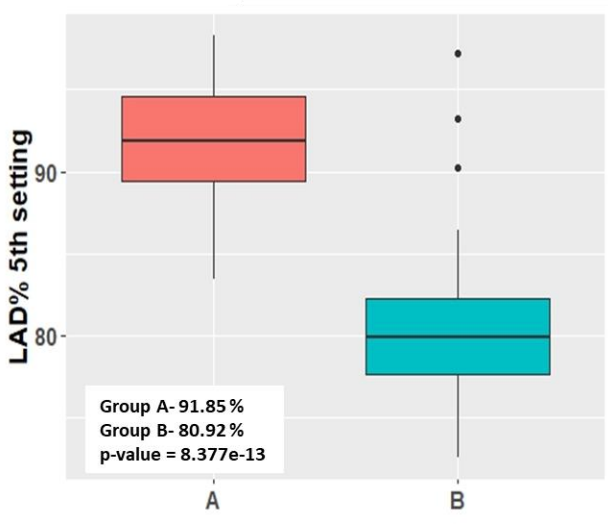
GRAPH – 14: GRAPHS SHOWING BOX PLOT PRESENTATION OF P – VALUES FOR QUANTITATIVE DATE – LAD PERCENTAGE OF IMPROVEMENT











P-value for GPA-Scale and LAD Score percentage of Improvement at the conclusion of the first, second, third, fourth, and fifth settings was 0.001. However, the GPA – Scale at the end of third setting was not < 0.001 (P-Value = 0.112). Hence the data of efficacy of both treatment modalities assessed at the end of 5 settings using GPA – Scale and LAD Score Improvement % were statistically significant.

P-values were <0.001 for VDS and VAS and they were statistically significant.

GROUP – A

FIGURE – 4 – PATIENT – 1:

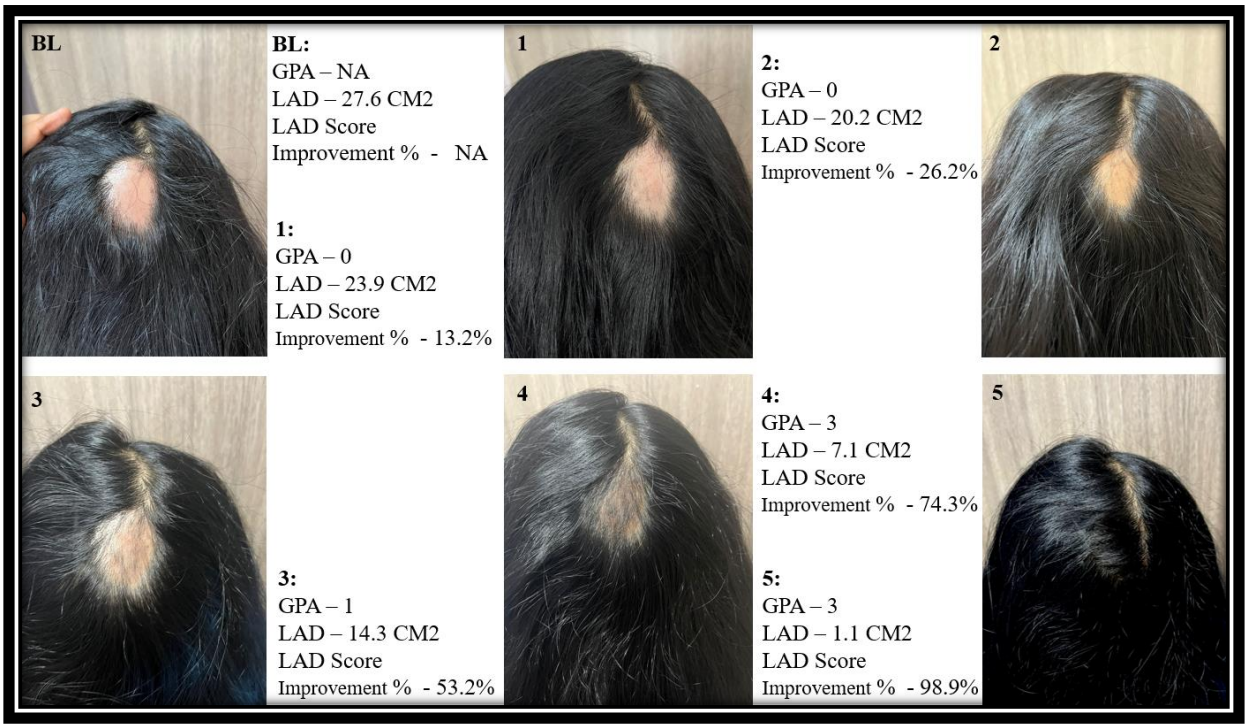
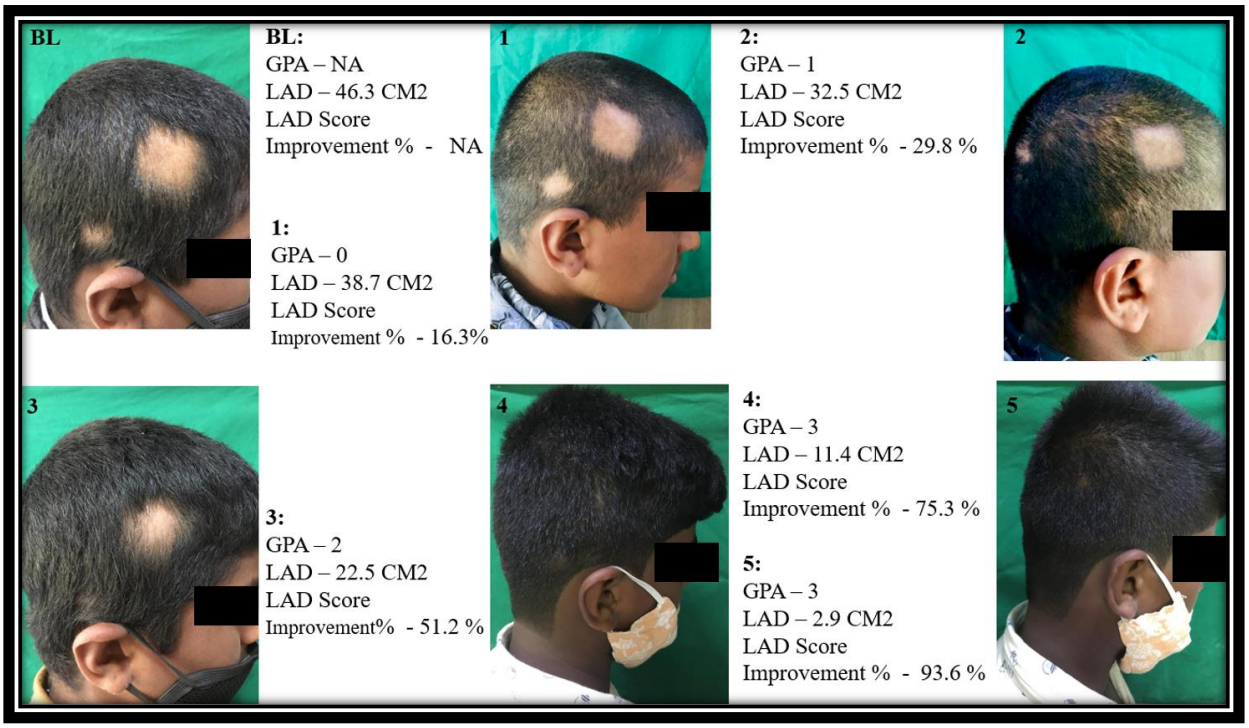


FIGURE – 5 – PATIENT – 2:



GROUP – B

FIGURE – 6 – PATIENT – 1:

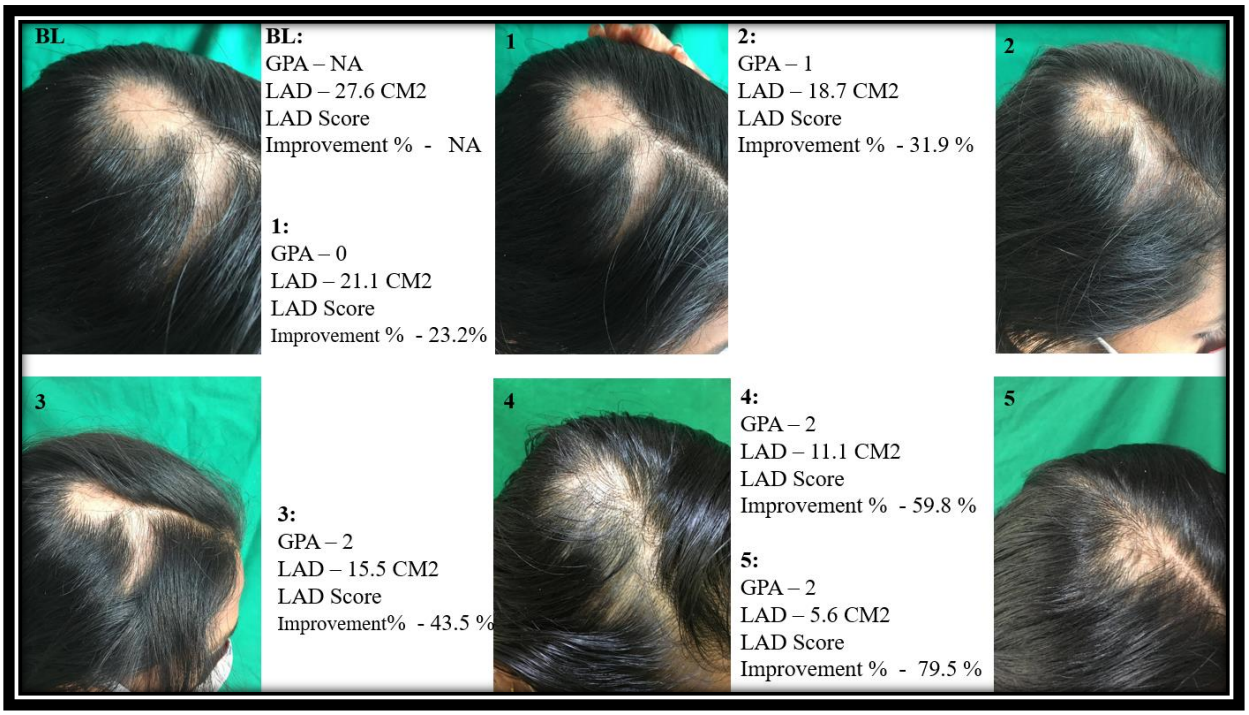
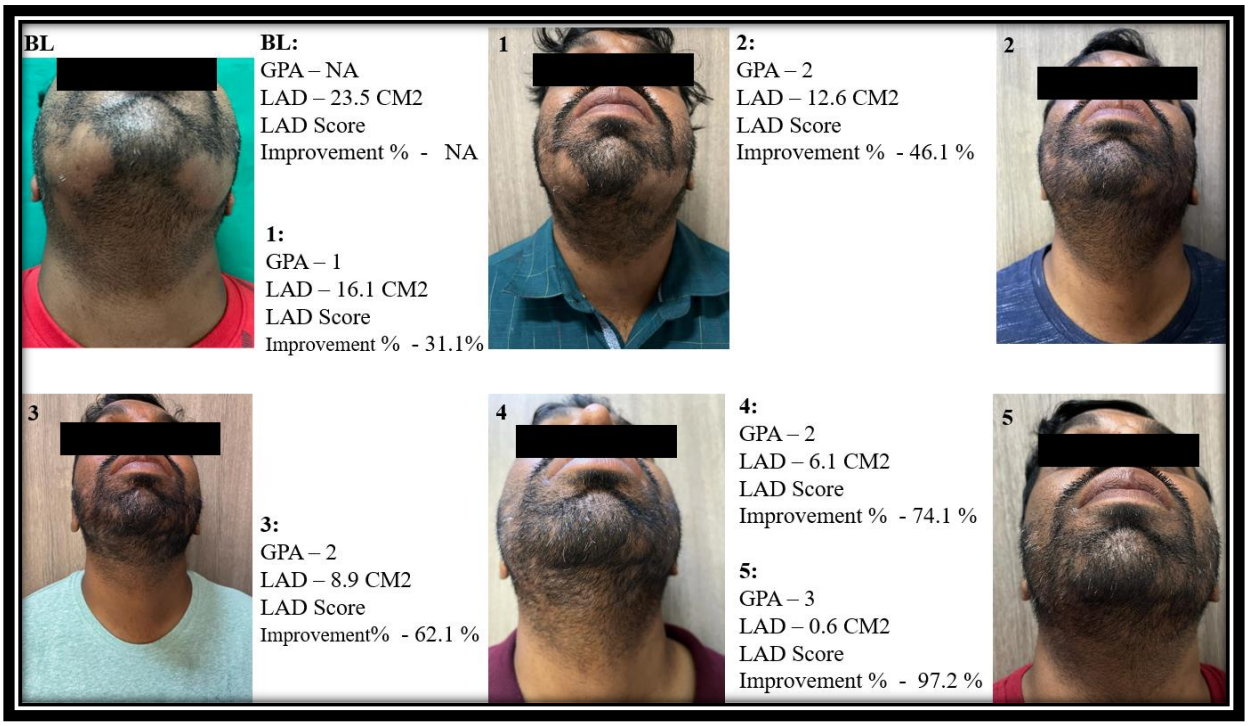


FIGURE – 7 – PATIENT – 2:



DISCUSSION

DISCUSSION:

In this study, The age range of 18 to 30 years comprised the majority of AA patients (41.6%), followed by 30 to 40 years of age (38.3%). This finding is in association with the observations of Juárez-Rendón et al[161] in their study where they conclude that the age range from 15 to 40 is when AA first manifests, with the age range from 10 to 25 having the highest prevalence (60%).[161]

In our study, 77% were men (46 cases) and 23% were women (14 cases). This finding is consistent with the observations of Juárez-Rendón et al[161] in their study where they conclude that majority of AA patients in India and Turkey are males.

In this study, 78.3% (47 cases) of the AA patients had a history of constant stress in their day-today activities. Minokawa[162] et al observed the association of stress in 23% of the AA cases. This result contradicts the findings of the study but suggests that stress has a role in the aetiology of alopecia areata as a trigger factor.

Regarding the site of Patchy AA in our study, 86.6% cases had Scalp involvement, 10% cases had Beard involvement and 3.3% cases had Moustache involvement. This result is congruent with the study conducted by Pratt[163] et al, where the majority of the cases recorded involved the scalp.

Most of the patients in our study were asymptomatic (95% cases). 5% of the patients in our study were associated with itching. The research of Strazzulla[164] et al. supports this conclusion.

76.6 % of our study population resorted to treatment for cosmetic non appealing nature of AA. 23.3% resorted to treatment for therapeutic benefit. This result is in line with those of

Strazzulla[164] et al and Liu[165] et al, who found that patients sought treatment primarily due to cosmetic concerns.

The underlying mechanism of action of Fractional CO2 laser as a therapeutic option for AA is presumed to be telogen hairs getting arrested due to the apoptosis of T cells and prolonged anagen hair stage.[155,166] Wnt/-catenin signalling pathways are shown to induce anagen hairs in a murine model study using Fr. CO2 laser.[167] Thermal effect caused by LASER over papillary dermis stimulate the stem cells in hair bulg.[156] Topical steroids can be delivered transepidermally by Microthermal Treatment Zones (MTZ) created by Fractional CO2 laser therapy.[155,156,166,167]

In our study, the efficacy of both treatment modalities was assessed using GPA – Scale and LAD Score Improvement %. At the end of 5th Setting, the GPA – Scale showed a score of 3 (> 75% improvement) to all cases treated with LASERS followed by Topical Steroids (100%) and 16.6% of cases treated with Intralesional steroids. > 90% LAD Score Improvement % was seen in 66.6% of cases treated with LASERS followed by Topical Steroids and 10% of cases treated with Intralesional steroids.

In a case series study of utilizing Fractional CO2 LASER followed by Topical Steroids for Recalcitrant AA by Majid J[156] et al observed seven out of eight cases showed > 75% regrowth at the end of 3 sessions with session a gap of 3 weeks. This finding is consistent with our study where mean LAD Improvement % at the end of 4th setting was 74.84% in patients who was treated with Fractional CO2 LASER followed by Topical Steroids.

In a study by Halim[157] et al., 10 patients getting fractional CO2 LASER followed by topical steroids for AA experienced a statistically significant decrease in SALT Score. This discovery is consistent with our research.

Using two distinct alopecia areata patches on the same person, Soror[158] et al. examined the efficacy of fractional CO2 laser with topical triamcinolone and intralesional steroids. When compared to patches treated with Ablative Fractional CO2 laser followed by topical steroids, their study revealed a statistically significant higher mean grading score for patches treated with intralesional steroids. This result was statistically significant for our study's first two settings where GPA and LAD Score Improvement % for patients treated with intralesional steroids was better than that of Fractional CO2 LASER followed by Topical Steroids. Although in subsequent settings, drastic statistically significant GPA and LAD Score Improvement % for patients who receive Topical Steroids after Fractional CO2 Laser Therapy occur in our study. In the study by Soror[158] et al two patches of same patient was given separate treatment whereas our research is a Randomized Controlled Trial (RCT) that includes two patient groups with various treatment plans.

In our study, despite having anesthesia over the patch, 83.3 percent of subjects treated with application of topical steroids after Fractional CO2 LASER had VDS > 5. 6.6% of cases treated with intralesional steroids had VDS >5. This result is similar with the study done by Majid[156] and Halim[157] where patients receiving LASER treatment for AA frequently documented discomfort.

In our study, all patients who were applied topical steroids after Fractional CO2 LASER (100% cases) had VAS ≥ 8 and 50 % of patients treated with Intralesional steroids had VAS ≥ 8. This result is in line with the observations of Majid[156], Halim[157] and Soror[158] in their research.

In our study, Patients who receive Topical Steroids after Fractional CO2 Laser Therapy had more transient adverse effects such as Erythema (80% cases) and Edema (16.6% cases) which fades away in a day or two. This finding is consistent with the research of Majid[156], Halim[157] and Soror[158]. Atrophy of skin was observed in 30% of patients treated with Intralesional Steroids and is consistent with the findings of Yee[168] et al.

CONCLUSION

CONCLUSION:

Majority of AA patients are from young population (18 – 40 years of age) who are mostly cosmetic concerned. Hence a patchy AA that disfigures their general appearance has a significant psychological impact over the mental status of the patient. The need for the treatment of AA is also cosmetic consciousness. This led to the hunt for a treatment modality which is cosmetically pleasing as well as therapeutically beneficial with minimal adverse effects. Therefore, we compared and documented the efficacy and safety of a novel procedure with a well-established treatment modality.

From the results of our study, it is evident that the patients who require cosmetic improvement for Alopecia Areata are suggested to be treated with Laser assisted drug delivery of potent steroids since it has less to no serious cosmetic adverse effects except few transient adverse effects, post procedure immediately which fades away in a day or two.

However, for patients who require immediate quick response within initial settings – Intralesional Steroids should be considered but complete remission cannot be guaranteed.

But on the long run in our study in subsequent settings, LASER assisted drug delivery of potent steroids is proven to be cosmetically pleasing and therapeutically beneficial with minimal adverse effects.

Hence, we are of the opinion that Fractional CO2 LASER with Topical Triamcinolone Acetonide is a better treatment modality than the Intralesional steroids for Alopecia Areata with respect to efficacy, safety, and adverse events.

SUMMARY

SUMMARY:

A total of 60 Alopecia Areata (AA) patients participated in the study as part of a Randomized Controlled Trial (RCT). The patients were divided equally into two groups, Groups A and B, each of which contained 30 individuals. An informed consent was procured from AA patients about the participation in the study, disease nature and the necessity to follow-up. Patients with Patchy Alopecia Areata who had not taken any treatment for the past 3 months were enrolled in the study. Systemically sick patients, Immunocompromised patients, Pregnant patients were excluded from the study. Patients in Group – A received Fractional CO2 Laser with Topical Triamcinolone acetonide aqueous solution and Group – B received Intralesional steroids. Both Groups received treatment for 5 settings with each setting a gap of 3 weeks. The effectiveness and security of treatment methods in both groups were assessed using Global Photograph Assessment (GPA) – Scale, Lesional Area Density Score Percentage of Improvement (LAD Score Improvement %), Visual Discomfort scale (VDS), Visual Analogue Scale (VAS), and documentation of adverse effects in each setting.

The study population's average age (∑) was 30.3. The mean age (∑) in Group – A and Group – B were 30.8 and 29.8 respectively. Age ranges for the population, both minimum and maximum in Group – A were 14 and 52 respectively. Age ranges for the population, both minimum and maximum in Group – B were 15 and 51 respectively. The majority of the participants in our study are between the ages of 18 and 30 (41.6 %) followed by the age group of 30 – 40 (38.3 %).

In our study, 77% of cases were males and 23% of cases were females. In our study, there was a strong familial history of AA in 43.3% of the individuals with AA. 23.3% had a past history of Patchy AA who were treated with various treatment modalities in the past.

In our study, 51.6% were Students (School/College going students), 31.6% were Skilled Professionals (which includes IT Professionals, Doctors, Bankers, Policemen), 10% were semi-skilled workers and 6.6% were unskilled workers. 78.3% of them gave a history of constant stress in their day-today activities.

At the baseline presentation, 26.6% were having a single Patchy AA and 73.3% were having more than one patchy AA. 86.6% had Scalp involvement, 10% had Beard involvement and 3.3% had Moustache involvement. 55% had AA surface area > 50 cm^2, 26.6% had AA surface area 30 – 50 cm^2 and 18.3% had AA surface area < 30 cm^2.

95% of cases were asymptomatic and 5% were associated with itching. 76.6% of cases resorted treatment for cosmetic non appealing nature of AA and 23.3% of cases resorted treatment for therapeutic benefit.

At the conclusion of the first, second, third, fourth, and fifth settings in Group A, the mean GPA-Scale score was 0.33, 1.13, 2.13, 3 and 3, respectively. In Group B, the mean GPA-Scale score at the conclusion of the first, second, third, fourth, and fifth settings was 0.93, 1.76, 2, 2, and 2.16, respectively. At the conclusion of the first, second, third, fourth, and fifth settings in Group A, the mean LAD Score Improvement percent was 14.84 percent, 26.39 percent, 54.09 percent, 74.84 percent, and 91.85 percent, respectively. At the end of the first, second, third, fourth, and fifth settings in Group B, the mean LAD Score Improvement percent was 24, 76, 48, 60, 82, and 80.92 percent, respectively.

P-value was < 0.001 for GPA – Scale and LAD Score Improvement % after the first, second, third, fourth, and fifth settings. However, the GPA – Scale at the end of third setting was not < 0.001 (P-Value = 0.112). Hence the data of efficacy of both treatment modalities assessed at the end of 5 settings using GPA – Scale and LAD Score Improvement % were statistically significant.

Groups A and B had mean VDS values of 6.1 and 4.3, respectively. Groups A and B had mean VAS values of 8.8 and 7.43, respectively. Both VDS and VAS were statistically significant. (P-Value < 0.001)

80 % of Group – A cases had erythema post LASER procedure. Atrophy of skin was observed in 30% of cases in Group – B and no cases in Group – A had documented the atrophy of skin.

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ANNEXURES

ANNEXURE – I

PROFORMA

Name:

Age:

Sex:

Occupation:

UHID number:

Phone number:

Address:

Date :

Chief complaints:

History of Presenting Illness:

1. Age of Onset:
2. Site of onset:
3. Duration:
4. Any Associated Symptoms: itching/ burning/ pain
5. Mode of spread: static/ growing/ receding
6. Use of any drugs before onset of illness
7. Aggravating factors: Occupational/ hobbies/ trauma/ drug/ work/ sunlight/ emotional factors/ menstruation/ pregnancy/ food/ cosmetics/ chemicals/ any other:
8. Recovery: Some/ good/ poor/ no response

Past history:

Associated systemic diseases: DM/ HTN/ Thyroid disease.

Associated cutaneous diseases:

Family history:

A. Similar complaints:
B. Other skin problems:

Personal history:

Diet: veg/ nonveg/ mixed
Bowel/ Bladder habits: regular/ altered.
Sleep- adequate/ disturbed
Appetite-
Habits: smoking/ tobacco chewing/ alcoholism

GENERAL PHYSICAL EXAMINATION :

- Built and nourishment

- Pallor/Icterus/Cyanosis/Clubbing/Generalised Lymphadenopathy/Edema

VITALS :

- Pulse :
- BP :
- Temperature :
- Respiratory Rate :

SYSTEMIC EXAMINATION :

1. CVS
2. RS
3. PER ABDOMEN
4. CNS

LOCAL EXAMINATION :

INSPECTION :

- SITE
- SIZE
- NUMBER
- SYMMETRY
- BORDER

PALPATION :

- LOCAL RISE OF TEMPERATURE
- TENDERNESS
- NUMBER
- SIZE
- SURFACE
- BORDER

Nail examination :

INVESTIGATIONS :

FINAL DIAGNOSIS :

TREATMENT :

REMARKS OF THE GUIDE :

ANNEXURE – II

INFORMED CONSENT FORM

I Mr./Mrs. _____ have been explained in my own understandable language, that I will be included in a study which is **"A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER WITH TOPICAL TRIAMCINOLONE ACETONIDE VERSUS INTRALESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF ALOPECIA AREATA"**

Hence as per the computer generated randomization of the study – I am allotted to Group - ____ for whom _____ will be given as a treatment modality for my illness.

I have been explained about the randomization of the treatment modality I receive and that my clinical findings, investigations, intra operative findings will be assessed and documented for study purpose.
I have been explained my participation in this study is entirely voluntary, and I can withdraw from the study any time and this will not affect my relation with my doctor or the treatment for my ailment.

I have been explained about the necessity of the intervention, possible benefits and adverse effects due to interventions, in my own understandable language.
I have understood that all my details found during the study are kept confidential and while publishing or sharing of the findings, my details will be masked.
I have principal investigator mobile number for enquiries.
I in my sound mind give full consent to be added in the part of this study.
No monetary benefits will be given to me during the study.

Signature of the patient	Signature of the witness
Name:	Name:
Date:	Relation to patient:
Place:	

ಮಾಹಿತಿ ನೀಡಿದ ಒಪ್ಪಿಗೆ ನಮೂನೆ

ನಾನು ಶ್ರೀ/ಶ್ರೀಮತಿ. _____ ಅನ್ನು ನನ್ನದೇ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ, ಅದು "ಪ್ರಾಕ್ಷಿಣ CO2 ಲೇಸರ್‌ನ ತುಲನಾತ್ಮಕ ಅಧ್ಯಯನದಲ್ಲಿ ಸಾಮಯಿಕ ಟ್ರಯಾಮಿಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡ್ ವಿರುದ್ಧ ಇಂಟ್ರಾಲೆಸಿಯನಲ್ ಟ್ರಯಾಮಿಸಿನೋಲೋನ್ ಅಸಿಟೋನಿಡೈಮೆಂಟೈಮೆಂಟೈಯೇಟ್ ಟೆಂಪ್ಲೇಟ್" ಎಂಬ ಅಧ್ಯಯನದಲ್ಲಿ ಸೇರಿಸಲಾಗುವುದು.

ಆದ್ದರಿಂದ ಕಂಪ್ಯೂಟರ್ ರಚಿತವಾದ ಅಧ್ಯಯನದ ಯಾದೃಚ್ಛಿಕತೆಯ ಪ್ರಕಾರ - ನನಗೆ ನಿಯೋಜಿಸಲಾಗಿದೆ ಗುಂಪು - ____ ಯಾರಿಗೆ _____ ನನ್ನ ಅನಾರೋಗ್ಯಕ್ಕೆ ಚಿಕಿತ್ಸಾ ವಿಧಾನವಾಗಿ ನೀಡಲಾಗುವುದು.

ನಾನು ಸ್ವೀಕರಿಸುವ ಚಿಕಿತ್ಸಾ ವಿಧಾನದ ಯಾದೃಚ್ಛಿಕತೆಯ ಬಗ್ಗೆ ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ನನ್ನ ಕ್ಲಿನಿಕಲ್ ಸಂಶೋಧನೆಗಳು, ತನಿಖೆಗಳು, ಇಂಟ್ರಾ ಆಪರೇಟಿವ್ ಸಂಶೋಧನೆಗಳನ್ನು ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುತ್ತದೆ ಮತ್ತು ಅಧ್ಯಯನ ಉದ್ದೇಶಕ್ಕಾಗಿ ದಾಖಲಿಸಲಾಗುತ್ತದೆ.

ಹಸ್ತಕ್ಷೇಪದ ಅಗತ್ಯತೆ, ಸಂಭವನೀಯ ಪ್ರಯೋಜನಗಳು ಮತ್ತು ಮಧ್ಯಸ್ಥಿಕೆಗಳಿಂದಾಗುವ ಪ್ರತಿಕೂಲ ಪರಿಣಾಮಗಳ ಬಗ್ಗೆ ನನಗೆ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ.

ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಪತ್ತೆಯಾದ ನನ್ನ ಎಲ್ಲಾ ವಿವರಗಳನ್ನು ಗೌಪ್ಯವಾಗಿ ಇರಿಸಲಾಗಿದೆ ಮತ್ತು ಸಂಶೋಧನೆಗಳನ್ನು ಪ್ರಕಟಿಸುವಾಗ ಅಥವಾ ಹಂಚಿಕೊಳ್ಳುವಾಗ, ನನ್ನ ವಿವರಗಳನ್ನು ಮರೆಮಾಚಲಾಗುತ್ತದೆ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ವಿಚಾರಣೆಗಾಗಿ ನಾನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಮೊಬೈಲ್ ಸಂಖ್ಯೆಯನ್ನು ಹೊಂದಿದ್ದೇನೆ.

ಈ ಅಧ್ಯಯನದ ಭಾಗದಲ್ಲಿ ಸೇರಿಸಲು ನನ್ನ ಉತ್ತಮ ಮನಸ್ಸಿನಲ್ಲಿ ನಾನು ಸಂಪೂರ್ಣ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ.

ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನನಗೆ ಯಾವುದೇ ಹಣಕಾಸಿನ ಪ್ರಯೋಜನಗಳನ್ನು ನೀಡಲಾಗುವುದಿಲ್ಲ.

ರೋಗಿಯ ಸಹಿ
ಹೆಸರು:
ದಿನಾಂಕ:
ಸ್ಥಳ:

ಸಾಕ್ಷಿಯ ಸಹಿ
ಹೆಸರು:
ರೋಗಿಗೆ ಸಂಬಂಧ:

ANNEXURE – III

PATIENT INFORMATION SHEET

STUDY TITLE:" A COMPARATIVE STUDY OF FRACTIONAL CO2 LASER WITH TOPICAL TRIAMCINOLONE ACETONIDE VERSUS INTRALESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF ALOPECIA AREATA"

STUDY SITE: R.L Jalappa Hospital and Research Centre, Tamaka, Kolar.

AIMS OF THE STUDY:

- To assess and compare the efficacy and safety of Fractional CO2 LASER in combination with Topical Triamcinolone Acetonide Aqueous Solution and Intralesional Triamcinolone Acetonide as a Monotherapy and in the treatment of Alopecia Areata.

Alopecia Areata is the patchy loss of hair on any part of the body affecting both gender, which gives psychological distress affecting quality of life of the patient, and it is also associated with other diseases. It is not contagious and not transmitted from one person to another by touching, eating together, sharing clothes.

Alopecia Areata can be diagnosed by clinical examination.In this study , two treatment modalities for alopecia areata are documented.

In this study, GROUP – A participants will be applied a topical anaesthetic, containing a mixture of LIDOCAINE – 7.0 % w/w and TETRACAINE – 7.0 % w/w in a cream base for 45 minutes on the treatment area. After satisfactory topical anaesthesia was achieved, the treatment area was cleaned with a gauze dipped in distilled water. Eyes was protected with eye shields. Fractional CO2 LASER will be then delivered to the Alopecia Areata site at the fluence of 45 mJ/cm2 – two times. Ice pack will be applied immediately. Then within 2 minutes of LASER procedure, Topical Triamcinolone Acetonide Aqueous solution (2.5 mg/ml to 10 mg/ml) was applied depending on the site. (10 mg/ml – Scalp, 5 mg/ml – Beard/Moustache, 2.5 mg/ml – Eyebrow). GROUP – B participants will be treated with Triamcinolone Acetonide was injected intradermally with an Insulin syringe as multiple 0.1ml injections (4 Units) at 1 cm intervals. (10 mg/ml – Scalp, 5 mg/ml – Beard/Moustache, 2.5 mg/ml – Eyebrow).

Both the study group participants must follow up for 5 sittings with an interval gap of 3 weeks.

During the procedure/post procedure all the discomforts experienced by the patient will be taken care by the principal investigator.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study, we will collect information (as per proforma) from you. Relevant blood investigations will be carried out if required. This information collected will be used for dissertation and publication only. NO MONETARY BENEFITS WILL BE MADE AVAILABLE FOR PARTICIPANTS OF THE STUDY.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. The expenses required for the above investigations will be taken care by the principal investigator. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

Left Thumb Impression/Signature of the Patient

Left Thumb Impression/Signature of The Witness

For any further clarification you can contact the study investigator:

Dr. Harish Prasanna.R
Mobile no: 8056890970
E-mail id: drharishprasannahp@gmail.com

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: "ಅಲೋಪೆಸಿಯಾ ಪ್ರದೇಶದ ಚಿಕಿತ್ಸೆಯಲ್ಲಿ ಟೋಪಿಕಲ್ ಟ್ರೈಅಮ್ಸಿನೋಲೋನ್ ಅಸೆಟೋನೈಡ್ ವರ್ಸಸ್ ಇಂಟ್ರಾಲೇಶನಲ್ ಟ್ರೈಅಮ್ಸಿನೋಲೋನ್ ಅಸೆಟೋನೈಡೊಂದಿಗೆ ಫ್ರ್ಯಾಕ್ಶನಲ್ ಸಿ 2 ಲೇಸರ್ನ ತುಲನಾತ್ಮಕ ಅಧ್ಯಯನ" .

ಅಧ್ಯಯನ ಸೈಟ್: ಆರ್.ಎಲ್ ಜಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ತಮಾಕಾ, ಕೋಲಾರ

ಗುರಿ:

1) ಅಲೋಪೆಸಿಯಾ ಅರೆಟಾದ ಚಿಕಿತ್ಸೆಯಲ್ಲಿ ಸಾಮಯಿಕ ಟ್ರಯಾಮ್ಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡೊಂದಿಗೆ ಸಂಯೋಜನೆಯಾಗಿ ಇಂಟ್ರಾಲೇಶನಲ್ ಟ್ರಯಾಮ್ಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡ್ ಅನ್ನು ಮೊನೊಥೆರಪಿ ಮತ್ತು ಫ್ರ್ಯಾಕ್ಷನಲ್ ಸಿಒ 2 ಲೇಸರ್ ಆಗಿ ಪರಿಣಾಮಕಾರಿತ್ವ ಮತ್ತು ಸುರಕ್ಷತೆಯನ್ನು ನಿರ್ಣಯಿಸುವುದು ಮತ್ತು ಹೋಲಿಸುವುದು.
2) ನಂತರದ ಕಾರ್ಯವಿಧಾನದ ಪ್ರತಿಕೂಲ ಪರಿಣಾಮಗಳು ಮತ್ತು ಗುಣಪಡಿಸುವ ಪರಿಣಾಮಗಳನ್ನು ದಾಖಲಿಸುವುದು ಮೊನೊಥೆರಪಿ ಮತ್ತು ಫ್ರ್ಯಾಕ್ಷನಲ್ ಕೋ 2 ಆಗಿ ಇಂಟ್ರಾಲೇಶನಲ್ ಟ್ರಯಾಮ್ಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡ್ ಚಿಕಿತ್ಸೆಯಲ್ಲಿ ಸಾಮಯಿಕ ಟ್ರಯಾಮ್ಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡೊಂದಿಗೆ ಲೇಸರ್ ಅಲೋಪೆಕೋವಾ ಅರೆಟಾ.

ಅಲೋಪೆಸಿಯಾ ಅರೆಟಾ ಎನ್ನುವುದು ದೇಹದ ಯಾವುದೇ ಭಾಗದಲ್ಲಿ ಕೂದಲನ್ನು ಕಳೆದುಕೊಳ್ಳುವುದು ಎರಡೂ ಲಿಂಗಗಳ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುತ್ತದೆ, ಇದು ರೋಗಿಯ ಜೀವನದ ಗುಣಮಟ್ಟದ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವ ಮಾನಸಿಕ ತೊಂದರೆಗಳನ್ನು ನೀಡುತ್ತದೆ ಮತ್ತು ಇದು ಇತರ ಕಾಯಿಲೆಗಳಿಗೆ ಸಹ ಸಂಬಂಧಿಸಿದೆ. ಇದು ಸಾಂಕ್ರಾಮಿಕವಲ್ಲ ಮತ್ತು ಸ್ಪರ್ಶಿಸುವ ಮೂಲಕ, ಒಟ್ಟಿಗೆ ತಿನ್ನುವ ಮೂಲಕ, ಬಟ್ಟೆಗಳನ್ನು ಹಂಚಿಕೊಳ್ಳುವ ಮೂಲಕ ಒಬ್ಬ ವ್ಯಕ್ತಿಯಿಂದ ಇನ್ನೊಬ್ಬರಿಗೆ ಹರಡುವುದಿಲ್ಲ.

ಅಲೋಪೆಸಿಯಾ ಅರೆಟಾವನ್ನು ಕ್ಲಿನಿಕಲ್ ಪರೀಕ್ಷೆಯಿಂದ ಕಂಡುಹಿಡಿಯಬಹುದು. ಈ ಅಧ್ಯಯನದಲ್ಲಿ, ಅಲೋಪೆಸಿಯಾ ಅರೆಟಾಗೆ ಎರಡು ಚಿಕಿತ್ಸಾ ವಿಧಾನಗಳನ್ನು ದಾಖಲಿಸಲಾಗಿದೆ. ಅಧ್ಯಯನದಲ್ಲಿ, GROUP A- ಭಾಗವಹಿಸುವವರಿಗೆ ಸ್ಥಳೀಯ ಅರಿವಳಿಕೆ ಸಿಂಪಡಣೆಯನ್ನು ಲಿಡೋಕೇಯ್ನ್ -2.5% w / w + ಪ್ರಿಲೋಕೇನ್ -2.5% w / w ಅನ್ನು ಕ್ರೀಮ್ ಬೇಸ್ನಲ್ಲಿ ಚಿಕಿತ್ಸೆಯ ಪ್ರದೇಶದ ಮೇಲೆ 1 ಗಂಟೆಗಳ ಕಾಲ ಚಿಕಿತ್ಸೆಯ ಸಮಯದಲ್ಲಿ ನೋವು ನಿವಾರಿಸಲು ನೀಡಲಾಗುತ್ತದೆ. ತೃಪ್ತಿದಾಯಕ ಅರಿವಳಿಕೆ ಸಾಧಿಸಿದ ನಂತರ, ಚಿಕಿತ್ಸೆಯ ಪ್ರದೇಶವನ್ನು ಸೌಮ್ಯವಾದ ಕ್ಲೆನ್ಸರ್ ಮೂಲಕ ಸ್ವಚ್ ed ಗೊಳಿಸಲಾಗುತ್ತದೆ. ಕಣ್ಣುಗುಡ್ಡೆಗಳಿಂದ ಕಣ್ಣುಗಳನ್ನು ರಕ್ಷಿಸಲಾಗುತ್ತದೆ. ಫ್ರ್ಯಾಕ್ಷನಲ್ CO2 ಲೇಸರ್ ಅನ್ನು 50-60 mJ / cm2 ನ ನಿರರ್ಗಳವಾಗಿ ಅಲೋಪೆಸಿಯಾ ಅರೆಟಾ ಸೈಟ್ಗೆ ತಲುಪಿಸಲಾಗುತ್ತದೆ. ಐಸ್ ಪ್ಯಾಕ್ ಅನ್ನು ತಕ್ಷಣ ಅನ್ವಯಿಸಲಾಗುತ್ತದೆ. ನಂತರ ಲೇಸರ್ ಕಾರ್ಯವಿಧಾನದ 2 ನಿಮಿಷಗಳಲ್ಲಿ, ಸಾಮಯಿಕ ಟ್ರಯಾಮ್ಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡ್ ಅನ್ನು ಅನ್ವಯಿಸಲಾಗುತ್ತದೆ. GROUP B- ಭಾಗವಹಿಸುವವರಿಗೆ ಇಂಟ್ರಾ ಲೆಸನಲ್ ಯಾಮ್ಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡೊಂದಿಗೆ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುತ್ತದೆ. ಟ್ರಿಯಾಮ್ಸಿನೋಲೋನ್ ಅಸಿಟೋನೈಡ್ ಅನ್ನು 0.5 ಇಂಚಿನ 30 ಗೇಜ್ ಸೂಜಿಯೊಂದಿಗೆ 1 ಸೆಂ.ಮೀ ಅಂತರದಲ್ಲಿ ಅನೇಕ 0.1 ಎಂಎಲ್ ಚುಚ್ಚುಮದ್ದಿನಂತೆ ಚುಚ್ಚಲಾಗುತ್ತದೆ. ಅಧ್ಯಯನದ ಗುಂಪಿನ ಭಾಗವಹಿಸುವವರು 3 ವಾರಗಳ ಮಧ್ಯಂತರ ಅಂತರದೊಂದಿಗೆ 5 ಆಸನಗಳನ್ನು ಅನುಸರಿಸಬೇಕಾಗುತ್ತದೆ. ಕಾರ್ಯವಿಧಾನ / ಪೋಸ್ಟ್ ಕಾರ್ಯವಿಧಾನದ ಸಮಯದಲ್ಲಿ ರೋಗಿಯು ಅನುಭವಿಸುವ ಎಲ್ಲಾ ಅಸ್ವಸ್ಥತೆಗಳನ್ನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ ನೋಡಿಕೊಳ್ಳುತ್ತಾರೆ.

ದಯವಿಟ್ಟು ಈ ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಒಪ್ಪಿದರೆ ನಾವು ನಿಮ್ಮಿಂದ ಮಾಹಿತಿಯನ್ನು ಸಂಗ್ರಹಿಸುತ್ತೇವೆ (ಪ್ರೊಫಾರ್ಮಾದ ಪ್ರಕಾರ). ಅಗತ್ಯವಿದ್ದರೆ ಸಂಬಂಧಿತ ರಕ್ತ ತನಿಖೆ ನಡೆಸಲಾಗುವುದು.

ಅಗತ್ಯವಿದ್ದರೆ ಸಂಬಂಧಿತ ರಕ್ತ ತನಿಖೆ ನಡೆಸಲಾಗುವುದು. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ. ಯಾವುದೇ ಹಣಕಾಸಿನ ಪ್ರಯೋಜನಗಳು ಅಧ್ಯಯನದ ಭಾಗವಹಿಸುವವರಿಗೆ ಲಭ್ಯವಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಸಿದ್ದರಿಲ್ಲದಿದ್ದರೂ ಸಹ, ವೈದ್ಯರೊಂದಿಗಿನ ಆರೈಕೆ, ಚಿಕಿತ್ಸೆ ಮತ್ತು ಸಂಬಂಧವು ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ.

ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತು ಬಹಿರಂಗಗೊಳ್ಳುವುದಿಲ್ಲ. ಮೇಲಿನ ತನಿಖೆಗೆ ಅಗತ್ಯವಾದ ವೆಚ್ಚಗಳನ್ನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ ನೋಡಿಕೊಳ್ಳುತ್ತಾರೆ. ಈ ಅಧ್ಯಯನವನ್ನು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯು ಪರಿಶೀಲಿಸಿದೆ ಮತ್ತು ಸಾಂಸ್ಥಿಕ ನೈತಿಕ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ನೀವು ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಈ ಅಧ್ಯಯನವನ್ನು ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಬಲವಂತವಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿ ಬದಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಕೊಂಡರೆ ಮಾತ್ರ ನೀವು ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ ಸಹಿ / ಒದಗಿಸುವ ಅಗತ್ಯವಿದೆ.

ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ / ರೋಗಿಯ ಸಹಿ ಎಡ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆ / ಸಾಕ್ಷಿಯ ಸಹಿ

ಯಾವುದೇ ಹೆಚ್ಚಿನ ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ನೀವು ಅಧ್ಯಯನ ತನಿಖಾಧಿಕಾರಿಯನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು:

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ANNEXURE – IV

KEY TO MASTER CHART

1. GRP – Group
2. GPA - Global Photograph Assessment Scale

    Score – 0: < 25 % Improvement

    Score – 1: 25-50 % Improvement

    Score – 2: 50-75 % Improvement

    Score – 3: > 75 % Improvement
3. LAD SCORE - Lesional Area and Density Score
4. LAD % - Lesional Area and Density Score Improvement Percentage from Baseline Presentation
5. VDS - Visual Discomfort Scale of the patients following the procedure

    Scale ranges from 0 – 10
6. VAS - Visual Analogue Scale of the patient's satisfaction of the treatment modality at the end of 5 settings. Scale ranges from 0 – 10
7. ER – Erythema
8. ED – Edema
9. AP – Atrophy of skin
10. PIH – Post Inflammatory Hyperpigmentation
11. BD – Bleeding
12. BL – Baseline presentation
13. 1 – At the end of 1st Setting
14. 2 – At the end of 2nd Setting
15. 3 – At the end of 3rd Setting
16. 4 – At the end of 4th Setting
17. 5 – At the end of 5th Setting

MASTER CHART