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Overview of Alopecia

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ABSTRACT-Alopecia has become a very common auto- immune and genetic hair disorder affected many people around the world characterized by sudden round or coined shaped patches of hair loss. It happens when the own immune system is misleading and attack the own body. They are of several types but most common is non-scarring alopecia areata (Alopecia totalis and univerals) affecting all age groups. Alopecia areata is depends on androgen also called androgenic alopecia. Treatment is limited and difficult to manage and no permanent cure. There are several synthetic compounds tends to treat alopecia the most common and well known is minoxidil, finasteride and DPCP approved by FDA.

Keywords- Alopecia totalis;Alopecia univerals; Minoxidril; Finasterids; DPCP.

I. INTRODUCTION:-

Alopecia is complex genetic disorder one of the most common hair loss condition also commonly known for hair loss. Alopecia is characterized by non-scarring and scarring hair loss which generally occurs in small round shaped and in small patches and diffuse pattern without any inflammation sign**. Cornelius celsus** was first described and the term introduced in 1760 by **sauvages** [1,2].

Alopecia is occurs in two forms scarring and non scarring but in general non scarring is common it Involves loss of hair from the scalp and also some parts of body such as beards, eyebrows, eyelashes, and limbs.[1,3]

It occus at any age if it can involves the whole scalp (alopecia totalis) or in whole body with scalp (alopecia universalis). according to the data it is less common in india only 0.7 percent but most common in UK and USA and China around 2-4percent in whole population. Males and females are equally affected by this. Highest affected age group is between 30-59 year but on the other hand it also affected any age group. On the current knowledge it represents an organ specific autoimmune diseases with genetic background.[4]

About 20 percent patient have a family history. in the beginning if the hair loss is less more the chances of regrowth within a year but hairs will be sometimes regrowth white and grayish in color. Most of the people get further attack and the total regrowth is less.[4,5]

1.1- Non scarring alopecia-also known as non-cicritical alopecia occurs due to the disturbance in hair cycle without inflammation which leads to hair loss also when hair follicles are blocked or disturbed in diameter or may be combination of all.[6]

Example- androgenic alopecia in males/ females, telogen effluvium, trichorillamania, traction alopecia, tinea capitis, short anagen syndrome, loosen anagen syndrome, temporal alopecia triangularis etc.

1.2- Scarring alopecia- also known as cicritiacal alopecia hair follicles are totally destroyed affected openings of hair follicles inflammated wit damage follicles.

Examples- lochen planopilaris, frontal fibrosing, chronic cutaneous lupus erythematosus, central centrifugal, folliculitis decalvans etc. [5,6,7]

II. DYNAMICS OF HAIR LOSS:-

skin is largest organ of human body and hairs are the pilosebaceous unit of skin. Skin has 3 main layers outer layer is epidermal layer, dermis and inner layer subcutaneous layer. Epidermal layer provides touch response and protection. Hair follicle is made up of three layers cuticle layer cortex and medulla.

Cuticle the outer most layer provides protection to the other inner layers act as barrier.

Cortex is Second layer below the cuticle layer more complex and tightly packed arrangements of cells contain melanin and alpha keratin filaments which provide color pigment, strength and elasticity to the hair.

Medulla The inner most layer composed of soft keratin contain all amino acids, fine hairs have lack medulla wavy and curly hairs have strong medulla.[6,8]

Hair shaft is extends from dermis to subcutaneous tissue and produce follicle and hair matrix base in binds with hair bulb. It consist of medulla, cuticle and cortex.[7,8]

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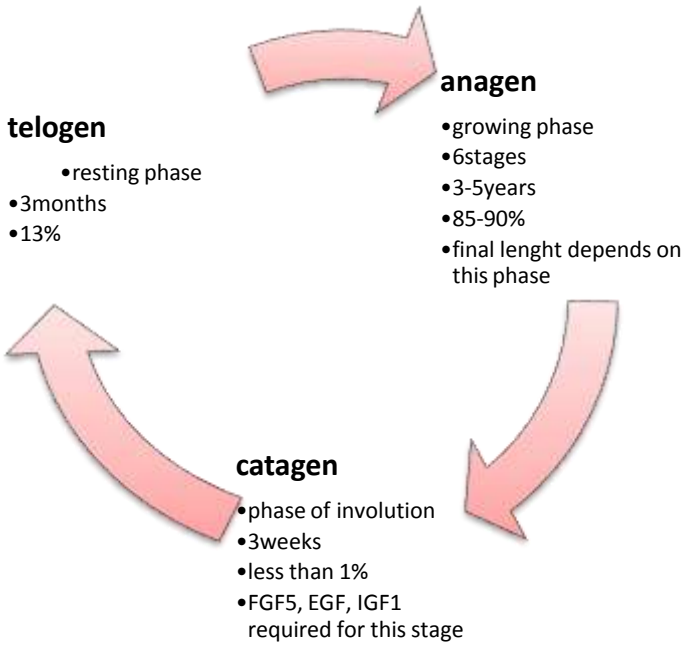
DERMAL PAPILLA AND PAPILLAE- it is composed of fibroblast, colleagen bundle,mucopolysaccharides rich stoma and fibers.dermal papilla located at the base of bulb attach to the epidermis with papillae follicle, arrector pilli muscles are attached underside of the hair at dermal papilla. keratinocytes growth factor (KGF) it is essential for the hair growth and cycling is generate by anagen dermal papilla. It is build up by the mesenchymal cells and their molecular activity determines the growth of hair shaft and hair bulb. Also change in the molecular weight disturb the hair growth cycle.[6,7,8,9,]

Hair follicle growth out in three phages or we can say it is in cycle which involves the growth phase, regeneration and hair loss phase. First phase is anagen which is also know as active phase and highly growing phase second is catagen phase known as tissue regression(short and transitional phase) and the last is telogan which is called resting phase and one another phase which is neogen called regeneration.[9,10]

Follicle is growing anagen phase and involving to catagen phase but it still is on the scalp(telogen phase) before discharge and enter in a new cycle. This cycle is ranges from few months to year. Alopecia areata auto reactive CD8+ lymphocytes attack anagen hair causing early conversion to catagen and telogen which results hair loss. Alopecia areata presence in the peribulbar lymphocytes around the bulb region of anagen hair follicles. Anagen phase is fully matured hair shaft contain melanin and stick from scalp to bulb in dermal adipose tissues. Several growth factors like fibroblast growth factor (FGF 5), epidermal growth factor (EGF), Insulin like growth factor(IGF 1) feast in the cortex layer during the later anagen phase which improve phase changes. External factor such as chemical , stress, radiation increases hair follicle to catagen phase[6]. Dermal papilla compact and shrinkage of sebaceous gland throught the later catagen phase increase removal of healthy hair and provides new hair follicles. The cell death causing transition to early telogen in which the follicle enters the resting phase and shedding of hairs occur.[6,7,10,13]



III. HISTOPATHOLOGY:-

Characteristics of alopecia areata based on the moment of the contemporary occurrence and do not differ with age, sex and race of the patient.

In the acute phase terminal hairs are surrounded by peribulbar lymphocytes pattern composed of CD4+ and CD8+ T cells around anagen follicles.

In subcutaneous phase- decrease anagen and increase catagen and telogen phase

In chronic phase decrease terminal and increase miniaturized hairs are found with variable inflammation number of telogen and catagen hair increased[14].

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3.1- CLASSIFICATION OF ALOPECIA:-

1- Based on extent- patchy alopecia
Alopecia Totalis
Alopecia U
2- Based on pattern- reticular
Ophiasis
3- New varients- acute and diffuse total alopecia
4- Unusual pattern- perinevoid alopecia
Linear

Other conditions that may be confused with alopecia include traction alopecia, temporal alopecia, androgenic alopecia, secondary syphilis, pressure related alopecia, telogen effuvium, chemotherapy induced alopecia etc[13].

✓ Three or less patches of alopecia with large diameter only on scalp not in eyebrows and eyelashes are considered as **mild alopecia areata.**

✓ More than three patches or diameter is more than 3cm excluded alopecia totalis or universalis are under **moderate alopecia areata**.

✓ Alopecia totalis and universalis consider as **severe**

IV. CAUSES OF ALOPECIA:-

it is caused by the abonormal behavior of immune system towords its own body normally immune system defends the tissue and body from the foreign particles or bacteria and virus but in case of alopecia our own immune system mistakenly attacks the hair follicles or we can say white blood cells attack the cells in hair follicles and disturbed the normal hair formation. The affected skin shows that the immune lymphocytes moving into the hair bulb of the follicles which leads to stop producing hair and cause hair loss or alopecia.[11,14]

4.1- hormomal- androgenic alopecia- it occurs in both male and in female and most common cause of hair loss. In men it is recorganized by retrogression of the hair line and shown as M shaped structure and after that complete blandness.
In case of women it generally affect mid frontal area of the skull without recession[13].
It occurs when androgen increases in hair follicle and to decrease the cycle and cause thinning of hair because slowdown the limited time of anagen phase[12,17].

4.2- Associated diseases- there are many diseases which associates wit alopecia areata like autoimmune thyroid diseases most common abnormality, vitiligo occurs with 3-8%, down syndrome, Addison diseases, psoriasis, lupus, rheumatoid arthritis, celiac diseases, type 1 diabetes most likely to be associated with alopecia areata and alopecia totalis[11,12,13].

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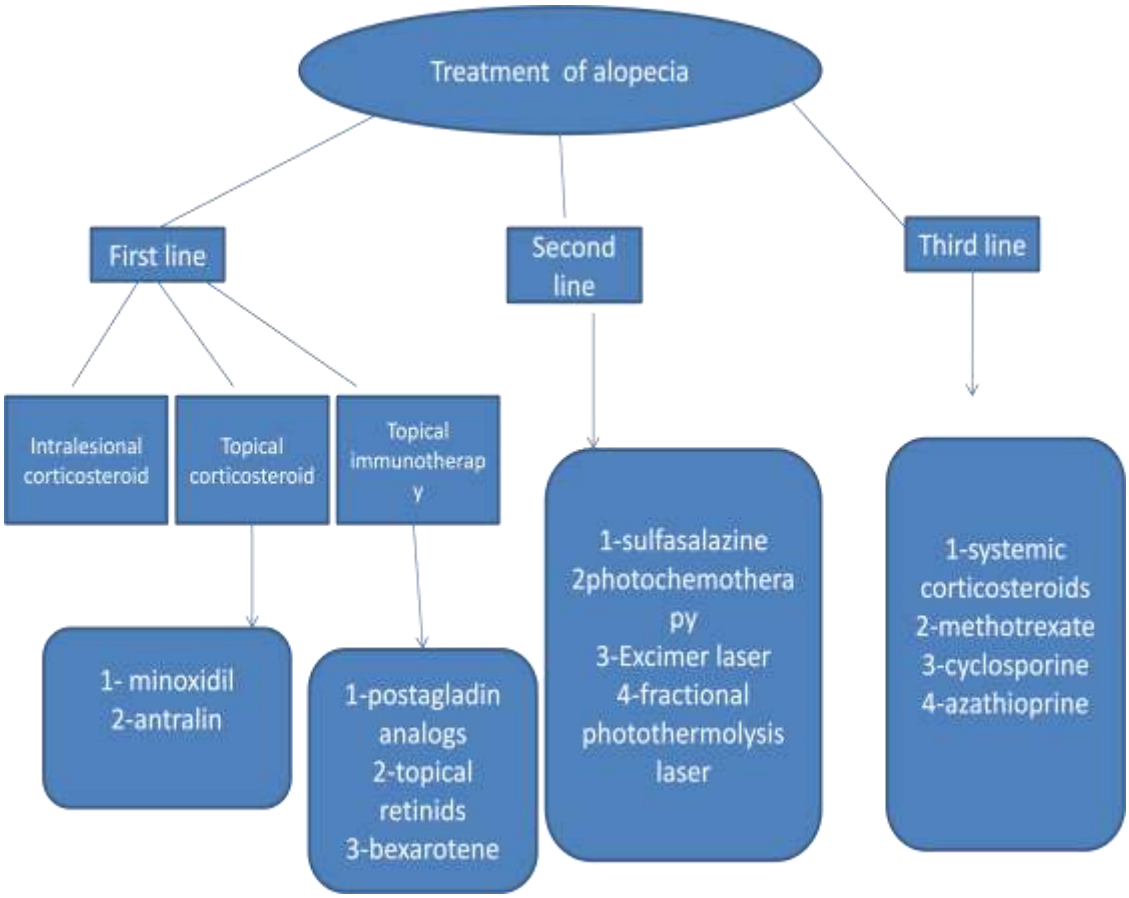
4.3- uses of other drugs- use of drugs in long terms cause hair loss and the most common drug induce hair loss is telogen effluvium. Appears in 2-4months usually. Other is anagen effluvium hair loss occurs in anagen phase of hair cycle this type of hair loss mostly occurs after the few weeks of medication in case of chemotherapy drugs for cancer. Other medications which induce hair loss is antidepresent, birth control pills, caners treating drugs, hormonal replacement therapy etc[12,13]

4.4- stress- excessive stress cause hair loss in many conditions.[13]

4.5- nutritional deficiency- lack of vitamins and minerals cause hair loss mostly the lack of vitamin D. it has immunomodulator effect involved in alopecia areata. Iron the most common deficiency in world specially in womens and also cause hair loss in womens[16].

V. TREATMENT:-

mild alopecia areata need no treatment as hair come back in few months or in a year but in case of sever condition treatment needed as soon as possible because as we know alopecia forms in coin shaped structure and hair loss is permanent to avoid this condition there are several treatment and alternatives which prevent hair loss. some treatment induce hair growth and those treatment which have high adverse effect or highly toxic should be avoided. As we know that alopecia areata itself a auto immune diseases so it has no adverse effect on physical health[15,17,18].



5.1- minoxidril is used antihypertensive agent but it shows some adverse effect by taken orally patients observe the hair growth specially in mens in clinical trials of androgenic alopecia.after that FDA approved it for the use of androgenic alopecia it found to regrowth 40% of the patients hair regrowth after the 3-6 months of treatment[18,20].

MOA-minoxidril has no direct effect on gair follicle but it provides commendatory environment around the hair follicle and on the vascular bed

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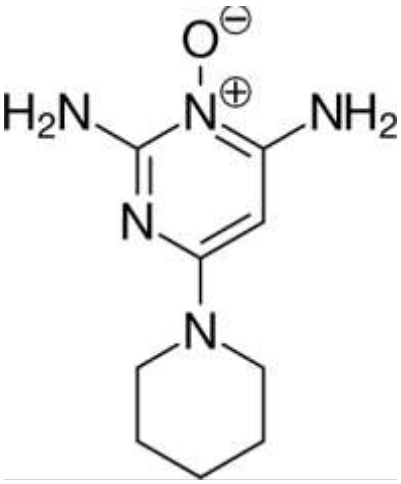
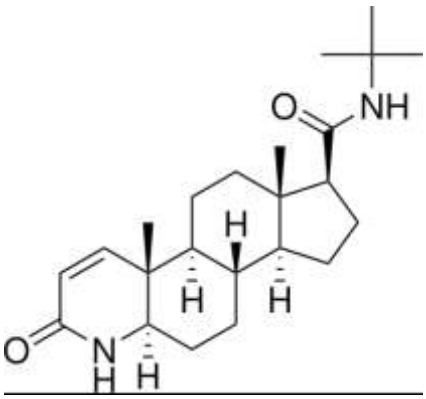
below which helps in hair regrowth. Minoxidril enhance the intraction between the bulb of hair follicle and vascular bed. It does not directly stimulates the hair follicles and the resulting hair is thin as compare to the normal hair. Response is not sustained if the treatment is discontinued than hair fall start again[22,36].



SIDE EFFECTS- as we know it is originated for the the use of hypertension so it lower the blood pressure by using orally some sother side effects are dizziness and fainting.
BY TROPICAL USE- itchiness, rash or some allergic reaction.[18]

5.2- FINASTERIDE- finasteride is developed by merck and developed as an oral anti androgenic agent. This inhibt the conversion of testestorone to dihydro testosterone. It is effective in male androgenic alopecia and for females in polycystic ovarian syndrome but it is more effective in male androgenic alopecia as compare to female PCOS alopecia. It is approved in the year 1997 for the treatment of alopecia in USA. It increases approximately 30% hair growth in alopecia areata and it is approved by FDA as minoxidril[18,20,22,36].



MOA- it inhibits the enzyme 5 alpha reductase it lowers the dihydrtestesterone in blood stream upto 70% and unaffected the level of testosterone . during the treatment androgen effect on the hair follicles remain the same. In the bulb of hair follicle androgen and testosterone receptor binds and the combination of androgen and testosterone tie up and use up intracellular beta catenin. If this holds back the conversion of hair follicle from the telogen to anagen phase dihydrtestesterone level decreseses and the changes reverse back.
SIDE EFFECTS- androgen potecy decreses means sexual dysfunctions in males and decreses sexual desires[25,36].

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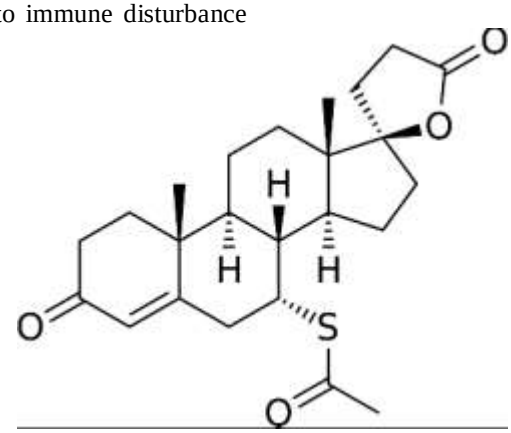
5.3-Glucocoticoid Therapy- Glucorticoid therapy is used for the auto immune alopecia therapy it is used in alopecia areata, alopecia tortial, alopecia universila no effect on androgenic alopecia. It is directly injected subcutaneously on the site of hair loss it means number of injection is more according to the hair loss if it is more. This therapy is not approved by FDA but used as the primary therapy of alopecia areata and response of this therapy is low approximetly 30%-50%.

MOA- they are anti inflammatory and given at high dose. Glucocoticoid are more effective if they are taken orally with high dose but shows more side effects to reduce these side effects the route of administration is altered and it is directly injected to the site of hair loss but efficacy is less with less side effects.it does not directly effect the hair follicle but decrease the auto immune disturbance of anagen hair follicles. In case of mild alopecia areata it is highly effective but in severe cases effect is low[35,36].

SIDE EFFECTS- increase apetite, increases weight gain, immune suppression and osteoporosis[36].

5.4-spironolactone-it is used as diuretic and adverse to aldosterone but it is similar to steroid hormone structurally. It has less androgen blocking activity and not especially approved for the treatment of alopecia because of it less androgen blocking activity which leads the off label use to decrease hair loss from polycystic ovarian syndrome with oral contraceptives therapy because of less androgen blocking activity it is not used in the treatment of male androgenic alopecia[32,33].



MOA-Used to block all forms of androgen induced hair loss and this blocking is not effective for the male androgenic alopecia, effective hair growth in females with polycystic ovarian syndrome and it has effective result in the condition of hirsutism[36].

SIDE EFFECTS- it is used as diuretic agent so it increases the urine output in patients.

5.5- DPCP(DIPHENYLCYCLOPROPENONE)- used in the treatment of alopecia areata 50% of the patient reported effective results og hair regrowth with this therapy in 6months of treatment. DPCP is not used and effective for the other forms of alopecia. It is applied weekly and tropically on the site of hair loss and left for 6-24hours. Response of DPCP is high as compare to other therapy with low cost and less side effect[36].

MOA- it induce contact dermatitis and alter the immune reaction from the hair follicles permit regrowth of hair, decreases the CD_4, CD_8 ratio on the site of application response is slow and result will be shown under 6months. In the starting of therapy patient feels some senstivity on the scalp but in continuity it is shortly disappeared[36]

SIDE EFFECT- redness, itching , swelling, burning and blistering.

5.5- SULFASALZINE- used as immunomodulatory and immunosuppresent agent inhibit T-cells polifiration and antibody production inhibit T- cells cytokinase IL-2,IL-1, TNF alpha and IL-6.

Sulfasalazine therapy regrowth hairs only 23% in severe alopecia areata. 27% complete hair regrowth after 4months of continue therapy.

SIDE EFFECTS- GI disturbance, rash and headache[26,27,29].

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Currently used drugs for different types of alopecia with its side effects.

S.NO	DRUGS	FDA APPROVED	TYPES OF ALOPECIA	SIDE EFFECTS	MARKETED PREPERATION	Refferences
1	MINOXIDRIL	APPROVED	ANDROGENIC AND ALOPECIA AREATA	HIRSUTISM,DRY SCALP, LOW BP,	OLSEN, ROGERS,AVRAM,MINTOP,REGAIN	[18,22,36]
2	FINASTERIDE	APPROVED	ALOPECIA AREATA	SEXULA DYSFUNCTIONING AND HORMONAL DISTURBANCE IN MALES	PROPECIA, FINPECIA,AINDECM	[36]
3	GLUCOCORTCOID	NOT APPROVED	ALOPECIA AREATA TOATLIS AND UNIVERSALIA	INCREASE WEIGHT, IMMUNO SUPPREESSION	KENOLOG-10 AND 40, ARISTOSPAN	[29]
4	SPIRONOLACTONE	NOT APPROVED	ANDROGENIC ALOPECIA IN FEMALES	INCREASE URINE OUTPUT	ALDACTONE	[21,22,24,36]
5	CYCLOSPORINE	NOT APPROVED	ALOPECIA AREATA	HYPERGLYCEMIA, INCREASE INFECTION POSSIBLITIES	NEUROL, NEUROSTAT,SANDIMMUNE,GENGRAF	[36]
6	CORTICOSTEROID	NOT APPROVED		ACNE, SKIN CANCER, INCREASE BP	DIANABOL, CORTISONE,HYDROCORTISONE ACETATE, KENOLOG	[25,27,29]
7	DPCP	APPROVED	ALOPECIA AREATA	REDNESS, ITCHING,SWELLING AND BURNING ON SITE OF APPLICATION	ANTON ALEXANDROFF	[36]

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8	CYPROTENE ACETATE	NOT APPROVED	ANDROGENIC ALOPECIA IN FEMALES	VARIATION IN MENSTURAL CYCLE, HEADACE, BREAST TENDERNESS	DIANE 35, ANDROCUR	[29,23]

VI. CONCLUSION-

Alopecia is common disorder and directly affect the appearance of individual there is no sustain treatment for alopecia right now because of the hidden reason behind the cause but there are many synthetic compounds approved and not approved by FDA used to treat and maintain the hair regrowth in patients but result are not promising those compounds are minoxidril, finasteride, DPCP, Glucocorticoid, JAK etc. some of the drugs are used as off label because not approved by FDA.

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