PAEDIATRIC PSORIASIS: A REVIEW ON DIAGNOSIS AND MANAGEMENT

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ABSTRACT

Psoriasis is a most common skin disease with genetic underpinnings.[1] Psoriasis is an itchy dry white scaly patches on the skin. About 40% of psoriatic patients have an age of onset before 16 years and 10% of them get it before their 10 years of life. Paediatric psoriasis may vary from mild moderate to severe, even though it's a lifelong condition without cure, symptomatic treatment with medications are available. Most of the paediatric cases are mild and get better with treatment. Treatment for paediatric psoriasis has no internationally standardised guidelines. It may include topical therapy, systemic therapy and phototherapy. while selecting a specific treatment factors such as age, quality of life, severity of psoriasis, location of psoriasis, type of psoriasis, tolerability, safety and patient preference is to be considered. topicals includes calcineurins, vitamin d analogues alone and in combination with topical corticosteroids. The disease can get controlled with intermittent therapy in most of the patients; but in some it get worsen with age and may require aggressive therapy. New innovations in the systemic, topical, phototherapy and biologic may provide a better future in paediatric psoriasis therapeutic armantarium.

***Keywords**: Paediatric psoriasis, Calcineurin, Phototherapy, Biologics, Dithranol*

INTRODUCTION

Psoriasis is a most common skin disease with genetic underpinnings.[1] Psoriasis is an itchy dry white scaly patches on the skin. About 40% of psoriatic patients have an age of onset before 16 years and 10% of them get it before their 10 years of life.

Paediatric psoriasis may vary from mild moderate to severe, even though it's a lifelong condition without cure, symptomatic treatment with medications are available. Most of the paediatric cases are mild and get better with treatment. This skin disease usually has a genetic background. Other factors like being obese, cold weather, cut scratches or rashes on skin, high stress level and certain medications like lithium, beta-blockers and anti-malarial drugs can also trigger the gene.[2]

EPIDEMIOLOGY

The epidemiological data regarding childhood psoriasis are limited even though it's a rather frequent condition in children.[3]

According to a study conducted by Swanbeck on *Age of onset and different types of psoriasis*, it revealed that in about 30-32% of adult patient had a disease onset before 15 years and another 20% in between 15-19 years.[4] Although the data concerning familial aggregation is inconsistent if a person with such history of psoriasis, the risk of developing diseases are high.[5, 6]

A German study revealed that about 49% of affected children had a first degree family member association. About 32 and 8% adult onset had either a second or third degree relative respectively.[7]

ETIOLOGY AND PATHOGENESIS

The precise etiology and pathogenesis of the disease is still remaining emegnatic. But it's likely to consider an interplay between genetic and environmental factors.[8] Psoriasis is a T cell mediated disease. Pathogenesis of adult psoriasis include the imbalance between regulatory and effecter T cells especially those T cells producing T_H-17. Since the adult and paediatric psoriasis vary in presentation, natural history, triggering factors and in

response to treatment, a pathogenetic variation is also there.[9] The cutaneous inflammatory cells infiltrates and cytokine profiles of psoriatic lesions from children are not much defined.[10]

From the study conducted by Kelly et.al CD_4:CD_8 ratio is not increased in children as compared to adult where the ratio is higher, in addition there was a minimal increase in the IL-17 producing T cells when compared to adult skin sample. Even though both adult and paediatric psoriatic patients produce IL-17(CD_8+), the increase was smaller in paediatrics. In contrast paediatric skin cells produce more IL-22 from CD_4+ cells.

T regs were increased in adults when compared to control but no such elevation in paediatrics is seen.[11]

CLINICAL FEATURES

Both adults and paediatric psoriasis present with same clinical subtypes they varies in morphology and distribution of lesions; so that differ in clinical symptoms.[12]

Paediatric psoriatic lesions are more often spread on face and flexural areas characterised by thinner and smaller white scaly erythmatous plaques. In addition, childhood psoriasis is characterised by macerated lesions.[13, 14] despite of the above mentioned area lesions can develop on any skin area and shows a symmetrical distribution.[15]

The paediatric diaper rashes are characterised by often macerated sharply demarcated minimally elevated psoriatic plaque in the diaper area also involving inguinal folds, and within 1-2 weeks it can develop into widespread eruption.[16] Diaper psoriasis is particularly difficult to treat.[17] when we consider the case of older children; about 75% are affected with plaque psoriasis.[18, 19]

Plaque psoriasis is the most common type of psoriasis seen in both adults and children and are characterised by plaques with overlying silvery white scale or erythematosquamous papules. Size of the lesion may vary and site of the first lesion can be scalp, face, extensors of elbow and knee. Scalp is the most frequently involved area.[20, 21]

Guttatte psoriasis is the second most common type in children.[22, 23] Griffith and Barker defined guttatte psoriasis as an acute form of psoriasis in which papules erupt on the trunk approximately after 2 weeks of viral or beta-haemolytic streptococci infection. So it is self limiting and can be resolved within 3-4 months of onset.[24]

Only 1-5.4% of paediatric patients shows pustular nature; studies demonstrated that those with pustular psoriasis shows IL-36 receptor antagonist(IL36RN) gene mutation and subsequent up regulation of IL-1 production.[25] Pustular psoriasis in children shows a classic von Zumbusch type are accompanied by fever, malaise and arthralgia and is characterised by either localised or generalised superficial sterile pustules.[26, 27]

Inverse psoriasis, palmoplantar psoriasis, isolated facial psoriasis, linear psoriasis and erythrodermic psoriasis are the other less common subtypes of psoriasis in children.[24] Erythrodermic psoriasis are extremely rare in children and can be life threatening because of the severe hypothermia, hypoalbuminemia and cardiac failure and this condition is characterised by erythema and scaling involving more than 90% od body surface area.[28]

Sometimes psoriatic skin changes are accompanied by nail changes in the nail plate and nail bed(in 40% of children, common in boys).[29] Changes may include pitting of nail plate, oil spots onycholysis, subungual hyperkeratosis, onychodystrophy and splinter hemorrhage.[30] paediatric psoriasis is often manifested with Juvenile Psoriatic Arthritis(JPsA) ie, about 1-10% of children.[31]

DIAGNOSIS

Apart from the above clinical features, paediatric psoriasis often characterised by thinner surface scale. Also show Auspitz sign*. Paediatric psoriasis can be result of isomorphic response or Koebner phenomenon and the residual pigmentation following healing of lesions are other typical diagnostic features of paediatric psoriasis.[19]

In children with atypical presentation, biopsy can be used as a diagnostic tool. On histological examination it shows parakeratosis, loss of the granular cell layer, elongation of the rete ridges, neutrophilic aggregation within the epidermis(microabscesses of munro), dialated blood vessels in the dermis and perivascular lymphocytic infiltrates.[32] But these features may vary depending upon site of biopsy, psoriasis subtypes or whether the child have been treated with topical or systemic medications. Usually morphology and distribution of lesions are used as a diagnostic tool.[33]

Dermoscopy is the standard diagnostic tool in dermatology which allow visualization of morphological features invisible to naked eyes, but is less commonly used in psoriasis diagnosis.[34] Dermoscopy of psoriatic plaque shows dotted vessel regularly distributed over a light red background and diffuse superficial white scales.[35]

MANAGEMENT

Paediatric psoriatic treatment is challenging and it require careful compliance to the specific treatment regimen. In addition to prescribing treatment modalities it's important to educate the patient and family about the chronicity of psoriasis, triggering factors. To enhance the patient adherence timing of first return visit is important, were return visit can induce white coat compliance.[36] Psychosocial support is another important component of therapy for paediatric psoriasis.[37]

Treatment for paediatric psoriasis has no internationally standardised guidelines. It may include topical therapy, systemic therapy and phototherapy. While selecting a specific treatment factors such as age, quality of life, severity of psoriasis, location of psoriasis, type of psoriasis, tolerability, safety and patient preference is to be considered.[38]

TOPICAL TREATMENT

Topical agents can be considered as the first-line therapy in psoriasis. Never the less, most are not approved for use in children.[39] while selecting vehicles for the treatment the factors such as lesion characteristics, location of psoriasis and patient preferences. Commonly used vehicles include cream, ointment, foams, gel and lotions.[40]

Topical Corticosteroids

It is the most commonly used topical agents in all age groups. Different strength and vehicles are available. In adult low- to mild-potency steroids are given for facial, flexural and genital psoriasis and for thick skin like soles and palms, high potency steroids with penetration enhancers are given. De Jagar ME et.al conducted study on *efficacy and safety of topical corticosteroid* and it concluded that in a total of 20 children included in the study, for a period of two weeks, 0.05% halobetasol cream and 0.05% clobetasol propionate emulsion are effective in plaque psoriasis. Reported side effects were relatively mild and included burning sensation at the site of application and mild skin atrophy.[41] Aside from these studies suggesting steroids, no data available on the use of such in paediatrics. Adults on treatment with corticosteroids show side effects like striae, telangiectasias, acneiform dermatitis, tachyphylaxis, periorificial dermatitis, hypertrichosis and less commonly suppression of the hypothalamic-pitutary-adrenal axis. So use of such agents in children should be rotational and and with caution.[20]

Vitamin D Analogues Alone and in Combination with Topical Corticosteroids

Vitamin D analogues includes calcitriol, calcipotriol etc. Topical preparations of these shown to have greater treatment efficacy with mild side effects like pruritis and localised skin irritation. So that application of these on thinner areas of skin such as faces genitalia and flexural areas are avoided. Calcitriol ointment is less irritating as compared with calcipotriol.[40] inappropriate use of vitamin D analogues may cause its systemic absorption and there by increased blood calcium level.[42] Dose of calcitriol upto $45g/m^2$/week is safe to use in children without changes in calcium level. But these are not recommended for the use in children below 2 years.[40]

Vitamin D monotherapy or combination therapy can be used in paediatric psoriasis which inturn cause a drug-synergysm and steroid sparing effect.[43]There is a commercially available product containing both calcipotriol and betamethasone propionate, the efficacy of which is illustrated by three studies

i. Van Geel MJ et al. on calcipotriol/betamethasone dipropionate cream for mild to moderate paediatric psoriasis: A prospective cohort study including 73 children with plaque psoriasis treated with above mentioned cream OD for 4 weeks and 4 days a week thereafter for a duration of 35 weeks. High response to treatment is observed in first week after which it seems to have stabilised the lesions. Only five of them reported adverse effects like striae.[44]
ii. Gooderham M et al. on safety and efficacy of calcipotriol and betamethasone dipropionate gel in the treatment of scalp psoriasis in adolescents: A multi-centric open label study, gel applied once daily for 8 weeks and was well tolerated and effective.[45]
iii. Oostveen et al. on the effectiveness of calcipotriene and betamethasone dipropionate gel in paediatric scalp psoriasis for the first 84 treatment episodes and maintained this for the following 48 weeks. Three patients described striae of skin in the arms, trunk and legs.[46]

Calcineurin Inhibitors

Commonly used calcinuerin inhibitors like tacrolimus(0.03% and 0.1%) and pimecrolimus(1%) proven as efficient to treat lesions of face, genitalia and flexures. It is the best alternative when the lesion areas are sensitive and the patient is more prone to adverse effects.[47] The safety and efficacy of tacrolimus 0.15% ointment has been evaluated by two nonramdomized clinical trials, which shows an improvement in condition within 30 days of treatment when applied twice daily. Pruritis was the only side effect reported.[48] There is no enough evidence for the safety and efficacy of pimecrolimus 1% ointment, as it was described only in two patients.[41] because of the possible increased risk of skin cancer and lymphoma, sun exposure and phototherapy should be avoided during this treatment.[49]

Dithranol

An anthralin derivative with both anti-inflammatory and anti-proliferative properties with least systemic absorption and it is the safe and effective treatment option for paediatric psoriasis.[28]Short contact dithranol in high concentration when applied for 10-30 min daily for shorter periods shows maintenance of effectiveness without irritation and staining. But it needs a day care setting and intense treatment schedule. About 73.2% of patients in a retrospective study show good response to treatment. For attaining such a remission of 5.5 month, a median treatment period of 2 months was needed.[50] A recent prospective observational study on *efficacy and safety of short contact dithranol therapy* in 34 patients shows a significant reduction in PASI score of 69.3% was found and skin irritation was the only reported adverse effect. In this study a telemedicine setup is compared with administration in a regular day care setting. Dithranol can produce local skin irritation and can stain clothes despite of its safety and effectiveness in paediatric psoriasis.[51, 52]

Phototherapy

nbUVB considered to be very effective and well tolerated treatment alternative for children with plaque and guttatte psoriasis especially when those are poorly controlled with topicals.[53] A retrospective study on paediatric psoriasis for a duration of 3.3 months shows complete clearance in about 51% and yielded a good response in about 40% of children.[54] PUVA is an another treatment option, but due to its long term toxicity it is rarely used.[55]

SYSTEMIC TREATMENTS

Children with moderate to severe psoriasis defiant to topical therapy, systemic agents are indicated. But selection of agent is difficult because of the limited number of clinical trial and lack of guidelines in paediatrics.[56] Usually off-label therapy is followed. Van Geel et al. demonstrated evidence based recommendations for the use of these agents in child population.[57]

Methotrexate

Even though it is one of the best used medicines in adults, but MTX is only approved for JIA, IBA and certain malignancies.[20] A prospective study conducted by van Geel et al on *safety and efficacy of oral and subcutaneous MTX* in 25 children suffering from plaque psoriasis. Based n the study it is concluded that it can be used as a treatment option for the children with moderate to severe psoriasis, given either orally or subcutaneously.[58] In children, after attaining a therapeutic control tapering of dose must be done while ensuring the effectiveness and a low maintenance dose to reduce any side effects if present.[59]

Most common side effects reported by paediatric patients include nausea, vomiting, fatigue, stomatitis, abnormal LFT, bone marrow suppression, pulmonary toxicity, infections, hepatotoxicity like liver fibrosis; some of them are fatal so a routine laboratory investigation must be done. Folic acid is given with MTX to lower the side effects.[49] Concomitant use of drugs like NSAIDs may increase the potential toxicity.

Cyclosporine

An immunosuppressant drug used to treat adult psoriasis. It has a rapid onset of action of 2-4 weeks, so it's considered as an ideal drug for controlling unstable psoriasis. Children may require a dose higher than adults due to changes in pharmacokinetics, body surface area and weight ratio. It is particularly effective in the treatment of psoriatic crisis, or other psoriasis with no response and those using rotational scheme of treatment. Appropriate selection and monitoring of patient may reduce the risk of side effects. Common side effects include nausea, diarrhoea, hypertension and nephrotoxicity. Due to unavailability of supporting data low doses

of drug for shorter period should be used. Non-melanoma skin cancer is also described as a long term effect. Concomitant phototherapy should be avoided to prevent these kinds of malignancies.[60, 49]

Retinoids

Retinoids had been used in treatment of pustular and erythrodermic forms of psoriasis. One of the best known medicines was etretinate, now it is replaced by acitretin, an active metabolite. Data regarding use and safety of acitretin are limited. It shows mucocutaneous side effects like cheilitis, xerosis, epistaxis, skin fragility, hair loss and other ocular toxities. It may elevate triglyceride and certain liver enzymes so that a regular laboratory investigation is needed. Long term retinoid use may lead to idiopathic skeletal hyperstosis, premature epiphyseal closure, and decreased bone mineral density. It is teratogenic. Patient is not allowed to conceive within 3 years after cessation of therapy to avoid any teratogenic outcome.[61, 62]

Fumeric Acid Esters

These are used for the treatment of moderate-severe plaque psoriasis and include a broad range of immunomodulatoy effects. In adult the dose titration can be done upto720 mg daily depending upon tolerability and clinical response. Even though data regarding use of esters are limited, Balak DM et al conducted a retrospective case series on 14 children with psoriasis for a median period of 10 months shows a complete clearance in 36%, good improvement in 7%, partial response in 21% and no response in 36%. A starting dose of 30 mg dimethylfumarate was given and increased up to 720mg OD.[63]

Flushing, gastrointestinal complaints, eosinophilia, transient shift in leucocyte count and elevated hepatic transaminases are the major side effects observed. Mild proteinuria and slight elevation in serum creatinine level may also occur. Even in the absence of sufficient supporting data, FAEs can be used in children if MTX is ineffective or contraindicated.[57]

BIOLOGICS

These are the new pharmacological agents which shows a targeted action towards mediators of inflammatory cascade ncluding TNF-α and IL-12/23. These agents also offer more favourable dosing regimen and do not require frequent laboratory investigation as compared to conventional therapy. There are no international guidelines regarding the use of biologics in paediatric psoriasis. Furthermore they shows various complications both in adults and children like more susceptibility towards opportunistic infections, reactivation of latent tuberculosis and malignancies especially lymphomas. Even though these side effects are rare, but are reported in arthritis, IBD and sarcoidosis patients.[64, 65]

Adalimumab, etanercept, infliximab, ustekinumab are the near future drugs to be used in treatment of psoriasis. Adalimumab was demonstrated in two studies, were it is prescribed after failure of systemic agents. Infliximab is the TNF-α inhibitor, administered by infusion is approved for the use in psoriasis treatment. Ustekinumab is recently approved by FDA

COMORBODITIES IN PAEDIATRIC PSORIASIS

When compared to healthy control, paediatric patients shows a twofold increased risk of hyperlipidemia, obesity, hypertension, diabetes mellitus and rheumatoid arthritis.[66]

CONCLUSION

Management of psoriasis in children are quite challenging. Children are usually presented with mild to moderate psoriasis and are best stabilised with topical treatment. Apart from giving specific treatment it is important to provide both supportive care and psychosocial involvement by avoiding ostracism. Comparing with adults, paediatric patients shows spontaneous remission. The disease can get controlled with intermittent therapy in most of the patients; but in some it get worsen with age and may require aggressive therapy. New innovations in the systemic, topical, phototherapy and biologic may provide a better future in paediatric psoriasis therapeutic armantarium.

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