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Pederm Insights

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Editor's Thoughts

Bidding Adieu from the Editor in chief

No Permanence is ours, we are a wave that flows to fit whatever form it finds

- Hermann Hesse

Dear Colleagues,

Welcome to the fourth edition of PDF newsletter!

The past few months have been exciting for all the team members with the second national 'Pediatric Dermatology Updates 2024' conference held on September 28th and 29th, 2024, at NIMHANS convention centre, Bengaluru. The two days of the conference were enriched with several insightful sessions with active participation from all the speakers, panelists, and delegates, adding depth and diversity to the discussion. Overall, the conference was an academic bonanza for all the dermatologists interested in the field of pediatric dermatology.

Diet and nutritional therapies play an important role in various dermatoses in pediatric age groups. It's unclear whether dietary supplements can improve or worsen specific skin diseases. This issue of 'Pederm Insights' features an evidence-based literature review on the role of antioxidants, probiotics, and biotin in various pediatric dermatoses. Akin to other issues, we have an interesting case vignette, photoquiz and tips and tricks while prescribing retinoids. We received an overwhelming response from many residents for the second PDF photoquiz. The resident's column yet again focuses on the views on pediatric dermatology of a postgraduate student from a medical college.

As the monsoon bids farewell and steps into autumn, a season of transition, I bid adieu as editor-in- chief of the 'Pederm Insights'. It has been a wonderful experience to work as editor-in-chief for the past one year, with the team of committed editorial board members. I thank Dr Deepak Parikh and all the editorial members for their constant support, guidance and contribution. I welcome our new editor-in-chief, Dr. Resham Vasani, and wish her all the best as I pass the torch to her!

Happy Reading!

Dr Sahana Srinivas

Editor in Chief

Contributors: Sahana M Srinivas, Preeti K Sheth, Jeta Buch, Divya Gupta,

1. **Andrade RDS, de Souza FIS, Aranda CS, Mallozi MC, Ferreira AC, Barreto TLN, et al. Antioxidant defense of children and adolescents with atopic dermatitis: Association with disease severity. Allergol Immunopathol. 2024;52(1):65-70.**

The authors of the study have aimed to compare the antioxidant defense in children and adolescents with atopic dermatitis with that of healthy individuals and to verify the association of antioxidant defense with disease severity and nutritional status. This cross-sectional study conducted at the Allergy outpatient clinic, evaluated 48 children and adolescents who were diagnosed with atopic dermatitis according to the diagnostic criteria of Hanifin and Rajka, and 25 healthy controls for nutritional assessment (body mass index z score [BMIZ] and height for age z score [HAZ]) and levels of vitamins A, C, E, and D, zinc (Zn), copper (Cu), antioxidant enzymes (superoxide dismutase , catalase , glutathione peroxidase), high-sensitivity C-reactive protein (CRP) and interleukin 33. The two groups, were homogenous in relation to gender and age. In the atopic dermatitis group, severe, moderate, and mild forms were observed in 14 (29.2%), 24 (50.0%), and 10 (20.8%) cases, respectively. The mean age was 10.3 ± 3.8; 24 (50%) were males, and 28 (58.3%) were prepubescent. There was no significant difference between the AD and control groups for vitamins and antioxidant enzymes and for copper. Zinc levels (98.3 ± 21.4 mcg/dL vs 76.9 ± 16.1 mcg/dL; $P < 0.001$) were significantly higher and IL-33 concentrations were lower (19.0 [0.18;929.6] pg/mL vs 2.8 [0.18;702.4] pg/mL; $P = 0.040$) in the atopic dermatitis group. There was no significant difference in terms of severity in patients with AD (moderate or severe vs mild) for vitamins A, C, and D, and antioxidant enzymes, zinc, and copper. The limitation of the study was the small sample size and the methodology.

Comments

In recent years, there has been a great deal of attention toward the field of free radical chemistry. Free radical's reactive oxygen species (ROS) and reactive nitrogen species are generated by our body by various endogenous systems, exposure to different physiochemical conditions or pathological states. A balance between free radicals and antioxidants is necessary for proper physiological function. Components of antioxidant defense include enzymes such as superoxide dismutase, catalase , and thioredoxin, as well as exogenous and endogenous nonenzymatic molecules such as vitamins A, C, and E, uric acid, coenzyme Q10, and the whole glutathione system, which comprises glutathione and the enzymes glutathione reductase and glutathione peroxidases. The trace elements such as zinc, copper, selenium, and manganese act as cofactors of antioxidant enzymes.

Chronic skin inflammation is associated with overproduction of ROS such as superoxide and hydrogen peroxide, which eventually accumulates and exceeds the defence capacity of the antioxidant system, giving rise to oxidative stress, a condition implicated in the pathogenesis of several skin disorders. Targeting oxidative stress has been an attractive strategy in the treatment of various skin disorders. Dermatologists often emphasise the importance of incorporating antioxidants for treatment of psoriasis, atopic dermatitis and vitiligo. However, the available evidence is not sufficient to establish their efficacy.

Review of articles on the association of atopic dermatitis and oxidative stress has shown inconclusive results. In the above article, zinc levels were found to be in higher concentrations, as compared to controls. However, systematic review and meta-analysis of the association of zinc and atopic dermatitis along with oral zinc supplementation has shown to have low or moderate quality of evidence. [Ref: Gray NA, Dhana A, Stein DJ, Khumalo NP. Zinc and atopic dermatitis: a systematic review and meta-analysis. J Eur Acad Dermatol Venereol. 2019 ;33(6):1042-1050]. At the present scenario, there is lack of evidence for recommendation of antioxidants for dermatological disorders like psoriasis or atopic dermatitis. Further, large scale studies are necessary to correlate the available data on antioxidants and its placement in the management of chronic skin disorders.

(Submitted by: Sahana Srinivas)

2. Xue X, Yang X, Shi X, Deng Z. Efficacy of probiotics in pediatric atopic dermatitis: a systematic review and meta-analysis. Clin Transl Allergy 2023; e12283.

Maintaining the structural integrity of the gut microbiome can resist the invasion of pathogenic bacteria and reduce the nutrient competition between the pathogenic and commensal bacteria. Gut microbiota is involved in the short chain fatty acid and amino acid metabolism that induce maturation of the innate and adaptive immune systems. Gut microbiota dysbiosis is one of the suggested pathogenic mechanisms leading to immune disorders like atopic dermatitis (AD). Thus, altering the gut microbiome may be helpful in modulating the immune response and improving AD.

Consumption of probiotics may actively fight pathogenic bacteria by release of antimicrobial factors and modulate the immune system to fight the pathogenic bacteria or induce immune tolerance thereby reducing inflammation in AD.

The role of probiotics in AD is though controversial. Some studies have suggested that probiotics can effectively improve AD while other observe no effect. With this premise, Xue et al.[1]conducted a systemic review and meta-analysis of randomized control trials (RCTs) to evaluate the efficacy of probiotics on SCORAD value in children of atopic dermatitis, as compared with a placebo group, between January 2010 to January 2023.

Ten outcomes from 9 RCTs involving 1000 patients (ages 0 to 18 years) were analysed. SCORAD was used as the outcome index in the studies. 3 of these 10 outcomes were evaluated as dichotomous variables in 373 patients whereas, 7 outcomes were analysed as continuous variables in 627 patients. Meta-analysis of dichotomous variables found no significant statistical difference between probiotics and control group ([OR = 1.75, 95% confidence interval (CI) (0.70, 4.35), p = 0.23, I2 = 68%]. The one on continuous variables found a significant difference between probiotics and control group [MD = −4.24, 95% CI (−7.78, −0.71), p = 0.002, I2 = 71%]. Continuous variables were further evaluated with subgroup analysis of effect of children's age, treatment duration and probiotic species on SCORAD values.

Effect of children's age: 2 studies with children < 3 years and 5 studies with children > 3 years were evaluated. Significant differences in SCORAD were found in children > 3 years, but not in children < 3 years. The difference between subgroups was insignificant.

Effect of treatment duration: 2 studies had an 8 weeks cycle, and 5 studies had a 12 weeks cycle. The results of both 8 weeks and 12 weeks treatment duration did not yield any significant difference. Statistically insignificant difference was found between both groups.

The study showed that the prognosis of AD was unrelated to the age of child at which probiotics was supplemented and its treatment duration.

Effect of probiotic strain number: single-strain probiotics were used in 4 studies and multi-strain probiotics in 3 studies. Significant difference was found between single-strain probiotics and placebo, but not between multi-strain probiotics and placebo. Probiotics helped to improve SCORAD value, with single-strain demonstrating more improvement in the values as compared to multi-strains. The bacterial load per bacterial strain was found to be comparable, both in the multi-strain mixture and single strain. The reason offered was the plausible suppression of strains on one another, leading to comparable concentrations. [2]

Limitations of the study: Small number of studies were included. Heterogeneity amongst the studies was high. Two studies were removed as one studied premature infants and in the other topical steroids were not discontinued. Probiotics in different studies used various number and type of strains and for various lengths of time.

Comments

AD is a complex disease with heterogenous clinical manifestations with multiple factors involved in the pathogenesis. Current understanding of the disease revolves around an impaired skin barrier with an underlying genetic defect, natural killer cell deficiency and gut microbial diversity. Gut dysbiosis early in life affects the host immune system by decreasing the short chain fatty acids and increasing Th2 cells, eventually leading to an increase in IL-4, IL-13, IgE production, culminating in an inflammatory response. Probiotics help regulate gut microbiota by encouraging T cell differentiation, increasing anti-inflammatory cytokines and hence, may play an adjuvant role in the treatment of AD. However, the type of strain of probiotic to be used, single or multiple, number, dose, administration, and duration is still unclear. Additionally, studies so far have yielded contradictory results. Majority of guidelines yet do not recommend probiotics in the therapeutic armamentarium of AD. Large, high-quality studies are the need of the hour.

1. Kim JE, Kim HS. Microbiome of the Skin and Gut in Atopic Dermatitis (AD): Understanding the Pathophysiology and Finding Novel Management Strategies. J Clin Med 2019; 8(4): 444.
2. Doege K, Grajecki D, Zyriax B-C, Detinkina E, zu Eulenburg C, Buhling KJ. Impact of maternal supplementation with probiotics during pregnancy on atopic eczema in childhood – a meta-analysis. British Journal of Nutrition. 2012;107(1):1-6.

(Submitted by: Preeti Sheth)

3. **Wang F, Wu F, Chen H, Tang B. The effect of probiotics in prevention of atopic dermatitis in children: a systematic review and meta-analysis. Transl Pediatr 2023; 12(4): 731-748.**

Owing to the inconsistency of results from previous research papers studying the efficacy of probiotics in prevention of pediatric atopic dermatitis (AD), this meta-analysis was undertaken to compare the efficacy of probiotics with placebo in prevention of atopic dermatitis.

Multiple Random Control Trials (RCTs) conducted to evaluate the role of probiotics in preventing pediatric AD were extracted from the time of establishment of database (details not mentioned) until November 2022. Thirty- seven RCTs were evaluated in the final count, with 2986 being in the probiotics group and 3145 in the placebo group. According to this meta-analysis, probiotics were superior to placebo in the prevention of AD [risk ratio (RR) (95% confidence interval): 0.83 (0.73, 0.94), I2=65.2%]. Sub group meta-analysis was also performed. It revealed the following:

On intervention objects: Probiotics proved to significantly prevent AD, when the recipients were both mothers and infants; but they did not have a significant effect when recipients were either mothers or infants. Details were not available whether infants were breast fed or not. For knowledge, probiotics are available in a capsule. The capsule is opened and contents poured into a feeding syringe. To this, 1 tsp i.e. 3-5ml of breast milk or formula milk is added. The mixture is then administered to the child once daily through a feeding tube.

On intervention timing: Probiotics had a significant effect on prevention of AD when the timing of intervention was both prenatal and postpartum; but did not have a significant effect when timing of intervention was either prenatal or postpartum. Most mothers were prescribed probiotics a month before delivery. Post-natally, probiotics were given to both mother and children (in most studies) for a varying time period ranging from 1 month to 2 years.

On type of probiotics: Significant effect on prevention of AD was appreciated when the type of probiotics used were Lactobacillus rhamnosus and mixed flora, but not when Lactobacillus or Bifidobacterium were used.
On trial region: Probiotics intervention had a significant effect on prevention of AD when the trial was conducted in Europe, but not in Oceania and Asia.
On the follow up time: Significant effect on prevention of AD was seen with probiotics intervention, when the follow-up time frame was less than 2 years; but not when it was for more than 2 years. Not much literature emphasizing the reason why, but it is speculated that probiotics work well before itch-cycle has commenced. Once the latter settles in, probiotics do not have much of a role to play.
Hence, to conclude the results of this meta-analysis, probiotics could effectively prevent the incidence of AD. Additionally, they could prevent the development of AD significantly when both mothers and infants took Lactobacillus rhamnosus and mixed flora, before and after delivery.
Limitations of the study: Being a meta-analysis of heterogenous studies, confounding factors were adjusted. However, dosage of probiotics and duration for which they were supplemented were not evaluated. Furthermore, criteria used to define AD differed in various studies. Differences in general characteristics such as age, sex, family factors were also noted.

Comments

Maternal microbes are transferred to the foetus during gestation. These microbes are essential for intestinal physiological regulation and immune function. Probiotics modulate structure of microbiota and function of immune cells, thereby regulating immunity development. They form tight junctions with intestinal epithelial cells, reduce the adhesion of pathogenic bacteria, stimulate the production of intestinal IgA and reduce IgE, thereby reducing inflammation. Hence, theoretically, administering probiotics pre – and postnatally to both mothers and infants may help in prevention of AD. However, further research is warranted with specific reference to the type of probiotic to be used, its dose and duration to be administered.

Reviewing both of the above meta-analyses, one may like to believe that probiotics may be a promising adjuvant therapy in the treatment and prevention of AD. Unfortunately, there's little scientific evidence backing them. A 2017 Cochrane review highlights the need of more high-quality trials to support the judicious use of probiotics (Sao Paulo Med J. 2017; 135(6):578-86). To the best of my knowledge, no good study has been published after the Cochrane review, that validates the use of probiotics in treatment or prevention of atopic dermatitis.

(Submitted by: Preeti Sheth)

4. **Venter C, Agostoni C, Arshad SH, Ben-Abdallah M, Du Toit G, Fleischer DM, et al. Dietary factors during pregnancy and atopic outcomes in childhood: A systematic review from the European Academy of Allergy and Clinical Immunology. Pediatr Allergy Immunol. 2020;31(8):889-912.**

Maternal diet during pregnancy has been linked to offspring allergy risk. Maternal diet is a potentially modifiable factor, which could be targeted as an allergy prevention strategy. In this paper, the authors undertook a systematic review of studies investigating the association between maternal diet during pregnancy and allergic outcomes (asthma/wheeze, hay fever/allergic rhinitis/seasonal allergies, eczema/atopic dermatitis (AD), food allergies, and allergic sensitization) in offspring. They searched three bibliographic databases (MEDLINE, EMBASE, and Web of Science) through February 26, 2019 and evidence was critically appraised.

Around 17 RCTs and 78 observational (case-control, cross-sectional, and cohort) studies were identified. Based on the meta-analysis, RCTs showed that vitamin D supplementation (OR: 0.72; 95% CI: 0.56–0.92) is associated with a reduced risk of wheeze/asthma. A positive trend for omega-3 fatty acids was observed for asthma/wheeze and allergic rhinitis, but this did not reach statistical significance (OR: 0.70; 95% CI: 0.45–1.08; OR: 0.76; 95% CI: 0.56–1.04 respectively). Neither vitamin D nor omega-3 fatty acids were associated with an altered risk of AD or food allergy. It was concluded that prenatal supplementation with vitamin D may have beneficial effects for prevention of asthma.

Comments

This systematic review and meta-analysis found insufficient evidence to provide clear dietary recommendations for preventing allergic diseases in offspring. Although Vitamin D supplementation was associated with a reduced risk of wheeze/asthma, higher than recommended doses were used in three of the RCTs (800,2400, or 4000 IU per day, as opposed to 600 IU Recommended Daily Allowance); also, Vitamin D supplementation showed no significant impact on atopic dermatitis (AD). The review was also limited by the quality of included studies (64% studies were of low quality) and focused primarily on Western countries. Since Indian dietary practices are markedly different from Western diet, it may not be appropriate to extrapolate the results to our population.

Previous studies have shown some role for probiotic supplementation along with various other macro- and micro-nutrients. However, the specific strain required, dose and the optimal timing of supplementation remain unclear. Also keep in mind that allergic outcomes can also be influenced by paternal factors and other family history, and not necessarily by maternal pregnancy exclusively.

The review highlights the need for more rigorous, large-scale studies to identify key factors influencing dietary impacts on allergy prevention during pregnancy. While vitamin D supplementation shows promise for reducing asthma/wheeze risk, routine high dose supplementation in pregnancy cannot yet be recommended without further research.

(Submitted by: Divya Gupta)

5. **Thompson, K. G., & Kim, N. (2020). Dietary supplements in dermatology: a review of the evidence for zinc, biotin, vitamin D, nicotinamide, and polypodium. Journal of the American Academy of Dermatology.**

Dietary supplements are recommended by majority of dermatologists for their purported benefits in skin, hair and nail disorders. The authors critically reviewed the available evidence for commonly recommended oral OTC supplements i.e. zinc, biotin, vitamin D, nicotinamide and polypodium in the management of common dermatologic disorders. Insufficient evidence exists to recommend the use of zinc in alopecia, acne, HS or wound healing and gastrointestinal side effects are common. Biotin supplementation has been shown to interfere with routine immunoassays which may lead to misdiagnosis of potentially serious conditions. Vitamin D may have a role in decreasing melanoma risk/progression, particularly in high –risk individuals with a history of non-melanoma skin cancer (NMSC), but there is insufficient evidence to recommend vitamin D for AD, psoriasis or prevention of NMSC. Studies on the use of nicotinamide in preventing NMSC are promising, but its chemoprotective effect does not persist after discontinuation. Preliminary studies indicate that PLE may prove to be a useful adjunct to standard-of-care treatments in photodermatoses, melasma and actinic damage, although the precise antioxidant and photoprotective mechanisms have yet to be fully elucidated.

(Submitted by: Jeta Buch)

6. **Elston DM. Letter from the editor: First do no harm-biotin for hair and nails. J Am Acad Dermatol. 2024 Apr 6:S0190-9622(24)00576-0.**

Biotin containing supplements are marketed over the counter as "dermatologist – recommended" for the treatment of hair and nail disorders. However, little evidence exists surrounding efficacy and safety of high dose biotin. Rare disorders like inherited biotin deficiency clearly benefit from high-dose biotin. Few anecdoctal reports of use in brittle nail syndrome and uncombable hair syndrome have also reported benefit. However, in healthy individuals, the benefits of supplementation are scant, but a risk of potential harm definitely exists. HCG detection is indicative of pregnancy and some forms of cancerous tumors. Biotin supplementation can also severely suppress urinary HCG values in assays utilizing biotin-streptavidin binding methods - particularly important in patients on isotretinoin. High dose biotin may interfere with laboratory testing of thyroid hormones, specific IgE, growth hormone, insulin-like growth factor, renin, aldosterone, bone alkaline phosphatase and most importantly cardiac enzymes. Biotin also interferes with pregnancy tests, particularly urine tests, essential in patients on isotretinoin.

Comments:

There is a general tendency to conclude that administration of aforementioned nutritional supplements would have a beneficial effect even without a proven lack. However, in clinical practice, the results are disappointing when confronted with problems. Inadvertent use of biotin may also mask detection of certain conditions doing more harm than good. High-quality investigations into the safety and efficacy of these supplements with standardized dosing, outcome measures, and adverse effects reporting are thus the need of the hour.

(Submitted by: Jeta Buch)

Case Vignette

Scaly patch on the scalp: unveiling the diagnostic features

Author: Rashmi Agarwal

Case report: An 8-year-old boy presented with a localized, single, itchy, scaly lesion on the scalp for the past 2 weeks. Cutaneous examination revealed a single well-defined plaque covered with thick whitish scales with matting of the hair (Figures 1 & 2). Surrounding erythema and mild scaling were present. On closer examination, a few broken hairs were seen. Other areas of the scalp were not involved. Cutaneous and nail examinations were normal. On dermoscopy, hairs were covered with thick silvery white scales, and the base had yellowish-brown, dirty-looking scales. Hairs showed the presence of multiple thin horizontal white bands (Figure 3), causing the hair to bend and break, giving rise to trichorrhexis nodosa (Figure 4). There was no comma hair or corkscrew hair. A KOH mount was done which showed the presence of multiple spores and a few branched septate hyphae, grouped and attached outside the hair cortex. After correlating the clinical examination, trichoscopic findings, and mycologic results, a diagnosis of tinea capitis (ectothrix) was made and the child was started on oral griseofulvin 250mg twice daily for 3 months. Post-treatment completion, repeat dermoscopic examination did not reveal any scales or morse code hair and KOH mount was negative for spores or hyphae.

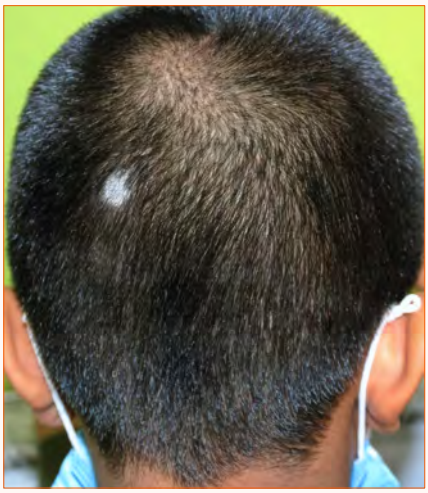

Fig 1

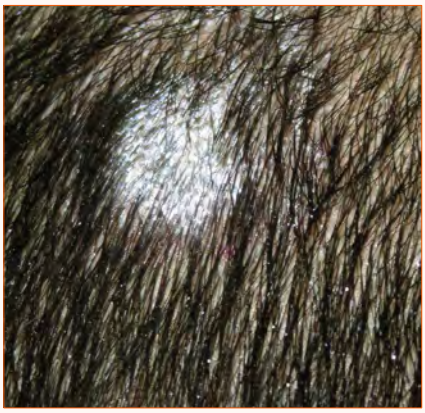

Fig 2

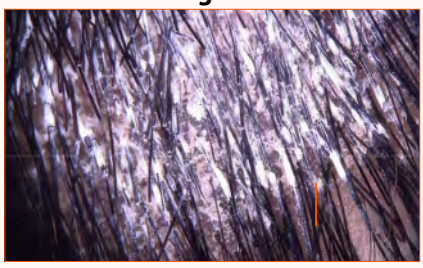

Fig 3

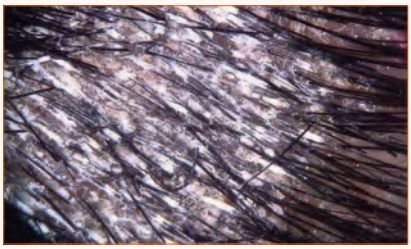

Fig 4

Discussion:

Tinea capitis mostly affects children, generally aged between 3 and 7 years, although cases in infants have also rarely been reported.[1] Children with tinea capitis usually complain of redness, itching, scaling, and patches of hair loss.

Different clinical patterns are associated with specific causative organisms.[2] The common clinical forms include the non-inflammatory variants: gray patch (circular patch of alopecia with fine scaling, caused by ectothrix Microsporum infection) and black dot (endothrix infection with Trichophyton species presenting with swollen hair stubs resulting from hair shaft breakage at the scalp level); and the severe inflammatory type, kerion celsi, presenting as a painful boggy swelling studded with pustules. It is usually associated with cervical lymphadenopathy and may lead to scarring alopecia if left untreated. Inflammatory tinea capitis, favus (yellow crusts known as scutula are observed at the base of the hair shafts) is now seen only sporadically.

Atypical presentations of tinea capitis include:[2,3,4]

- Subtle hair loss accompanied by scalp scaling
- Seborrheic dermatitis-like (diffuse scaling or severe dandruff-like appearance on various places on the scalp)
- Diffuse pustular (patchy alopecia with scattered pustules or low-grade folliculitis)
- Moth eaten syphilitic alopecia-like presentation
- Pityriasis amiantacea-like presentation

Tinea capitis usually has a good prognosis when treated early and appropriately. Owing to the changing and varied clinical patterns, causative organisms, and close resemblance to other scalp conditions (like alopecia areata, trichotillomania, scalp psoriasis, seborrheic dermatitis, dissecting cellulitis, abscess formation) it poses dia gnostic and therapeutic challenges in children. Though direct examination with 10%–20% KOH and mycological culture of infected hair is the gold standard for

diagnosing tinea capitis, sampling errors can give false negative results. Also, culture requires around a month, delaying effective treatment and increasing the risk of transmission. Trichoscopy presents with characteristic features of tinea capitis (sensitivity of 94% and specificity of 83%)[5], making it useful for providing a preliminary diagnosis during initial patient evaluations and monitoring treatment progress.

Table 1: Characteristic trichoscopic features of tinea capitis:[6,7]

Trichoscopic features	Description	Associated diseases
Comma hair	Short, C-shaped hairs, homogeneous in pigmentation and thickness formed due to subsequent cracking and bending of a hair shaft filled with hyphae	Endothrix- > ectothrix-type tinea capitis Occasionally in alopecia areata and trichotillomania
Corkscrew hair	Multiple twisted and coiled short hairs	Endothrix- > ectothrix-type tinea capitis Occasionally in ectodermal dysplasias
Bar code–like hair/ Morse-code like hair	Multiple thin white bands across the hair formed due to the accumulation of spores around the hair shaft causing a transverse perforation of the hair shaft	Ectothrix-type tinea capitis
Zigzag hair	Bent hairs with multiple sharp angles formed from incomplete, transverse fractures along the hair shaft	Ectothrix-type tinea capitis Occasionally in alopecia areata
Bent hair	Bending of the hair shaft with homogeneous thickness and pigmentation, but without hair shaft shortening (unlike comma hair)	Ectothrix-type tinea capitis
i-hair	block hairs with an accented dark distal end	Also observed in alopecia areata and trichotillomania
Block hair	very short hairs with a transverse horizontal distal end	

Broken hairs, black dots, and perifollicular and interfollicular scaling are not characteristic, but commonly observed trichoscopic findings of tinea capitis. Trichoscopy thus serves as a useful tool in differentiating between Microsporum and Trichophyton tinea capitis, which is important from the perspective of a different therapeutic approach (Table 2).[5,6]

Table 2:

Trichoscopic findings	Associated organism causing tinea capitis	Treatment (Oral Antifungals)
Predominantly curved findings (comma and corkscrew hair)	Trichophyton spp	Terbinafine (preferred; but syrup form unavailable) Griseofulvin Itraconazole
Predominantly straight findings (bar code–like, zigzag hair and bent hair) and diffuse scaling	Microsporum spp	Griseofulvin (microsize formulation: 15–25 mg/kg/day; ultramicrosize formulation: 10–15 mg/kg/day Itraconazole (3-5mg/kg/day) *Longer duration of treatment is needed for ectothrix (Microsporum spp.) than endothrix (Trichophyton spp.) infections.
Polymorphic pattern (both curved and straight findings)	Microsporum spp (as ectothrix fungi proliferate both inside and outside the shaft, lesions may present with several different signs simultaneously)	

Oral antifungals are the treatment of choice as topical antifungal agents do not penetrate the hair follicle root. Antifungal shampoos can be part of the treatment plan and often help in preventing spread of spores. The use of topical antifungal agents alone results in the development of carriers, who exhibit minimal symptoms and clinical signs but remain mycologically positive, thereby increasing the risk of transmission.

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Answer to PDF - Photoquiz 2

Authors: Preeti K Sheth, Resham Vasani

Clinical data

A three and half years old boy, born of a non-consanguineous marriage, presented with asymptomatic, raised, solid, skin coloured lesions on the trunk, progressively increasing in the past 1 year. He weighed 2.1 kg, had a short stature and stiffness of the joints. Family history was non-contributory.

General examination findings revealed a coarse facial phenotype with bushy eyebrows, depressed short bridge of the nose, widened nostrils and thickened lips (Figure 1). He had broad hands with short stubby fingers (Figure 2) and a protuberant abdomen. Cutaneous examination revealed small, firm, skin coloured papules like pebbles, arranged close together to form ridges in a reticular array. The papules (marked with black arrow) were present bilaterally symmetrically between angles of scapulae, posterior axillary line and lateral side of the trunk. (Figure 3, 4). Bluish-black, ill-defined macules were spotted on the back (Figure 4). Mild hypertrichosis was seen over thigh and trunk.

A punch biopsy was done and sent for histopathological analysis with special stains (Figures 5 and 6).

Please answer the following questions

1. What is your diagnosis?

   Answer: **Hunter's syndrome**

1. The presence of one of the following is crucial to the diagnosis:

   a) Mongolian spots

   b) Hypertrichosis

   c) Pebbly papules

   d) Corneal clouding

   Answer: **Pebbly papules**

3. The gold standard test leading to diagnosis is

   a) Urine examination

   b) Skin biopsy

   c) Enzyme assay

   d) Skeletal survey

   Answer: **Enzyme assay**

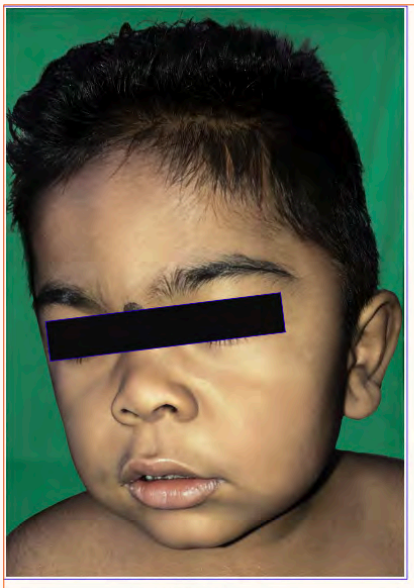

Fig 1

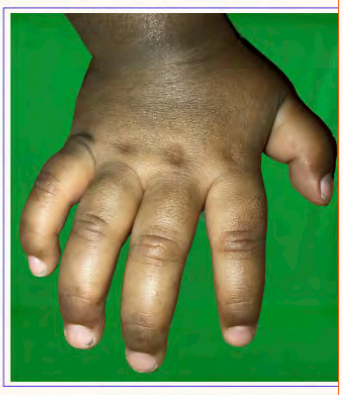

Fig 2

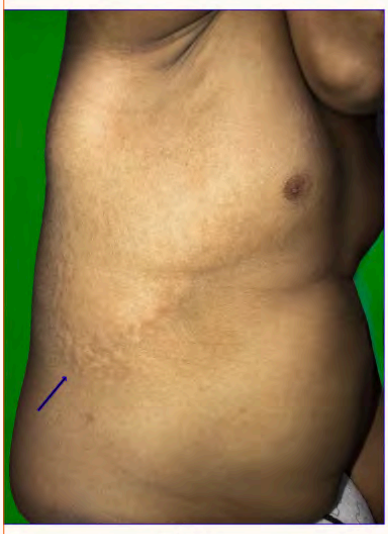

Fig 3

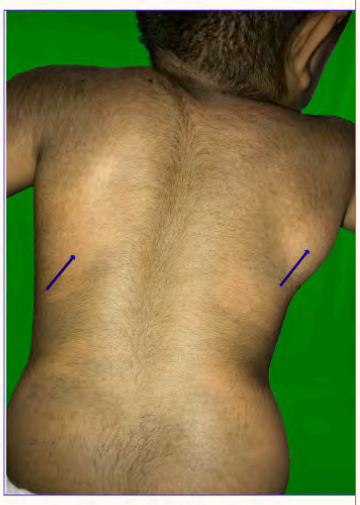

Fig 4

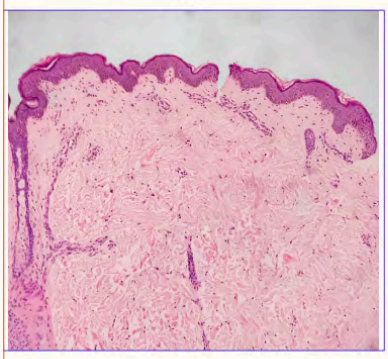

Fig 5

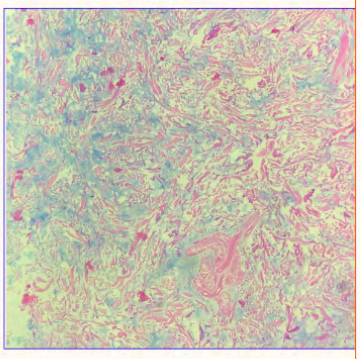

Fig 6

4. Which special stain was used to confirm the diagnosis?

    a) PAS stain

    b) Aniline blue stain

    c) Colloidal iron stain

    d) Alcian blue stain

Answer: **Alcian blue stain**

Discussion

A presumptive diagnosis of Hunter's syndrome/Mucopolysaccharidosis II (MPS Type-2) was made in view of the coarse facies, short stature, protuberant abdomen, pebbly papules on the trunk and extensive mongolian spots. As a screening test, urine electrophoresis was carried out which demonstrated significantly raised glycosaminoglycans with high excretion of dermatan sulphate with lower levels of chondroitin sulphate and heparan sulphate. Bowing of skull bone was seen on radiological examination. Ultrasonography of the abdomen revealed mild hepatosplenomegaly and bulky pancreas. Ophthalmologic examination was normal. Histopathology of the papules demonstrated mucin deposition between the collagen bundles in the dermis, which was substantiated with Alcian blue positivity. Molecular diagnosis using lysosomal storage disorder panel showed a pathogenic hemizygous deletion of exon 9 of IDS gene, with X linked recessive inheritance, which confirmed the diagnosis of MPS-type 2/Hunter's syndrome.

MPS type 2 is an X linked recessive, multisystemic, lysosomal storage disorder. Although affecting mostly males, the syndrome is observed in a few numbers of females too. Mutation in the IDS gene leads to deficiency in the enzyme iduronate-2-sulfatase which thereby leads to decreased degradation of mucopolysaccharides. In turn there is accumulation of glycosaminoglycans within the lysosomes in multiple organs of the body, including skin. [1]

Hunter's syndrome, has distinct skin eruptions, apart from Mongolian spots and hypertrichosis. Although the latter are observed in other mucopolysaccharidoses, the 'pebbly papules' are unique to Hunter's syndrome. They are found to be present in both the attenuated and severe phenotypes of the syndrome. These are ivory white, small 2mm to 10mm papules, closely grouped to form ridges in a reticular fashion. They develop symmetrically between the angle of the scapulae and posterior axillary lines, nape of neck, pectoral area and lateral aspect of the arms and thighs. They erupt before the age of 10 years and help in diagnosing the condition in its early stages, particularly in the attenuated form of the syndrome. Hence, the papules are the cutaneous marker of Hunter's syndrome. Differential diagnosis of pebbly papules include, connective tissue nevi (unlike pebbly papules, these nevi do not follow a pattern), localized amyloidosis (inflammation and pruritus are present, while pebbly papules are asymptomatic) and papular mucinosis (papules and nodules are usually translucent versus pebbly papules that are skin colored).[2]

Hunter's syndrome is a heterogenous disorder involving a constellation of signs and symptoms with respect to various organs, with relevance to musculoskeletal, nervous and cardiorespiratory systems. Only the ocular system is not largely affected, which helps to differentiate from Hurler's syndrome.

Clinical suspicion coupled with battery of investigations help to arrive at the diagnosis. On histopathological front, special stains like Alcian blue confirm the presence of mucin in the dermis. Definite diagnosis is achieved with enzyme assay and molecular analysis.

Management is multidisciplinary. Enzyme replacement therapy with recombinant iduronate 2 sulfatase, hematopoietic stem cell transplant, serum or plasma infusion gene therapy offer a ray of hope to this complex disease.[3]

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The correct answers to the PDF photoquiz 2 are given by

1. Dr Shashidhar K.C, Fellowship student in Pediatric Dermatology, Dept of Pediatric Dermatology, Indira Gandhi Institute of Child Health, Bengaluru.
2. Dr ArulSelvan M, Final year post graduate, Dept of Dermatology, Pondicherry Institute of Medical Sciences.
3. Dr Anmol Godara, Post graduate resident, ESIC Medical College and Hospital, Faridabad.
4. Dr Asha B Panchagavi, Consultant Pediatric Dermatologist, Sai Aadhar Hospital, Mudhol

The Editorial board congratulates all the winners. Free complimentary registration will be provided to all the winners for the upcoming 'Pediatric Dermatology Updates 2025' conference, Mumbai. Further information will be emailed.

PDF - Photoquiz 3

Authors: Manjyot Gautam, Akanksha Ghodke

Clinical data

A sixteen-year-old boy, presented with a mildly painful lesion on right upper back noted since 4 months. The lesion was small to begin with and gradually progressed to the current size. The patient denied any history of trauma prior to this lesion. There was no history of any pre-existing mole at the site of this lesion. Cutaneous examination revealed a single, well-defined, oval hyperpigmented plaque measuring 2.5cm x 1.5 cm with elevated erythematous margin and atrophy in the centre, situated over the right scapula (figure 1a,1b). It was mildly tender.

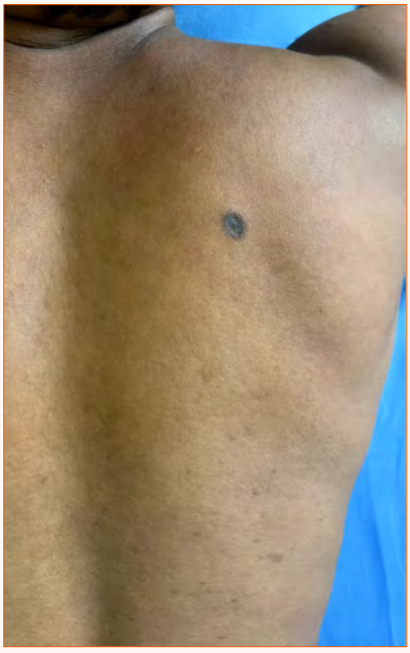

Fig 1a

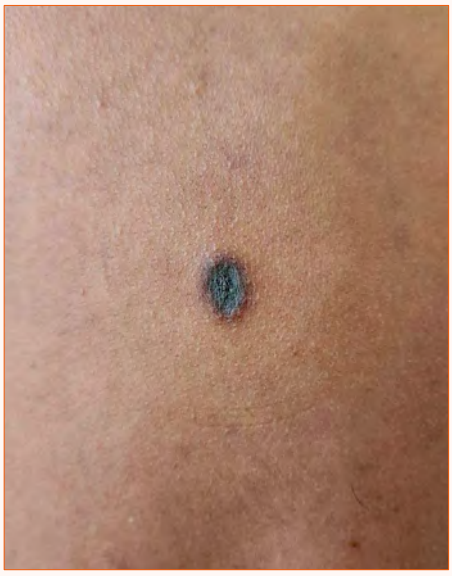

Fig 1b

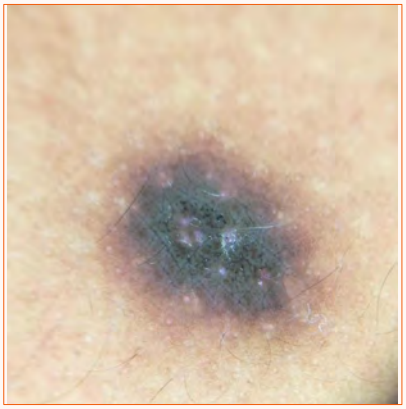

Fig 2 On Dermoscopy- central irregular white scar like patch with pesudofollicular openings and peripheral erythematous homogenous macules is seen.

Dermoscopy of the lesion showed central irregular white scar like patch with pesudofollicular openings and peripheral erythematous homogenous macules (figure 2).

A 4mm punch biopsy was done and sent for histopathological examination. (figure 3a,3b,3c,3d)

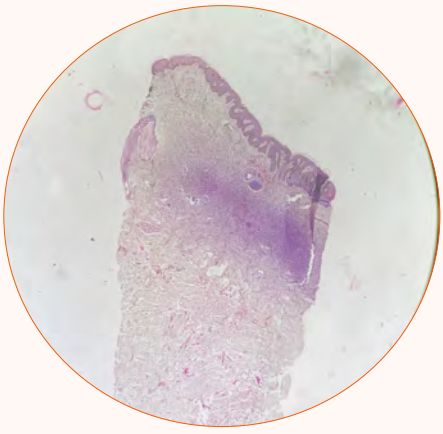

Figure 3a-Scanner view [H&E 4X] showed acanthosis in the epidermis with elongation of rete ridges and an infiltrate was noticed in the papillary and mid dermis.

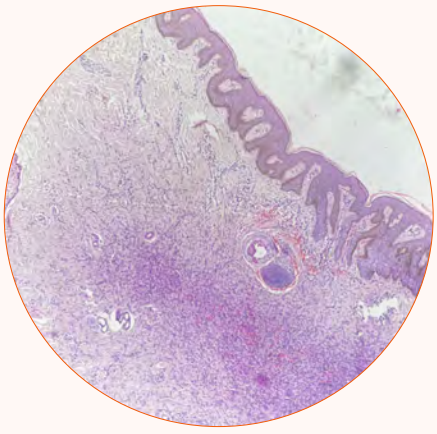

Figure 3b-A higher magnification confirmed an acanthotic epidermis with hyperpigmented basal keratinocytes known as 'dirty feet sign'. A clear Grenz zone is seen in the papillary dermis with spindle cells entrapping collagen bundles. [H&E 10X]

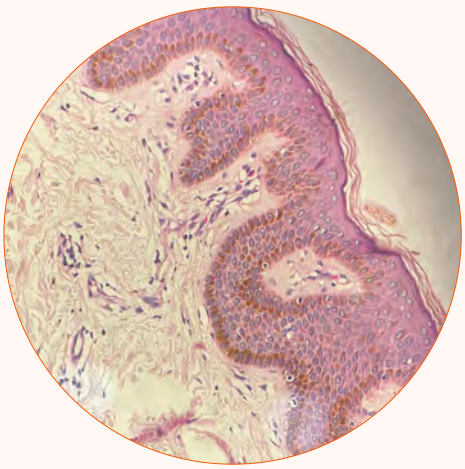

Figure 3c- Acanthotic epidermis with scanty perivascular infiltrate in the papillary dermis and hyperpigmentation of basal keratinocytes (Dirty feet sign).[H&E 40X]

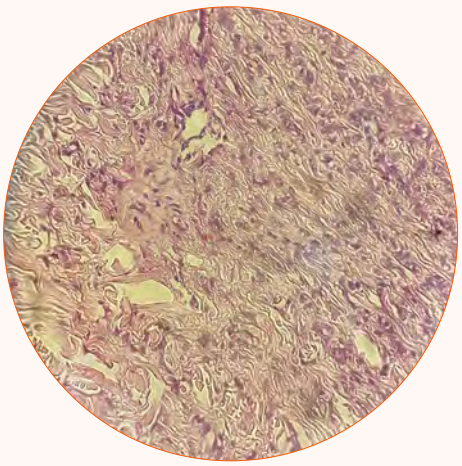

Figure 3d-Storiform arrangement of spindle cells with entrapment of collagen bundles in the papillary and mid dermis. [H&E 40X]

What is your diagnosis?

[Kindly mail your answers along with your affiliation **to** peddermfoundation@gmail.com before 20th December 2024. The winners of the **PDF Photoquiz 3** will be announced in the next issue]

Pediatric Dermatology Foundation

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My Understanding and Views on Pediatric Dermatology: Insights from a Dermatology Resident

Authors: Praveen Raj, Pramodh Kumar

Junior Residents, Department of Dermatology, Command Hospital Airforce, Bengaluru

Introduction

Pediatric dermatology, a subspecialty within dermatology, focuses on diagnosing and treating skin conditions specific to babies, children, and teenagers. Given the unique physical and mental needs of youths, this field is crucial for early diagnosis, intervention, and parental counseling, significantly impacting the quality of life and health outcomes in pediatric patients.

Historical Perspective

The recognition of pediatric dermatology as a distinct subspecialty is relatively recent. Historically, children's dermatological care was integrated into general dermatology. However, the unique needs of pediatric patients led to the establishment of dedicated pediatric dermatology units and training programs. Pioneers like Dr. Alvin Jacobs and Dr. Lawrence Schachner played significant roles in developing and recognizing pediatric dermatology through their research and clinical contributions.

Scope and Significance

Pediatric dermatology addresses common conditions such as atopic dermatitis and diaper rash, as well as rare genetic disorders like epidermolysis bullosa. Unlike adult dermatology, pediatric dermatology requires expertise in pediatric or developmental biology and an understanding of the unique skin physiology of young individuals. Due to their increased body skin surface area to mass ratio, newborns and infants are more prone to dermatoses. Effective management of pediatric dermatological conditions is essential to prevent lifelong morbidity and improve quality of life. Early intervention also offers psychosocial benefits by reducing the negative impact of visible skin diseases and emotional distress.

Training and Education

Becoming a pediatric dermatologist requires extensive training, including a dermatology residency followed by specialized fellowship training. Throughout my residency, handling the nervousness of juvenile patients and their families and devising treatment strategies for specific pediatric needs has been challenging. Pediatric dermatologists must communicate effectively with both patients and parents, especially when explaining serious prognoses, and work empathetically with other pediatric specialists.

Clinical Experiences

During my residency, I encounter approximately 5-10 pediatric dermatology cases daily in the outpatient department. These cases range from common conditions like atopic dermatitis and tinea capitis to rare genetic disorders such as epidermolysis bullosa and ichthyosis. Treating severe atopic dermatitis in young children involves medical intervention and educating families on skincare routines and environmental modifications. Success stories, such as significant improvements in a child's quality of life after effective treatment, underscore the importance of specialized care in pediatric dermatology.

One profound experience during my residency involved counseling a family whose child was diagnosed with epidermolysis bullosa, a rare and debilitating genetic skin disorder. This condition, characterized by fragile skin that blisters and tears easily, poses significant challenges in medical management and psychological support. Counseling sessions included detailed explanations of the disease process, management strategies to prevent skin trauma, and guidance on wound care. Addressing the emotional toll of the condition and providing support resources to the family was equally important.

Witnessing the resilience of the child and the family's commitment to providing the best care was both humbling and inspiring, reinforcing my dedication to pediatric dermatology.

Prenatal Diagnosis and Genetic Counseling

Prenatal diagnosis and genetic counseling are vital components of pediatric dermatology, especially for families affected by genetic skin disorders. Advanced prenatal tests, such as chorionic villus sampling (CVS) and amniocentesis, can identify conditions like epidermolysis bullosa and ichthyosis before birth, allowing early planning and management. Techniques such as non-invasive prenatal testing (NIPT) and preimplantation genetic diagnosis (PGD) further enhance the detection of genetic anomalies. Genetic counseling provides essential information about the nature, inheritance patterns, and potential impacts of these conditions, helping families understand risks and make informed decisions. This process supports emotional well-being and offers guidance on reproductive options, including in vitro fertilization (IVF). Integrating prenatal diagnosis and genetic counseling into pediatric dermatology practices enhances early intervention strategies, improves patient outcomes, and supports families managing complex genetic skin disorders.

Present Stature of Pediatric Dermatology in India

In India, pediatric dermatology is gradually gaining recognition as an essential subspecialty. While specialized training programs and dedicated pediatric dermatology units are emerging, there is still a need for greater awareness and resources. The prevalence of pediatric dermatological conditions in India, such as infectious diseases, genetic disorders, and nutritional deficiencies, necessitates a robust pediatric dermatology infrastructure. However, access to specialized care is often limited to urban centers, highlighting the need for broader dissemination of expertise and resources.

Comparative Analysis: India vs. Western Countries

Pediatric dermatology practices differ significantly between India and Western countries. In the West, pediatric dermatology is well-established with extensive research, advanced technology, and comprehensive training programs. In contrast, Indian pediatric dermatologists face challenges related to limited resources, socioeconomic disparities, and cultural factors influencing healthcare delivery. Despite these challenges, there is tremendous potential for growth and development in pediatric dermatology in India, driven by a dedicated workforce and increasing awareness of the importance of specialized care for children.

Research and Advancements

Recent advances in pediatric dermatology, such as the development of biologic therapies for severe atopic dermatitis and genetic research on rare skin disorders, have revolutionized the field. Ongoing research is crucial for improving patient outcomes and developing new treatment modalities. In India, there is growing interest in research focused on pediatric dermatological conditions prevalent in the region, such as infectious diseases and genetic disorders. Collaborations between Indian and international researchers can further enhance the field, leading to innovative solutions and improved care for pediatric patients.

Future of Pediatric Dermatology in India

The future of pediatric dermatology in India holds immense promise. With increasing awareness and recognition, there is potential for substantial growth in specialized training programs, research initiatives, and healthcare infrastructure. Opportunities for innovation, such as teledermatology and community outreach programs, can bridge the gap in access to care, especially in rural areas. As a dermatology resident, I aspire to contribute to the advancement of pediatric dermatology in India, focusing on research, education, and community engagement to ensure comprehensive care for young patients.

Interdisciplinary Collaboration

Effective pediatric dermatology care often involves collaboration with pediatricians, allergists, geneticists, and other specialists. A multidisciplinary approach is essential for addressing complex cases and ensuring holistic care. For instance, managing a child with a genetic skin disorder may require input from geneticists for diagnosis and counseling, pediatricians for overall health management, and dermatologists for skin-specific treatment. Collaborative efforts enhance patient outcomes and provide comprehensive support to families.

Patient and Family-Centered Care

In pediatric dermatology, building trust and rapport with patients and their families is paramount. Effective communication, empathy, and understanding the emotional and psychological impact of skin conditions are essential components of patient care. Strategies for managing anxiety and fear in young patients, such as using age-appropriate explanations and involving parents in the treatment process, can significantly improve the patient experience. Patient and family-centered care fosters a supportive environment, promoting better adherence to treatment plans and overall satisfaction.

Challenges and Opportunities

Pediatric dermatology practice presents several challenges, including limited resources, high patient load, and the need for continuous education and training. However, these challenges also present opportunities for growth and innovation. Enhancing awareness, increasing access to specialized care, and promoting research and education can address these challenges and pave the way for a brighter future for pediatric dermatology in India. As a dermatology resident, I am committed to overcoming these challenges and contributing to the field's development through dedicated clinical practice, research, and advocacy.

Conclusion

Reflecting on my journey as a dermatology resident, I recognize the profound impact pediatric dermatology has on the lives of young patients and their families. The subspecialty offers unique challenges and rewards, requiring a dedicated and compassionate approach. The future of pediatric dermatology in India holds great promise, with opportunities for growth and advancement through research, education, and community engagement. As I continue my career, I am dedicated to contributing to this field, ensuring comprehensive and compassionate care for all pediatric patients.

Drug dosing in children: Tips and tricks

Retinoids

Author: Shibhani Hegde

Retinoid group of drugs are analogues of vitamin A. It is available in both topical and systemic formulations. As they are not immunosuppressive medications, their safety profile is high. Adequate safety of retinoid in adults has been established but concerns persist about systemic retinoid use in children. Their effects on keratinocyte differentiation and immunity has made them a compelling therapeutic option in disorders of keratinization and papulosquamous disorders in children. With currently no treatment options available for severe forms of inherited ichthyoses and keratoderma, use of systemic retinoids has truly been revolutionary.[1,2] Various generations, retinoids, formulations and uses are mentioned in table below.[2-4]

Table: Various retinoids and their features

Generation	Chemical Structure	Compounds	Topical/systemic	Available dosages	Used In
1st Generation	Nonaromatics	Tretinoin	Topical	Micronized: less tretinoin degradation 0.04% gel 0.1% gel Other forms: 0.05%, 0.025% cream	Acne vulgaris Warts Acanthosis nigricans
		Isotretinoin	Systemic	Soft gelatin capsule: 5mg, 10mg, 20mg, 30mg, 40mg	Acne vulgaris, other forms acne Rosacea Psoriasis
2nd Generation	Monoaromatic	Acitretin	Systemic	Hard gelatin capsule: 10mg, 25 mg	Plaque psoriasis, generalized pustular psoriasis, palmoplantar pustular psoriasis, palmoplantar pustulosis Pityriasis rubra pilaris (PRP) Inherited ichthyosis and palmoplantar keratoderma Darier disease Lichen planus Recalcitrant warts
		Etretinate	--	Phased out in 1988 due to long term teratogenicity	--
3rd Generation	Polyaromatic	Tazarotene	Topical	0.05% gel	Acne vulgaris Plaque psoriasis, nail psoriasis, guttate psoriasis, Ectropion in lamellar ichthyosis
		Adapalene	Topical	0.1% gel	Acne vulgaris Acanthosis nigricans
4th Generation	Pyranones	Trifarotene	Topical	0.005% cream	Acne vulgaris ≥9 years Lamellar ichthyosis

Pediatric dosage and administration[2]

- Starting dose of 0.25-0.5mg/kg/day and subsequent dose escalation of 0.5-1mg/kg/day is usually advised. However, minimum effective dose is adequate.
- For dosages requiring <10mg, freezing the capsule, cutting it as per requirement and dispensing the same in milk/infant formula is suggested. Residual capsule must however be disposed off due to light sensitivity.
- Alternatively, certain pharmacists can formulate capsules into syrups in black-out jars but shelf lives of such formulations are not adequately tested.

Adverse effects and monitoring[2,5,6]

- All clinical and laboratory adverse effects are reversible dose dependent (except for teratogenicity).
- Mucocutaneous adverse effects like lip xerosis, cheilitis, retinoid dermatitis, ocular and nasal mucosal involvement can be seen.
- Transient elevation of liver enzymes and hyperlipidemia warrants their baseline evaluation. Repeat testing in 2-4 weeks for the first 2 months followed by every 3 months thereafter ensures timely detection of these side effects.
- Escalation of transaminase levels to 3 times the upper limit warrants discontinuation of systemic retinoids.
- Laboratory adverse effects were uncommon after 2 years of uneventful treatment.
- Although 1-year absolute risk of suicides, self-harm and suicidal ideation among isotretinoin users is <0.5% each, continued vigilance is necessary as 1-year absolute risk depression is 3.83%.
- Although not routine, systemic retinoids can cause hypoglycemia in diabetic children so adequate monitoring is necessary.

Retinoids and skeletal safety[1,5]

- Concern about the use of acitretin in children has arisen from occasional reports of premature epiphyseal closure, skeletal hyperostosis and extra-osseous calcification in children on long-term treatment with etretinate.
- Two long-term retrospective studies involving repeated radiological surveys detected no evidence between hyperostosis and prolonged retinoid therapy. Another prospective study of 51 patients treated with acitretin for over 2 years revealed bone exostoses in only two patients.
- Skeletal adverse effects are a major concern in paediatric population especially in disorders of keratinization where long duration of treatment is necessary. Long term safety of acitretin has been documented in various studies.
- Baseline vitamin D in such patients ensures avoidance of erroneously associating skeletal effects to retinoid drugs.
- Present recommendations advocate no routine skeletal monitoring. Routine growth charting and diet monitoring growth charting is adequate and skeletal monitoring is only required if patient develops atypical musculoskeletal pain.

Systemic retinoids in disorders of keratinization[1,2,7-9]

- Acitretin is highly effective in inherited disorders of keratinization, albeit indefinite therapy might be required especially in lamellar ichthyosis and lifesaving in Harlequin ichthyosis.
- Retinoids have been effective in autosomal recessive congenital ichthyosis (ARCI) and other ichthyosis like erythrokeratoderma variabilis (EKV), keratitis ichthyosis deafness (KID) syndrome, Sjogren-Larsson syndrome and palmoplantar keratoderma (PPK) especially Papillon-Lefevre syndrome, Mowinckel syndrome, and punctate PPK.
- In bullous congenital ichthyosiform erythroderma, it can aggravate skin fragility so careful lowest effective dosage to be administered.
- Topical and systemic retinoid are not tolerated in Netherton syndrome and SAM syndrome (severe dermatitis, multiple allergies and metabolic wasting)

- Systemic retinoids are less tolerated in congenital ichthyosiform erythroderma when compared to other ARCI.
- Systemic retinoids are effective in EKV and Darier disease.
- Severe forms of PRP and Darier disease also respond to systemic retinoids. Dosage varies from 0.5-1mg/kg/day in PRP to 0.2mg/kg/day in Darier disease.

Tips and tricks

- Topical retinoids are usually sandwiched with moisturizers and concomitant use of petrolatum jelly over lips ensures avoidance of cheilitis.
- Absorption of systemic retinoid is improved when taken with fatty food.
- Minimum effective dose to be maintained especially in conditions here long-term use of retinoids are required. Retinoid holidays can also be observed.
- In harlequin ichthyosis, they serve as life-saving adjunct to supportive therapy initiated at birth.
- Acitretin and adolescence: re-esterification of acitretin can take place when consumed with alcohol hence it must be carefully administered in adolescents. Females in late adolescence and possible sexual activity must also be warned regarding possible teratogenicity. Isotretinoin has been preferred over acitretin during reproductive age group.
- For their protective role in development of skin cancers, systemic retinoids are given in patients of xeroderma pigmentosum and nevoid basal cell carcinoma syndrome.
- Careful dispensing of vitamin A to be done in children to avoid side effects of overdosing.

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