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Itching dermatosis with chronicity in children: modern methods of treatment and effective relief of subjective complaints

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The article illustrates present-day data on features of the etiology and pathogenesis of pruritic dermatoses with chronicity in children. The classification of the various forms of itching and pathophysiological mechanism of its development, underlying chronic skin diseases, is presented. The results of clinical research on the effectiveness and safety of methylprednisolone aceponate in the treatment of itching dermatoses in children are described.

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Definition

An itching — is localized, unpleasant sensation, causing stress and a strong desire to scratch, which it is impossible to adapt to [1].

Pathogenesis

Itching is the most common symptom, described in dermatology. Various triggers are known to provoke itching, such as stress, hidrosis, dryness of the skin, physical exercise, nutrition. All of these can activate sensory nerve fibers, which are involved in the formation of itching [2]. The endings of these fibers are located at the connection of epidermis and dermis. Receptor stimulation is accompanied by the release of inflammatory mediators (histamine, kinins, interleukins, protease, neuropeptides, prostaglandins, cysteine, gastrin-releasing peptide etc.), as a result, the pulse is supplied dorsal root ganglia, reaching spinal cord and brain [3]. A more detailed examination of non-myelinated nerve fibers showed that the afferent C-fibers with particularly thin axons have a very low rate of impulses conduction and extensive ultimate ramifications. In the pathways of the spinal cord and in

the central nervous system there may be mechanisms that can both alleviate the itching sensations and strengthen them (temperature, pain). For example, an alternative to scratching an itch and pain induction in the usual way to ease the itching.
If untreated, the itching may chronizate the course of the skin disease. Excoriated lesions on the surface of the skin lead to the aggravation of the dermal barrier disorders and create the preconditions for infectious complications.

Classification

There are many published classifications of itching, based on etiology and clinical morphology of chronic itching [1]. The International Forum for the Study of Itch (IFSI) suggests a classification that separates patients with chronic itch into 3 groups based on clinical and distinguishing diagnostic features [4].
The first group (Group I — itching in the primary inflamed skin) includes patients with primary dermatological diseases; the second group (Group II — itching in the primary not inflamed skin) — systemic diseases and certain dermatoses — asteatotic eczema in elderly people, polymorphic photodermatosis, the third group (Group III —itching with secondary leasons after scratching) — patients suffering from chronic simple lichen, lichen amyloidosis, nodular prurigo, patients with somatic diseases (diseases of the kidneys and liver), with itching during pregnancy or medication or related neuropathological and psychiatric disorders [3, 4].
Through careful study of the pathophysiological mechanism of itching development, which is the base of chronic diseases of the skin, the need for modern and individualized approach to the treatment of chronic itching in pediatric patients should be emphasized. "Eppendorf itch questionnaire" is proposed as a tool of assessment the intensity of itching, it should collect the information about the subjective sensation of itch by patients [5]. There have also been developed a diary for itching assessment, itching index, severity scale for itching and 5D-scale for itching assessment.
The most common itching dermatoses in childhood, occurring in practice dermatologist, are atopic dermatitis, chronic urticaria and psoriasis. In 2009 E. Weisshaar and F. Dalgard presented data on itching in 87% of patients with psoriasis, in case of atopic dermatitis and chronic urticaria, this figure was 100% [6].

Atopic dermatitis

According to various sources, the proportion of children with atopic dermatitis (AD) is 8-20% [7]. Most often, the disease onset occurs in infancy: in 45% of cases it occurs in the first 6 months, in 60% — in the first year of life, in 85-95% — in the age of 5 [8].
Clinical picture of AD varies with age. For example, in infancy, rashes appear in form of papules and vesicles are prone to oozing lesion, and are accompanied by intense itching. During 2 years before the onset of puberty, the skin pathological process is less exudative, lichenification is being formed locally, the most "favorite" localizations are the folds of the elbow, wrist, knee and ankle joints, xerosis phenomenon is progressing [9]. An important medical and social aspect of itching is its ability to lead to sleep disturbances, concentration of attention of children at school [10]. Itching and xerosis — are one of the key criteria for AD.
Constant itching and leads to a number of secondary issues that affect the emotional state of the child and his parents. The children have problems in behavior, characterized by impaired attention, learning, self-confidence and self-esteem can be effected adversely [11]. Parents impose additional obligations, they have to spend a huge amount of time on the child care, which, in turn, negatively affects the social and emotional well-being of the family as a whole. Works, which have been carried out, have proved the necessity of psychological

support for parents of children suffering from AD in greater amount than for families with a child with diabetes [12-14].
A huge amount of negative emotions associated with intractable itching, induces the intensity and frequency of an even greater extent.
In acute AD, lasting longer than 6 weeks, the itching becomes chronic [1].
For a long time, antihistamine drugs has been used as an antipruritic remedy. This treatment is prescribed in case of sleep disorders, which come as a result of non-durable itching and is recommended as a routine method of itching treatment. The main disadvantage of this group of drugs are associated side effects: sedation, dry mouth, vision disorders, tachycardia and others [15].
The is not enough evidence at the moment, supporting the effectiveness of antihistamine drugs in relieving pruritus in children with AD [16]. This fact is explained by the existence of other mechanisms, forming itchy at AD, such as mast cell degranulation during intradermal injection of R substance, related to neuropeptides; acetylcholine overactivity in the skin of patients with AD. In addition, tryptase, cathepsin S, interleukin 8, leukotrienes and some others are itching indicators [17].

Chronic urticaria

Chronic urticaria is the only known "histamine" itchy disease. Chronic urticaria is a common and a severe itching dermatosis, seriously violating many facets of everyday life. It commonly has the day or almost day formation of recurrent and strongly itching blisters with concomitant angioedema or without it for more than 6 weeks [18-20].
Although the causes of chronic urticaria are rather vague and require deeper further research of triggers and pathophysiology, there are potential risk factors of itching dermatosis: viral and bacterial infections, food allergies, etc. [3].

Psoriasis

In psoriasis, itching is normally localized and causes inconvenience only in places of psoriatic plaques, most often it is observed in the evening. Subjectively it feels as something tickling, burning or like a "goose bumps". Itching in psoriasis becomes the main complaint at a very high index of PASI. In such patients generalized itching is observed, which is not only psoriatic plaques, hence it is characterized by being torpent to therapy. The study of nerve fibers and the distribution of neuropeptides provides evidence in favour of neuropathic origin of pruritus in these patients. Antihistamine drugs, as means of itching relief in psoriasis, are ineffective [21, 22]. In this regard, the differential diagnosis of pruritus in children needs to be made for excluding somato-, neuro- and psychogenic diseases, where itching characteristics may be similar to those of chronic dermatoses. Itching at AD is clinically similar to rarer itching in hematological diseases and obsessive-compulsive disorders. In psoriasis vulgaris, especially in case of extensive lesions of the skin, itching is similar to itching during schizophrenia. Liver itching and itching during depression are similar to the one that bothers the patients suffering from chronic urticaria [3].

Treatment

Currently, one of the modern methods for the relief of itching is the use of topical glucocorticoids. Actual problems, associated with the introduction of external glucocorticoid drugs during the treatment of pruritus in children and infants, were linked to a vast area of skin lesions, which led to an increased absorption of any active ingredient. External therapy with hydrocortisone resulted in a significant increase in the cortisol content in serum in

children, especially, in children under 18 months of age [23]. With the advent of generation IV glucocorticoid drugs, it became possible to stop the itching safely and effectively, without observing any side effects. One of these drugs is methylprednisolone aceponate (MPA), which, unlike many others, combines the qualities of a strong anti-inflammatory action, relative safety and is approved for use since four months of age.

The principal difference between MPA during its development was the introduction of methyl group C_6 for a higher activity of the drug and the absence of fluorine or chlorine, which, if used, may lead to a strong dissociation between the expected therapeutic effect and systemic side effects. Due to esters groups C_{17} and C_{21}, MPA is a high lipophilic drug, which easily penetrates into the stratum corneum where enzymatically active metabolite is released — methylprednisolone propionate. This substance has a higher binding affinity with glucocorticoid receptors (6,1 times higher) than hydrocortisone. Due to a higher level of enzyme activity (esterases), acceleration of bioactivation of MPA is indicated in the damaged skin [24]. After functional binding and subsequent detachment from the receptor of corticosteroid methylprednisolone, propionate is rapidly inactivated by glucuronic acid. Then, the resulting inactive metabolite is excreted with the urine, which also contributes to low serum concentrations of MPA.

Alleviation of itching with topical glucocorticoids occurs due to an increase in the intensity of binding of histamine and serotonin in the skin and a decrease in the sensitivity of nerve endings to neuropeptides and histamine, and due to regression of inflammatory process of the skin. The drug activity leads to the break of the vicious circle "itching-scratching-subsequent irritation and severe-itching", thereby improving the skin pathological process. While studying the mechanisms of effective relief of itching with MPA its ability to inhibit one of the powerful pruritogen mediators, enzyme phospholipase A_2, was established, which leads to suppression of liberation of arachidonic acid and to inhibition lipoxygenase pathway of prostaglandin synthesis [25].

Methylprednisolone aceponate — non-halogenated glucocorticoid of IV generation — was comprehensively assessed in the application in children with mild, moderate and severe AD both in acute and stationary phases. MPA therapy caused a rapid and effective regression of symptoms of AD in children and newborn (within 2-3 days) with a low frequency of local and systemic side effects.

The optimization of MPA application results from the variety of forms of the drug: oily ointment, ointment, cream and emulsion. The choice of the drug form depends on skin lesions and localization of the lesions.

Several researches proved higher efficiency of MPA, than of tacrolimus ointment 0.03%, which is characterized in the improvement of sleep due to more effective alleviation of itching. MPA is applied 1 time a day, unlike tacrolimus [3, 26].

After the relief of AD exacerbation, it is recommended to apply MPA 2 times a week, combined with daily use of emollients [26].

Conclusion

The chosen topical remedy should provide fast and safe reduction of itching, which is one of the main priorities of therapeutic tactics in complex treatment of pruritic dermatoses in children.

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