A.V. KUDRYAVTSEVA, O.A. MOROZOVA
First Moscow State Medical University n.a. I.M. Sechenov

The colonization by staphylococcus of skin children with atopic dermatitis as a criterion of the effectiveness of external treatment

The article presents data for the study of colonization by staphylococci affected skin of children with the various manifestations of atopic dermatitis in the period of exacerbation, after the external treatments CSG and on the background of the use of cosmetic product Losterin®. It is shown that the period of exacerbation of the disease is accompanied by the colonization of the skin of the S. aureus, the subacute period and a decrease in the frequency of infection of the skin on the background of the treatment of external CSG-medications. It was noted that the application of the in the period of remission of atopic dermatitis cosmetic cream Losterin® allows to combat dryness of skin, to prevent the occurrence of acute illness and re-colonization of the skin Golden Staphylococcus.

Keywords: *atopic dermatitis*, *treatment*, *losterin*

Atopic dermatitis (AtD) is a chronic allergic skin disease, the beginning of which usually takes place in an early childhood period. The disease growth, formation of chronic, constantly reoccurring forms of atopic dermatitis, makes specialists to look for the reasons behind severe acute disease. AtD is a multifactorial disease, the beginning, character and severity of which depend on interaction of predisposing factors and external environmental triggers. Pathogenic base of the disease is a skin barrier defect. Allergens penetrating into skin provoke sensibilization process, development of allergic inflammation involving such immune cells as dendritic, T- lymphocytes, keratinocytes, labrocytes and eosinophils [1, 2]. At present, there has been revealed the reasons for skin barrier damage, which play an important role in AtD pathogenesis. Together with increased skin dryness due to trans-epidermal loss of water and hyperhidrosis, there is a high sensitivity of skin receptors to metacholine and the absence of natural protective lipid film, preventing a direct contact of environmental antigens with a horny layer.

At present it has been defined that a key role belongs to a key protein – filaggrin, which takes part in epidermis cells differentiation with skin barrier formation. [3]. Combining keratin and stimulating keratinocyte apoptosis in horny zone, filaggrin prevents trans-epidermal fluid loss [4, 5]. Identifying gen mutation coding filaggrin (FLG) essentially allowed to decode one of genetic markers of predisposition to AtD development [6].

The number of external factors, capable to encourage AtD is vast [7]. Together with a food allergy, irritants, aero-allergens and stress, the important part in supporting allergic inflammation is played by infection agents: bacteria, viruses, funguses. Not only it deepens the inflammation process, but also promotes organism sensibilization. According to data of different authors, more than 25 – 35% of patients have AtD process complicated by staphyloderma and strepto-staphyloderma, they are often diagnosed with virus dermhelminthiasis (up to 25%), candidiasis of mucous coats and skin folds (7-15%) [8, 9, 10].

There is a large number of scientific works dedicated to the study of skin staphylococcus in our country, as well as abroad. It is proven, that more than 80% of cases patients' affected skin are colonialized by Staphylococcus aureus (SA), in stains of which there were found enterotoxic producing properties, more expressed among the patients with severe AtD process [11].

AtD treatment is directed towards skin allergic inflammation resolution. Modern strategy of external application includes the usage of steroid and non-steroid topic anti-inflammatory medications during AtD exacerbation and the usage of cosmetic products, allowing to maintain skin care, smoothening, moisturizing it and affecting different biochemical, physical, chemical and morphological skin processes.

Usage of cosmetic products for AtD is pathogenically reasonable. Combat with skin dryness, reduction of trans-epidermis water loss leads to restoration of its barrier function and its ability to resist Staphylococcus aureus infection.

One of the goals in AtD treatment is a remission support for a disease with a chronic, continuous relapsing course. On the bases thereof it is possible to assume that prevention of secondary skin colonization with Staphylococcus aureus and regeneration of skin wholeness may be effective marker for the conducted therapy.

Losterin cream is a non-hormonal cosmetic product, designed for daily skin care. It is recommended for people with different forms of dermatitis/dermatosis with excessive skin dryness, such as: psoriasis, eczema, atopic dermatitis, simple contact dermatitis, seborrhea, seborrhea dermatitis, ichthyosis, xerosis.

"Losterin" cream possess significant anti-inflammatory, antipruritic, exfoliating and anti-microbial action, promotes skin regeneration, increases skin barrier, prevent the feeling of dryness and irritation. "Losterin" cream may be used as a monothepary, as well as in a combination with external hormonal medications (it decreases the need in using topic steroids, helps to reduce exacerbation and promotes the remission duration). Losterin has a high safety level, does not have any counter

prescriptions, does not cause addiction and abstinence symptoms. It contains resin free naphtalan (3%), urea (10%), D-panthenol, salicylic acid, Japanese pagoda tree extract and almond oil.

Naphtalan oil has been used for a long time for skin disease treatment. Its healing properties are defined by the naphthenic hydrocarbon (cyclopentaneperhydrophenantrene product – CPP), which stimulate a natural steroid hormone biosynthesis, reduce synthesis and inactivate inflammation mediators action, increase skin sensitivity level, stimulate local microcirculation processes, improve gemolymphatic drainage, activate metabolism, promote tissue homeostasis regeneration.

Resin free naphtalan possesses significant anti-inflammatory, anesthetic, densensitise and antibacterial action, promotes skin trophic functions.

Urea is a classic hydrant, which helps epidermis cells to absorb aqueous vapor from the air, absorbs the moist, possesses the ability to penetrate inside the skin depth, serves as conductor for other active ingredients contained in medication. The concentration of 10% dissolves epidermis keratin, provides removal of horny masses from effected areas, slows down repeated excessive growth of horny cells.

Salicylic acid stimulates production of adrenocorticotropic hormone (ACTH) and 17 oxycorticosteroids, restrains the action of hyaluronidase (ferment causing decay of hyaluronic acid), reduces penetrance of tissue barriers, possesses significant anti-inflammatory action.

D-panthenol (provitamin B5) promotes skin regeneration, erosion and cracks healing. Japanese pagoda tree extract contains flavonoids, including rutin, which strengthens blood vessels, improves blood microcirculation locally.

The study goal was to investigate particularities of strain colonization of effected skin by Staphylococcus aureus among children with different atopic dermatitis during disease exacerbation prior and after external treatment with glucocorticosteroids (GCS) and basic application of Losterin cosmetic cream.

Materials and methods

Effectiveness of anti-relapsing external treatment with Losterin cream was evelauated among 26 patients with AtD. AtD was diagnosed according to criteria, offered by J. Hanifin and G. Rajka (1980) [12]. The following criteria were used to evaluate AtD severity level: exacerbation and remission duration, lesion area [13]. Prevalence rate, pathological process localization, exudation, itching and lymph gland local reaction were taken into consideration for all patients. Severity of affected skin was performed on base of semi-quantitative SCORAD scale (Scoring of Atopic Dermatitis).

Average age of patients equaled to 4,3 ± 0,7 years (from 3 months to 13,5 years). Average AtD duration coincide with an average patients' age and due to the early beginning of disease equaled to 3,9 ± 0,6 years. Breakdown of patients (depending on disease severity) was as follows: 8 (30,8% of patients with mild disease, 11 (42,3%) – with moderate disease, 7 (26,9%) – with severe disease. 16 children out of this group were examined during exacerbation and remission of disease, 10 – during remission. During the study of patients' breakdown character depending on the disease form, it was noted that 7 (26,9%) patients were diagnosed with erythematosquamous form, 4 (15,4%) – with lichenous and 1 (3,8%) – with exudative disease form [13]. Average SCORAD index during AtD exacerbation was equal to 64,4 ± 6,5, during remission – 26,4 ± 2,5.

External treatment during exacerbation was performed with GCS medications of medium biological activity [14]. After 2 weeks of treatment, Losterin cream was prescribed to use 3 times a day within 2 weeks. In order to identify Staphylococcus aureus, a smear of affected skin was taken prior to GSC therapy, 2 weeks after beginning of treatment course and 2 weeks after the beginning of Losterin application.

Microbiological study was performed according to common method: culture of skin discharge was performed to identify a number of standard culture agar medium, allowing to maximize identification of Staphylococcus strain. St. aureus skin seeding level was evaluated by semi-quantitative method known as "swab/loop (number of colony-forming units per swab – NCFU/swab).

Specific identification of Staphylococcus strains was performed with help of automatic microbiological analyzer WalkAway-96SI (Siemens Healthcare Diagnostics) and by common methods, with a use of Bergey's manual.

Sensitivity to antibacterial medications was defined by disk-diffusion method (DDM) with a usage of Becton Dickinson discs(BD) and WalkAway-96SI analyser.

Received data was processed with statistic analysis Biostat program under Windows XP and standard Excep application for Miscosoft Office 2005. Pearson method was used (with Yeats corrections), correlation analysis (Pearson's coefficient was evaluated), differentiation significance point was considered accurate at $p<0,05$.

Study results

Performed study had shown, that AtD exacerbation was accompanied by skin colonization by staphylococcus in 75% of cases (table 1), coagulase-negative staphylococcus strains (CNS) in 18,2 cases. During study of SA and SNS discharge resistance to antibiotics, it was noted, that in majority of cases bacteria were resistant to penicillin group and demonstrated 100% sensitivity to vancomycin and gentamicin. Staphylococcus epidermidis was more resistant to chloramphenicol, than SA, and SA was more resistant to tetracycline ($\chi 2 = 1,6$, which is less than $\chi 2\ (0,05,\ 1) = 3,84$).

It was noted, that after a treatment with external GCS medications after achieved clinical remission, frequency of identified skin colonization by staphylococcus aureus reduced to 30,8%. During Losterin cream application, together with skin condition normalization, it was also noted a greater reduction of skin infection by staphylococcus areus 11,5% ($\chi 2 = 4,2$, which is less than $\chi 2\ (0,05,\ 2) = 5,99$).

SCORAD index dynamics had a tendency to reduction from 64,4 ± 6,5 during AtD exacerbation to 46,2 ± 5,4 in a period of incomplete remission after conducted treatment by GCS medications index had a minimal figure during disease remission – 26,4 ± 2,5 ($p < 0,05$) after 2 weeks of Losterin cream usage.

After external treatment with GCS there was noted a positive dynamics such as itching and erythema intensity reduction (table 3), with a further application of Losterin cream, reduction of skin dryness and almost complete itching jugulation was noted ($p < 0,001$).

No side effects or irritating reactions were noted during Lorestin cream application. Most patients during anti-relapsing did not note recrudescence. Only 3 patients with severe AtD noted disease exacerbation during cream application on 10 ± 1,4 days, which was accompanied not only by worsening of skin conditions and itching increase, but also repeated skin colonization by staphylococcus aureus.

Thus, conducted study proved, that Losterin cream possesses a significant preventive effect, and is well tolerated. With Losterin cream use, it is possible not only to reduce the probability of exacerbation, but to also prevent skin infection by staphylococcus aureus. Cream daily use during AtD remission period allows to control disease flow and improve life quality for children and their parents.

Patients with severe Atd should also use intermittent courses of GCS medications as preventive exacerbation therapy. Correct usage of medical cosmetic products for skin care of children with Atd allows to protect it from negative external factors, and significantly increase remission period and optimize disease treatment.

Table 1

Staphylococcus aureus skin discharge among children with Atd during external treatment

	Prior to GCS treatment (during AtD exacerbation) n = 16	After GCS treatment n = 26	During Losterin cream Treatment n = 26
Staphylococcus aureus	n = 12 (75%)	n = 8 (30,8%)	n = 3 (11,5%)
Coagulase-negative staphylococcus	n = 6 (37,5%)	n = 6 (23,1%)	n = 9 (34,6%)
SA + CNA	n = 3 (18,8%)	n = 4 (15,4%)	n = 1 (3,8%)
No growth	n = 2 (12,5%)	n = 15 (57,7%)	n = 17 (65,4%)

Table 2

Sensitivity of discharged strains of staphylococcus aureus (n = 19) and coagulase-negative staphylococcus (n = 10) to antibiotics

	Staphylococcus aureus		Coagulase-negative staphylococcus	
Antibiotic	Number of discharged strains	Sensitivity (%)	Number of discharged strains	Sensitivity (%)
Benzylpenicillin	0	0	0	0
Azithromycin	18	94,7	8	80
Amoxycillin/clavulanate	17	89,5	8	80
Ampicillin	0	0	0	0
Oxacillin	17	89,5	8	80
Tetracycline	11	57,9	9	90
Cefazolin	15	89,5	8	80
Erythromycin	17	89,5	7	70
Gentamicin	19	100	9	90
Chloramphenicol	8	42,1	2	20
Vancomycin	19	100	10	100
Clindamycin	15	78,9	8	80

Table 3

Dynamics of clinical manifistations during external therapy among patients with Atd (maximum – 3 point)

	Prior to GCS treatment (during AtD exacerbation) n = 16	After GCS treatment n = 26	During Losterin cream treatment n = 26
Dryness	2,57 ± 0,4	2,32 ± 0,21[2]	1,21 ± 0,1
Erythema	2,22 ± 0,2[1]	1,76 ± 0,3[2]	1,00 ± 0,15
Crusting	1,63 ± 0,22	1,3 ± 0,14[2]	0,6 ± 0,13
Skin itching	6,39 ± 0,5[1]	4,37 ± 0,7[2]	1,25 ± 0,4

Note:

1 – difference between received data before and after external GCS treatment is accurate ($p < 0,001$);

2 – difference between received data before and after external GCS and during Losterin cream treatment is accurate ($p < 0,001$).

LITERATURE

1. Geppe N. A. An issue of atopic phenotype development / N. A. Geppe, O. A. Pakhomova, N. S. Glyushkina // Pediatric pulmonology: digest – Issue 2 – Moscow – Ivanovo, 2002. – P.96-98
2. Batchelor J.M. What's new in atopic eczema? An analysis of systematic reviews published in 2008 and 2009 / J.M. Batchelor,D.J. Grindlay, H.C. Williams // Clin. Exp. Dermatol. — 2010. — Vol. 35, № 8. — P. 823-827.
3. Brown S.J. Intragenic Copy Number Variation within Filaggrin Contributes to the Risk of Atopic Dermatitis with a Dose-Dependent Effect / S.J. Brown, K. Kroboth, A. Sandilands et al. // J. Invest. Dermatol. — 2011. — Vol. 10. — P. 2011-2022.
4. Cork M.J. New perspectives on epidermal barrier dysfunction in atopic dermatitis: Gene-environment interactions / M.J. Cork, D.A. Robinson // J. Allergy Clin. Immunol. — 2006. — Vol. 118. — P. 3-21.
5. Greene R.M. Sweeting patterns in atopic dermatitis patients / R.M. Greene, R.K. Winkermann, T.L. Opfer-Gehrking // Arch. Dermatol. Res. — 1989. — Vol. 281. — P. 373-376.
6. Meyer M.W. Filaggrin gene mutations are frequent and increase the risk of skin disease / M.W. Meyer, J.P. Thyssen // Ugeskr Laeger. — 2011. — Vol. 173, № 43. — P. 2705-2708.
7. Galli E. Atopic dermatitis: molecular mechanisms, clinical aspects and new therapeutical approaches / E. Galli, R. Cicconi, P. Rossi et al. // Curr. Mol. Med. — 2003. — Vol. 3. — P. 127-138.
8. Katosova L. K. Role of staphylococcus aureus in atopic dermatitis among children / L. K. Katosova, I. I. Balabolkin, V. G. Aseeva // Pediatrics. – 2003. - № 6. P. 32 – 36.
9. Smirnova G. I. Kaposi eczema herpeticum among children with severe atopic dermatitis / G. I. Smirnova // Challenging issues in infection pathology among children. – 2003. – P. 181 – 182
10. Gately M. Bacterial superantigens induce T cell expression of the skin-selective homing receptor, the cutaneous lymphocyte- associated antigen, via stimulation of interleukin 12 production / M. Gately, D.Y. Leung, A. Trumble et al. // J. Exp. Med. — 1995. — Vol. 181. — P. 747-753.

11. Atopic dermatitis severity rate dependency from toxin-producing strains properties of staphylococcus aureus / A. V. Kudryavtseva, F. S. Fluer, I. I. Balabolkin. Katosova L. K. and others // Russian pediatric magazine. – 2009. - № 3. – P. 31 – 37.
12. Hanifin J.M. Diagnostic features of atopic dermatitis / J.M. Hanifin, G. Rajka // Acta Derm. Venerol. — 1980. — Vol. 92. — P. 44-47.
13. Balabolkin I. I. Atopic dermatitis among children / I. I. Balabolkin, N. V. Grebenyul. – M: Medicine, 1999 – P. 240
14. Miller J.A. TCS: clinical pharmacology and therapeutic use / J.A. Miller, D.D. Munro // Drugs. — 1980. — Vol. 19. — P. 119- 134.