Skin and nasal vestibule colonisation by Staphylococcus aureus and its susceptibility to drugs in atopic dermatitis patients

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Abstract

Introduction. Atopic dermatitis (AD) is a chronic and recurrent disease with an inflammatory background. Genetic and environmental factors are responsible for the occurrence and development of this dermatosis.

Objective. The aim of the study was to assess the frequency of colonisation of the nasal vestibule and apparently healthy skin by S. aureus, and to assess dermal lesions for superinfection with S. aureus in AD patients.

Materials and method. The research was performed on a population of 100 AD patients. Three smears were collected for microbiological investigations: from the anterior nares, from apparently healthy skin and from lesioned skin. On collection, the material was cultured on mediums provided by the bioMerieux and Argenta companies. The strains were identified and their sensitivity to antibiotics assessed by means of the Vitek2 system (bioMerieux).

Results. S. aureus was present in at least one location in 90%. 44% presented S. aureus colonization of apparently healthy skin and within skin lesions. In the case of 23%, this particular pathogen was detected only in skin lesions, whereas 6% had a positive result within the area of apparently healthy skin. In total, S. aureus was detected in the skin of 73%. In 61%, apparently healthy skin had been colonized with S. aureus, whereas in 81% colonization was proved within the skin lesions. S. aureus was detected in the nasal vestibule of 85%. Among the group with S. aureus in their anterior nares, the pathogen was also found on the skin surface of 77%.

Conclusions. S. aureus colonises skin in most AD patients. Most AD patients carry S. aureus in their nasal vestibules. S. aureus does not seem to colonise healthy skin as often as skin lesions in young people. The vast majority of S. aureus strains were sensitive to local antibiotics. Most S. aureus strains produced penicillinase.

Key words

microbiota, antibiotic resistance, atopy, skin barrier, eczema, superinfection, colonisation

INTRODUCTION

Atopic dermatitis (AD) is a chronic and recurrent disease with inflammatory background [1]. Like bronchial asthma, allergic rhinitis and conjunctivitis, it belongs to the group of atopic diseases. Genetic and environmental factors are responsible for the occurrence and development of this dermatosis [2]. There are elaborate descriptions of disorders in the structure and function of the epidermal barrier [3]. The significance of microbiological factors in the pathogenesis of eczema and the resulting therapeutic implications have been under discussion for over 100 years [4]. It is widely known that inflammation in the course of AD is stimulated by the antigens of skin-colonising microorganisms. Damage to the epidermal barrier facilitates their penetration into the epidermis and dermis [5]. *Staphylococcus aureus* (*S. aureus*) has a predominant role among the pathogens responsible for exacerbation of the dermatological condition in AD patients [6, 7].

OBJECTIVE

The aim of the study was to assess the frequency of colonisation of the nasal vestibule and apparently healthy skin by *S. aureus*, and to assess dermal lesions for superinfection with *S. aureus* in AD patients.

MATERIALS AND METHOD

The research was performed on a population of 100 AD patients (48 males and 52 females) aged 2–76 years, consecutively admitted to our Department. The recruitment of patients followed the AD diagnostic criteria developed by Hanifin & Rajka [8]. Children were qualified for the research with their parents’ written consent. Three smears were collected for microbial tests: one from the nasal anterior nares, one from the skin where lesions appeared at the moment of investigation, and one from the skin which was free from eczema. Healthy skin smears were not collected from patients suffering from erythroderma.

Other patients, who had been consulted at the dermatological outpatient clinic for a follow-up examination, had no inflammatory lesions after remission of the disease.
Patients with a history of a systemic or local antibiotic therapy in the last four weeks were excluded from the study group. Only those patients who had received the last dose at least two weeks earlier were included to the study population. Patients taking immunosupression drugs or with other kind of immunosupression were also excluded. The patients suffering from upper respiratory tract infections did not have their smear collected from the nasal vestibule to prevent false research results due to the possible predominance of another aetiological factor of the infection. Smears were collected from the following three places: the anterior nares and/or apparently healthy skin and/or diseased skin to sterile swabs which had been moistened with sterile saline for better adsorption of microorganisms from the surface of the mucosa and/or skin.

On collection, the material was cultured on solid and broth mediums provided by the bioMerieux and Argenta companies. After incubation, each medium was thoroughly analysed for the presence of \textit{S. aureus}. The strains were identified and their sensitivity to antibiotics was assessed by means of the Vitek 2 system (bioMerieux).

\section*{RESULTS}

100 of evaluated AD patients had their nasal vestibules examined for the presence of \textit{S. aureus}, and their apparently healthy skin as well as skin lesions were examined. 12 patients (12\%) had only their nasal vestibules examined. 18 patients (18\%) had only their skin examined and their anterior nares were not assessed for the presence of the pathogen, 14 patients (14\%) had both their apparently healthy skin and skin lesions examined, whereas 4 patients (4\%) had only their skin lesions examined. 5 AD patients (5\%) were examined for the presence of \textit{S. aureus} and had their apparently healthy skin examined (there were no skin lesions during the examination), 2 patients (2\%) were examined for the presence of \textit{S. aureus} and had their skin eczema examined (erythroderma). Among the 100 patients, \textit{S. aureus} was present in at least one location in 90 patients (90\%). In 10 patients (10\%) it was not found at any location. 44 patients (44\%) presented \textit{S. aureus} colonization of apparently healthy skin and within skin lesions. In the case of 23 patients (23\%) this particular pathogen was detected only in skin lesions, whereas 6 patients (6\%) had a positive result within the area of apparently healthy skin. In total, \textit{S. aureus} was detected in the skin of 73 patients (73\%). In 50 out of 82 patients (61\%), apparently healthy skin had been colonized with \textit{S. aureus}, whereas in 67 out of 83 patients (81\%) colonization was proved within the skin lesions.

\textit{S. aureus} was detected in the nasal vestibule of 70 out of 82 AD patients (85\%) tested for the presence of the pathogen. Among the group of the 70 patients with \textit{S. aureus} in their anterior nares, the pathogen was also found on the skin surface of 54 patients (77\%). Results were negative in case of the skin of 6 patients (8.6\%). 10 patients did not have their skin examined for the presence of \textit{S. aureus} (14.3\%).

The methicillin-resistant \textit{Staphylococcus aureus} (MRSA) was detected in 4 patients (4\%). 3 patients (3\%) presented colonization of their anterior nares. In the case of 1 person (1\%), colonization of apparently healthy skin was also proved. The skin surface of 2 patients (2\%) was not examined in terms of \textit{S. aureus} colonization. 1 patient (1\%) presented the MRSA strain both in their apparently healthy skin and within skin lesions, whereas methicillin-sensitive \textit{Staphylococcus aureus} (MSSA) was found in this patient’s nasal vestibule. Antibiograms were made for all the \textit{S. aureus} strains cultured from the skin lesions. 90\% of the strains produced penicillinase (Fig. 1). 90\% of the strains were sensitive to tetracyclines and 100\% were sensitive to levofloxacin, vancomycin, teicoplanin, tigecycline and linezolid. The strains were also assessed for sensitivity to macrolides (sensitivity to erythromycin amounted to 87\%), clindamycin (91\%) and trimethoprim/sulfamethoxazole (98\%). As far as the external use drugs are concerned, the strains were sensitive to gentamicin (94\%), fusidic acid (99\%), fosfomycin and mupirocin (100\%) (Fig. 2).

As far as the nasal vestibule smear is concerned, \textit{S. aureus} was more often isolated in the group of children aged under 15 years (72\%). As far as the colonisation of apparently healthy skin and the superinfection of skin lesions with \textit{S. aureus} are concerned, there were higher values in the group of adults, i.e. patients aged over 15 years (54\% and 66\%, respectively). Apart from that, in the population of young people aged under 15 years the percentage of positive results of the microbial test for the presence of \textit{S. aureus} in apparently healthy skin was twice as small than the percentage of positive results showing the presence of \textit{S. aureus} in AD skin lesions. These values were similar in the group of patients aged over 15 years (Tab. 1).
Table 1. Skin and nasal colonisation by _Staphylococcus aureus_ in different age groups of patients with atopic dermatitis

<table>
<thead>
<tr>
<th>Age category (years)</th>
<th><em>S. aureus</em> colonisation in patients, n (%)</th>
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<tr>
<td></td>
<td>Nasal</td>
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<tr>
<td>&lt; 15 (n=32)</td>
<td>23 (72)</td>
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<tr>
<td>&gt; 15 (n=68)</td>
<td>44 (65)</td>
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**DISCUSSION**

The human skin is a complex ecosystem. In a surface area of about 2 m² there is a unique diversity of habitats characterised by different physicochemical conditions, i.e. moisture, pH [9]. Numerous species of bacteria, fungi, mites and viruses find favourable conditions for their existence, and simultaneously make a specific microbiome [10]. The composition of this group is an individual trait [2]. It is necessary to stress the fact that most of these microorganisms are not pathogenic, but constitute a physiological protective barrier, which is important for the maintenance of skin homeostasis [11].

Skin dryness is the leading symptom of AD and results from the damaged epidermal barrier which causes increased transepidermal water loss. The epidermal barrier dysfunction facilitates contact between environmental allergens and cells of the skin immune system. It intensifies inflammation [3]. Moreover, barrier disruption is associated with the deficit of lipids, pH alkalinisation, increased serine protease activity, and decreased production of antimicrobial peptides (AMPs) [12]. All these factors favour _S. aureus_ colonisation, which intensifies changes in the course of AD. There are age-dependent predilection areas for the occurrence of typical AD eczemas; for example, in children these are flexion areas of knee joints, elbow, wrist and ankle joints, and the cervical fold. To a certain extent, this fact could be attributed to differences in the microbiome [9].

Latest studies prove that staphylococci, especially _S. aureus_, are predominant in the skin lesions of AD patients. The microbial diversity in skin lesions is smaller than in the skin without eczema [13]. According to the present state knowledge, _S. aureus_ colonisation reaches 75 – 100% in lesional skin of AD patients, and 30 – 100% of AD patients have this bacteria in their nonlesional skin. By contrast, only 5 – 30% of healthy people are carriers of _S. aureus_ [5, 14, 15, 16, 17]. The results of this study were consistent with the above observations – _S. aureus_ was isolated from the skin lesions of 81% of AD patients.

_S. aureus_ proliferates in the nasal vestibule and the skin surface may be temporarily colonised [18, 19]. Usually, the pathogen is transferred from there to the skin, especially damaged skin, or other parts of the mucosa [19]. Colonisation with _S. aureus_ is not found in all patients. This may be because of the fact that about 60% of patients are temporarily colonised, and _S. aureus_ may be absent at the moment of examination [19, 20].

If a patient carries _S. aureus_, there is higher frequency of infections with this aetiology. By contrast, the eradication of the pathogen from the nasal vestibule may decrease the incidence of infections [18]. In the presented study, 85% of AD patients (i.e. 70 patients) carried _S. aureus_ in their nasal vestibules. 77% of the patients in this group, i.e. 54 patients, also carried the pathogen in their skin.

Bilal et al. studied a population of AD children and found that the colonisation of skin lesions was much more intense than the colonisation of apparently healthy skin – 38% vs. 15% [21]. The current observations were similar. In the group of patients aged under 15 years, _S. aureus_ was found in 62.5% of skin lesions, whereas it was found in 28% of the cases of skin without eczema. In the group of patients aged over 15 years, these values were more similar. However, it is noteworthy that the percentage of colonisation of apparently healthy skin was twice as high (54%). Bilal et al. suggest that the presence of the bacteria on apparently healthy skin may have been caused by contamination with _S. aureus_ from the anterior nares and skin lesions [21]. Hon et al. proved that the notable increase in the count of _S. aureus_ obtained from nasal vestibule smears may be related with the higher total score in the SCORAD scale (Scoring Atopic Dermatitis), more extensive lesions, oozing and the presence of scabs [6]. Thus, they confirm the widely accepted thesis that _S. aureus_ is the most significant pathogen in moderate to severe AD, and the nasal cavity may be the habitat of the pathogen [6, 17, 19]. In view of this fact, it can be supposed that carrying _S. aureus_ is usually the first stage of development of infection. _S. aureus_ is undoubtedly the most common factor of bacterial infections in AD patients [6]. Hauser et al. reported that the count of _S. aureus_ in the apparently healthy skin of AD patients was much greater than in skin of healthy people [22]. In the presented study, the presence of _S. aureus_ in the apparently healthy skin was found in 61% of the cases. Abeck et al. also stressed the big contrast between the frequency of skin colonisation by _S. aureus_ in healthy people (2–25%) and the occurrence of these bacteria in AD patients, where it ranged from 76% on apparently healthy skin to as much as 100% in oozing lesions. Apart from that, they observed that colonisation of the nasal anterior nares was much more common (71%) than colonisation of the armpits (45%). At the same time, the study showed the significance of the nasal vestibule as the preferable habitat of _S. aureus_. In view of this fact, the researchers suggest taking anti-staphylococcal treatment into consideration. They studied the role of proteins responsible for adhesion to keratinocytes and proved that there was a wide range of proteins, such as staphylococcal protein A, coagulase, the aggregation factor and fibronectin-binding protein. The inflammation development mechanism was another aspect under discussion. Staphylococcal proteins and toxins are listed here, especially those which are superantigens [4]. The study by Goh et al. resulted in the following findings: _S. aureus_ was isolated in 69.7% of eczematous lesions and 42% of cases of apparently healthy skin in AD patients. Only in 5% of the cases _S. aureus_ was found in the control population of healthy subjects. The incidence of nasal colonisation in AD patients was higher than in healthy subjects, i.e. 51.5% vs 35.0%. The researchers think that in view of these findings, the decision to apply an antibiotic therapy in cases of severe AD enables control of the course of the disease and inflammation. Systemic rather than local antibiotic therapy is recommended due to the risk of allergic contact dermatitis [23]. Jung et al. noted that most _S. aureus_ strains were sensitive to a wide range of antibiotics. They proved that _S. aureus_ was usually resistant to benzylpenicillin, erythromycin, clindamycin, and fusidic acid. All _S. aureus_ strains isolated from acute lesions were sensitive to treatment with vancomycin, tigecycline, teicoplanin, linezolid and trimethoprim/sulfamethoxazole [24]. In the presented study, antibigrams revealed the lowest percentage of sensitive...
strains after the following antibiotics: erythromycin (87%), tetracycline (90%), β-lactam antibiotics (90%), clindamycin (91%), and trimethoprim/sulfamethoxazole (98%). As far as local antibiotics are concerned, antibiograms revealed the lowest percentage of sensitive strains to gentamicin (94%) and fusidic acid (99%). Jung et al. compared resistance to drugs in individual age groups and noted that there was a higher percentage of methicillin-resistant strains among infants, regardless of the fact whether pathogens were isolated from acute or chronic lesions. In the group of adults, the strains were characterised by lesser sensitivity to fusidic acid, regardless of the clinical state. As far as mupirocin is concerned, the sensitivity of *S. aureus* was higher in the group of infants and children with acute lesions [24].

Researchers stress the fact that in recent years there has been increasing resistance to local antibiotics, which is undoubtedly the consequence of their abuse [25]. In the presented population of patients, the cases of carrying or being infected with the MRSA strain were predominantly found in young people (3 patients aged 16–29 years, and only one patient aged 62 years). Only one patient, i.e. a 4-year-old boy (1%), did not exhibit sensitivity to fusidic acid. This fact still proves very high sensitivity to the drug in comparison with the findings of the study by Jung et al. Likewise, Salah et al. proved that penicillinase-producing *S. aureus* strains were mostly isolated in AD patients. In the current study, these strains amounted to 90%. It is noteworthy that in comparison with the global data there was a low percentage of MRSA strains among a group of Swedish patients [26]. There were 100 patients in the presented group and the presence of MRSA was confirmed in 4 patients (4%). Adamek-Guzik et al. stress the fact that some patients should receive local antibiotic therapy to eradicate *S. aureus* from the skin and to improve the patient’s clinical state [15]. Sabtu et al. suggest that during local antibiotic therapy *S. aureus* carriers and AD patients with infections of staphylococcal aetiology should adhere to the dosage regimen to minimise the risk of drug resistance [25].

**CONCLUSIONS**

1. *S. aureus* colonises skin in most AD patients.
2. *S. aureus* also colonises apparently healthy skin in AD patients.
3. Most AD patients carry *S. aureus* in their nasal vestibules.
4. *S. aureus* does not seem to colonise apparently healthy skin as often as skin lesions in young people (aged under 15 years).
5. The vast majority of *S. aureus* strains were sensitive to local antibiotics, i.e. fusidic acid and mupirocin.
6. Due to the fact that most *S. aureus* strains produced penicillinase (90%) in AD patients, the application of antibiotic therapy with β-lactamase inhibitors is recommended.

**REFERENCES**