Silver-coated textiles reduce *Staphylococcus aureus*-colonization in patients with atopic eczema

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**Key words:** *Staphylococcus aureus*, silver ions, antibacterial effect, atopic eczema, skin barrier, textiles
Abstract

In atopic eczema (AE), skin colonization with *Staphylococcus aureus* is known to play a major triggering and possibly pathophysiological role.

In this open-labeled controlled side-to-side comparative trial affected sites (flexures of both elbows) in 15 patients diagnosed with generalized or localized AE were evaluated regarding *S. aureus*-colonization and clinical severity of AE over a two weeks period. Flexures of the elbows were covered with silver-coated textiles on one arm and cotton on the other for seven days followed by a seven day control period.

A highly significant decrease of *S. aureus*-colonization could be seen on the silver-coated textile site already two days after initiation lasting until the end of the treatment. Seven days after cessation, *S. aureus*-density remained significantly lower compared to baseline. In addition, significantly lower numbers of *S. aureus* were observed on the silver-coated textile site in comparison to cotton at the end of treatment as well as at timepoint of control.

Clinical improvement correlated with reduction of *S. aureus*-colonization.
Introduction

*Staphylococcus (S.) aureus* is recognized as an important triggering factor for maintenance of skin inflammation and acute exacerbations of the genetically determined skin disease atopic eczema (AE) [1,2]. The degree of colonization is associated with disease severity [3,4,5]. The knowledge of the pathophysiological role of *S. aureus* in AE has increased during the recent years. The organism produces a variety of immunmodulatory toxins with superantigenic properties like the well characterized staphylococcal enterotoxins A-E as well as the toxic shock syndrome toxin 1 [6]. In addition, *S. aureus* produces a variety of enzymes with direct cell damaging properties, several hazardous toxins (including haemolysins and exfoliative toxins) as well as elaborate defense mechanisms against the majority of currently used antimicrobial drugs [7,8,9]. Although there is controversial discussion about topical glucocorticoid and antibiotic combination, antibiotic as well as antiseptic substances of good antistaphylococcal activity have been well established and are successfully used for treatment of AE. By reduction of *S. aureus* density they are able to contribute to the antiinflammatory effect of topical corticosteroids and emollients [10,11,12,13]. Silver products have been under investigation during recent years with special regard to wound healing processes. They demonstrate two key advantages: they are broad-spectrum antibiotics and are not yet associated with drug resistance [14]. Silver-coated materials are already frequently used e.g. in surgery (external fixation), urology (catheter) or odontology [15,16,17]. Padycare®-textiles consist of micromesh material containing woven silver filaments with a silver content of 20% in total. In vitro-studies of these silver-coated textiles demonstrated a significant decrease of bacteria (*Staphylococcus aureus* and *Pseudomonas aeruginosa*) as well as *Candida albicans* [18]. The aim of our study was to investigate the influence of silver-coated textiles in patients with atopic eczema with special consideration of *S. aureus* colonization.
Materials and Methods

Patients and clinical evaluation

15 consecutive out-patients clinically diagnosed with generalized or localized AE [19] presenting eczematous lesions on the flexures of both elbows were included in the study. All fulfilled the inclusion criteria, i.e. a steroid-free interval of at least two weeks and no systemic or topical antibiotic treatment within four weeks. The study was performed during the months February and March with low temperatures simplifying compliance during day and night. Local disease severity was assessed using the local SCORAD protocol [20] comprising the following six intensity items: erythema (1); edema/papulation (2); oozing/crusts (3); excoriations (4); lichenification (5) and local pruritus (6). Each item was graded on a 4-point scale: 0 = absent, 1 = mild, 2 = moderate, 3 = severe. A total severity score was calculated as the sum of the grading resulting in a highest possible score of 18. Patients were instructed to wear especially designed elbow-covers for seven days and nights in total: the left elbow was covered with pure cotton material, the right elbow with silver-coated material (Padycare®) (Fig.1). Due to the diversity of patients, different sizes of elbow covers were used: European size 92-104-128-164 for children, size S(mall), M(edium) and L(arge) for adults. During the seven day wearing period the same elbow covers -without cleaning- were applied during night and day and removed only while taking a shower. Basic skin care with emoillents was allowed, the patients’ washing and cleaning behaviour was continued as usual. After cessation of the wearing period, a control period of seven days followed, where no elbow covers were applied. Clinical evaluation using the local SCORAD was performed at baseline (day 0), day 2 and 7 after the onset of wearing elbow covers as well as seven days thereafter (day 14) for control. The mean age of our patients was 24.6 years (range 3 to 55 years).
**Microbiological exams**

Bacterial solutions were collected from the affected sites of both arms at baseline (day 0), day 2 and 7 as well as seven days thereafter (day 14) - in accordance with clinical evaluation. A standardized scrub method developed by Williamson and Kligman [21,22] was used: a perspex-lined cylinder (contact area of 6,158 cm²) was put on the eczematous lesion followed by continuous scrubbing of the surface with 1000 µl of a standardized washing solution (0.15% Twen/PBS Dulbecos) for one minute. The solution was immediately diluted up to level 10⁻⁶ using PBS-buffer and an aliquot of 100µl was inoculated onto Columbia agar plates containing 5% sheep blood (bioMerieux, Nürtingen, Germany) at 37 °C for 24 hours. Identification of *S. aureus* was performed using the Slideex Staph-Kit test (bioMerieux). Positive cultures were further characterized using the api-Staph system (bioMerieux). Colonization of *S. aureus* was quantified by counting the numbers of colony-forming units per agar plate and subsequent calculation of colonies per square centimeter.

**Statistical analysis**

The Wilcoxon ranked pair test was applied for comparisons of the *S. aureus*-colonization (a) on silver-coated site (right elbow flexure) against cotton-site (left elbow flexure) as well as (b) on one affected site in comparison to baseline at different timepoints of evaluation. A significance level of p=0.05 was chosen. Spearman’s correlation coefficient was chosen for the overall correlation of the density of *S. aureus* and the clinical severity.
Results

*S. aureus* was isolated in all of the 15 patients from both sites with density numbers between $10^{2.2}$ and $10^{5.2}$ CFU/cm² on the right flexure site and between $10^{2.1}$ and $10^{5.1}$ CFU/cm² on the left flexure site of the elbow at initiation. During treatment period with elbow covers density numbers ranged between 0 to $10^{4.1}$ CFU/cm² on the silver-coated textile site/right flexure site and $10^{2.3}$ to $10^{5.3}$ CFU/cm² on the cotton/left flexure site. At timepoint of control (day 14), density numbers were between 0 and $10^{4.9}$ CFU/cm² and between $10^{2}$ and $10^{5.1}$ CFU/cm² respectively.

At initiation, clinical severity of right and left flexure site of the elbows was comparable: it was assessed between 6 and 15 on the right and 5 to 15 on the left flexure site. During treatment period, local severity of eczema ranged between 2 and 13 on the silver-coated textile site/right flexure site and 4 to 14 on the cotton/left flexure site. At control, severity scores were between 2 and 11 and between 4 and 12 respectively.

*Staphylococcus aureus* colonization

At baseline, no significant difference regarding the density of *S. aureus* colonization could be observed.

After initiation of the trial a constant decrease in *S. aureus* colonization could be seen on the silver-coated textile site (right elbow flexure). The steepest decline was noted between day 2 and day 7. After termination the density numbers of *S. aureus* remained constant or rose again (a general view of *S. aureus* colonization density numbers in all patients is demonstrated in Fig. 2). In contrast, density numbers in *S. aureus* colonization on the Cotton-site (left elbow flexure) remained nearly constant during course of time in all 15 patients, one patient being an exception with an unsteady course of bacteria colonization (Fig. 3).

In statistical analysis, a highly significant decrease of *S. aureus* colonization could be observed already at day 2 on the silver-coated textile site (p=0.002). Also at day 7 and even at
timepoint of control (seven days after termination) *S. aureus* density numbers remained highly significant (p=0.002 and p=0.008, respectively) reduced compared to baseline (Figure 4). On the other hand, cotton treatment did not significantly reduce the density of *S. aureus* during the whole treatment period, there was even an increase in bacteria density. Numbers of *S. aureus* remained high at day 14, seven days after termination of treatment (Figure 4).

Comparison between silver-coated textile site- and cotton-treatment revealed a significantly lower *S. aureus*-colonization at day 7 (p=0.002) and at timepoint of control (day 14; p<0.05) on the silver-coated textile site (data not shown). At baseline as well as at day 2, no significant difference between the two treatment modalities could be seen.

*Clinical evaluation - local SCORAD*

Clinical severity, expressed by local SCORAD, was comparable between the two treatment arms at baseline, a significant difference could not be assessed.

After already two days a constant decrease in local SCORAD could be seen on the silver-coated textile site (right elbow flexure) in nearly all patients and continued to fall until termination of treatment (day 7). Thereafter, severity of eczema was assessed constant in 5 and declined in 6 of 15 patients (Fig. 5). In contrast, the course of clinical evaluated eczema severity remained fairly unchanged on the cotton-site (left elbow flexure) during and after treatment in all 15 patients (Fig. 6).

Excellent clinical response was seen on the silver-coated textile site: reduction of local SCORAD was highly significant at all timepoints of evaluation (day 2, 7 and 14) in comparison with baseline (p=0.003, p=0.001 and p=0.004, respectively) (Fig. 7). On the cotton site, a slight clinical improvement could be seen at day 2 of evaluation without statistical significance, however at days 7 and 14 local SCORAD values were even higher than at baseline (Fig. 7).
Comparing the two treatment arms, the local SCORAD was constantly lower at all timepoints of clinical evaluation on the silver-coated textile site (right elbow flexure), reaching high statistical significance at day 7 and even seven days after termination of treatment (day 14) (data not shown).

**Correlation of Staphylococcus aureus density and local SCORAD**

The reduction of *S. aureus* colonization paralleled with clinical improvement on the silver-coated textile site. A significant correlation between local SCORAD and bacteria density was seen only at day 14 (p=0.01).
Discussion

In the present study a superior clinical improvement by silver-coated comparing to cotton textiles paralleled by a potent anti-\textit{S. aureus}-efficacy was demonstrated.

Silver-coated textiles induced a highly significant reduction of \textit{S. aureus} already two days after initiation of textile treatment and lasted throughout the whole therapy phase. Even seven days after cessation, \textit{S. aureus}-density was significantly lower compared to baseline. The reduction of \textit{S. aureus} was paralleled by a reduction of clinical severity.

The mechanisms of the antibacterial activity of silver ions are not yet fully understood. Silver ions seem to cause a detachment of the cytoplasm membrane from the bacterial cell wall. The existence of elements of silver and sulfur in the electron-dense granules and cytoplasm suggest the antibacterial mechanism of silver by loss of the ability of DNA-replication and protein-inactivation after Ag(+) treatment [23]. To our knowledge, the antibacterial effect of silver ions in \textit{S. aureus}-colonized skin in patients with atopic eczema has not yet been investigated in vivo.

The disruption of the skin barrier function in patients with AE is known to be one of the major pathophysiological aspects of the disease [24]. Quantitative and qualitative changes in lipid composition [25,26,27] result not only in an increased transepidermal water loss (TEWL) [28] but also in a higher susceptibility for external irritants in affected and non-affected skin [24,29]. By textile protection, external provocation factors of the AE can be diminished, e.g. aeroallergens or UV-irradiation as well as contact with irritating material. In addition, due to textile protection the itch-and-scratch cycle can be disrupted. In this context, the clinical improvement on the cotton treated site at day 2 was probably due to the textile protecting effect, since no antiinflammatory therapy had been used. Our results showing a clinical improvement paralleled by a reduction of \textit{S. aureus} counts indicate that antiseptic therapy is essential for an efficient therapy of affected lesions in AE. These findings are in accordance with earlier studies implicating that antibiotic or antiseptic therapy contributes to a faster
clearance of AE [11,30]. Of interest was the observed prolonged effect on staphylococcal reduction exhibiting the period of active wearing. This is in contrast to the effects seen by the antistaphylococcal dye gentian-violet where cessation of therapy resulted in immediate subsequent recolonization [11]. These findings could indicate that overnight wearing of silver-coated textiles might be able to sustain a constant *S. aureus*-reduction.

Since the effectiveness of combining topical antibiotic or anti-infective agents with glucocorticosteroids is still controversially discussed [31], textiles with antibacterial qualities may offer the advantage to enhance the clinical efficacy of glucocorticosteroid or other antiinflammatory therapy. In addition, an identical clinical efficacy might be achieved by combining textile antistaphylococcal treatment and steroids of less potency and in this way reducing possible side effects of glucocorticosteroids. Concerning possible toxicologic side effects of silver coated textiles, toxicity is related to absorption through dermal wounds into the systemic circulation [32]. In further studies, silver absorption in patients wearing silver-coated textiles needs to be investigated.
References


18) BioService: Test 001118. 2001


Legends:

Figure 1:
Example of elbow covers used: silver-coated textile (right elbow flexure) and cotton (left elbow flexure) in a patient with atopic eczema

Figure 2:
Bacterial colonization of *S. aureus* in affected sites on silver-coated textile site (right elbow flexure) at different timepoints of evaluation: days 0, 2, 7 and 14.
Results of *S. aureus*-colonization in all 15 patients are expressed in CFU/cm².

Figure 3:
Bacterial colonization of *S. aureus* in affected sites on cotton-site (left elbow flexure) at different timepoints of evaluation: days 0, 2, 7 and 14.
Results of *S. aureus*-colonization in all 15 patients are expressed in CFU/cm².

Figure 4:
Difference in *S. aureus* density within affected silver-coated textile site (right elbow flexure) and cotton-site (left elbow flexure) in patients with AE during study period (day 0 vs. days 2, 7 and 14), expressed in CFU/cm².
Reduction of *S. aureus* was highly significant at day 2, 7 and 14 on silver-coated textile site (right elbow flexure) (**p<0,01) compared to baseline (day 0). On the cotton site, no significant reduction could be seen.

Figure 5:
Clinical severity in affected sites on silver-coated textile site (right elbow flexure) at different timepoints of evaluation: days 0, 2, 7 and 14.
Results in all 15 patients are expressed in local SCORAD values (0-18)

Figure 6:
Clinical severity in affected sites on cotton-site (left elbow flexure) at different timepoints of evaluation: days 0, 2, 7 and 14.
Results in all 15 patients are expressed in local SCORAD values (0-18)

Figure 7:
Clinical eczema severity differences within affected silver-coated textile site (right elbow flexure) and cotton-site (left elbow flexure) in patients with AE at different timepoints of evaluation: days 2, 7 and 14 compared to baseline (day 0).
A highly significant reduction of the local *SCORAD* could be seen at days 2, 7 and 14 (**p<0,01) on the silver-coated site compared to baseline. No significant reduction could be noted on the cotton-site.
Clinical eczema severity is expressed in local SCORAD (0-18) in all 15 patients.

Extreme values beyond statistical analysis
Figure 2

Figure 3
Figure 4

Figure 5
Figure 6

Figure 7