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SPECIFIC LYSIS OF STAPHYLOCOCCUS AUREUS BY THE BACTERIOPHAGE ENDOLYSIN STAPHEFEKT SA.100: IN VITRO STUDIES AND HUMAN CASE SERIES

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New strategies in the treatment of infections are warranted, as antibiotic resistance is emerging. Endolysins originating from bacteriophages combine two characteristics essential for such new strategies: powerful killing of bacteria and limited likelihood of emerging resistance.

The endolysin Staphefekt SA.100TM selectively targets S. aureus. It is the first registered endolysin and it has already been used by over a thousand patients on intact skin.
In vitro data from turbidity assays and bactericidal assays with clinical strains of methicillin susceptible (MSSA) and resistant (MRSA) S. aureus showed that lysis of S. aureus by Staphefekt is dose dependent, specific and efficient, compared to control strains of coagulase negative staphylococci. MSSA and MRSA proved to be equally susceptible to the endolysin, and MIC's did not differ between them, with a median MIC of 64 µg/ml in a specified setup.

No naturally occurring resistance against Staphefekt could be inferred from the MIC distribution amongst strains of S. aureus. Moreover, induction of resistance against Staphefekt could not be achieved in vitro. In contrast, resistance could be induced against another naturally occurring anti-staphylococcal enzyme (lysostaphin) and the frequently used antibiotic mupirocin. This supports the hypothesis that resistance against phage-derived endolysins is not likely to happen. The lytic activity seems such an essential part of the life cycle of the bacteriophages, that during over a billion years of co-evolution of bacteria and bacteriophages, natural selection has yielded endolysins that effectively target highly conserved essential structures in the bacterial cell wall that cannot easily be changed.

The in vivo effect of Staphefekt was evaluated retrospectively in two case series of S. aureus associated dermatitis. Of seven rosacea patients, three were lesional S. aureus carriers. After the local application of Staphefekt for one week, S. aureus was eradicated from the lesion in all positive rosacea patients, while other skin inhabitants remained present.

In another case series of eight patients, lesional S. aureus carriership, symptom relief and corticosteroid use were analysed after Staphefekt treatment. In six cases, S. aureus was found in skin cultures before treatment (three patients with constitutional eczema, two with contact dermatitis and one with peri-oral dermatitis). In 5 of 6 patients, symptoms diminished during treatment with Staphefekt, and patients reported less or no need of corticosteroids. In one patient with severe constitutional eczema, the burden of S. aureus carriership was very high and symptoms diminished only moderately, necessitating the use of corticosteroids and eventually cyclosporin. In the remaining two cases of eczema, no S. aureus was found. In one of them, Staphefekt had no effect on symptoms and corticosteroid use remained unchanged. In the other case, symptoms did diminish, but corticosteroid use was not completely abandoned.

The two case series provide evidence of the in vivo applicability of Staphefekt to specifically eradicate S. aureus without disturbing the normal skin flora. The reported corticosteroid use suggests that a quick relief of symptoms at the stage of local inflammation could best be achieved by combining symptomatic short term corticosteroid therapy with eradication of etiological S. aureus carriership by Staphefekt. These results support further clinical studies in a placebo controlled setting on the effect of Staphefekt on S. aureus related skin diseases.