No resistance after 100 days repeated incubation of \textit{Staphylococcus aureus} with polihexanide

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\textbf{Introduction}

Infection is the main cause of delayed healing in surgical, traumatic and burn wounds, and may lead to the formation of a chronic wound. Therefore, wound dressings with antiseptics are increasingly utilized in the treatment of critical colonized or infected chronic wounds. Antiseptics have a lower potency to induce bacterial resistance than antibiotics; however, concerns have been expressed regarding their overuse and the emergence of bacterial adaptation. \textit{Staphylococcus aureus} is one of the most important pathogens of nosocomial infections and is a common complication during the treatment of chronic wounds. Antiseptics have a lower potency to induce bacterial resistance than antibiotics; however, concerns have been expressed regarding their overuse and the emergence of bacterial adaptation. \textit{Staphylococcus aureus} is one of the most important pathogens of nosocomial infections and is a common complication during the treatment of chronic wounds. We have used an experimental system employing microplate-laser nephelometry to test the adaptation capacity of \textit{S.aureus} to polihexanide and silver nitrate, two commonly used antimicrobial agents in the treatment of infected chronic wounds.

\textbf{Material & Methods}

\textit{Staphylococcus aureus} was incubated with different concentrations of polihexanide (0.1 - 0.6 $\mu$g/mL) and silver nitrate (1 - 40 $\mu$g/mL). Bacterial growth was investigated by laser nephelometry (NEPHELOstar, BMG Labtech, Germany). IC$_{50}$ concentrations (half maximal inhibitory concentration) of the antiseptics were determined. Subsequently, the microorganisms were repeatedly incubated with the respective IC$_{50}$ concentration for 100 days. Influence of the continued treatment was determined by calculation of the current IC$_{50}$. Additionally, a polihexanide containing wound dressing (Suprasorb$^\circledR$ X + PHMB) has been tested according to the JIS L 1902 for antibacterial activity using untreated and treated \textit{S. aureus}.

\textbf{Results}

As figure 3 shows, the calculated IC$_{50}$ of polihexanide increased only slightly over time (m=0.002). In contrast, a dramatic increase of the IC$_{50}$ was observed for silver nitrate (m=0.087). Furthermore, the tests of antimicrobial activity against \textit{Staphylococcus aureus} according to the JIS L 1902 showed a comparable reduction of treated and untreated \textit{S. aureus} growth using the polihexanide containing wound dressing (fig. 4).

\textbf{Conclusions}

The IC$_{50}$ for silver nitrate was found to increase with repeated treatment of \textit{S.aureus}. Polihexanide on the other hand showed a much lower potency to induce adaptation in \textit{S. aureus}. Furthermore, the antibacterial activity of a polihexanide-containing wound dressing against PHMB-treated and untreated \textit{S. aureus} tested according to the JIS L 1902 was not altered. These results indicate that the clinically very effective silver-based products are microbicidal but should be used for short-term only in critically-contaminated or infected wounds due to a possible risk of adaptation after a longer treatment. Alternatively, polihexanide seems to be a valid option for an antimicrobial substance in wound dressings for treating chronic wounds as it possess a low risk to induce adaptation and shows a high biocompatibility.