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Pexiganan Acetate

A Viewpoint by Richard Wise

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Short chain synthetic cationic peptides are being studied as potential antimicrobial agents. These peptides are found widely in nature in mammals, fish, insects and amphibians. They apparently work by interacting with cell membranes, causing holes to form and hence the membrane to be disrupted.

As with other novel therapeutic agents, such as oligonucleotides, the practical problems with these agents are associated with targeting: namely, how to get the peptide to the site of infection. Studies with some compounds when given systemically show that they can disrupt red cell membranes, which of course limits their therapeutic potential.

There has therefore been a move towards using the agents in the topical treatment of superficial infections. Pexiganan acetate is the most clinically advanced compound that has been developed for the treatment of skin and soft tissue infections, such as those found in diabetic patients with infected leg and foot ulcers.

The *in vitro* activity of this compound is not too dissimilar from that of other peptides, inhibiting the majority of Gram-positive pathogens at concentrations of ≤8 mg/L. The Gram-negative organisms commonly found in foot ulcers, such as *Acinetobacter, Pseudomonas aeruginosa* and *Escherichia coli*, are inhibited at slightly higher concentrations. The reason why certain other Gram-negative organisms, such as *Serratia marcescens*, are resistant is unknown, but presumably relates to differences in the bacterial cell wall. Animal models of superficial infections, when treated with pexiganan acetate, show reductions in colony counts of infecting pathogens similar to that found with gentamicin (for *P. aeruginosa* infections) or mupirocin (for staphylococcal infections).

Clinical trials of diabetic patients with infected foot ulcers are difficult to perform and interpret. Topical pexiganan acetate gave clinical results similar to those obtained with oral ofloxacin. It is interesting to note that, in these trials, some haemolysis was observed as an adverse effect of pexiganan acetate, as might be predicted from our knowledge of peptides. Minor haemolysis may not be a significant clinical problem, but far more data are required before this phenomenon can be accurately assessed.

The use of a topical antibacterial agent with no cross-resistance to other antimicrobial agents is undoubtedly a welcome addition to the antimicrobial armamentarium, especially for the treatment of difficult infections such as those found in the diabetic foot. Further information on efficacy and tolerability should be obtained, as should any evidence concerning the emergence of resistance. As previous experience suggests, the topical use of a compound is an ideal way of selecting for resistance. ▲