The bioavailability of mupirocin in nasal secretions in vitro

R L R Hill

**Aim:** To determine the bioavailability of mupirocin in human nasal secretions and to assess whether the contents of nasal secretions interact appreciably with this antibiotic.

**Methods:** The comparative bioavailability of mupirocin and chlorhexidine in nasal secretions was determined by bioassay after one, four, and eight hours of incubation with pooled secretions from three subjects. The interaction of mupirocin with nasal secretions was characterised by matrix assisted laser desorption time of flight mass spectrometry (MALDI-TOF).

**Results:** MALDI-TOF analysis showed that mupirocin was not absorbed by the main fraction of pooled nasal secretions and should remain active. In bioassay, mupirocin retained 100% of its antistaphylococcal activity in nasal secretions, whereas chlorhexidine was significantly reduced from 100 mg/litre to 1.5 mg/litre and from 1000 mg/litre to 38.5 mg/litre, irrespective of incubation time.

**Conclusions:** The high bioavailability of mupirocin in nasal secretions results from the lack of appreciable molecular interactions.

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**Table 1** Effect of nasal secretions on the activity of mupirocin or chlorhexidine at 37°C

<table>
<thead>
<tr>
<th>Concentration (mg/l)</th>
<th>50</th>
<th>100</th>
<th>250</th>
<th>500</th>
<th>1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mupirocin</td>
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<tr>
<td>Chlorhexidine</td>
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<td>Average amount recovered from initial concentrations (mg/l) of nasal secretions</td>
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**RESULTS**

MALDI-TOF analysis showed that mupirocin, which had a mass/charge peak of 592 (fig 1A), was not absorbed by the main fraction of pooled nasal secretions (fig 1B) and should still remain active (fig 1C). This was confirmed in bioassay when, unlike chlorhexidine, the activity of mupirocin remained unaltered when incubated with nasal secretions for up to eight hours at 37°C. Table 1 shows that the activity of chlorhexidine was significantly reduced from 1.5% to 38.5% of the initial concentration of 100 and 1000 mg/litre, respectively. Recoverable activities of mupirocin and chlorhexidine were unaffected by time.

**DISCUSSION**

In a molecular assessment, MALDI-TOF mass spectroscopy, which allows direct capture and characterisation of complex spectra,10 showed that the extract of nasal secretions did not significantly absorb mupirocin. This has not been described previously. Nasal secretions serve to eliminate substances introduced into the nose, and consist of mucopolysaccharides and mucoprotein11 which, like mupirocin, possess an overall
negative charge. It is probable that negative charges on the major components of nasal secretions repel mupirocin, preventing any appreciable interactions.

“Nasal secretions serve to eliminate substances introduced into the nose, and consist of mucopolysaccharides and mucoprotein”.

This is the opposite to chlorhexidine, which has highly positively charged quanido groups and is known to be inactivated by saliva which, like nasal secretions, contains negatively charged molecules. Indeed, bioassay confirmed that chlorhexidine is unlikely to have valuable intranasal activity because only the equivalent of 1.5 mg/litre remained from the initial 100 mg/litre and 385 from 1000 mg/litre. This is important because minimum inhibitory concentrations of chlorhexidine for several strains of MRSA have been reported to be from 2 to 8 mg/litre. By extrapolating our results it can be calculated that 0.26 ml of a 1% cream would be needed in each nostril to achieve a dose of 10 mg, compared with the “match head” sized amount required for mupirocin (∼40–50 µl). Thus, the unreliability of chlorhexidine used intranasally to control MRSA carriage might result from the use of an insufficient amount.

Bioavailability in, and interaction with, nasal secretions could be a useful model for the development of newer analogues of mupirocin or similar agents, such as SB 205952. Indeed, using MALDI-TOF together with bioassay and the evaluation of killing kinetics predicted the effectiveness of 5% povidone-iodine against *S. aureus* in a controlled trial (RLR Hill and JJ Wade. Presented at the 40th international congress on antimicrobial agents and chemotherapy, Toronto, 17–20 September 2000).

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