Not all chlorhexidine containing antiseptics kill multidrug resistant Klebsiella pneumoniae

The best way to treat an infection is to prevent it in the first place. As resistance to antibiotics becomes increasingly prevalent, the reliance on disinfectants and antiseptics to prevent the spread of bacteria becomes ever more important. However, bacteria can also develop increased resistance to antiseptics, reducing their efficacy.

Chlorhexidine is a commonly used antiseptic, with formulations designed for mouthwashes, catheter maintenance and pre-surgical skin antisepsis containing a large range of chlorhexidine concentrations (0.02% to 4%). This large variation in concentrations means that bacteria are likely to be exposed to concentrations of chlorhexidine that will not kill them. This in turn will allow them to adapt and increase their resistance to chlorhexidine, making formulations containing chlorhexidine less effective against these bacteria. Exposure time to formulations is another important factor, as a short exposure time can allow bacteria to survive concentrations that would kill them with longer exposure times. For most applications, manufacturers recommend an exposure time of 1 minute.

In this study we looked at the inherent resistance of fourteen multidrug resistant *Klebsiella pneumoniae* strains to chlorhexidine and formulations containing it. *K. pneumoniae* is a Gram-negative bacterium, which can cause a variety of infections such as pneumonia, urinary tract infections, septicaemia, meningitis, diarrhoea and wound infections. *K. pneumoniae* is an opportunistic pathogen, meaning that it will only infect patients with a weakened immune system, which may be due to age, trauma or underlying health conditions. The *K. pneumoniae* strains used in this study all came from patient samples and are thus likely to be similar to strains found in the healthcare environment.

We found that *K. pneumoniae* strains that had been isolated before the widespread use of chlorhexidine (pre-1950s) were more sensitive to chlorhexidine than those isolated since the use of chlorhexidine became routine. This may indicate that *K. pneumoniae* has adapted to chlorhexidine over time or that less sensitive strains have become dominant. The formulations varied hugely in their ability to kill the bacteria within five minutes of exposure, which was the shortest exposure time we were able to test in the laboratory. One of the tested formulations killed all *K. pneumoniae* strains at 0.006% of the working concentration, whereas a different formulation was unable to kill strains, even when they were exposed to 50% working concentration. The concentration of chlorhexidine in the formulation was important, though this was not the only factor for efficacy of the formulation.

When we adapted strains to chlorhexidine by exposing them to low and increasing concentrations of chlorhexidine, six out of 14 strains were able to survive 8 to 32 times the original chlorhexidine concentration. These adapted strains also showed increased resistance to most of the

chlorhexidine formulations: they were 128 times more resistant to one formulation than the non-adapted strains. However, different formulations showed the same activity against the adapted strains as against the original ones, showing how important formulation and added ingredients can be to maintain efficacy of a disinfectant. The variety and commercial nature of formulations and added ingredients did not allow us to define a specific “best” combination with chlorhexidine, though there was an indication that chlorhexidine may have a synergistic bacteriostatic (halting growth) rather than a bactericidal (killing of bacteria) effect when combined with alcohol.

In conclusion, we showed that not all chlorhexidine formulations kill multidrug resistant *K. pneumoniae* after the exposure time recommended by the manufacturer. Effectiveness of formulations, especially against chlorhexidine adapted strains, depends on additional ingredients. Careful formulation of products containing chlorhexidine is therefore important to maintain and enhance their activity and avoid potential breakdown in infection control.

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