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WHAT'S NEW IN INTENSIVE CARE

Chlorhexidine use in adult patients on ICU

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Chlorhexidine (CHG) is a biguanide cationic antiseptic molecule, which has been incorporated into mouthwash solutions, dental gels, dressings, washcloths and central venous catheters (CVC). It has become the first-choice antiseptic to reduce healthcare-associated infections. However, the widespread use of CHG has raised concerns about increasing rates of resistance and cross-resistance to antibiotics. In this short review the antimicrobial characteristics of CHG including microbial resistance and its main clinical applications in ICU are presented.

Antimicrobial activity

CHG is available in a range of concentrations from 0.05% to 4% (w/v) in aqueous solutions and in combination with different alcohols. Formulations that contain both CHG and alcohol, such as 70% (v/v) isopropyl alcohol, advantageously exhibit the relatively rapid antimicrobial activity of the alcohol with the persisting activity of residual CHG.

CHG has broad-spectrum non-sporicidal antimicrobial activity against gram-positive bacteria (GPB) and gram-negative bacteria (GNB), yeasts, and some lipid-enveloped viruses, including HIV [1]. CHG is generally more active against GPB than GNB. In comparison mycobacteria are generally less susceptible to CHG. The positively charged CHG molecule is attracted to the negatively charged phospholipids in the bacterial cell wall. At low concentrations (< 0.5%), CHG is bacteriostatic, altering the cell wall leading to loss of cell membrane integrity and leakage of intracellular components. At higher concentrations (≥ 0.5%) CHG is bacteriocidal, causing cell death following coagulation of the cytoplasmic components and precipitation of proteins and nucleic acids.

Intrinsic microbial resistance to CHG is partly due to degradative enzymes and cellular impermeability. The cell wall of GNB is more complex as compared to GPB, and often permeation of high molecular weight compounds to its cellular targets is hindered as a result of the outer cell membrane, which is absent in the GPB. Bacteria in biofilms are also less susceptible to biocides. GNB bacteria that exhibit a high level of intrinsic resistance to CHG include *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Proteus* spp., and *Providencia stuartii*. In comparison, efflux pumps are the most widely reported mechanism of acquired resistance to CHG. Unfortunately multisubstrate (biocide and antibiotic) efflux pumps genes are present in both GPB and GNB, and concern has been raised that encouraging emergence of resistance to CHG with widespread clinical use may also simultaneously result in antibiotic resistance increasing [2, 3].

Clinical applications

CHG for skin preparation prior to invasive procedures

According to international recommendations CHG > 0.5% (w/v) in alcohol is the most efficacious antiseptic for skin preparation prior to invasive procedures in patients [4–7]. Strong clinical evidence suggests that 2% (w/v) CHG in 70% (v/v) isopropyl alcohol for skin antisepsis prior to placement of any short-term arterial, central, and hemodialysis catheters in patients located on ICU reduces the risk of catheter-related infection in comparison to ≤ 0.5% (w/v) CHG or povidone-iodine in alcohol [7]. Similarly there is evidence that the use of CHG as a skin preparation prior to venipuncture for blood cultures will reduce contamination rates [4–6]. It would therefore seem appropriate to use the CHG for all types of skin preparations prior to invasive procedures.

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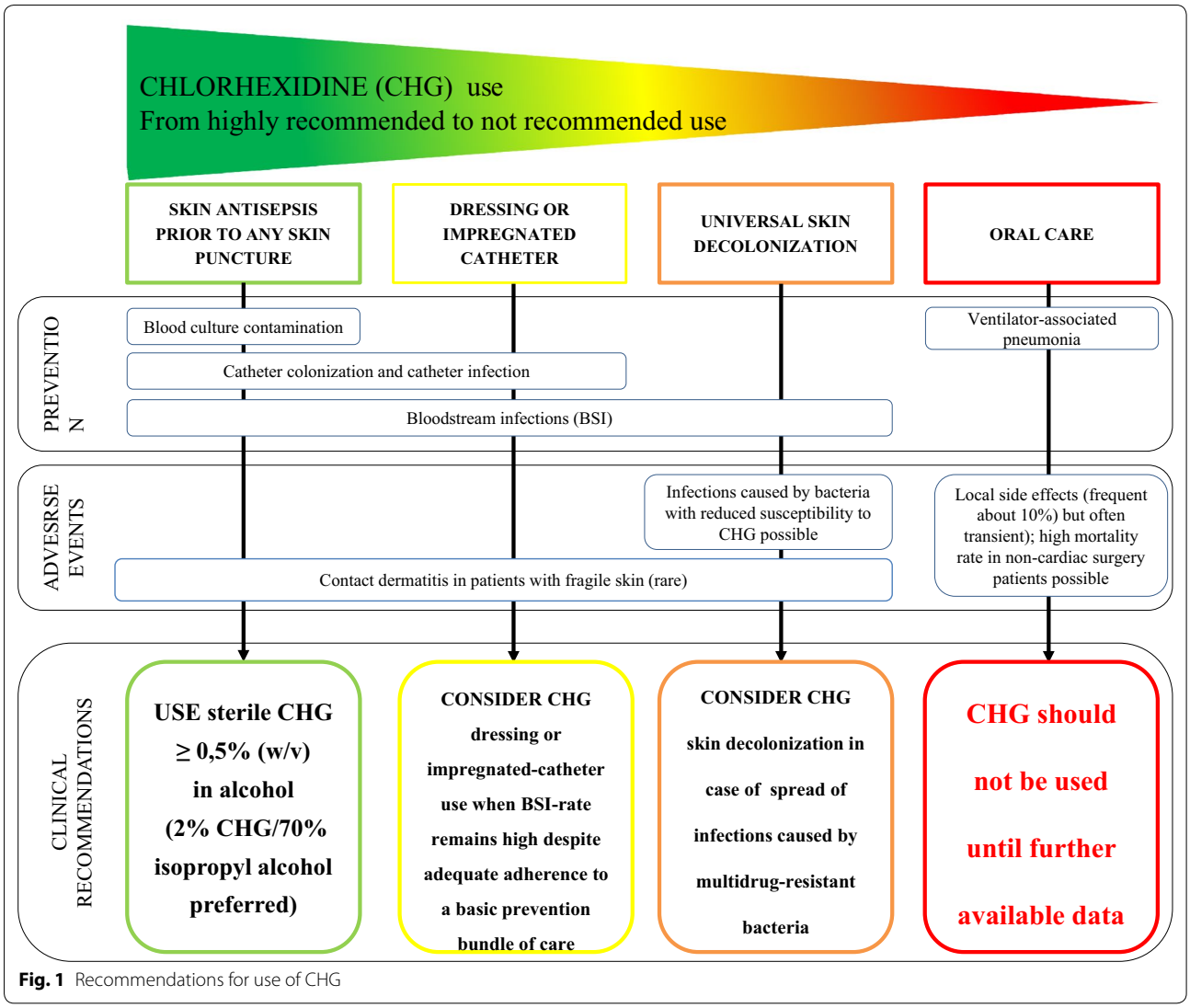

Fig. 1 Recommendations for use of CHG

CHG dressings

Both CHG-impregnated sponges and CHG–gel dressings have been used for the care of indwelling intravascular devices and have resulted in an up to 60% decrease in the risk of arterial and CVC infections, including catheter-related bloodstream infections (CR-BSI) [8, 9]. Their use has been recommended in high-risk adult patients when the risk of infection remains high despite the application of an appropriate catheter care bundle. These CHG-containing dressings have, however, been associated with contact dermatitis in adults.

CHG-impregnated CVC

A meta-analysis of five randomized controlled clinical trials evaluating CVC with CHG–sulfadiazine on both the internal and the external surfaces has shown the risk of CR-BSI to be significantly reduced in comparison to standard CVC [OR = 0.51 (0.56–1.00)] [10]. However, this analysis found significant heterogeneity between investigations. More importantly, the pooled level of CR-BSI in the control groups was unacceptably high in two studies (7.2% and 14%). These factors make universal application of these antimicrobial catheters for all patients in all situations less clear. However, the use of CHG–silver sulfadiazine catheters seems appropriate when the background rate of CR-BSI is greater than 1 per 1000 catheter-days despite adherence to a comprehensive infection prevention bundle strategy.

Universal skin decolonization with CHG

The use of CHG washcloths significantly reduces GPB but not GNB bacterial bloodstream infections [11]. Their

use is, however, associated with an increased risk of infections caused by bacteria with reduced susceptibility to CHG [11]. This raises the concern of the development of CHG resistance that could limit its future use prior to invasive procedures. The implementation of universal skin decolonization with CHG warrants caution and further consideration. It should only be considered where there is, for example, evidence of spread of infections caused by multidrug-resistant bacteria.

Oral decontamination with CHG for ventilated patients

CHG use for oral care in ICU patients has been recently challenged despite previous consistent data showing the beneficial effect of CHG in preventing ventilator-associated pneumonia (VAP) [12]. Firstly, oral mucosa adverse events with 2% (w/v) CHG mouthwash in ICU are frequent but often transient. Adverse events described were erosive lesions, ulcerations, plaque formation (which are easily removed), and bleeding mucosa in 29 of 295 patients (9.8%) who received 2% (w/v) CHG [13]. Secondly, despite a decrease in the rate of VAP in cardiac surgery patients, recent meta-analyses suggested that oral CHG paradoxically increased the risk of death, which may have resulted from toxicity of aspirated CHG in the lower respiratory tract [14, 15]. Consequently, it remains unclear whether using CHG for oral care affects outcomes in critically ill patients and CHG should not be used until further data become available.

Conclusions

CHG has a wide range of antimicrobial activity and is used for a variety of clinical applications some of which are supported by strong evidence. Other applications, however, are disputable in certain scenarios. Considering the possible risk of bacterial resistance and side effects, it is therefore prudent to restrict the use of CHG to those applications with a clear patient benefit (Fig. 1), and alternative antiseptics need to be developed.

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