Topical Antibacterial Agents

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- Bacitracin • Polymyxin

The skin presents a first line of defense against a wide range of bacterial invaders. When the integrity of the skin is compromised accidentally or intentionally, its natural defenses weaken and a role for antibacterials emerges. The topical route of application offers several advantages over systemic administration, including the avoidance of systemic toxicity and side effects, the decreased induction of bacterial resistance, and the high concentration of antibacterial agent at the site of infection. However, a treatment that must be physically applied to the skin is limited by patient compliance, local side effects such as allergic contact dermatitis, and the depth of penetration of the agent. Despite their shortcomings, topical antibacterial agents are highly versatile and can be used successfully for both prophylaxis and treatment of bacterial infections.

Outside of the hospital setting, *Staphylococcus aureus* and group A streptococci are classically considered the pathogens most often involved in infections of the skin. Recent data from hospitalized patients demonstrate that *S aureus*, *Enterococcus* spp, coagulase-negative staphylococci, *Escherichia coli* and *Pseudomonas aeruginosa* are the most prevalent pathogens involved in skin and soft tissue infections.[1]

These well-known offenders, as well as the panoply of more exotic pathogens that have been reported to cause skin infections, must be kept in mind while exploring the topical antibacterial agents at one's disposal.

PROFILES OF SELECTED ANTIBACTERIAL AGENTS

Antiseptics

Antiseptics, also known as disinfectants, are chemical agents primarily used to decrease the risk of infection in intact skin or in minor wounds. Alcohol and iodophors have rapid action against bacteria but little persistent activity, whereas chlorhexidine

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and triclosan are slower to act but persist on the stratum corneum for continued antimicrobial effects.[2,3] Most antiseptics are not suitable for open wounds as they may impede wound healing by direct cytotoxic effects to keratinocytes and fibroblasts.[4]

Hydrogen peroxide

Hydrogen peroxide is a common antiseptic agent used on intact skin and minor wounds. It is thought to kill bacteria in two distinct modes: rapidly by way of DNA damage from highly reactive hydroxyl radicals, and more slowly in a manner that may involve the inactivation of housekeeping enzymes.[5,6] It has limited bactericidal activity, however. In one study of mixed microorganism disinfection of a glass, it was found to be entirely ineffective.[7] A prospective study in human appendectomy wounds found that there was no statistical difference in the infection rate between a control group and a group receiving hydrogen peroxide.[8]

Hydrogen peroxide may be detrimental to wound healing, however, as it has been shown to be directly cytotoxic to keratinocytes, and even at very low concentrations inhibits keratinocyte migration and proliferation.[9]

Chlorhexidine

Chlorhexidine's role continues to expand as an effective and versatile agent for both infection control and prevention.[10] Chlorhexidine gluconate is active against a wide range of gram-positive and gram-negative bacteria, yeast, and molds.[11] Chlorhexidine acts by disrupting cytoplasmic membranes and remains active for hours after application.[3,12,13] It has a major role in antisepsis for both general skin cleansing and preoperative bathing and surgical site preparation. Chlorhexidine is consistently superior to povidone-iodine and a number of other antiseptics in reducing colonizing flora immediately and several days after application.[2,14,15] It is useful in decolonization of methicillin-resistant *Staphylococcus aureus* (MRSA) carriers and has been shown to reduce MRSA infection in ICU patients treated with a combination of chlorhexidine bath along with intranasal mupirocin.[16,17] Daily chlorhexidine baths alone reduced contamination and acquisition of vancomycin-resistant enterococcus.[10,18] In addition, chlorhexidine is widely used for skin preparation before catheter insertion. More recent developments include chlorhexidine-impregnated dressings or sponges for maintenance of indwelling catheters and impregnated or coated catheters and catheter cuffs.[19,20] Finally, chlorhexidine is playing an emerging role in decontamination of the oropharynx as it impacts on nosocomial pneumonia. A meta-analysis found that chlorhexidine decontamination was responsible for a 30% decrease in the incidence of ventilator-associated pneumonia.[10,21]

Triclosan

Triclosan is a broad-spectrum cationic antimicrobial agent that is widely used in consumer products such as soaps, detergents, toothpastes, and cutting boards. Its mechanism of action is bacterial membrane disruption through blockade of lipid synthesis. This was elucidated recently when triclosan resistance was found in *E coli* strains. These strains were found to have a mutation in the *fabI* gene, which encodes an enzyme involved in fatty acid biosynthesis.[22] The emergence of resistance, although not yet clinically relevant, has sparked concern about the widespread use of this agent promoting resistance.

Iodophors

The iodophors are complexes of iodine and organic carrier compounds that have a broad spectrum of activity against bacteria and fungi. Its mechanism is thought to be by way of destroying microbial protein and DNA.[23] They were formulated to be