Published online: 2019-11-27

Original Article

A comparative study of the effect of different topical agents on burn wound infections

Katara Gunjan, Chamania Shobha[1], Chitnis Sheetal, Hemvani Nanda, Chitnis Vikrant[2], Dhananjay Sadashiv Chitnis

Department of Microbiology, Immunology and Molecular Biology, [1]Department of Burn Surgery, Choithram Hospital and Research Centre, Manik Bagh Road, [2]Department of Microbiology and Immunology, Aurobindo Medical College, Sanwer Road, Indore, Madhya Pradesh, India

Address for correspondence: Dr. D. S. Chitnis, Department of Microbiology, Immunology and Molecular Biology, Choithram Hospital and Research Centre, Manik Bagh Road, Indore – 452 014, Madhya Pradesh, India. E-mail: ds_chitnis@rediffmail.com

ABSTRACT

Background: Topical agents are used to treat burn wound infections. **Aims and Objective:** The present work was aimed to find out the *in vitro* efficacy of different topical agents against burn wound pathogens. **Settings and Design:** Randomly selected gram-positive (29) and gram-negative bacterial (119) isolates from burn wound cases admitted in burn unit of Choithram Hospital and Research Centre, Indore, were included in the *in vitro* activity testing for silver nitrate, silver sulphadiazine (SSD), chlorhexidine, cetrimide, nitrofuran, soframycin, betadine, benzalkonium chloride and honey by growth inhibition on agar medium. **Materials and Methods:** Multidrug-resistant isolates of gram-positive and gram-negative bacteria were checked for different topical agents. 1% topical agent was mixed with Mueller-Hinton agar. Two microlitres of bacterial suspension adjusted to 0.5 McFarland turbidity standard was spread over the topical agent containing plates. The plates without the topical agent were used as control plates. The plates were incubated for 48 h at 37°C. **Results:** SSD (148/148), silver nitrate (148/148) and chlorhexidine (148/148) showed excellent activity against all the pathogens. Neosporin had poor activity against *Pseudomonas aeruginosa*, (4/44) *Proteus* spp. (2/4) *and* group D streptococci (1/4). Betadine did not show activity against the bacterial isolates in the presence of organic matter. Honey did not exert any antimicrobial activity under the study conditions. **Conclusion:** SSD, silver nitrate and chlorhexidine have excellent activity against all the bacterial pathogens and could be used empirically, while identification of the infective agent is required for selecting the alternative topical agents such as nitrofuran, soframycin, and benzalkonium chloride.

KEY WORDS

Benzalkonium chloride; burn wounds; cetrimide; chlorhexidine; nitrofuran; silver nitrate; silver sulphadiazine; topical gents

Access this article online	
Quick Response Code:	Website: www.ijps.org
	DOI: 10.4103/0970-0358.101320

INTRODUCTION

Infections in burn patients continue to be the primary source of morbidity and mortality. Growing multiple drug resistance among pathogens in wound infections is a major concern today. Wound colonisation with these organisms results in difficult of management of the

wound, complicated by a greatly limited choice of therapeutic antibiotics. Nearly 10 million patients with traumatic wounds are treated annually in the United States.[1]

Topical use of antimicrobial agents has played an important role in the control of burn wound infection. Topical antimicrobial therapy may be especially helpful to overcome the deleterious effects of bacteria in specific circumstances.

The management of the microbial contamination of burns to prevent sepsis is a routine requirement of acute care that has led to the development of a variety of therapeutic agents for topical use.[2] Prior to the advent of topical antimicrobial agents, the overall mortality rate in the typical burn population was reported as 38–45%.[3] However, after the use of topical antimicrobial therapy, the overall mortality was reduced to 14–24%.[3] Further, the risk of development of superinfection and antibiotic-resistant bacteria, as well as organ toxicity, is minimal as compared to the use of systemic antibiotics in clean operations. The combination of systemic and topical chemotherapeutic drugs is a valuable adjunct in the treatment of contaminated wounds and high-risk patients.[4]

The use of silver in wound management can be traced back to the 18th century, during which silver nitrate (AgNO3) was used in the treatment of ulcers.[5] Silver began to be used again for the management of burn patients in the 1960s, this time in the form of 0.5% AgNO3 solution.[6,7] Silver has the advantage of having broad antimicrobial activities against Gram-negative and Gram-positive bacteria and there is also minimal development of bacterial resistance. The use of these compounds and the mechanisms of silver resistance have been reviewed.[8] One major advantage of its use is the limited side effect of topical silver therapy.[9,10]

Silver sulphadiazine (SSD) has been used clinically as a standard treatment for burns over the past three decades, since Fox first synthesised SSD from silver nitrate and sodium sulfadiazine for an increased potency and negligible adverse effects including minimal pain on application.[11,12] At the present time, SSD is the most frequently used topical prophylactic agent.

Many effective antibacterial substances are now available for topical application in the prophylaxis of sepsis in burn. Other topical agents including mafenide acetate (Sulfamylon), bismuth tribromophenate (Xeroform), Dakin's solution (0.25% sodium hypochlorite), bacitracin zinc, neomycin with polymyxin B and bacitracin (Neosporin), mupirocin (Bactroban), gentamicin sulphate, and nystatin have been used individually and in combination to control microbial growth in burn wounds and on healing meshed skin graft.[13-15] Other agents, such as nitrofuran or chlorhexidine preparations, may be useful in isolated clinical situations. Multiple topical agents may be used for cleansing, barrier protection, and antimicrobial control. However, occasional complications of contact and/or irritant dermatitis may further complicate re-epithelialisation and eventual wound healing.

The goal of prophylactic topical antimicrobial therapy is to control microbial colonisation and prevent burn wound infection. In selected clinical circumstances, topical agents may be used to treat incipient or early burn wound infections.

At present, the available preparations meet the majority of characteristics of an ideal topical agent.[16] However, much effort must be put into finding better and more cost-effective products, especially for developing countries that experience burn accidents more frequently than developed nations. Hence, it was aimed presently to study the *in vitro* activity of various topical agents against the bacterial isolates from burn wound in Central India.

MATERIALS AND METHODS

One hundred and forty-eight consecutive isolates from burn wound cases admitted in Choithram Hospital and Research Centre, Indore, India, during 2007–2008 were included in the study. The bacterial isolates included 44 *Pseudomonas aeruginosa,* 27 *Escherichia coli,* 31 *Klebsiella pneumoniae*, 25 *Staphylococcus aureus,* 13 *Acinetobacter baumanii*, and 4 *Proteus* spp. *a*nd 4 group D streptococci. All the isolates of *E. coli* and *Klebsiella* were extended spectrum beta-lactamases (ESBL), and 4/27 *E. coli* and 5/31 *Klebsiella* were resistant to carbapenems as well. Twenty-nine of the 44 *Pseudomonas* were resistant to all the conventional antibiotics and sensitive only to Polymixin. Similarly, *Acinetobacter* were also susceptible only to Polymixin. Twenty of 25 *S. aureus* were Methicillin-resistant *Staphylococcus aureus* (MRSA). *Pseudomonas* ATCC 27853, *Staphylococcus* ATCC 25923, *E. coli* 25922 and *Klebsiella* 700603 were included as control strains.

Overnight growth of these organisms on nutrient agar slants was harvested in normal saline and opacity adjusted to McFarland standard 0.5 was used for the susceptibility testing. The details of topical agents used in the study are given in Table 1.

One gram (one millilitre for liquids) of topical agents was mixed with 100 ml molten Muller-Hinton agar (Hi-Media, Mumbai, India), cooled to 45°C–48°C, and an aliquot of 25 ml poured in 100-mm-diameter sterile Petri dish was used for "no drug" control plates. Two microlitres of the bacterial suspension adjusted to 0.5Mc Farland turbidity standard was spread over an area of 1.5 cm diameter for both topical agent containing plates and control plates. The plates were incubated for 48 h at 37°C before observation for growth.

Table 1: The details of topical agents used in the study

Topical agent	*Brand*	*Final concentration used*
Silver sulphadiazine	Solvay Pharma, Mumbai, India	0.1 mg/ml
Silver nitrate	Biolab Diagonistics, Mumbai, India	10 µg/ml
Neosporin	Glaxo Smithkline Pharma, Mumbai, India	0.1 mg/ml
Cetrimide	Hi-Media Laboratories, Mumbai, India	10 mg/ml
Nitrofuran	Martin and Harris laboratories, Gurgaon, India	500 µg/ml
Soframycin	Aventis Pharma, Mumbai, India	0.1 mg/ml
Benzalkonium chloride	Benzyl Septol antiseptic liquid, Meridine Enterprises, Mumbai, India	0.03%
Chlorhexidine	Microshield, Johnson and Johnson, Mumbai, India	0.2% 0.01% 0.05%
Honey	Dabur, Ghaziabad, India	10 mg/ml
Betadine ointment	G. S. Pharmbutor, Win Medicar, Mumbai, India	0.5 mg/ml

RESULTS

Susceptibility of various bacterial isolates to various topical agents is displayed in Table 2. SSD and silver nitrate showed excellent activity against all the bacteria. Neosporin had poor activity against *Pseudomonas*, *Proteus* and group D streptococci. Overall activity of cetrimide was good except for *Pseudomonas*, while nitrofuran showed poor activity against *Pseudomonas* and *Acinetobacter.* Soframycin had fair activity against only *E. coli*, *Klebsiella* and staphylococci. Chlorhexidine was checked at three different concentrations and had excellent activity up to 0.5% concentration; the effect was marginally reduced for 5/44 *Pseudomonas* at 0.25% concentration. Honey could not show *in vitro* activity at the 1% concentration against any of the bacterial isolates and surprisingly betadine ointment or liquid did not show *in vitro* activity against the bacterial pathogens tested.

DISCUSSION

Although there is some controversy as to the effectiveness of topical chemotherapy in certain types of local infections, there are several clinical situations in which topical therapy is apparently beneficial.[17] Topical antimicrobial formulations are widely used in the field of dermatology.[17]

Table 2: Susceptibility of bacterial isolates to different topical agents

Topical agents	*No. of strains*						
	E. coli (n = 27)	*Klebsiella (n = 31)*	*Pseudomonas (n = 44)*	*Acinetobacter (n = 13)*	*Proteus (n = 4)*	*Staphylococci (n = 25)*	*Group D streptococci (n = 4)*
SSD	27	31	44	13	4	25	4
Silver nitrate	27	31	44	13	4	25	4
Neosporin	27	31	4	11	2	24	1
Cetrimide	27	30	1	13	4	25	3
Nitrofuran	26	31	0	3	4	25	2
Soframycin	24	23	1	3	0	8	1
Benzalkonium chloride	25	26	0	3	0	24	4
1% Chlorhexidine	27	31	44	13	4	25	4
0.5% Chlorhexidine	27	31	44	13	4	25	4
0.25% Chlorhexidine	27	31	39	13	4	25	4
Honey	0/12	0/12	0/24	0/4	-	1/8	0/4
Betadine ointment	0/12	0/12	0/24	0/4	-	0/8	0/4

The primary purpose of the present study was to compare the various topical antimicrobial agents and the preparations, most of which are employed in the hospitals. As topical agents may be either synthetic compounds or antibiotics, representatives of both types were included in this study. SSD, silver nitrate and chlorhexidine showed excellent activity against all the bacterial isolates. It needs to be mentioned that the gram-negative bacterial isolates were multidrug resistant. Thus some of the *E. coli, Klebsiella* and most of the *Pseudomonas, Acinetobacter* isolates were multi drug resistant. Staphylococcus bacteria were largely MRSA. Thus, the choice for systemic antibiotic usage had several limitations and we often encountered resistance to all antibiotics except polymyxin B.

Resistance to SSD has been reported, but is rare.[18] A variety of topical silver preparations have been evaluated on chronic wounds in controlled trials with favourable results.[19,20] Recently, a number of silver-containing dressings have become available.[21-25]

Other agents, such as nitrofuran or chlorhexidine preparations, may be useful in isolated clinical situations. 0.5% Silver nitrate and chlorhexidine were equally effective as 1% SSD against gram-positive and gram-negative bacteria. There were equally effective in reducing the colonisation and also preventing the infection.[2] Silver nitrate was probably the first silver compound used on wounds with an astringent and irritating effect.[26] The undesirable side effects of silver nitrate solution limit its use by most clinicians at the present time.[2]

Neosporin, cetrimide, soframycin, benzalkonium chloride and nitrofuran had poor activity against *Pseudomonas* and *Proteus* spp. adherence is not likely to be efficient topical agent in such situations. Thus, the present study also points out limitations of the available topical agents. Honey is used for topical applications in many developing countries, but the present study revealed poor antibacterial activity for it. The lack of demonstrable activity of betadine in the study is not surprising, as at the concentration checked it failed to show activity against the bacterial pathogens in the study model. The lack of activity of betadine appears to be due to the masking of iodine in the protein-based nutrient media, and the presence of organic matter in the burn wounds is likely to be a limiting factor for the activity of betadine.

To conclude, SSD, silver nitrate and chlorhexidine preparations can be recommended for the empirical usage as topical agents for burn wound, but identification of the infective agent is required for selecting the alternative topical agents.

ACKNOWLEDGEMENT

The authors are thankful to the management, Choithram Hospital and Research Centre, Indore, India, for the research facility support.

REFERENCES

1. Dale RM, Schnell G, Wong JP. Therapeutic efficacy of Nubiotics against burn wound infection by *Pseudomonas aeruginosa*. Antimicrob Agents Chemother 2004;48:2918-23.
2. Monafo WW, West WA. Current treatment recommendations for topical burn therapy. Drugs 1990;40:364-73.
3. Vu H, McCony LF, Carino E, Washington J, Dang T, Villarreal C, *et al*. Burn wound infection susceptibilities to topical agents: The Nathan's agar well diffusion technique. Pharmacy and Therapeutics 2002;27:390-96.
4. Moylan AJ. The proper use of local antimicrobial agents in wounds. World J Surg 1980;4:433-7.
5. Chopra I. The increasing use of silver based products as antimicrobial agents: A useful development or a cause for concern. J Antimicrob Chemother 2007;59:587-90.
6. Price WR, Wood M. Silver nitrate burn dressing. Treatment of seventy burned persons. Am J Surg 1966;112:674-80.
7. Moyer CA, Brentano L, Gravens DL, Margraf HW, Monafo WW. Treatment of large human burns with 0.5 percent silver nitrate solution. Arch Surg 1965;90:812-67.
8. Silver S. Bacterial silver resistance: Molecular biology and uses and misuses of silver compounds. FEMS Microbial Rev 2003;27:341-53.
9. Lansdown AB. Silver. 2. Toxicity in mammals and how its products aid wound repair. J Wound Care 2002;11:173-7.
10. Marshall JP, Schneider RP. Systemic argyria secondary to topical silver nitrate. Arch Dermato 1977;113:1077-9.
11. Lee AR, Moon HK. Effect of topically applied silver sulphadiazine on fibroblast cell proliferation and biochemical properties of wound. Arch Pharma Res 2003;26:855-60.
12. Fox CL Jr, Rappolg BW, Standford W. Conrol of Pseudomonas infection in burns by silver sulphadiazine. Sur gyneecol Obstet 1969;128:1021-6.
13. Heggers JP, Robson MC, Herndon DN, Desai MH. The efficacy of nystatin combined with topical microbial agents in the treatment of burn wound sepsis. J Burn Care Rehabil 1989;10:508-11.
14. Lindberg RB, Moncrief JA, Mason AD. Control of experimental and clinical wound sepsis by topical application of sulfamylon compounds. Ann N Y Acad Sci 1968;150:950-72.
15. Strock LL, Lee MM, Rutan RL, Desai MH, Robson MC, Herndon DN, *et al*. Topical Bactroban (mupirocin): Efficacy in treating burn wounds infected with methicillin-resistant staphylococci. J Burn Care Rehabil 1990;11:454-9.
16. Ross DA, Phipps AJ, Clarke JA. The use of cerium nitrate-silver sulphadiazine as a topical burn dressing. Br J Plast Surg 1993;46:582-4.
17. McRipley JR, Witney RR. Responsiveness of experimental surgical wound infections to topical chemotherapy. Antimicrob

Agents Chemother 1976;10:45-51.
18. Modak SM, Fox CL. Sulphadiazine silver-resistant Pseudomonas in burns. New topical agents. Arch Surg 1981;116:854-7.
19. O'Meara SO, Cullum N, Majid M, Sheldon T. Systematic review of wound care management: (3) Antimicrobial agents. HealthTechnol Assess 2000;4:1-237.
20. O'Meara SO, Cullum N, Majid M, Sheldon T. Systematic review of antimicrobial agents used for chronic wounds. Br J Surg 2001;88:4-21.
21. Wright JB, Iarn K, Burell RE. Wound management in an era of increasing bacterial antibiotic resistance: A role for topical silver treatment. Am J Infect Control 1998;26:522-77.
22. Wright JB, Hansen DL, Burrell RE. The comparative efficacy of two antimicrobial barrier dressing: *In vitro* examination of two controlled release silver dressing. Wounds 1998;10:179-88.
23. Furr JR, Russell AD, Turner TD, Andrew SA. Antibacterial activity of Actisorb plus, Actisorb and silver nitrate. J Hosp Infect 1994;27:201-8.
24. Bowler PG, Jones SA, Walker M, Parsons D. Microbicidal properties of a silver containing hydrofibre dressing against a varity of burn wound pathogens. J Burn Care Rehab 2004;25: 192-6.
25. Jones SA, Bowler PG, Walker M, Parsons D. Controlling wound bioburden with novel silver containing hydro fibre dressing. wound repair and regeneration 2004;12:288-94.
26. Viala J, Simon L, Le Pommelet C, Philippon L, Devictor D, Huault G. Agranulocytosos after application of silver sulfadiazine in a 2-month old infant. Arch Pediatr 1997;4:1103-6

How to cite this article: Gunjan K, Shobha C, Sheetal C, Nanda H, Vikrant C, Chitnis DS. A comparative study of the effect of different topical agents on burn wound infections. Indian J Plast Surg 2012;45:374-8.

Source of Support: Nil, **Conflict of Interest:** None declared.