Nanocrystalline silver reduces the need for antibiotic therapy in burn wounds

Catherine Tonkin • Fiona Wood

Abstract

Wound infection is a serious consequence of burn injury. This study aims to compare the effectiveness of Acticoat™ and silver sulphadiazine (SSD) in relation to antibiotic use during a product trial at Royal Perth Hospital (RPH) in Western Australia (WA). This investigation consisted of four periodic clinical audits (n=72) comparing SSD and Acticoat wound dressing regimens for burn injury, with the primary outcome variable being antibiotic use.

Of the 72 patients audited, 81.9% were male and 18.1% female, with a mean age of 35.7 years. The most common burn agent was flame (58%); 36% had partial depth burns. The mean percentage total body surface area (%TBSA) of burn was 9.3%. Antibiotic use was prescribed for 24 (36.1%) of the 72 patients reviewed. There was a statistically significant (p=0.016) decrease (50%) of antibiotic usage with Acticoat dressings compared to SSD. The mean length of stay (LOS) for those patients receiving Acticoat showed a statistically significant decrease (p=0.045); 8.8 days compared with a LOS of 15.1 days in the SSD group. It was therefore concluded that Acticoat is a more effective dressing for reducing infection than SSD in burn wounds.

Tonkin C, Wood F. Nanocrystalline silver reduces the need for antibiotic therapy in burn wounds. Primary Intention 2005; 13(4): 163-168.

Introduction

The release in November 2001 of Acticoat™ onto the Australian market prompted a product trial of this new silver dressing in the nine bed acute care burn unit at Royal Perth Hospital (RPH) in Western Australia. The unit averages approximately 200 adult admissions each year; the average size of burn is 10% total body surface area (TBSA).

The Center for Disease Control (CDC) defines burn wound infection as follows:

- The appearance or character of the burn wound changes. For example, rapid separation of eschar, discolouration of the eschar or oedema at the burn wound margins.
- Histologic examination confirms micro-organism invasion into adjacent viable tissue. A positive blood culture or herpes simplex isolated.
- Fever or hypothermia, oliguria, hyperglycaemia or mental confusion [1].

Catherine Tonkin
BScHlth (Nursing)
Clinical Nurse
Burns Unit, Royal Perth Hospital
Wellington Street, Perth, WA
GPO Box X2213 Perth WA 6847
Tel: (08) 9224 2154 pager 2154
E-mail catherine.tonkin@health.wa.gov.au

Fiona Wood
FRACS, AM
Director
Burn Unit, Royal Perth Hospital, Perth, WA

The standard treatment for burn injuries within the burn unit at RPH is silver sulphadiazine (SSD), a white, water based cream [1, 2]. SSD was developed in the 1960s and has been acknowledged worldwide as the gold standard in the treatment of burn wounds [3, 4]. Clinical trials show that SSD reduces bacterial load and inhibits colonisation of the burn wound with Gram-negative and some Gram-positive organisms [2, 5, 6]. SSD, however, does not reliably control these organisms in burn injuries of greater than 40% TBSA [2, 6].

Acticoat is a three-layered dressing; an absorbent rayon polyester core between two layers of a high-density polyethylene mesh, coated with nanocrystalline silver. It is a non-adherent dressing that promotes moist wound healing [5, 7, 8]. *In vitro* studies show that Acticoat is an effective dressing that protects against a broad spectrum of Gram-negative and Gram-positive organisms, including multi-resistant organisms [2]. An inflammatory and pro-healing role for this product is also postulated [7, 9, 10].

Burn wounds treated with Acticoat and SSD differ in appearance. SSD forms a yellow-grey slough over the wound surface of partial thickness burns, whereas Acticoat does not.

This SSD slough may impede the accurate assessment of the depth of the burn [11]. Clinical experience has found that, as Acticoat does not form a slough, it may not amplify the depth of the burn wound [10].

An important issue in the treatment of burn wound infection is the need to avoid prophylactic antibiotic therapy. This is due to the risk of developing multi-resistant infection and drug reactions which may complicate recovery [12]. This study therefore aims to compare the effectiveness of Acticoat and SSD in relation to antibiotic use.

Methods

Study design

This investigation consisted of four periodical clinical audits (two retrospective and two prospective) comparing SSD and Acticoat wound dressing regimens for burn injury. The primary outcome variable was antibiotic use. The secondary outcome variables were length of stay (LOS) in hospital in the burn unit, and surgical intervention, debridement, skin grafting, cultured epithelial autograft (CEA) and wound breakdown.

Recruitment

The clinical audits included men and women admitted to the unit over a 3-year period from January 2001 to December 2003. These patients were included from all those identified, in the burn unit admission register, with a burn injury of less than 35% during the years of the audit. When the initial two audits were conducted, patients were dressed with SSD on admission, as per protocol. For the later audits, the dressing on admission was Acticoat. As it is community practice to dress burns with SSD prior to transfer to the burn unit, those patients treated with SSD prior to admission to the burn unit were excluded from the Acticoat audits (Table 1).

Routine management of patients in the burn unit

The burn unit at RPH comprises seven positive pressure single rooms and a two bed positive pressure room with a negative pressure anteroom where patients with multi-resistant organisms are nursed. The unit is designed to decrease cross contamination and thus the risk of infection [2, 13].

Staff members wear gowns, sterile gloves and hats during dressings and observe strict hand washing procedures when undertaking other aspects of patient care. Patients are showered daily to reduce the bacterial load and precautions, such as reducing patient visitors and ensuring visitors wash their hands and wear a plastic apron, are undertaken. These protocols aim to further reduce cross contamination [13].

Table 1. Description of audit groups and dressing types.

Audits	Year and month	No.	Group	Dressing
Audit 1	1st-12th 2001	18	1	SSD cream
Audit 2	11th 2001-12th 2002	18	2	Acticoat
Audit 3	1st -12th 2003	18	1	SSD cream
Audit 4	1st -12th 2003	18	2	Acticoat

Routine antibiotics prescribed

Antibiotic usage is defined as the prescription and administration of antibiotics, including the number of doses of each antibiotic administered. For the prescription of antibiotics, the standard practice in the RPH burn unit is based on a combination of elevated body temperature in excess of 38.5ºC, and on the visual assessment of cellulitis at the burn margin of greater than 2cm, in contrast to the appearance of inflammatory process related to wound healing.

Proactive prescription of antibiotics for suspected infection with the risk of extension of the wound is also made on the basis of clinical examination wound appearance, including inflamed burn wound margins, elevated body temperature (not necessarily 38.5ºC) and environment of the occurrence of the burn injury (i.e. potential infection). Some microbiological tests for the presence of organisms are undertaken as clinically indicated.

At the time of the audits, the common antibiotics and dosages used to treat suspected wound infections for all patients admitted to the burn unit included Flucloxacillin (1g), Benzlypenicillin (1.2g), Gentamicin (varying dose dependent on body weight and renal function), Cephalothin (1g), Ciprofloxacin (400mg), Clindamycin (600mg), Ticarcillin sodium and potassium clavulanate (3.1g), Amoxycillin (1g), and Ceftazidime (1g).

Routine dressing practice

SSD dressings are undertaken twice daily by nursing staff and incorporate a shower using Chlorhexidine 4% pre-operative liquid soap. The shower is used to reduce the risk of infection by decreasing surface bacteria and wound colonisation. The burn wound is debrided of crusting, loose slough and non-viable skin, as required, and SSD cream applied to the burn wound. Gauze is applied over the cream and secured using crepe bandages. This practice continues until the patient either requires surgery, the wound healing progresses, or he or she is discharged.

When using Acticoat dressings, the shower and debridement of the burn wound is performed as with that of the practice with SSD dressings. The Acticoat is moistened with sterile water and applied to the burn wound, with minimal overlap onto unburnt skin. As recommended by the manufacturer and if clinically indicated (that is the burn is not infected and the dressing has not changed from blue to copper, signifying diminished silver in the dressing), the Acticoat remains in place for up to 3 days.

The secondary dressing of gauze is moistened with sterile water and applied directly to Acticoat. This is covered with paraffin gauze, to keep the dressing moist, and then more burn gauze is applied and secured with a crepe bandage. The inner burn gauze dressing is moistened with sterile water, as required, but at least once a day. If the burn is not clinically infected, from Day 3 post burn injury, an alternative dressing practice is used – the application of a hydrocolloid directly over the Acticoat to promote moisture retention [8].

Analysis of data

Data on demographic characteristics (age, gender), clinical characteristics (%TBSA, agent, burn depth, antibiotic use, LOS in the burn unit and surgery) and outcomes (antibiotic use) were obtained from patient integrated notes and reported in counts and percentages.

Comparative analysis by dressing product used non-parametric chi-square (antibiotic usage) and Mann-Whitney (LOS) using the p=0.05 level of significance. Data analysis used SPSS v12.5.

Ethical issues

These clinical audits were conducted under the auspices of the burn unit with access to clinical notes using non-identifiable clinical data.

Results

The following results report on the demographic and clinical characteristics, antibiotic usage, LOS and surgical requirements of the 72 patients audited.

Demographic and clinical characteristics

Table 2 shows that, of the 72 patients audited, 81.9% were male and 18.1% female, with an age range of 14-76 years (x=35.7 years). The %TBSA of patients ranged from 1% to 33% (x=9.7%). Table 3 shows that, of the 72 patients, the most common burn agent was flame (58%), followed by hot oil (15%) and scald (13%), with other agents the cause of injury for eight of the total.

Table 2. Demographic characteristics of patients in the two groups.

Gender	Group 1	Group 2	Total	%
Female	6	7	13	18.1
Male	30	29	59	81.9
Age (mean, range)	38.1	33.4		
%TBSA (mean, range)	8.9	9.5		

Table 3. Common agents causing burn injury in the two groups.

Agent	Group 1	Group 2	Total	%
Flame	18	25	43	59.7
Hot oil	7	4	11	15.3
Scald	7	3	10	13.9
Other	4	4	8	11.1
Total	36	36	72	100

Table 4 shows that deep partial burns were the most common depth of injury (41%), followed by superficial burns (20%), partial thickness burns (20%) and mixed depth burns (16%). There were no full thickness burns.

Antibiotic usage

There was a statistically significant (p=0.016) decrease (50%) of antibiotic usage with Acticoat dressings compared to SSD. Antibiotic use was required by 26 (36.1%) of the 72 patients reviewed. Of those patients receiving SSD dressings (audits 1 and 3), 61.1% required antibiotic therapy, compared with 11.1% who received Acticoat dressings (Table 5).

Table 6 shows swab results and corresponding antibiotic use. Of the 22 patients in the SSD group receiving antibiotic therapy, 22.7% returned a positive wound swab result, 50% returned a result where no pathogens were isolated, and 27.2% had no wound swab taken.

In comparison, of the four patients in the Acticoat group receiving antibiotic therapy, 50% returned a positive wound swab result, 25% returned a result where no pathogen was isolated, and 25% of patients did not have a wound swab taken.

Therefore more patients received antibiotic therapy when dressed with SSD cream despite no microbiological evidence of infection in the wound swabs.

Surgical requirements

Table 7 shows that approximately half of the patients reviewed in the audit required surgical intervention, including debridement and split skin grafting, or cultured epithelial autograft. This included 24 patients who received SSD and nine who received Acticoat dressings. A total of 11 patients, nine who received SSD dressings and two who received Acticoat, experienced wound breakdown. In this study,

Table 4. Clinical characteristic of patients in the two groups.

Factor (depth)	Group 1	Group 2	Total	%
Superficial	7	8	15	20.8
Partial	6	9	15	20.8
Deep	14	16	30	41.7
Full	0	0	0	0
Mixed	9	3	12	16.7
Total	36	36	72	100

Table 5. Comparison of antibiotic usage Acticoat and SSD cream.

Group		Antibiotic usage events No.	%	Significance Chi square
Group 1	SSD	22/36	61.1	p=0.016*
Group 2	Acticoat	4/36	11.1	

*Statistically significant at the p=0.05 level

Table 6. Swab results and corresponding antibiotic use.

Group		Antibiotic therapy		Positive swab		No pathogen isolated on swab		No swab taken	
		n	%	n	%	n	%	n	%
Group 1	SSD	22/36	30.5	5/22	22.7	11/22	50	6/22	27.2
Group 2	Acticoat	4/36	5.5	2/4	50	1/4	25	1/4	25.0

Table7. Surgical intervention and wound breakdown in the Acticoat and SSD cream groups.

Group		Debridement and skin grafting	Debridement and CEA	Debridement, CEA and skin grafting	Total no. requiring surgery	Wound breakdown
Group 1	SSD	4	2	18	24/36	9
Group2	Acticoat	2	2	5	9/36	2

CEA = Cultured Epithelial Autograft

wound breakdown is defined as a healed burn or graft that has suffered skin loss, resulting in a further wound to the area.

Length of stay

The mean LOS for those patients receiving Acticoat showed a statistically significant decrease (p=0.045); 8.8 days compared with a LOS of 15.1 days in the SSD group.

Discussion

Every intervention from the time of burn injury influences the ultimate healing of the burn wound. Tissue salvage and consequently minimising infection is paramount. The healing process is initiated as the acute inflammatory response at the time of injury. At the site of injury, the blood vessels dilate and become more permeable. Macrophages migrate into the site of injury and, through phagocytosis of debris and bacteria, attempt to control infection. Nutrients are released to sustain the cells, protecting against infection, and fibrin is formed, preventing the spread of infection. A layer of yellow slough or eschar also becomes visible due to the debris from phagocytosis.

During the inflammatory response, the site of injury is characterised by erythema, heat, oedema, pain and loss of function of the area, which are the signs of suspected infection [14]. It is widely recognised that the inflammatory response is a vital element of the process of wound healing. Optimal inflammatory response is essential in achieving healing. If this response is impaired or its progression impeded, the wound healing process is also affected [15].

Burn injury results in impairment to the skin barrier, providing access for bacteria; it has been shown to initiate inflammatory and immune impairment [16]. In patients with burn injuries over 25% TBSA, this response is further compromised [6].

In determining whether Acticoat is a more effective antimicrobial agent than SSD, there is conflicting evidence. Previous *in vitro* research has found SSD to be a more effective topical antimicrobial agent compared to Acticoat [5]. Other studies, however, report the reverse, with Acticoat being more valuable than other topical antimicrobial products [2, 7, 17].

Antibiotic usage

In the present study, 11% of patients receiving Acticoat were prescribed antibiotic therapy, compared to 61% in the SSD group. This is of major significance, considering the mean %TBSA of both groups was similar – Acticoat 9.5%, SSD 8.9%.

Is it possible that the inflammatory response, or the appearance of inflammatory response, is exacerbated by the use of SSD dressings? Of the 22 patients receiving SSD dressings and antibiotics, half returned a wound swab where no pathogens were isolated. Five patients receiving SSD and antibiotics returned a positive wound swab and six did not have swabs taken yet still received antibiotic therapy. Of the four patients receiving Acticoat dressings and antibiotics, two returned positive wound swabs, one patient's swabs did not isolate pathogens and one patient did not have swabs taken.

SSD may exacerbate the appearance of inflammatory response but not necessarily constitute clinical wound infection. Therefore wound appearance is not a reliable gauge of burn wound infection.

The question raised is the whether wound swabs should be routine practice in burn wound care prior to the commencement of antibiotic therapy. There is conflicting evidence on this matter. Whilst it is acknowledged that wound swabs are routinely performed to verify a suspicion of infection, there is minimal research to support the sole use of swabbing in the diagnosis of infection [18]. One study, however, reported that wound swabs are adequate to determine appropriate antibiotic therapy [19]. The present audit supports the practice of the routine swabbing of wounds for the presence of infection prior to the prescription of antibiotics.

While the inflammatory response may be heightened by SSD, as discussed previously, SSD forms a yellow-grey eschar over the wound surface [11]. This eschar is a moist or macerated and irregular surface, which promotes the proliferation of bacteria [6]. Acticoat does not form this eschar. Therefore the higher number of positive swab results ad increased use of antibiotic therapy in the SSD group may be due to the formation of an eschar, which may promote the migration of bacteria.

Surgical requirements

The present study also found that the Acticoat group required less surgery than the SSD group. This may be indicative that less patients in the Acticoat group received antibiotic therapy than those in the SSD group, and the healing time was reduced due to a normal inflammatory response [20].

Other authors have reported that both dressings delay wound healing due to the impairment of re-epithelialisation by the silver in both products [8, 21, 22]. In the RPH burn unit, routine dressing practice is to apply a hydrocolloid dressing directly over the Acticoat, if the burn is not clinically infected, from Day 3 post burn injury. This may also contribute to the need for less surgery in the Acticoat group, in contrast to the SSD

group, as hydrocolloids promote moisture and thus re-epithelialisation[8]. Due to the use of hydrocolloid dressings, moist wound healing may increase the rate of epithelialisation and therefore decrease the need for surgical intervention in the Acticoat group.

The ability of Acticoat to prevent eschar formation may also account for that group's reduced need for surgical intervention. Over partial thickness burns, a yellow-grey pseudo eschar is formed when dressed with SSD. This eschar may mask the depth of burn, making assessment difficult, which may have impacted on the number of surgeries in the SSD group compared with the Acticoat group.

It is suggested that the heightened need for surgical intervention in the SSD group compared to the Acticoat group may have also impacted on the occurrence of wound breakdown. Nine patients in the SSD group experienced wound breakdown, compared with two patients in the Acticoat group.

Length of stay

The increased use of antibiotics, surgical intervention, and further treatment due to wound breakdown in the SSD group may account for the mean LOS in the burn unit of 15.1 days. This is 6.3 days more than those patients receiving Acticoat dressings.

Conclusion

The findings of this study indicate that Acticoat is more effective than SSD in relation to the reduction in antibiotic use. The basis for this finding may originate on the false assumption that antibiotic use equates with the presence of infection.

This study has demonstrated that antibiotic use equates with suspicion of infection. This suspicion of infection is assessed using visual inspection of signs and symptoms and, infrequently, wound swabs. Compared to Acticoat, SSD alters the appearance of the burn wound, which may affect the visual assessment of the wound, resulting in the prophylactic prescription of antibiotic therapy, surgical intervention, wound breakdown and increased LOS in the burn unit.

Acknowledgments

The authors wish to acknowledge the contribution of Bess Fowler in the preparation of this manuscript.

References

1. Garner JS, Jarvis WR, Emori TG, Horan TC & Hughes JM. CDC definitions for nosocomial infections. Am J Infect Control 1988; **16(3)**:128-40.
2. Tredget EE, Shankowsky HA, Rennie R, Burrell RE & Logsetty S. Pseudomonas infections in the thermally injured patient. Burns 2004; **30(1)**:3-26.
3. Lansdown ABG. Silver 1: its antibacterial properties and mechanism of action. J Wound Care 2002; **11(4)**:125-130.
4. Fox CL & Modak SM. Mechanism of silver sulfadiazine action on burn wound infections. Antimicrob Agents Chemother 1974; **5(6)**:582-588.
5. Frazer JF, Bodman J, Sturgess R, Faoagali J & Kimble RM. An *in vitro* study of the anti-microbial efficacy of a 1% silver sulphadiazine and 0.2% chlorhexidine digluconate cream, 1% silver sulphadiazine cream and a silver coated dressing. Burns 2004; **30**:35-41.
6. de Gracia CG. An open study comparing topical silver sulfadiazine and topical silver sulfadiazine-cerium nitrate in the treatment of moderate and severe burns. Burns 2001; **27(1)**:67-74.
7. Tredget EE, Shankowsky HA, Groeneveld A & Burrell R. A matched-pair, randomized study evaluating the efficacy and safety of Acticoat silver-coated dressing for the treatment of burn wounds. J Burn Care Rehabil 1998; **19(6)**:531-7.
8. Innes ME, Umraw N, Fish JS, Gomez M & Cartotto RC. The use of silver coated dressings on donor site wounds: a prospective, controlled matched pair study. Burns 2001; **27(6)**:621-7.
9. Voigt DW & Paul CN. The use of Acticoat as silver impregnated telfa dressings in a regional burn and wound care centre: the clinicians' view. Wounds: A Compendium of Clinical Research and Practice 2001; **13(2, Supp B)**:11-20.
10. Demling RH & DeSanti L. Effects of silver on wound management. Wounds: A Compendium of Clinical Research and Practice 2001; **13(1, Supp A)**:4-15.
11. Eldad A, Icekson M, Zur T, Slosser D, Maly A, Arielli D *et al.* Silver-sulfadiazine eschar pigmentation mimics invasive wound infection: a case report. J Burn Care Rehabil 2003; **24(3)**:154-7.
12. Pillai TA, Jalewa AK & Chadha IA. Antibiotic prophylaxis – Hobson's choice in burns management. Burns 1998; **24(8)**:760-2.
13. Apelgren P, Bjornhagen V, Bragderyd K, Jonsson CE & Ransjo U. A prospective study of infections in burn patients. Burns 2002; **28**:39-46.
14. Gardner SE, Frantz RA & Doebbeling BN. The validity of the clinical signs and symptoms used to identify localized chronic wound infection. Wound Repair Regen 2001; **9(3)**:178-86.
15. Hart J. Inflammation. 1: Its role in the healing of acute wounds. J Wound Care 2002; **11(6)**:205-9.
16. Heinrich SA, Messingham KA, Gregory MS, Colantoni A, Ferreira AM, Dipietro LA *et al.* Elevated monocyte chemoattractant protein-1 levels following thermal injury precede monocyte recruitment to the wound site and are controlled, in part, by tumor necrosis factor-alpha. Wound Repair Regen 2003; **11(2)**:110-9.
17. Yin HQ, Langford R & Burrell RE. Comparative evaluation of the antimicrobial activity of Acticoat antimicrobial barrier dressing. J Burn Care Rehabil 1999; **20(3)**:195-200.
18. Miller M. How do I diagnose and treat wound infection? Br J Nurs 1998; **7(6)**:335-338.
19. Slater RA, Lazarovitch T, Boldur I, Ramot Y, Buchs A, Weiss M *et al.* Swab cultures accurately identify bacterial pathogens in diabetic foot wounds not involving bone. Diabetic Med 2004; **21(7)**:705-709.
20. Wright JB, Lam K, Buret AG, Olson ME & Burrell RE. Early healing events in a porcine model of contaminated wounds: effects of nanocrystalline silver on matrix metalloproteinases, cell apoptosis and healing. Wound Repair Regen 2002; **10(3)**:141-51.
21. Poon VK & Burd A. *In vitro* cytotoxicity of silver: implication for clinical wound care. Burns 2004; **30(2)**:140-7.
22. Bugmann P, Taylor S, Gyger D, Lironi A, Genin B, Vunda A *et al.* A silicone-coated nylon dressing reduces healing time in burned paediatric patients in comparison with standard sulfadiazine treatment: a prospective randomized trial. Burns 1998; **24(7)**:609-12.