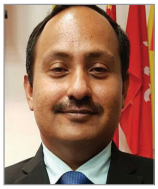
Managing infection in chronic wounds with nano colloidal silver



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Wound infections present a significant clinical challenge that impacts on patient morbidity and treatment cost. This case study evaluated patients receiving standard wound management coupled with a nano colloidal silver (NCS) spray of 30 ppm. The evaluation included 17 patients (12 male, 5 female) aged between 27 to 77 years who presented with chronic non-healing wounds and treated using NCS. The patients were assessed using the hospital's standard protocol and received a minimum of two NCS applications per week, which was sprayed directly onto the wound prior to a secondary dressing application. This was continued until the symptoms of infection had cleared fully and wound healing was observed. The criteria used for wound healing was based on clinical observations which included reduction in signs of infection, such as inflammation, redness, exudate, odour, suspected biofilm and pain, and the observation of proper epithelialization of the wound. The majority of non-healing wounds were venous ulcers in origin and the average wound healing time was around 5 weeks. Swabs were not taken for this case study but will be needed for a more robust study.

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Wound infections present a significant clinical challenge, impacting on patient morbidity and treatment cost (Wilkinson et al, 2011). A chronic wound is a wound that does not heal in an orderly set of stages and in a predictable amount of time. Wounds that do not heal within three months can also be considered chronic (Iqbal et al, 2017). These commonly include diabetic foot ulcers (DFUs), venous ulcers (VUs) and other non-healing wounds, such as infected wounds, traumatic wounds and others. Management of these chronic non-healing wounds poses a great challenge because they are associated with underlying disorders and are prone to complications, including secondary infections and risk of amputation. Any wound that does not heal within a few weeks should be examined by a healthcare professional because it might be infected, or might reflect an underlying disease (Iqbal et al, 2017).

Recently, NCS received considerable interest for treating chronic non-healing wounds where it has shown its effectiveness by reducing bioburden and inflammation (Wilkinson et al, 2011). This may be due to the ability of NCS to release bigger Ag+ ions at a greater rate than any other silver-based treatments due to the form and size of the nanoparticles (Wang et al, 2017). The Ag+ ion is an active antimicrobial entity as it is capable to interfere with thiol (–SH) groups and provokes the generation of reactive oxygen species (ROS) — a major contributor to its antibacterial efficacy (Wilkinson et al, 2011). NCS can release Ag+ ions at a greater rate than bulk silver by virtue of their large surface area, so if released via a dressing, these also have the potential to cross biological compartments. This review aims to consolidate recent findings with regards to the efficacy and safety of different formulations of silver used as an antiseptic agent in dressings, summarising the features

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SPRAY

Nano Colloidal Silver, 30ppm

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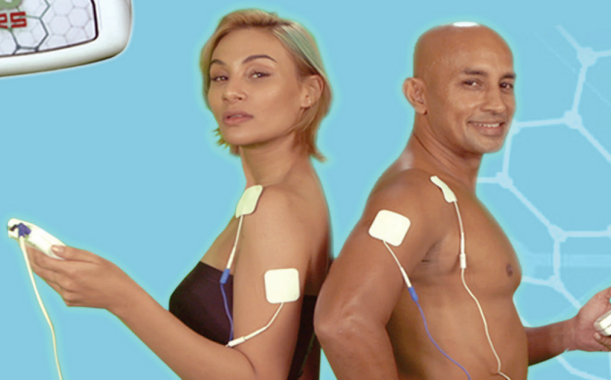

Table 1. Wound type and time to reduction in the bacterial bioburden (weeks)

No	Wound Type	Age	Gender	Initial size (cm^2)	Final size (cm^2)	Slough (initial) present	Slough (final) present	Biofilm (initial) present	Biofilm (final) present	No of weeks
1	VU	27	M	Multiple	N/A	No	No	Yes	No	7
2	VU	39	M	Multiple	Fully closed	No	No	Yes	No	9
3	VU	43	F	13.5	1.25	No	No	Yes	No	5
4	VU	63	F	37.5	12.5	No	No	Yes	Yes	6
5	VU	63	F	2.25	Fully closed	Yes	Yes	Yes	Yes	1
6	VU	36	M	36.0	26	No	No	Yes	No	7
7	VU	64	M	18.0	16.5	No	No	Yes	No	3
8	VU	51	F	10.0	6	No	No	Yes	No	3
9	VU	69	M	2.25	Fully closed	No	No	Yes	No	5
10	VU	37	M	4.0	3.28	No	No	Yes	No	5
11	DFU	65	M	11.25	10.5	No	No	Yes	No	3
12	DFU	59	M	42.9	22.65	No	No	Yes	No	7
13	DFU	67	M	5.0	1.0	Yes	No	Yes	No	7
14	DFU	65	M	35.0	13.0	No	No	Yes	No	5
15	TW	77	M	22.5	19.5	No	No	Yes	No	4
16	TW	77	M	25.5	241	No	No	Yes	No	7
17	IW	52	F	8.75	8.25	No	No	Yes	No	6

of NCS, with particular attention to the dose-dependencies for biological effects, highlighting the need for information on their uptake and potential biological effects (Wilkinson et al, 2011).

In the past, silver has been employed as an anti-microbial agent to prevent the transmission of bacteria. Medical applications are documented in the literature throughout the 17th and 18th centuries. The bactericidal activity of silver is well established. Silver nitrate was used topically throughout the 1800s for the treatment of burns, ulcerations, and infected wounds, and although its use declined after World War II (Roberts et al, 2017)and the advent of antibiotics, Fox revitalized its use in the form of silver sulfadiazine in 1968 (Politano et al, 2013).

This article reports on wound management using NCS as primary treatment in a Wound Care Clinic at the Department of Internal Medicine, Hospital Kuala Lumpur.

Material and methods

This clinical study was conducted at the Wound Care Unit, Department of Internal Medicine, Kuala Lumpur Hospital. The following materials and methods were used during the treatment:

- The wounds were cleansed with distilled water only
- NCS (30 ppm) was applied generously in two layers from a spraying distance of 10 cm
- After spraying the wound bed, the wound was closed with a secondary dressing (such as melolin, or polyurethane foam)
- For patients with VUs additional compression system bandages were used.

Study participants

A total of 17 outpatients (12 male and 5 female) between the age of 27 and 77 years with non-healing wounds were included for this observational case report. These patients had different types of chronic wounds, which included 2 Trauma Wounds (TWs), 1 Infected Wound (IW), 4 DFUs and 10 VUs.

Results

The patient distributions based on wound type and the results are displayed in *Table 1*. Out of the 17 patients, 10 (59%) had VUs with wound sizes ranging from 2.25 cm^2 to 25 cm^2, 4 (23%) had DFUs with wound size ranging from 5 cm^2 to 42.9 cm^2 and 3 (18%) had other non-healing wounds with wound size ranging from 8.75 cm^2 to 25.5 cm^2.

Out of the ten patients with VUs, 9 (90%) patients had exudating wounds with suspected biofilm, slough, heavy odour with signs of maceration *[Table 2]*. The average time to completely clear the infection in patients with VUs was observed to be around

5 weeks. Meanwhile, there were 4 (100%) patients with DFUs and 2 (75%) patients with TWs, all their wounds were suspected of have biofilm.

The infection signs in the DFUs and other non-healing wounds subsided in an average of 5 weeks. A limitation is that the swabs were not taken as this is a pilot study observing the usage of the new NCS.

The longest suspected infection eradication time, up to 9 weeks, was observed in patients with VUs. Out of all the patients, 3 experienced full wound closure.

Discussion

All of the 17 patients underwent a wound assessment, using the hospital's standard protocol, where trained wound care nurses look at the tissue visually for slough and suspected biofilm. On assessment, there were signs of infection and inflammation such as redness, suspected biofilm, slough and increased exudates in those patients with macerated wounds. The clinicians used NCS spray to clear infections. The products contained in the spray are active against a broad range of bacteria, fungi and viruses, including antibiotic-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococci* (VRE). Furthermore, there may be significant topical anti-inflammatory and analgesic effects that encourages blood vessel formation (neovascularization).

NCS has been shown to be active against bacteria because of its ability to be absorbed into the wound environment and the bacteria wall due to its nano form and size (Tian et al, 2007).

All the 17 patients showed good improvement in terms of wound size and reduction of signs of infection without any allergic reactions. It has been noted that all 17 cases had a 30% improvement. Depending on the wound size, the treatment was continued for around 4 to 5 weeks until the signs of infection was completely cleared. However, in patients with large wounds it took 7 to 8 weeks. NCS application was stopped once the infection symptoms had been cleared while dressings, such as foam dressings, continued to be applied until the full closure of the wounds.

Figures 1 to 7 show pictures of wounds of seven patients taken before NCS was applied and at the time the infection had fully cleared.

It appears that treating chronic wounds has become more of a challenge recently. Electron microscopy of biopsies from chronic wounds found that 60% of the specimens contained biofilm structures in comparison with only 6% of biopsies from acute wounds (James et al, 2008). These wounds are mainly those

Table 2. Wound type and infection signs

No	Type	Age	Gender	Biofilms suspected	Maceration	Exudate	Swelling	Pain	Odour
1	VU	27	M	√	√	√	0	0	√
2	VU	39	M	√	√	√	0	0	√
3	VU	43	F	√	√	√	√	√	√
4	VU	63	F	√	√	√	0	0	√
5	VU	63	F	√	√	√	√	√	√
6	VU	36	M	√	√	√	0	0	√
7	VU	64	M	√	√	√	0	0	√
8	VU	51	F	√	√	√	√	√	√
9	VU	69	M	√	√	0	0	0	√
10	VU	37	M	√	√	√	0	0	√
11	DFU	65	M	√	√	√	0	0	√
12	DFU	59	M	√	√	√	√	√	√
13	DFU	67	M	√	√	√	0	0	√
14	DFU	65	M	√	√	√	0	0	√
15	TW	77	M	√	√	√	√	√	√
16	TW	77	M	√	√	√	√	√	√
17	IW	52	F	0	√	0	√	√	0

Figures 1 to 7. Images of wounds taken before starting NCS application and at the time the infection had fully cleared.

Figure 1. A 59-year-old male with a DFU improved within 7 weeks

Figure 2. A 39-year-old male with a VU completely healed within 9 weeks

Figure 3. A 67-year-old male with a DFU improved within 7 weeks

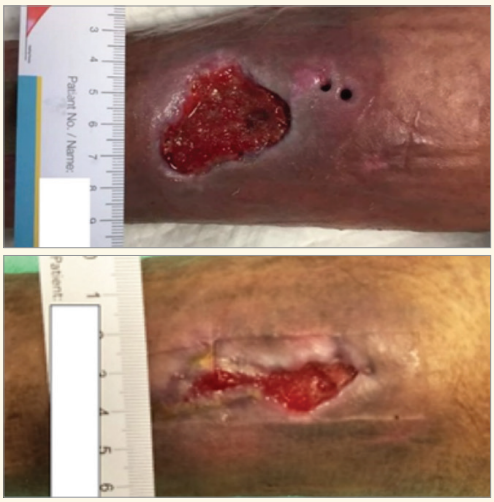

Figure 4. A 77-year-old male with a TW improved within 4 weeks

Figure 5. A 52-year-old female with a IW, which closed fully after 6 weeks

Figure 6. A 77-year-old male with a TW, which showed improvements within 7 weeks

Figure 7. A 51-year-old female with a VU, which improved within 3 weeks

associated with antibiotic-resistant bacteria which form biofilms that can resist the action of antibiotics and the human immune system (Phillips et al, 2010). It is known that both Gram-negative and Gram-positive bacteria can form biofilms, while the most common biofilm-forming bacteria associated with human disease are *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus viridans*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Pseudomonas aeruginosa* (Markowska et al, 2013).

Nevertheless, it has been known that biofilms are not resistant to nano silver particles (Richter et al, 2017) and the author observed in this clinical evaluation that NSC had been effective in reducing infection and managing the bio-burden, even though none of these patients were on any antibiotics.

Conclusion

In summary, it is safe to mention that NCS exerted a positive effect resulting in faster healing time and reduction in the bacterial bioburden, which has been proven to be an excellent option to achieve accelerated wound healing in managing wounds at primary health care centers. WAS

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