

Original Research Article

Silver colloid dressings score over conventional dressings in diabetic foot ulcer: a randomized clinical trial

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ABSTRACT

Background: Topical silver treatments and silver dressings are increasingly used for the local treatment of contaminated or infected wounds; however, there is a lack of clarity regarding the evidence for their effectiveness. To compare the outcome of silver colloidal based dressing in comparison to conventional dressing in management of diabetic foot ulcers.

Methods: This was a single institution prospective randomized controlled trial. Patients with Wagner grade 1 and 2 diabetic foot ulcer were enrolled in this study. Patients were assessed on day one and then at two weeks interval for twelve weeks for ulcer size by planimetry.

Results: Out of 25 patients, 13 were randomized to silver colloid group and 12 in conventional dressing group. Age and sex distribution was comparable among two groups. Total 29 ulcers were present in silver colloidal and conventional dressing group. Mean wound area in silver colloidal dressing group and conventional dressing group on admission was 36.8 and 20.46 cm² respectively. After 12 weeks of dressing mean wound area in silver colloidal dressing group and conventional dressing group decreased by 31.52 (85.65%) and 14.04 (68.62%) and after 12-week complete healing was seen in 11 (84.62%) patients in silver colloidal dressing group and 5 (41.67) patients in conventional dressing group.

Conclusions: The results suggest that silver colloidal based dressing had significantly better outcome in form of complete healing and decrease in ulcer size in comparison to conventional dressing in diabetic foot ulcers (p value <0.05).

Keywords: Diabetic ulcer, Nano silver in diabetic ulcer, Silver colloid in diabetic ulcer

INTRODUCTION

Wounds are either acute or chronic and can result from venous or arterial insufficiency, diabetes, burns, trauma, chronic pressure or surgery.^{1,2} Antiseptic agents also may control bacterial load and prevent the development of infection but may also be toxic to fibroblasts and other viable cells.³⁻⁶ However, Silver has only a very weak toxic potential and only rarely induces microbial resistance in vitro studies have demonstrated the

effectiveness of silver-based dressings against pathogenic bacteria.⁷⁻¹⁰ Thus, use of silver-releasing dressings in conjugation with debridement on wounds at risk of developing infection is beneficial.^{3,11,12} Nanotechnology has facilitated the production of very small size silver particles with increasingly large surface area to volume ratios. Which imparts greater antimicrobial efficacy and most importantly lowers their toxicity to human tissue cell.¹³ The use of silver as a prophylactic and treatment for infection and other diseases dates back to about 1000

BC, when the ancient Greeks and the Romans used it as a disinfectant.^{14,15}

The purpose of this single centre randomized control study was to compare the efficacy of silver colloidal dressings versus conventional dressings in management of diabetic foot ulcers.

METHODS

All the cases of diabetic foot either admitted or attending Out Patient Department with diabetic foot over a period of one year with Wagner Grade 1 and 2 were enrolled in this study. Patients with foot ulcer and fasting blood glucose level more than 126 mg/dL or patients with known diabetes mellitus were included in the study. In addition to detailed history thorough clinical examination included assessment of foot ulcer according to Meggitt-Wagner Grading, examination of peripheral pulses, examination of peripheral nerves for sensory, motor or autonomic loss and systemic complications of diabetes mellitus if any. All the patients were subjected to routine investigations including lipid profile, glycosylated hemoglobin (Hb1Ac), 24 hours urinary proteins, urinary ketone body, bacteriological culture, X-ray foot, fundus examination, ECG, USG kidneys and Doppler's study of lower limb.

Inclusion criteria

All adults with a diabetic foot ulcer of at least 2 cm² falling under Wagner grade I and II of at least 30 days duration.

Exclusion criteria

- All causes of foot ulcer, which can be attributed to other coexisting disease like paraplegia, varicose, vein etc.
- Patients suffering from a condition that interfered with wound healing e.g., carcinoma, vasculitis, connective tissue disease, an immune system disorder, treatment with corticosteroids, immunosuppressive agents, radiation therapy, chemotherapy
- Patient with known hypersensitivity to colloidal silver gel.

Evaluation of role of colloidal silver dressing

37 patients were divided into two groups: Conventional dressing group and silver colloidal dressing group. Conventional dressings group managed with debridement and povidone iodine/saline dressings. Silver colloidal dressing group was managed with debridement and application of silver colloidal gel dressing. Patients were assigned to these groups by alternate manner i.e. first patient of grade 1 or 2 was assigned to conventional group and second patient was assigned to silver colloidal group. Patients were managed and followed up for 12

weeks at two weeks interval and progress was assessed as follows:

- Evaluation of ulcer by planimetry on first day and subsequently after every two weeks; greatest length and width of wound was measured in centimeters
- Pus culture for aerobic and anaerobic microorganism on first day and subsequently every two weeks
- Debridement as and when required
- In conventional dressing group, daily dressing was done with povidone iodine/saline
- In silver colloidal group, wound was thoroughly debrided and colloidal silver gel was applied to either completely fill the deep ulcers or cover the entire superficial ulcers. No other chemical was used
- Amoxicillin clavulanic acid was started empirically for all patients and thereafter switched over to other culture sensitivity guided antibiotics.

Primary study point

At the end of study period of 12 weeks, the patients were categorized as follow:

- *Complete responder*: Complete healing of leg ulcer
- *Partial responder*: 50% or greater reduction in the product of the two longest perpendicular diameters from baseline
- *Non-complete responder*: Less than 50% reduction in the product of the two longest perpendicular diameters from the baseline
- *Non-responder*: No reduction in ulcer area or increase in ulcer area over baseline.

RESULTS

Total 37 patients of Wagner grade 1 and 2 ulcer recruited in this study. These patients were further divided in to two groups; 18 patients who received silver colloidal based dressing were labeled as "Silver group" and 19 patients who received conventional dressing were labeled as "Conventional group". Almost all patients were diabetic for 6-15 years. 05 patients in silver group and 07 patients in the conventional group were lost to follow up or opted out of the study, leaving 13 and 12 patients in each group at the end of 12 weeks. The two groups were comparable for age and sex. The mean age of silver group was 58.23±11.59 (male-9, female-4) and in conventional group the mean age was 54.08±10.33 year (male-8, female-04). Most patients had single ulcer except for three in the silver group and one in the conventional group with two ulcers each in the same limb. Thus, total 29 ulcers were present in silver and conventional group. According to Wagner's classification, in silver colloidal group out of 16 ulcers, 08 (50%) ulcers were grade I and 08 (50%) ulcers were grade II. In conventional group out of 13 ulcers, 07 (53.85%) ulcers presented with grade I and 06 (46.15%) ulcers presented with grade II. Mean wound area in silver and conventional group on admission was 36.8 and

20.46 cm² respectively, and at 12 weeks it decreased 5.28 and 6.42 cm² respectively (Table 1). After 4th week of dressing, in silver group, there were 02 complete responders, 08 partial responders, and 03 non-complete responders. In conventional group, 04 patients were partial responders and 08 patients were non-complete responders (Table 2). After 8th week of dressing, in silver group, there were 03 complete responders, and 10 partial responders. In conventional group, there were 07 partial responders and 05 non-complete responders (Table 2).

After 12 weeks, complete healing was seen in 11 (84.62%) patients in silver colloidal dressing group and 5 (41.67) patients in conventional dressing group (p value < 0.05) (Table 2).

The percentage decrease in wound area after 12 weeks of dressing in silver and conventional group was 85.63% and 68.63% respectively (Table 1).

Table 1: Response to dressing in term of decrease in wound area in cm² (n=25).

	On admission	2 nd week	4 th week	6 th week	8 th week	10 th week	12 th week	Decrease in wound area after 12 weeks (%)
Silver group (Mean area in cm ²)	36.8	29.89	21.65	16.84	11.8	7.185	5.28	85.63%
Conventional group (Mean area in cm ²)	20.46	18.23	15.2	12.94	9.96	8.01	6.42	68.63%

Table 2: Healing response in silver and conventional dressing group after 4th/8th/12th week (n - 25).

Patients	Silver colloidal group number (%)			Conventional group number (%)		
	4 th week	8 th week	12 th week	4 th week	8 th week	12 th week
Complete responders	2 (15.38)	3 (23.7)	11 (84.6)	0	0	5 (41.6)
Partial responders	8 (61.53)	10 (76.9)	2 (15.38)	4 (33.33)	7 (58.3)	7 (58.33)
Non-complete responders	3 (23.07)	0	0	8 (66.66)	5 (41.76)	0
Non-responders	0	0	0	0	0	0

DISCUSSION

One of the earliest publications to mention silver was a textbook, The Surgeons Mate, published in 1617 by John Woodall, surgeon-general to the East India company.¹⁶ By the early 20th century, silver and its compounds were readily used by medical professionals to counter bacterial infections in acute and chronic wounds, including burns.¹⁷ Silver dressings contain silver atoms that are slowly released as positively-charged silver cations (Ag⁺), which have a strong antimicrobial effect: they bind to bacterial cell wall, causing disruption of the wall and the death of the bacteria.^{18,19} Ag⁺ ions also bind to bacterial enzymes thereby preventing them from performing their function as well as to bacterial cell DNA, thus interfering with cell division and replication.¹⁸

Although the multifaceted effect of silver carries a low risk of resistance, studies in burn wounds have shown that bacteria (in particular *Pseudomonas* species) may become resistant to SSD and silver nitrate.²⁰ The amount of silver incorporated in the various dressings and the rate

of release of Ag⁺ ions appear to influence the resulting antimicrobial effect.^{21,22}

Another potential concern is that silver does not act specifically against bacteria, but acts on any alien and host proteins. Hence, when relatively few bacteria are present in the wound the effect on host tissue is greater, and that could slow down healing.²³

Nanotechnology has facilitated the production of smaller silver particles with increasingly large surface area to volume ratios. Which impart greater antimicrobial efficacy and most importantly lowers their toxicity to human tissue cell Evolution of nano silver (NS) particles has overcome the toxicity limitations posed by silver ions. NS in contrast to silver ions, actually possesses beneficial anti-inflammatory activity, thus leading to greater efficacy in wound healing along with lower toxicity.^{24,25}

It is thought that dressings act as barriers against exogenous bacteria and, therefore, prevent wound contamination or infection.²⁶ Topical agents used with

dressings to treat wound infections include antibiotics, antiseptics or disinfectants, as these agents destroy micro-organisms or limit their growth. The choice of dressings and topical agents for contaminated and infected wounds is not always based on a firm rationale.²⁷ In the trial of Münter, patients treated with silver-containing foam experienced less pain, showed a quicker reduction of odour, and required less frequent dressing changes due to leakage. These secondary advantages of silver can be used in balancing the pros and cons for the use of silver.¹²

The mean age in this study group in different Wagner grade was, 56.2 year in Grade I, 54.2 year in Grade II. Most of the patients in our study were between the ages of 41-70 years. Highest numbers of diabetic foot ulcers were persons aged 45-64 years. The older the patient, the more likely are the chances of developing peripheral vascular disease there by the diabetic foot.^{28,29} Mean age of presentation in silver colloidal dressing group was 58.23±11.59 year, conventional dressing group was 54.08±10.33 year. In this study, high incidence of diabetic foot was seen in the patients with the previous history of Diabetes mellitus for last 6-15 years. The duration of diabetes is well established risk factor for diabetic foot.³⁰ Late complications of diabetes mellitus including diabetic foot generally develop about 15 years after appearance of hyperglycemia.²⁸

History of antecedent trauma to foot was present in majority of patients (76%). Minor trauma often footwear related has been reported as most frequent cause leading to development of lower extremity ulcers in diabetic patients.³¹ In this study, 62% patients had inadequate blood sugar control. Mean of random blood sugar (RBS) was 241.94±86.65 mg/dL and fasting blood sugar (FBS) was 197.04±88.79 mg/dL. In present study, mean wound area in silver and conventional group on admission was 36.8 and 20.46 cm² respectively. After 12 weeks of dressing mean wound area in silver and conventional group was 5.28 and 6.42 cm² respectively (Table 1). The percentage decrease in wound area after 12 weeks of dressing in silver and conventional group was 85.63% and 68.63% respectively (Table 1).

After 12th week of dressing, in silver group there were 11 complete responders and 02 were partial responders. In control group, 05 patients were complete responders and 07 were partial responders (Table 2). While comparing the healing response in silver and conventional group it was noticed that diabetic foot ulcers showed accelerated healing in silver group.

It is reported that colloidal (nano) silver particles promote wound healing and reduce scar appearance and that cytokines play an important role in these processes by their capacity to decrease wound inflammation and modulate fibrogenic cytokines. Nanosilver induces apoptosis primarily in inflammatory cells in the dermis and clearly resolve inflammation by removing the inflammatory cells safely. It increases the rate of wound

closure, which occurs through promotion of proliferation and migration of keratinocytes and helping differentiation of fibroblasts in to myofibroblasts, thereby promoting wound contraction.³²

Nanocrystalline silver dressing achieves the highest silver concentration with sustained release of silver. It acts as an antimicrobial barrier apart from antibacterial action and help to reduce the risk of cross-contamination and cross infection of multi-resistant pathogen like MRSA.³³ Reduction in the use of antimicrobial medicine has been seen in diabetic ulcer cases with the use and application of topical NS. On the other hand, use of iodine preparations have been criticized because povidone-iodine, unless highly diluted, is toxic to most cell types and implicates in healing process.³⁴ The Contop trial evaluated 352 chronic non-healing ulcers in which venous leg ulcers were present in 43-48%, mixed venous/arterial in 20-24%, pressure ulcers in 10% and diabetic foot ulcers in 5-9%. The primary dressing type consisted of a foam or alginate in 45%, hydrocolloid or film in 15%, gauze in 4%, antimicrobial in 30% (silver foam in 48% of these) and a range of other dressings in the remaining 6%. There was a 50% reduction in wound size by Week 4 in those treated with the silver foam, compared to a 30% reduction in the (combined) standard-care groups, with p=0.002 for the difference.¹²

In an another non-randomised trial, 27 patients with diabetic foot ulcers, a silver-containing foam was used for 4 weeks. Six ulcers in these patients were not treated with a silver dressing and served as a control group. Four treated patients healed completely and the average healing with the silver dressed ulcers was 56% of initial area.³⁵

CONCLUSION

The silver colloidal based dressing had better results in comparison to conventional dressing in the management of diabetic foot both in form ulcer healing as well as reduction in ulcer size. Further, considering the cost of hospitalization and reduced burden on health care system the silver colloidal dressing is a cost effective option in chronic non-healing diabetic ulcers as compared to conventional dressing.

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Ethical approval: The study was approved by the institutional ethics committee

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