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Original research article

A comparative assessment of wound healing with normal saline and ionized nano-crystalline silver dressing given among patients with chronic diabetic foot ulcer

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Abstract

Background: Diabetic foot is a broad spectrum term which includes infection, ulceration and foot gangrene. Proper assessment of wound along with an aggressive multidisciplinary approach can reduce the risk of limb amputation. Wound dressings play an important role in diabetic foot care management. Nano crystalline silver ion dressing is a newer modality that has been in consideration for the treatment of diabetic wounds.

Aim: This study was aimed to compare on the wound healing effectiveness of with normal saline and ionized nano-crystalline silver dressing among chronic diabetic foot ulcer patients.

Material and methods: A Prospective study was conducted in the Department of General Surgery, Patna Medical College and Hospital, Patna, Bihar, India for 15 months. Total 80 diabetic patients with leg and foot ulcers with age 20 to 75 years were include in this study. In 40 patients, ionized nano-crystalline silver dressing was given. In another 40 cases, normal saline was used for wound dressing. Area of the ulcer, development of granulation tissue and size of the ulcer were measured over 2 days interval. Each patient was studied for three weeks or until discharge of the patient. **Results:** Total 80 diabetic patients were included in the study. No statistically significant difference could observe among any of the demographic details between the groups. 40 patients were included in the group 1 whose ulcer was dressed with normal saline. 40 patients included in the group 2, whose ulcer were dressed with ionized nano-crystalline silver. Reduction width of wound on 15th day was found to be almost double in the ionized nano silver dressed group when compared to the normal saline group ($p=0.001$). The mean areas of reduction of wound on 15th day in the saline and ionized nano silver dressings were 22.36±10.37 and 40.58±19.87, respectively. The areas of reduction of wound on the 1st day of dressing were 1.39±0.73 and 2.77±1.41, respectively in the normal saline and ionized nano crystalline silver dressed groups. All the parameters were found statistically significant between the groups ($p<001$). The healing rate was found maximum of 1.6 mm/day with an average value of 0.7 mm/day in the silver dressed group. In the group 1 patients where the ulcer was dressed with normal saline; the healing rate was found 1.3 mm/day with an average value of 0.5 mm/day. The dull red and unhealthy observation was found in the normal saline treated group while in the ionized nano crystalline silver treated group, the granulation tissue was bright red and healthy. The percent reduction of ulcer with ionized nano crystalline silver was 2.82% per day and with normal saline dressings is 1.39% per day, which was significant (<0.001). **Conclusion:** we conclude that the nano-crystalline silver, a cost-effective agent as an early intervention in the management of diabetic foot ulcer along with systemic antibiotics to reduce the rate of amputations. **Keywords:** Diabetic foot ulcer, Neuropathy, Nano-crystalline silver, Normal saline

Introduction

The prevalence of diabetes is increasing rapidly with more than 62 million cases in India.[1,2] Long-term effects of diabetes include retinopathy, nephropathy and neuropathy. Diabetic foot is a blanket term for foot disorders such as infection, ulceration or destruction of deep tissues due to peripheral neuropathy and ischemia from peripheral vascular disease.[3] The diabetic foot ulcers take time to heal and require great care. Offloading and debridement of the wound expedites the healing process, however in wounds of advanced grade and stage vascular repair or amputation might be required. At least 40% of these amputations can be prevented with a team approach to wound care.[4] The selection of wound dressings plays a pivotal role in diabetic wound care management. An ideal dressing should be cheap, easy to use, non adherent, non allergic, maintain a moist wound environment, absorb excessive exudates, allow gaseous exchange, control wound odour, provide thermal insulation and mechanical protection, prevent wound contamination and lower the risk of infections.[5] Numerous dressings are available like Saline, hydrogels, hydrocolloid, foam, alginate, Paraffin (Tulle), Polyurethane, silver impregnated dressings. Saline dressings are inexpensive and provide an atraumatic moist environment but the maintenance of the moist environment is a problem with these dressings. Hydrogel dressings provide adequate hydration and analgesic effect for dry wounds with necrotic eschar.[6,7] Hydrocolloid dressings provide more consistent moisture retention, absorb low to moderate level of exudates and retain growth factors which promote granulation.[6,7] Foam and alginate dressings are highly absorbent and can aid in decreasing the risk for maceration in wounds with heavy exudates.[6,7] Paraffin dressings offer the advantage of low adherence with lesser trauma during dressing removal.[7] Polyurethane dressings are transparent and enable proper wound monitoring.[7] Hyperbaric oxygen therapy, vaccum assisted devices and culture skin substitutes are other wound therapies that have been advocated.[6,7] Silver dressings using silver nitrate or silver sulfadiazine have the limitation of rapid inactivation of silver by the wound fluid, which is compensated by frequent replacement but it results in excess of silver being delivered to the wound. Nano crystalline silver ion dressing is an effective antimicrobial barrier composed of an absorbent inner core that maintains a moist environment optimal for wound healing and outer layers of silver coated polyethylene nets which prevent wound contamination and exhibit bactericidal effect.[8] Waterproof top film with visible strike through indicates when dressing change is required. To achieve a broad spectrum bactericidal effect, silver ions concentration must be at least 30-40 mg/l. Nano crystalline silver ion dressings provides concentration of silver at 70-100 mg/l which is bactericidal and kills over 150 types of pathogens. It releases as much as 30 times silver ions which allows dressing changes to be reduced from once or twice daily to every second or third day.[9] A continuous equilibrium of aqueous silver is maintained for over 48 hours and silver is released at good concentration levels even when water volume is doubled at 24 hours. Nano crystalline silver ion dressings have been in use for burns and chronic wounds.[8,10-13] , but the literature on their use in diabetic wounds is limited. So, the present study was conducted to study the effect of nanocrystalline silver ion dressings and its comparison with standard normal saline dressings in diabetic foot ulcers. Therefore, this study was aimed to compare effectiveness of standard normal saline dressing and ionized nano-crystalline silver dressing.

Material and methods

A Prospective study was conducted in the Department of General Surgery, Patna Medical College and Hospital,Patna, Bihar, India for 15 months, after taking the approval of the protocol review committee and institutional ethics committee.

Inclusion criteria

- Total 80 diabetic patients with leg and foot ulcers,
- Age 20 to 75 years

Exclusion criteria

- Patients suffering from immunodeficiency,
- Malignancy
- Patients under treatment with steroids

Methodology

All patients underwent a detailed history and clinical examination. Systemic antibiotics were given in culture positive cases. Complete control of diabetes was done. Blood sugar was monitored and maintained the euglycemic state using insulin and oral hypoglycemic agents during the therapy. After removing slough from the wound, dressing was given. In 40 patients, ionized nano-crystalline silver dressing was given. In another 40 cases, normal saline was used for wound dressing. Clinical assessment was done with serial photography of the ulcer. Area of the ulcer, development of granulation tissue and size of the ulcer were measured over 2 days interval. Each patient was studied for three weeks or until discharge of the patient.

Results

Total 80 diabetic patients were included in the study. The demographic data of the patients were given in Table 1. No statistically significant difference could observe among any of the demographic details between the groups. All the patients were followed up until the completion of the study. No adverse effect or incident was observed during the period of the study.

Table 1: Demographic and clinical profile of the patients

Demographic and clinical parameter	Groups		P value
	Ionized nano- crystalline silver dressing (n=40)	Normal saline (n=40)	
Age (years)	57.8±10.12	58.2±11.7	0.758
Gender	Male 33 Female 7	Male 34 Female 6	0.455*
Duration of diabetes (years)	11.7±8.1	14.7±11.22	0.487
Serum glucose (mg/dl)	312.1±51.65	278.7±68.98	0.0658
HbA1C (%)	7.7±0.4	7.3±0.6	0.914
Initial ulcer width length (mm)	33.2±19.5 80.9±40.36	29.1±20.2 72.4±25.66	0.522 0.236

*Fisher's exact test

40 patients were included in the group 1 whose ulcer was dressed with normal saline. 40 patients included in the group 2, whose ulcer were dressed with ionized nano-crystalline silver. The rate of wound healing and observation of the granular tissue were given in Table 2. Reduction of both wound length or width was evidenced in the ionized nano silver dressed group with the normal saline dressed group. Reduction width of wound on 15th day was found to be almost double in the ionized nano silver dressed group when compared to the normal saline group (p=0.001). The mean areas of reduction of wound on 15th day in the saline and ionized nano silver dressings were 22.36±10.37 and 40.58±19.87, respectively. The areas of

reduction of wound on the 1st day of dressing were 1.39±0.73 and 2.77±1.41, respectively in the normal saline and ionized nano crystalline silver dressed groups. All the parameters were found statistically significant between the groups (p<001). The observation of the granulation tissue developed was given in Table 3

Table 2: Effect of nano-crystalline silver and normal Saline dressing on diabetic foot ulcer

Observation	Group	N	Mean±SD	P value
Reduction of length on 15th day (mm)	Normal saline	40	7.11±2.65	0.001
	Nano crystalline silver	40	17.11±15.37	
Reduction of width on 15 days (mm)	Normal saline	40	3.55±2.69	0.001
	Nano crystalline silver	40	7.36±4.68	
Reduction of length on 1st day (mm)	Normal saline	40	0.38±0.22	0.003
	Nano crystalline silver	40	1.16±0.97	
Area of reduction on 15th day (mm^2)	Normal saline	40	22.36±10.37	0.001
	Nano crystalline silver	40	40.58±19.87	
Area of reduction 1st day (mm^2)	Normal saline	40	1.39±0.73	0.001
	Nano crystalline silver	40	2.77±1.41	

Table 3: Effect of nano-crystalline silver and normal saline on granulation tissue

Groups	Material used for ulcer dressing	Maximum and average healing rate/day (mm)	Granulation tissue developed
1 (n=40)	Normal saline	1.3, average: 0.5 mm	Dull red and unhealthy
2 (n=40)	Nano crystalline silver	1.6, average: 0.7 mm	Bright red and healthy

The healing rate was found maximum of 1.6 mm/day with an average value of 0.7 mm/day in the silver dressed group. In the group 1 patients where the ulcer was dressed with normal saline; the healing rate was found 1.3 mm/day with an average value of 0.5 mm/day. The dull red and unhealthy observation was found in the normal saline treated group while in the ionized nano crystalline silver treated group, the granulation tissue was bright red and healthy. The percent reduction of ulcer with ionized nano crystalline silver was 2.82% per day and with normal saline dressings is 1.39% per day, which was significant (<0.001).

Discussion

The present study reported that wound dressing with ionized nano-crystalline silver showed a healing rate of maximum of 1.6 mm/day and average healing rate of 0.7 mm/day with bright red and healthy granulation tissue. Ulcer dressed with normal saline showed a maximum healing rate of 1.3 mm/day and average healing rate of 0.5 mm/day and the granulation tissue developed was dull red and unhealthy. Silver has efficacy against wide spectrum of bacteria, virus and fungal infections.[14] Silver-based compounds have been using in wound care since early 1970. Among them, silver nano compounds attracted recently as silver nano particles may enter into the cell via pinocytosis and endocytosis. Entry into the cell is followed by damage to deoxyribonucleic acid (DNA) and bacterial proteins that eventually resulting in bacterial death.[15] One parts per million (ppm) silver is sufficient to achieve bactericidal action. Nano crystalline technology appears to give the highest, sustained release of silver to a wound without clear risk of toxicity.[16] Silver nano particles can release Ag+ ions at a greater rate than bulk silver, by virtue of their large surface area.[17] Use of a newer, relatively nontoxic antiseptic (example: silver dressings) is preferable to use of topical antibiotics, especially agents that are available for systemic use was concluded in previous study.[18] An ionized nano-crystalline silver dressing was evaluated through an uncontrolled, prospective study of a case series of 29 patients with a variety of chronic non-healing wounds. The results showed a marked clinical improvement for the majority of wounds treated with the dressing.[19] Previous study found that the use of silver foam dressings resulted in a greater reduction in wound size and more effective control of leakage and odour than did use of non-silver dressings.[20] Another study concluded that infected diabetic foot ulcer could benefit from the antibacterial effectiveness of silver phosphate cellulose fibers.[21] Our results was also consistent to those previous studies.

In DM, there is imbalance between matrix degrading enzymes, matrix metalloproteases (MMP), their tissue inhibitors, inhibitor MMP. Loss of collagen which is associated with DM can be due to decreased levels of its synthesis, enhanced metabolism or a combination of both. Non healing of diabetic foot ulcer display elevated MMP activity, with 30 to 60 fold increase in MMP 2 and MMP 9.[17] Dysregulated cellular function also play a part, such as T-cell immunity, leukocyte chemotaxis, phagocytosis, and bactericidal capacity.[22] Increased T-lymphocyte apoptosis which inhibit healing, has been observed in patients with DM. In DM, the accumulation of glycation end products causes the up regulation of pro-inflammatory cytokines, interleukin-1 and tumor necrosis factor- alpha.[23] There is increased risk of infection and poor wound healing due to decreased cell and growth factor response, diminished peripheral blood flow and decreased local angiogenesis. In hyperglycemia, endothelial dysfunction leads a decrease of vasodilators and increase of plasma thromboxane-A2 levels. The result is vasoconstriction and plasma hyper coagulation in peripheral arteries leading to ischemia and increased risk of ulceration. Patient with infected diabetic foot ulcer should be prescribed a targeted antibiotic regimen based on wound culture results. Aggressive antibiotic treatment is essential. Wounds are commonly infected with Pseudomonas and Staphylococcus. Ischemia complicates matter further by reducing defense mechanisms.

Conclusion

We conclude that the nano-crystalline silver, a cost-effective agent as an early intervention in the management of diabetic foot ulcer along with systemic antibiotics to reduce the rate of amputations.

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