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Original Research Article

A randomized comparison study of conventional normal saline and silver nanocrystalline gel as topical wound dressings in non-healing wounds

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ABSTRACT

Background: Non-healing wounds and chronic ulcers are being consequence of the abnormality in healing process and disturbance in the recovery pathway. Picking an ideal choice of topical application and dressing helps in enhancing the wound heal in addition to the antibiotics administration. To identify the outcome of topical dressing in chronic ulcers by using, silver nanocrystalline gel dressing (AgNP) and conventional normal saline dressing (NS).
Methods: This study was an open label randomized study in patient with chronic non-healing wound. The wound healing outcomes of two different dressing methods were compared, which was evaluated by independent assessor. The primary outcome is area reduction of wound and duration of healing. The secondary outcome is the formation of healthy granulation, slough and discharge and wound site infection control.
Results: The outcome of AgNP and conventional NS dressing was compared. The 100 patients with non-healing wounds were randomized in the ratio of 1:1. The primary outcome was study group had better area of reduction of 41.97% (SD-7.41) with statistical significance ($p<0.0001$) and mean duration of healing, 15.64 weeks. The secondary outcome of healthy granulation tissue and reduced slough and discharge at the end of 3 weeks with topical silver nanocrystalline dressing was significant.
Conclusions: Topical silver nanocrystalline dressing shall be an effective dressing option to achieve apposite recovery of healing process in non-healing wounds.

Keywords: Non-healing wounds, Chronic ulcer, NS, Silver nanocrystalline gel, Surgical dressings, Wagner's ulcer grade

INTRODUCTION

Chronic non-healing ulcers was considered as a condition, in patients featured with poor process of wound healing and recovery. Many factors attribute this condition and presence of co-existing conditions, still delays and disturbs the normal pathological and healing process.[1]

Non-healing ulcers have an abnormal pathological process where there was a copious neutrophil infiltration and chronic infiltration state. The state of uncontrolled inflammatory process brings in destructive enzymes and reactive oxygen species.[2] This cause abnormal healing process which disturbs the phases of recovery viz, hemostasis, inflammation, proliferation and remodelling. The healing cascade was chronically interrupted. This state of affected cell signalling events would alter the repairing process such as new cell formation, etc. and results in chronic non-healing wounds.[3] Re-infection or cross infection of the non-healing wounds over mounts the repairing task with the addition fight against the infectious agents.[4]

The rational choice and application of the surgical dressings depend on basic qualities of the dressings such as a protective barrier, absorption of wound discharge and retaining required moist to aid re-epithelialization. In addition, the wound dressings may have feature such as antimicrobial and pain managing support.

The wound type, cause and its anatomical nature decides the choice of dressings to be selected. The wound nature should be assessed, before choosing the surgical dressing, say wound depth, and its drainage level. Culture study reveals the infection status. The assessment during the follow-up visit reveals status of healing process. Healing process may have normal/abnormal recovery process. A non-healing wound may lead to chronic ulcers.

An ideal surgical dressing should have the salient features to fit the healing requirements such as moisture retention, antimicrobial activity, infection control at the wound site, etc. In case of non-healing wounds, the surgeon has challenges to re-establish promotion of healthy granulation; arresting exudates; protection from re-infection/cross infection etc.[5] A favourable healing environment could be achieved for the non-healing wound through optimization of healing factors.[6]

Conventional NS as surgical dressing in non-healing wounds was exploited due to its isotonicity and maintaining adequate moist for healing. Repeated cleaning and dressing with NS dressing contribute in draining fluid and drying up the wound.[7]

Silver as topical application can exhibit a wide spectrum antibacterial activity including multidrug resistant bacteria. Use of silver in wound healing was a grand old remedy and available in various pharmaceutical formulations. The silver as a nanoparticle preparation can be formulated as nanoparticle gel for topical applications. It was more potentially active against microbes.[4]

The study objective was to compare the conventional NS dressings and AgNS dressings among non-healing wounds; to estimate the appropriateness of dressings and its recovery outcomes regarding wound area reduction, new granulation, wound site re-infection control and time taken to heal.

METHODS

The study was an open label, prospective, randomized study, carried out in Tirunelveli medical college hospital from March 2017 to June 2018. The study was approved by the Institution ethical committee. The patients with non-healing wounds due to diabetes mellitus, wound infections, post-operative wound ulcers, traumatic ulcers, burn ulcers and venous ulcers. The patients were identified from in-patient admissions with prolonged hospitalization due to non-healing wounds. A total of 100 patients were enrolled in the study, and randomized in to two groups of surgical dressing method. The calculated sample size was based on anticipated SD-7.65 with desired margin of error 3. Therefore 50 patients in each group will be able to reject the null hypothesis with probability 0.95.

Group-A received silver nanocrystalline gel (0.02 wt% Ag) which was applied to one fourth thickness of shallow wounds or completely fill deep wounds. It was then covered with secondary dressing such as gauze or pad depending on the wound drainage. Group-B received conventional dressing with sterile gauze soaked with NS (0.9%) over the wound.

Study inclusion criteria include patients, aged more than 20 years with a Wagner's ulcer grade-II and grade-III; the duration of ulcer 3 weeks & above with a size of ulcer less than 15 x 15 cm and willing to give consent for the study.

Study exclusion criteria included patients, ulcers with severe active infections: Wagner's ulcer grade more than III; X-Ray features of underlying osteomyelitis; Diabetic foot with major vascular disease; Uncontrolled diabetes mellitus; Patients with severe hepatic, renal, and haematological diseases which impair wound healing; Patients on immunosuppression drugs, long-term steroid therapy, radio therapy or chemotherapy.

All patients during initial treatment phase underwent surgical debridement and devitalised tissue was removed. Daily cleaning and dressing done till ulcer became stable (i.e., no progression in size of ulcer). Good glycaemic control was achieved in diabetic patients and maintained throughout the treatment phase.

Clinical assessments like, tissue assessment and area of ulcer was completed at the time of inclusion. Tissue assessment was done for devitalized tissue and ulcer tissue. Sterile gauze and graph paper method was followed to measure ulcer area in sq.mm. Culture, and sensitivity were done during the phase and appropriate antibiotics were started. Daily cleaning and dressing were done in both groups for a period of 3 weeks.

The patients were assessed and the chart was filled in by an independent assessor at 0 (randomization), weeks -1, 2, 3 for parameters viz. slough and discharge, formation of healthy granulation tissue, wound size (initial and final) in mm^2. Final reduction in wound size was expressed in %; pus cultured at 0, 1, 2 and 3 weeks. Induration, discharge and odour were noted weekly during this phase.

The results obtained from 0 weeks to 3 weeks, in both the groups were compared and analysed for the presence of slough and discharge; formation of healthy granulation tissue; pus culture report and wound size. The study data were subjected for descriptive analysis and the parametric variables were statistically analysed by independent sample T test.

RESULTS

There were 100 patients recruited in our study. The mean age of patients in topical silver dressing group-A (AgNP) was 60.68 years while in conventional NS dressing group-B mean age was 60.48 years (Table 1).

Table 1: Demography data.

Variables	Group-A (AgNP)	Group-B (NS)
	Number (%)	Number (%)
Age (Years)		
21-30	1 (2)	1 (2)
31-40	0 (0)	4 (8)
41-50	10 (20)	5 (10)
51-60	12 (24)	12 (24)
61-70	22 (44)	16 (32)
71-80	05 (10)	12 (24)
Gender		
Male	26 (52)	25 (50)
Female	24 (48)	25 (50)

The aetiology of non-healing wounds was, diabetic foot ulcer, venous ulcers, traumatic wounds, burns, pressure ulcer, and post infective. Diabetes was the leading cause for non- healing wound in both the groups comprising 74 percentage and 66 percentage in group A AgNP dressing and B NS respectively in Table 2.

At the end of 3rd week, the slough and discharge were present in 12% and 44%, of silver dressing and saline dressing, respectively. The topical silver dressing group had manifested a significant reduction in slough and discharge by the end of 3rd week ($p<0.0001$). Healthy granulation tissue at the end of 3 weeks, in silver dressing and saline dressing, was 80% and 28% respectively. There was significantly higher healthy granulation tissue formation in silver dressing group ($p<0.0001$) in Table 3.

The mean duration of ulcer in the topical silver dressing group was 15.64 weeks, and in the NS dressing group was 13.66 weeks. The mean, wound area reduction was 41.97 % (SD-7.41) and 18.37% (SD-13.43) in silver dressing group, and saline dressing group, respectively. It was statistically significant on independent sample T test ($p<0.0001$) in Table 4.

The pus culture sensitivity was done in both the study groups across three weeks. The negative culture report on 3rd week was in 48 patients of silver crystalline treatment and in 42 patients of NS group with $p=0.046$ in Table 5.

Table 2: Aetiology of ulcer.

Etiology	Diabetic		Venous		Traumatic		Burns		Pressure		Post infective	
	Nos	%	Nos	%	Nos	%	Nos	%	Nos	%	Nos	%
Group-A (AgNP)	37	74	1	2	3	6	1	2	7	14	1	2
Group-B (NS)	33	66	1	2	8	16	2	4	6	12	0	0

Table 3: Ulcer grading with health granulation and slough/discharge, (n=50).

Variables	Group-A (AgNP)	Group-B (NS)
	Number (%)	Number (%)
Grading of ulcer		
Grade 2	21 (42)	21 (42)
Grade 3	29 (58)	29 (58)
Slough and discharge (at 3rd week)		
No	44 (88)	28 (56)
Yes	6 (12)	22 (44)
Healthy granulation tissue (at 3rd week)		
No	10 (20)	36 (72)
Yes	40 (80)	14 (28)

Table 4: Wound healing-outcome comparison.

Variables	N	Mean	SD	P value
Duration of ulcer (in weeks)				
Group-A (AgNP)	50	15.64	4.13	0.063
Group-B (NS)	50	13.66	3.63	
Wound area reduction (mm^2)				
Group-A (AgNP)	50	41.97	7.41	0.0001
Group-B (NS)	50	18.37	13.43	

Table 5: Pus culture infection-outcome comparison, (n=50).

Visits	Group-A (AgNP)	Group-B (NS)	P value
	Number	Number	
Week 1			
No	31	22	0.071
Yes	19	28	
Week 2			
No	43	38	0.202
Yes	7	12	
Week 3			
No	48	42	0.046
Yes	2	8	

DISCUSSION

Non-healing wounds were affecting the patient's quality of life. The morbidity widens if the wound site gets fibrosis. It is a big challenge in opting for a quick recovery and preventing fibrosis.[8] Different methods of dressings were in use. An ideal choice of topical application to be made to achieve reasonable recovery, and healing of wound.

A choice of appropriateness is mandated among elderly patients. As the associated illness may challenge the healing process, random choice in topical dressings may even prolong the healing and lead to poor prognosis.[6]

Topical applications of conventional NS and AgNP were used in wounds and ulcers. The benefit of these formulations in case of non-healing wounds was studied here.

The conventional saline solution dressing has the water content, and it was lost through conduction. Therefore, the saline solution gets concentrated, and the dressing becomes hypertonic, aiding in pulling of the exudates from the wound. Silver crystalline topical gel has anti-bacterial effect by easing membranes disruption, penetration, and intracellular absorption.

Isotonicity of NS dressing drains out the exudate and cleanse the infection causing microbes. Silver nanocrystalline gel exerts its effect by acting as a physical barrier to superficial infections.

Saline dressing forms a thin semipermeable membrane as a physical barrier and provides protection from superficial infection.[4,9] Silver nano preparation prevent infection, when applied as thin layer with an optimal contact time.[10]

In addition, silver nanocrystalline gel increases the reactive oxygen species (ROS) inside the microbial cells leading to metal-induced oxidative stress and cell damage.[2]

The infection frequency was very frequent with NS dressing. The average wound healing time was significant with AgNP than conventional NS dressing.

Topical silver dressings may reduce slough and discharge, induces healthy granulation tissue formation, improves pus culture sensitivity, reduces wound size considerably. Silver formulations exerts its action through bactericidal action, anti-inflammatory action, cell infiltration, infection control, coping with natural healing process.[11-13]

The study outcome was inadequate to be generalized for the real population due to the limitations like, individualized antibiotic regimen and exemption of patient with Wagner's ulcer grade >3, uncontrolled diabetes and severe ulcer infection.

CONCLUSION

The result of the study appears to show more favourable results for topical silver dressing group than for conventional dressing. It can be used as an adjunct to conventional mode of treatment (conventional dressings and debridement). However, the results are highly significant, the strength of evidence depend upon the study design. The results of the study justify further research into the use of topical nano silver preparations in the treatment of various wounds and ulcers.

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