



A CLINICAL STUDY ON EFFICACY OF NANOCRYSTALLINE SILVER DRESSING IN DIABETIC FOOT ULCERS

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Abstract

Background: Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia, leading to long-term microvascular and macrovascular complications. Among these, diabetic foot ulcer (DFU) is one of the most common and serious complications, affecting nearly 15% of diabetic patients during their lifetime and often resulting in prolonged hospitalisation and limb amputation. Effective wound management is crucial for improving healing rates and reducing morbidity. Nanocrystalline silver dressings have emerged as an advanced wound care modality due to their potent antimicrobial properties and ability to maintain an optimal moist wound environment.

Aim: To evaluate the efficacy of nanocrystalline silver dressings compared to conventional dressings in the management of diabetic foot ulcers.

Methodology: This prospective interventional comparative study was conducted over a period of two years at Government Medical College and Hospital, Kadapa, after Institutional Ethical Committee approval. A total of 100 patients aged 18–75 years with Wagner's grade II diabetic foot ulcers were selected using simple random sampling and divided into two groups of 50 each. Group A received nanocrystalline silver dressings, while Group B received conventional dressings. Outcome measures included number of dressings required, percentage reduction in ulcer size measured by ulcer planimetry, and length of hospital stay. Data were analysed using SPSS version 16, with $p < 0.05$ considered statistically significant.

Results: The mean number of dressings required was significantly lower in Group A (10.28 ± 2.82) compared to Group B (21.74 ± 3.89). The mean hospital stay was shorter in Group A (20.26 ± 5.64 days) than in Group B (43.16 ± 7.87 days). The mean percentage reduction in ulcer size was higher in Group A ($95.24 \pm 2.64\%$) compared to Group B ($83.32 \pm 6.11\%$). These differences indicate superior wound healing outcomes with nanocrystalline silver dressings.

Conclusion: Nanocrystalline silver dressings are safe, effective, and more patient-compliant than conventional dressings in the management of diabetic foot ulcers. They significantly reduce the number of dressings required, shorten hospital stay, and enhance ulcer size reduction, thereby offering a superior option for DFU management.

Keywords: Diabetic foot ulcer, Nanocrystalline silver dressing, Conventional dressing, Wound healing, Hospital stay

Introduction

Diabetes is a metabolic disease characterised by hyperglycaemia, which may be due to defect in insulin secretion, insulin action or both. The chronic hyperglycaemia of diabetes is associated with long term damage and dysfunction, which eventually leads to failure of different organs, especially the eyes, kidneys, nerves and heart.^{1, 2} India with approximately 42 million cases is ranked first in the list of ten nations most affected with diabetes.³

Among diabetes mellitus related complications, foot ulceration is the most common, affecting approximately 15% of diabetic patients during their lifetime.^{4,5} The diabetic patients with foot ulcers require prolonged hospitalisation and carry the risk of limb amputation.⁶ Peripheral neuropathy, peripheral vascular disease, and foot trauma were risk factors in the pathophysiology of foot ulcer.^{7,8,9,10}

Numerous dressings are available like Saline, hydrogels, hydrocolloid, foam, and 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. Hydrocolloid dressings provide more consistent moisture retention, absorb low to moderate level of exudates and retain growth factors which promote granulation. Foam and alginate dressings are highly absorbent and can aid in decreasing the risk for maceration in wounds with heavy exudates. Paraffin dressings offer the advantage of low adherence with lesser trauma during dressing removal. Polyurethane dressings are transparent and enable proper wound monitoring. Hyperbaric oxygen therapy, vacuum assisted devices and culture skin substitutes are other wound therapies that have been advocated.^{11, 12}

Nanocrystalline silver ion dressing is an effective anti microbial 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.¹³ 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.¹⁴ There are several mechanisms by which Ag NPs can destroy the bacteria. They include bacterial membrane destruction, the crossing of the microbial body and initiation of intracellular destruction, removal of lipopolysaccharide with cellular disintegration, the induction of oxidative stress, and metal release ions in addition to non oxidative stress mechanisms.^{15,16,17}

In addition to antimicrobial properties that have been well demonstrated in vitro in the literature, silver dressings are proven to reduce the bacterial load present in an infected wound, in turn reducing the inflammatory response and further aiding the healing process.¹⁸ Silver based dressing materials contain Silver nano particles - which expand the surface area of contact with the wound and also are in the ionic form Ag cations which cause cell toxicity to bacteria both gram positive and negative, including multi drug resistant strains and also promoting wound healing by the inhibition of MMPs and are also effective against bio films.^{19,20}

Hence in this study, we compared the efficacy of Nanocrystalline Silver dressings with conventional dressings.

Aim: To study the efficacy of Nano crystalline silver dressing in the management of diabetic foot ulcer. **Objective:** The efficacy of Nano crystalline silver dressings over conventional dressings is assessed in terms of Number of dressing required, Percentage reduction in the ulcer size, Length of hospital stay

Patients and methods: This was a Prospective Interventional and Comparative study done in 100 patients were selected using Simple Random Technique and divided into two Groups with 50 patients in each group, admitted with diabetic foot ulcer in Government Medical College and Hospital, Kadapa for a period of 2 years and has got approval from Institutional Ethical Committee meeting held on 14.10.2022.

Inclusion Criteria: Patients aged 18 – 75 years with diabetic foot ulcer. Ulcers of Wagner's grade II, Patients giving consent to the study. **Exclusion Criteria:** Patients with comorbidities like Cardiovascular, Respiratory, Neurological, and Osteomyelitis. Patients with Ischemic/ malignant/

venous insufficiency wounds. Ulcers of Wagner’s grade III, IV, and V. Patients under Immunosuppressive treatment. Patients not giving consent for the study

Method of Collection of Data: Patients admitted to Government Medical College and Hospital, Kadapa were divided by Simple random technique into Group A Test Group who had Nano silver crystalline dressings and Group B Control Group who had conventional dressings.

Upon admission a detailed history was taken including history of the mode of onset, duration, progress of ulcer and information about diabetes status with duration and medication. Ulcer examination was performed. All the patients underwent the following investigations: Hemoglobin, Blood Sugars, Serum Creatinine, Urine Ketone Bodies, X ray foot, Doppler (both arterial and venous). Ethical clearance was obtained from Ethical committee of our institution for this study.

Group A Test Group (Nanocrystalline Silver Dressings): After cleaning the ulcer with help of normal saline, nanocrystalline silver gel applied and the wound was closed with gauze pad and roller bandage. Dressings are changed accordingly if there is soakage of dressing.

Group B Control Group (Conventional Dressings): If ulcer contained slough, patients underwent debridement to have clean ulcer base. Following debridement, base was cleaned once with wet gauze piece soaked in normal saline. Wet gauze piece soaked in betadine solution was kept over the ulcer which was covered with gauze pad and roller bandage.

Patients are discharged from the hospital after significant reduction in ulcer size or in some cases after formation of granulation tissue and after applying partial thickness split skin graft. Percentage reduction in the ulcer size was measured at the time of discharge using Ulcer Planometry. Number of dressings required for each group, Number of days of hospital stay were recorded. Patients are re-evaluated on the outpatient basis for 2 months.

Statistics: Data was entered in Microsoft excel and analyzed. The results are presented in frequencies, percentages and Mean, Standard Deviation. Relevant statistical analysis was done using SPSS version 16. Differences in the groups was analysed with Chi square test, Continuity Correction, Likelihood Ratio, Fisher’s Exact Test, McNemar Test. Significance was defined when the p value is less than 0.05.

RESULTS

TABLE NO 1: DISTRIBUTION OF AGE RANGE IN TWO GROUPS

		Group 1		Group 2	
S.No	Age in range(years)	N	%	N	%
1	20-30	1	2	1	2
2	31-40	4	8	3	6
3	41-50	12	24	13	26
4	51-60	21	42	19	38
5	61-70	10	20	11	22
6	71-80	2	4	3	6
	TOTAL	50	100	50	100

TABLE NO 2: COMPARISON OF GENDER PREVALENCE IN TWO GROUPS

Binomial Test					
	Category	N	Observed Prop.	Test Prop.	Exact Sig. (2-tailed)
Group 2	Female	17	.34	.50	.033
	Male	33	.66		
	Total	50	1.00		
Group 1	Female	19	.38	.50	.119
	Male	31	.62		
	Total	50	1.00		

TABLE NO 3: COMPARISON OF DRESSING TYPE

Crosstab				
		Case-Control		Total
		Control	Case	
Dressing type	Nanocrystalline Silver Dressing	0	50	50
	Conventional Dressing	50	0	50
Total		50	50	100

The results of the Chi-Square test indicate a significant association between the type of dressing (NS or CD) and the case-control status ($\chi^2 = 100.000$, $df = 1$, $p < .001$). This suggests that the choice of wound dressing is significantly related to the likelihood of being a case or control in the study population. The Fisher's Exact Test also supports this association, further emphasizing its significance ($p < .001$).

TABLE NO 4: BINOMIAL ANALYSIS OF ULCER ONSET IN GROUPS

Binomial Test					
	Category	N	Observed Prop.	Test Prop.	Exact Sig. (2-tailed)
Ulcer in Group 1	Traumatic	37	.74	.50	<.001
	Spontaneous	13	.26		
	Total	50	1.00		
Ulcer In Group 2	Spontaneous	18	.36	.50	.065
	Traumatic	32	.64		
	Total	50	1.00		

TABLE NO 5: BINOMIAL ANALYSIS OF ULCER SITE IN GROUPS

Ulcer Site Binomial Test					
	Category	N	Observed Prop.	Test Prop.	Exact Sig. (2-tailed)
Group 1	Plantar	38	.76	.50	<.001
	Dorsal	12	.24		
	Total	50	1.00		
Group 2	Plantar	31	.62		.119
	Dorsal	19	.38	.50	
	Total	50	1.00		

TABLE NO 6: BINOMIAL ANALYSIS OF TREATMENT IN GROUPS

Binomial Test					
	Category	N	Observed Prop.	Test Prop.	Exact Sig. (2-tailed)
Group 1	OHA	17	.34	.50	.033
	Insulin	33	.66		
	Total	50	1.00		
Group 2	Insulin	22	.44	.50	.480
	OHA	28	.56		
	Total	50	1.00		

TABLE NO 7: A DESCRIPTIVE ANALYSIS OF OUTCOME MEASUREMENT AND DEPENDENT VARIABLES

Statistics		Group 1			Group 2		
		No of Dressings	LOS	% reduction in ulcer size	No of Dressings	LOS	% reduction in ulcer size
N	Valid	50	50	50	50	50	50
	Missing	80	80	80	80	80	80
Mean		10.2800	20.2600	95.2400	21.7400	43.1600	83.3200
Std. Deviation		2.82149	5.64172	2.64621	3.89039	7.86716	6.11936
Range		12.00	24.00	11.00	13.00	26.00	24.00
Percentiles	10	7.0000	12.2000	91.1000	16.1000	32.1000	72.2000
	20	8.0000	16.0000	94.0000	18.0000	35.0000	78.0000
	30	8.0000	16.0000	94.0000	19.0000	36.3000	80.0000
	40	9.0000	17.4000	95.0000	20.4000	40.4000	84.0000
	50	10.0000	20.0000	96.0000	22.0000	43.5000	86.0000
	60	12.0000	23.2000	96.0000	23.6000	46.0000	86.0000
	70	12.0000	24.0000	97.0000	24.0000	48.0000	88.0000
	80	13.0000	26.0000	98.0000	25.0000	50.0000	88.0000
	90	14.0000	28.0000	98.0000	27.0000	54.0000	90.0000

DISCUSSION

As of routine practice there are many methods of dressings that are done for the Diabetic foot. They include: Povidone Iodine that acts by iodinating and oxidizing microbial protoplasm, rapidly killing bacteria, fungi, and viruses. These are available as Tincture iodine (2% in alcohol), Mandl's paint (1.25% with potassium iodide), non-staining iodine gel (e.g., Iodex 4%). Some individuals may experience rashes or systemic manifestations due to iodine sensitivity.²¹ Cadexomer Iodine: Consists of hydrophilic beads of cadexomer starch, gradually releasing iodine into the wound. It acts by Slow and sustained release of iodine for antimicrobial activity.

Hydrogen Peroxide has limited impact on wound healing or bacterial control, but effervescence aids in cleansing or debriding wounds. Typically diluted to half strength and rinsed off with saline after application as a part of dressing. Acetic Acid acts by reducing various bacteria, including *Pseudomonas aeruginosa* and *Staphylococcus aureus*, without cytotoxic effects. It is effective against a range of bacteria but non-toxic in in vivo studies. Metronidazole Activity: Broad-spectrum activity against protozoa (e.g., *Giardia lamblia*), anaerobic bacteria (e.g., *Bacteroides fragilis*, *fusobacterium*, *clostridium perfringes*, anaerobic streptococci), and helminths (e.g., *Dracunculus medinensis*). It enters microorganisms, where it is reduced to cytotoxic compounds, possibly damaging DNA or interfering with electron transport. There has been minimal resistance reported among targeted parasites.²²

In our study we used Nanosilver as a dressing material and compared with conventional dressing materials. Silver nanocrystalline technology utilizes nano-scale silver particles to enhance the antimicrobial properties of silver, making it highly effective against various microorganisms. This technology has revolutionized wound management by providing a potent antimicrobial agent with multiple benefits for wound healing.

Mechanism of Action:

- **Antimicrobial Effectiveness:** Silver ions (Ag^+) bind to tissue proteins, causing structural changes in bacterial cell membranes, inhibiting cell replication, and denaturing bacterial DNA and RNA.
- **Broad Spectrum:** Effective against bacteria, fungi, yeast, mold, and antibiotic-resistant strains like MRSA and VRE.

- **Residual Activity:** Maintains adequate concentrations of silver (>70mg/L) with prolonged residual activity, preventing microbial resistance.^{23,24}

Benefits:

- **Moisture Regulation:** Provides moisture to the wound bed, preventing dehydration of granulation tissue and promoting autolytic debridement.
- **Antiseptic Barrier:** Allows gaseous exchange while forming a barrier against microbial entry into the wound.
- **Pain Relief:** Offers a cooling effect, soothing pain associated with wounds.
- **Extended Antimicrobial Release:** Releases active ionic silver slowly over time, ensuring broad antimicrobial effectiveness and preventing contamination.
- **Reduces Contamination:** Decreases wound surface contamination, aiding in the healing process.
- **Inhibition of Matrix Metalloproteinases:** Promotes wound healing by inhibiting MMPs involved in tissue breakdown.

Clinical Applications:

Indications: Pressure ulcers, venous ulcers, dermal lesions, second-degree burns, and donor sites.

Precautions: Use caution in heavily exudating wounds or wounds covered with thick eschar. When signs of infection are present, proper antibiotics should be used in conjunction with silver nanocrystalline technology.

Contraindications: There are no absolute contraindications but its utility is limited when used in heavily exudating wounds or wounds covered with thick eschar.

In this study Group A included 50 patients treated with Nanocrystalline Silver Dressings. Group B included 50 patients treated with conventional dressings. The results in both groups were compared in terms of following factors.

For Group 1: The mean number of dressings was approximately 10.28, with a standard deviation of 2.82. The minimum and maximum number of dressings was 4 and 16, respectively.

The mean length of stay was about 20.26 days, with a standard deviation of 5.64. The minimum and maximum LOS was 8 and 32 days, respectively.

TABLE NO 8: DESCRIPTIVE ANALYSIS OF TREATMET VARIABLES

Descriptive Statistics						
		Statistic	Bootstrap ^a			
			Bias	Std. Error	95% Confidence Interval	
					Lower	Upper
Group 1						
No of dressings	N	50	0	0	50	50
	Minimum	4.00				
	Maximum	16.00				
	Mean	10.2800	.0052	.3834	9.5600	11.0995
	Std. Deviation	2.82149	-.03608	.19788	2.40442	3.17343
LOS	N	50	0	0	50	50
	Minimum	8.00				
	Maximum	32.00				
	Mean	20.2600	.0134	.7682	18.8000	21.8390
	Std. Deviation	5.64172	.07634	.40052	4.74610	6.33363
% reduction in ulcer size	N	50	0	0	50	50
	Minimum	88.00				
	Maximum	99.00				
	Mean	95.2400	.0018	.3724	94.5200	95.9600
	Std. Deviation	2.64621	.04883	.32859	1.95891	3.19422

Group 2						
No of dressings	N	50	0	0	50	50
	Minimum	16.00				
	Maximum	29.00				
	Mean	21.7400	.0017	.5511	20.6410	22.9000
	Std. Deviation	3.89039	.04437	.27101	3.29025	4.35740
LOS	N	50	0	0	50	50
	Minimum	32.00				
	Maximum	58.00				
	Mean	43.1600	.0018	1.1160	41.0200	45.4600
	Std. Deviation	7.86716	.08685	.54607	6.66899	8.83068
% reduction in ulcer size	N	50	0	0	50	50
	Minimum	68.00				
	Maximum	92.00				
	Mean	83.3200	-.0192	.8369	81.6800	84.8795
	Std. Deviation	6.11936	.08322	.56093	4.92512	7.07785
Valid N	N	50	0	0	50	50
a. Unless otherwise noted, bootstrap results are based on 1000 bootstrap samples						

The mean percentage reduction in ulcer size was approximately 95.24%, with a standard deviation of 2.65%. The minimum and maximum reduction percentages are 88% and 99%, respectively.

For Group 2: The mean number of dressings was around 21.74, with a standard deviation of 3.89. The minimum and maximum number of dressings was 16 and 29, respectively.

These descriptive statistics provide information on the number of dressings, length of stay (LOS), and percentage reduction in ulcer size for two groups, Group 1 and Group 2. The mean length of stay was approximately 43.16 days, with a standard deviation of 7.87. The minimum and maximum LOS was 32 and 58 days, respectively.

The mean percentage reduction in ulcer size was about 83.32%, with a standard deviation of 6.12%. The minimum and maximum reduction percentages were 68% and 92%, respectively.

The descriptive statistics reveal notable differences between Group 1 and Group 2 in terms of wound care management. In Group 1, patients received an average of 10.28 dressings, stayed for approximately 20.26 days, and experienced a mean reduction in ulcer site size of 95.24%.

Conversely, in Group 2, patients received more dressings on average (mean was 21.74), had a longer length of stay (mean = 43.16 days), and exhibited a slightly lower mean reduction in ulcer site size (mean = 83.32%). These findings suggest that Group 2 patients required more intensive wound care management, reflected in the increased number of dressings and longer hospital stays, while still achieving a substantial reduction in ulcer size.

TABLE NO9: MEAN AGE DISTRIBUTION IN VARIOUS STUDIES

Study	Mean Age Distribution in years	
	Cases	Control
N. V. Ramanaiah et al. ²⁵	52.73 ± 9.88	55.50 ± 12.11
Theresa hurd et al. ²⁶	56.35	56.67
Gupta, V et al. ²⁷	54.47	59.93
Mohamed S. Essa et al. ²⁸	55.8 ± 2.38	54.64 ± 3.54

TABLE NO10: GENDER DISTRIBUTION IN VARIOUS STUDIES

Study	Sex distribution	
	Male	Female
Malligurki VK et al ²⁹	78%	22%
Rahaman, Abdur et al ³⁰	67%	33%
Dr. P. Nancharaiah MS et al ³¹	60%	40%
N. V. Ramanaiah et al ²⁵	65%	35%
Gupta, V et al ²⁷	66.7%	33.3%
Kanneedi naresh kumar et al ³²	62.5%	37.5%

Onset of Diabetic Foot ulcer:

Trauma is the most common cause in patients with diabetic foot ulcer, which is mostly due to neuropathy developed from diabetes. In our study 69 patients were developed ulcers following trauma and the rest developed spontaneously by means of rupture of bullae. In Dr. P. Nancharaiah MS et al³¹ 80% ulcers were due to trauma, and 20% were spontaneous. In N. V. Ramanaiah et al²⁵ study 69% ulcers were traumatic origin and 31% were spontaneous in onset.

SITE OF ULCER:

Diabetic foot ulcers were more common on plantar aspect of foot. In our study 69 patients developed ulcers over plantar aspect of the foot and the remaining 31 patients developed ulcers over dorsum of foot. In N. V. Ramanaiah et al²⁵ study 69% ulcers are on plantar area; and in Kanneedi naresh kumar et al³² study also plantar ulcers were more common than ulcers on the dorsum.

TABLE NO 11: MEAN DURATION OF STAY IN HOSPITAL IN VARIOUS STUDIES

Study	Mean duration of stay in hospital	
	Cases	Controls
Dr. P. Nancharaiah MS et al ³¹	19.31 ± 6.01	33.83 ± 8.35
N. V. Ramanaiah et al ²⁵	20.54 ± 7.04	36.19 ± 7.24
Dr. Shiva kumar. S et al ³³	23.16 ± 8.16	48.34 ± 18.06
Present study	20.26 ± 5.64	43.16 ± 7.86

TABLE NO 12: MEAN OF NUMBER OF DRESSINGS IN VARIOUS STUDIES

Study	Mean of number of dressings	
	Cases	Controls
Dr. P. Nancharaiah MS et al ³¹	11.38 ± 4.00	20.46 ± 3.46
N. V. Ramanaiah et al ²⁵	10.92 ± 3.05	17.54 ± 6.00
Dr. Shiva kumar. S et al ³³	11.50 ± 4.09	24.04 ± 9.09
Present study	10.28 ± 2.82	21.74 ± 3.89

TABLE NO 13: MEAN PERCENTAGE OF REDUCTION IN ULCER SIZE IN VARIOUS STUDIES

Study	Mean percentage of reduction in ulcer size	
	Cases	Controls
Dr. P. Nancharaiah MS et al ³¹	92.41 ± 4.47	85.37 ± 7.59
N. V. Ramanaiah et al ²⁵	94.81	84.69
Dr. Shiva kumar. S et al ³³	66.76 ± 16.81	22.71 ± 24.53
Present study	95.24 ± 2.64	83.32 ± 6.11.
Tsang. K. K. et al ³⁴	97.45	81.91
Kanneedi naresh kumar et al ³²	38.44 ± 2.68	13.67 ± 7.85
Rakesh sharma et al ³⁵	84.06 ± 3.20	76.48 ± 3.17
Gupta, V et al ²⁷	55.67	54.93

Conclusion: From the study we conclude that Nanocrystalline silver dressings are safe, effective, with a slight beneficial edge when compared to conventional dressings in terms of promoting wound healing, and more patient compliant in terms of

- 1) Less pain while changing the dressing.
- 2) Less number of dressings required.
- 3) Shorter hospital stay.
- 4) More percentage reduction in ulcer size.

The above results indicates that nanocrystalline silver dressings mau be used in the management of diabetic foot ulcers and are seems to be more efficient than conventional dressings.

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