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ORIGINAL RESEARCH

Comparison of efficacy of cadexomer iodine with silver alginate in ulcer healing

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ABSTRACT

Introduction: Ulcers pose a significant burden on patients and healthcare systems due to prolonged healing times and the risk of infection. Effective wound management strategies are essential to improve healing outcomes. This study compares the efficacy of nanocrystalline silver (NCS) and cadexomer iodine (CI) dressings in ulcer healing.**Methods:** A prospective randomized comparative study was conducted at SSIMS Hospital, Davangere, from November 2022 to July 2024, enrolling 45 patients with leg and foot ulcers. Patients were randomly assigned to either the NCS group (n=23) or the CI group (n=22). Wound healing was assessed through parameters such as reduction in wound surface area, granulation tissue formation, and secondary outcomes, including the need for grafting and secondary suturing.**Results:** The NCS group demonstrated a significantly greater reduction in wound surface area (mean improvement: 33.03 cm^2 vs. 15.27 cm^2, $p=0.025$) and a higher percentage of wound healing (80.64% vs. 56.15%, $p<0.001$) compared to the CI group. While both groups had comparable Wagner grade distributions, purulent discharge was lower in the NCS group (8.7% vs. 19.0%). Additionally, more patients in the NCS group underwent grafting (30.4% vs. 19.0%), suggesting faster wound healing.**Conclusion:** Nanocrystalline silver dressings demonstrated superior wound healing outcomes compared to cadexomer iodine dressings. The antimicrobial properties and moisture-retaining characteristics of NCS dressings contributed to enhanced healing. Further large-scale studies and cost-effectiveness analyses are recommended to establish its widespread clinical use.

Key words: Ulcer healing, cadexomer iodine, silver alginate, wound management, granulation tissue formation

INTRODUCTION

Ulcers are burden to patient and society in terms of economically, morbidity and mortality. Wounds are easily prone for infection thus delaying wound healing which can be tackled/treated by local or systemic use of antimicrobials. Many local antimicrobials have been used since ages (from historical times) and are adopted in modern times as per their effectiveness and compliance of the patient[1, 2]. The local management of depends on the condition/nature of the wound. Silver-impregnated dressings are typically used for a limited period, usually a few weeks, to control excessive inflammation in ulcers. This practice is based on the understanding that silver dressings effectively reduce bacterial load and inflammation during the critical early stages of wound healing. However, prolonged use is generally discouraged, as once the inflammation subsides and the wound enters the regenerative phase, continued exposure to silver may delay healing by affecting healthy cells. Therefore, once the infection and excessive inflammation are managed, switching to a non-silver dressing is recommended to support optimal wound recovery[9]. Our study compares the effectiveness of Nanocrystalline silver and cadexomer iodine used in dressings of the ulcers.

AIM OF THE STUDY

To evaluate and compare the clinical effectiveness of nanocrystalline silver and cadexomer iodine dressings

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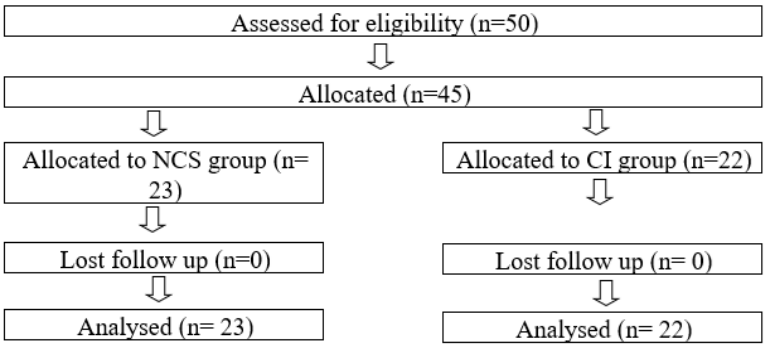
MATERIALS AND METHODS

SOURCE

All the OPD and IPD patients with leg and foot ulcers from November 2022 till July 2024 in SSIMS Hospital Davangere.

3.2 STUDY DESIGN

Prospective randomised comparative study.



INCLUSION CRITERIA

1) Age >18 years.
2) Diabetic ulcers, venous ulcers, traumatic ulcers.
3) Wound area ≥ 1 cm^2
4) Wagner Grade 1 to 2.
5) PVD with restored blood flow by revascularisation.
6) Thigh, Leg & foot ulcers.
7) Post operative ulcers.

EXCLUSION CRITERIA

1) Allergy to silver or cadexomer iodine.
2) Active arterial insufficiency.
3) Wagner grade 3 to 4.
4) Severe infections like cellulitis, abscess and osteomyelitis.
5) Malignancy in extremities near target ulceration
6) Malignant ulcers.
7) Immunodeficiency.
8) Uncontrolled medical conditions.

PROCEDURE AND METHODOLOGY

All the patients with ulcers over lower extremities, after applying inclusion and exclusion criteria were enrolled in the study.

Patient general condition and wound assessment is done. Wound is cleaned using sterile sodium chloride solution and mechanically debrided if needed. Wound culture is sent for antibiotic susceptibility and oral or intravenous antibiotics are started accordingly. Parameters like wound surface area, peripheral vascular circulation, ulcer location, microbial isolate are noted and wound is classified according to Wagner classification. Patients are then allocated randomly into 2 groups nanocrystalline silver (NCS) group and cadexomer iodine (CI) group to a 6-8 weeks course of treatment. NCS group received silver alginate dressings while CI group cadexomer iodine dressings.

SURGICAL INTERVENTION

Mechanical and chemical debridement of the ulcer done if indicated, in both the groups to remove slough and necrotic tissue.

PROTOCOLS OF DRESSING

NCS GROUP

Ulcer is cleaned using betadine (5%), non-adhesive silver foam is directly applied along the floor of the ulcer which is then covered with conventional dressings in aseptic precautions.

CI GROUP

Ulcer is cleaned using betadine (5%),cadexomer iodine is applied to the ulcer and is then covered with conventional dressings.

ASSESSMENTS & PROCEDURES

FOLLOW-UP

Four weekly visits scheduled at week 1, week 2, week 3 and week 4 is done for NCS group.

Weekly twice visits scheduled at day 0, day 3 or 4, day 7, day 10/11, day 14, day 17/18, day 21, day 24/25, day 28 for CI group.

Wound parameters are noted. Wound area is determined by measuring the longest ulcer length, then the width of a line that ran perpendicular to the longest length.

OUTCOMES

PRIMARY OUTCOMES

1) Reduction in the wound surface area
2) Healing area calculated as
   Healing area = Surface area of the wound in the first visit-Surface area of the wound at the present visit.
3) Healthy granulation tissue filling the ulcer.

SECONDARY OUTCOMES

1. Secondary suturing.
2. Grafting.
3. Non healing ulcer.
4. Amputations.
5. Need of second debridement surgery.

Statistical analysis

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4.RESULTS

Table1:Demographic and Clinical details of study participants between groups

Variables	Groups				p Value
	Ulcer silver dressing		Cadexomer iodine dressing		
	n=23	%	n=22	%	
Age (Mean ± SD)	53.61 ± 15.17		50.19 ± 17.37		0.490
Sex					
Male	17	73.9	14	66.7	0.599
Female	6	26.1	7	33.3	
Co-morbidities					
HTN	11	47.8	4	19.0	0.044
DM	10	43.5	9	42.9	0.967
CAD	3	13.0	0	0.0	0.234
CVA	1	4.3	2	9.5	0.599
IHD	2	8.7	1	4.8	1.000

The mean age was 53.61 ± 15.17 years in ulcer silver dressing and 50.19 ± 17.37 in cadexomer iodine dressing. In ulcer silver dressing, 17 (73.9%) cases were male and 6 (26.1%) were female. Whereas in cadexomer iodine dressing, 14 (66.7%) were male and 7 (33.3%) were female. The proportion of hypertension was significantly higher in ulcer silver dressing (47.8%) compared to cadexomer iodine dressing (19.0%).

Table2: Comparison of wound surface area between groups

Wound surface area	Ulcer silver dressing (n=23)		Cadexomer iodine dressing (n=21)		p Value
	Mean	SD	Mean	SD	
First Visit	43.52	54.90	27.46	20.95	0.312
Last Visit	10.49	14.11	12.19	9.72	0.133
Improvement of Healing Area	33.03	40.94	15.27	11.51	0.025
Percentage of Wounded Heal	80.64	9.56	56.15	4.65	<0.001

The baseline mean wound surface area was 43.52±54.90 in ulcer silver dressing and 27.46±20.95 in cadexomer iodine dressing. The follow up mean wound surface area was 10.49±14.11 in ulcer silver dressing and 12.19±9.72 in cadexomer iodine dressing. The mean improvement of healing area was significantly higher in ulcer silver dressing (33.03±40.94) compared to cadexomer iodine dressing (15.27±11.51). The percentage of improvement of healing area was significantly higher in ulcer silver dressing (80.64±9.56) compared to cadexomer iodine dressing (56.15±4.65).

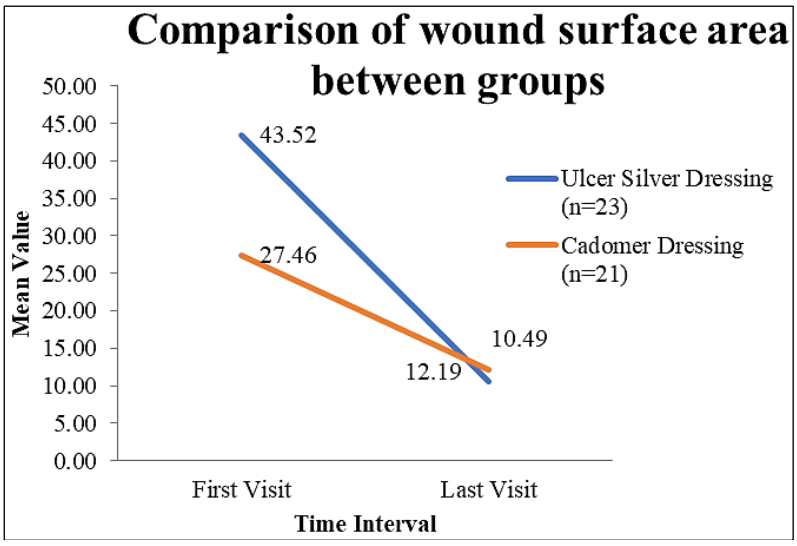

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Table3:Comparison of WAGNER grade between groups

WAGNER Grade	Groups				p Value
	Ulcer silver dressing		Cadexomer iodine dressing		
	n=23	%	n=22	%	
Grade 1	3	13.0	2	9.5	0.713
Grade 2	20	87.0	19	90.5	

Out of 23 cases in ulcer silver dressing, 3 (13.0%) cases were grade I Wagner and 20 (87.0%) were grade II. Whereas in cadexomer iodine dressing, 2 (9.5%) were grade I and 19 (90.5%) were grade II.

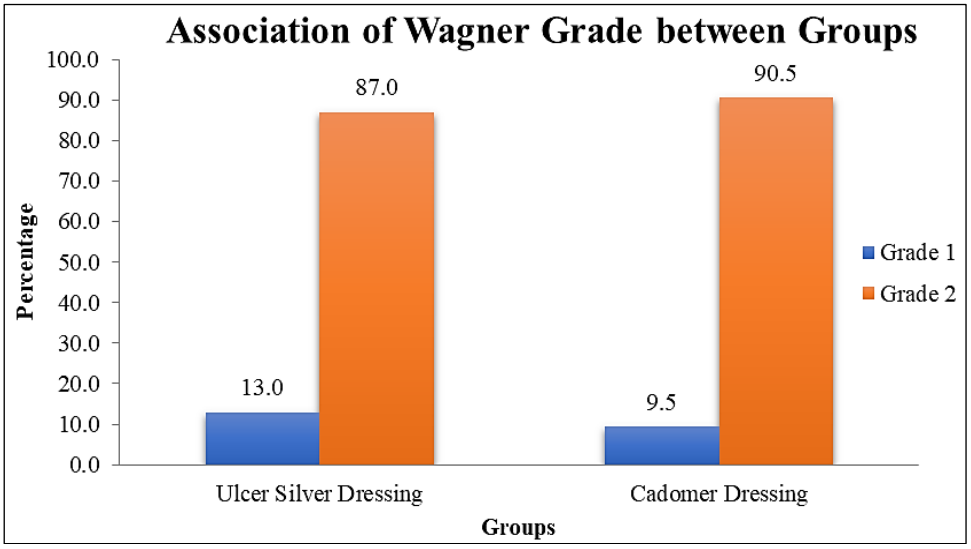

Table4: Association of discharge between groups

Discharge	Groups				p Value
	Ulcer silver dressing		Cadexomer iodine dressing		
	n=23	%	n=22	%	
Greenish	4	17.4	2	9.5	0.468
Purulent	2	8.7	4	19.0	
Serosanguinous	0	0.0	1	4.8	
Serous	17	73.9	14	66.7	

In ulcer silver dressing method, 4 (17.4%) cases were greenish, 2 (8.7%) were purulent and 17 (73.9%) cases were serous. Whereas in Cadexomer iodine dressing method, 2 (9.5%) were greenish, 4 (19.0%) were purulent, 1 (4.8%) was serosanguinous and 14 (66.7%) were serous.

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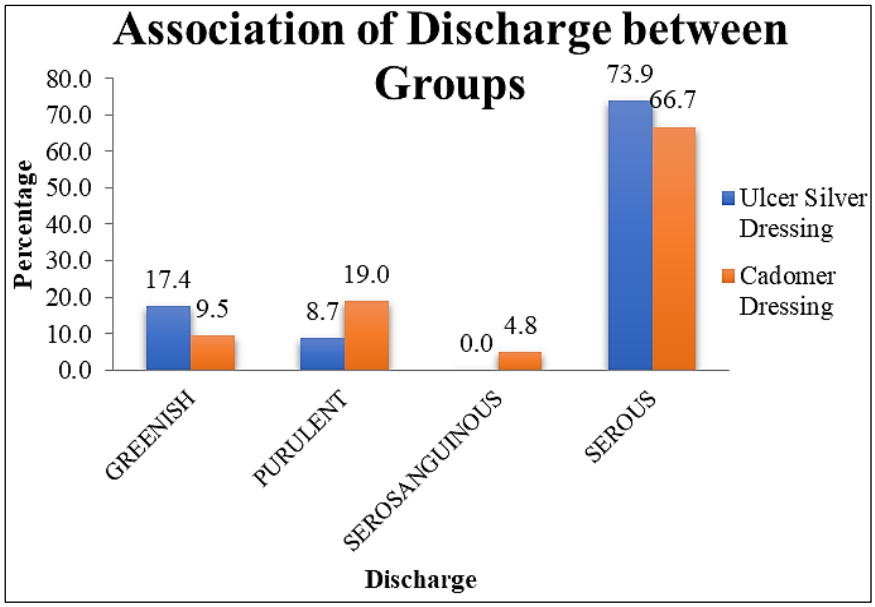

Table5:Association of outcome between groups

Outcome	Groups				p Value
	Ulcer silver dressing		Cadexomer iodine dressing		
	n=23	%	n=22	%	
Grafting	7	30.4	4	19.0	0.488
Healed by secondary intention	14	60.9	13	61.9	
Secondary suturing	2	8.7	4	19.0	

30.4% (7/23) cases were grafting, 14 (60.9%) cases were healed by secondary infection and 2 (8.7%) cases were secondary suturing in ulcer silver dressing. Whereas in cadexomer iodine dressing, grafting, healed by secondary intention and secondary suturing were 19.0%, 61.9% and 19.0% respectively.

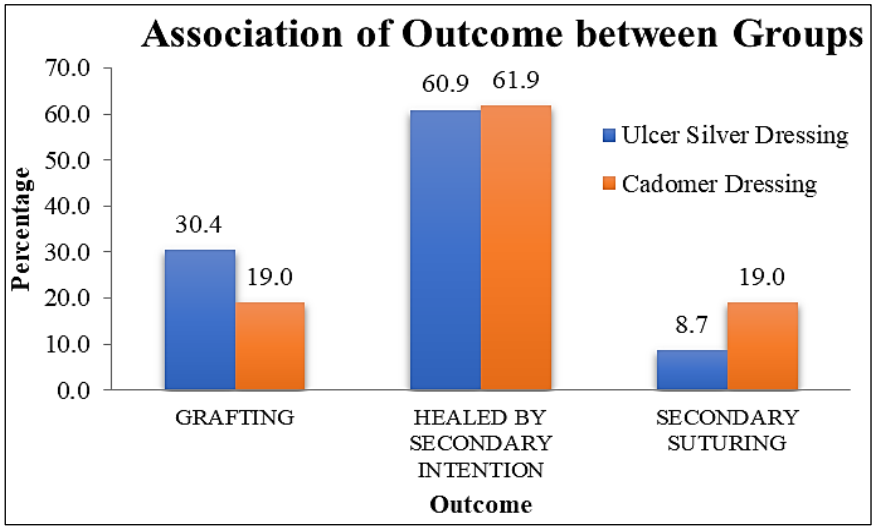

Table6:

Purulent discharge	Groups				p Value
	Ulcer silver dressing		Cadexomer iodine dressing		
	n=23	%	n=21	%	
Yes	2	8.7	4	19.0	0.318
No	21	91.3	17	81.0	

The purulent discharge was 8.7% in ulcer silver dressing and 19.0% in cadexomer iodine dressing. There is no association of purulent discharge between groups (p=0.318).

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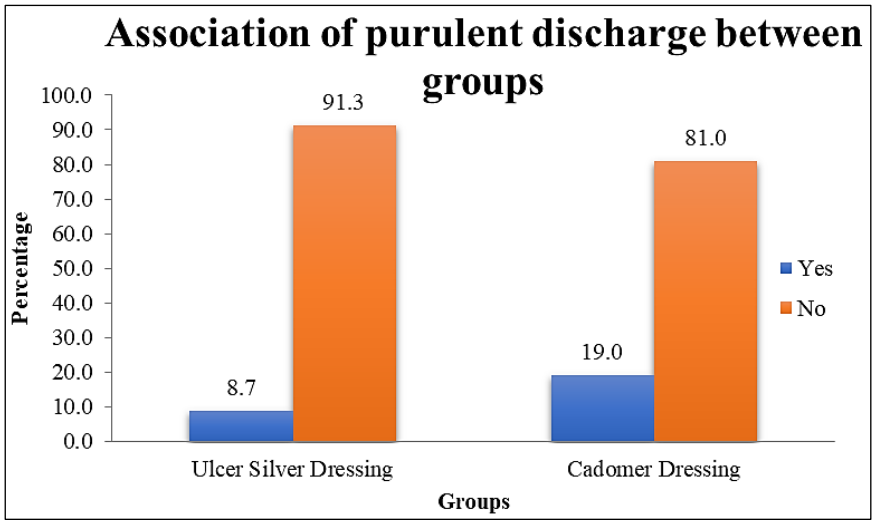

DISCUSSION

Silver nanoparticles have effective action against both, Gram negative and Gram-positive bacteria[1]. Silver inhibits bacterial growth by incorporating it as silver nitrate or silver sulfadiazine in creams and dressings to treat burns and ulcers, in food packaging to prevent contamination, in home appliances as refrigerators and washing machines and several applications in the industrial area[2-6].

Silver's antibacterial mechanism can be categorized into six key pathways. First, it inhibits the bacterial respiratory chain by interfering with enzymes involved in ATP production, ultimately leading to cell death. Second, silver ions disrupt protein synthesis and folding by binding to ribosomes, preventing essential cellular functions. Third, they induce bacterial genetic toxicity by interacting with DNA, causing structural damage and inhibiting replication. Additionally, silver facilitates photocatalytic protein destruction, where light exposure generates reactive species that degrade bacterial proteins. Another critical mechanism is cell membrane rupture, in which silver ions embed into the bacterial membrane, increasing permeability and causing leakage of cellular contents. Lastly, silver induces oxidative stress by promoting the production of reactive oxygen species (ROS), which damage proteins, lipids & DNA[8]. AQAg silver dressings were associated with favourable clinical outcomes compared with CA dressings, specifically in ulcer depth reduction and in infected ulcers requiring antibiotic treatment[7].

The present study compared the efficacy of ulcer silver dressing and cadexomer dressing in wound healing among patients with ulcerations. The findings indicate that ulcer silver dressing led to significantly better healing outcomes compared to cadexomer dressing, with a higher percentage of wound healing and a greater reduction in wound surface area.

The demographic analysis showed no significant differences in age and gender distribution between the groups, ensuring comparability. However, a higher prevalence of hypertension was noted in the ulcer silver dressing group, which could have influenced healing outcomes. Other comorbidities, including diabetes mellitus (DM), coronary artery disease (CAD), and cerebrovascular accident (CVA), were comparable between groups.

One of the most significant findings was the improvement in healing area. The ulcer silver dressing group demonstrated a higher mean improvement of 33.03 cm^2, which was statistically significant ($p = 0.025$) when compared to the cadexomer dressing group (15.27 cm^2). Furthermore, the percentage of wound healing was 80.64% in ulcer silver dressing versus 56.15% in cadexomer dressing ($p < 0.001$), highlighting the superior efficacy of ulcer silver dressing in promoting wound closure.

The distribution of wagner grades was similar between the groups, with the majority of patients presenting with grade 2 ulcers, indicating that both dressings were used on patients with comparable severity of ulceration.

Regarding wound discharge, ulcer silver dressing showed a lower rate of purulent discharge (8.7%) compared to cadexomer dressing (19.0%), though the difference was not statistically significant. A higher proportion of patients in the ulcer silver dressing group had serous discharge, which is often indicative of a cleaner wound-healing process.

The outcome analysis demonstrated that a greater percentage of patients in the ulcer silver dressing group underwent grafting (30.4%) compared to the cadexomer dressing group (19.0%), suggesting that faster wound healing in this group may have facilitated earlier surgical intervention. The proportion of patients who healed by secondary intention was comparable between groups, while secondary suturing was more frequent in the cadexomer dressing group (19.0% vs. 8.7%), possibly due to delayed wound healing.

The findings suggest that ulcer silver dressing is a more effective option for promoting wound healing, potentially due to its antimicrobial properties and ability to maintain a moist wound environment, which

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facilitates granulation tissue formation and epithelialization. The results align with existing literature supporting silver-based dressings as an optimal choice for managing chronic wounds and ulcers.

However, the study is limited by its sample size, and further large-scale randomized trials are recommendedto validate these findings.Additionally, a cost-benefit analysis may be needed to determine the economic feasibility of using ulcer silver dressing over cadexomer dressing in routine clinical practice.

CONCLUSIONS

The study concludes that ulcer silver dressing is superior to cadexomer dressing in terms of wound healing, wound area reduction, and overall clinical outcomes. It can be considered a preferred dressing choice for ulcer management, particularly in cases requiring enhanced wound healing and infection control.

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