Original Research Article

# Clinical study on the efficacy of nanocrystalline-silver in diabetic foot

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## Abstract

**Background:** Diabetic foot is a major complication of diabetic patients; with about 3-4% of individuals with diabetes currently having foot ulcers. If untreated they end in amputation. This puts a staggering load on healthworkers to provide an organised diabetic foot care service. Nanocrystalline silver has been gaining increasing popularity. This study aims to compare the efficacy of silver and conventional saline dressings, to provide a basis for popularising the use of silver ointments.**Methods :**This study is an RCT with 2 groups .We have categorized 50 diabetic foot patients admitted under the department of general surgery of government medical college, Kottayam, during the time period 2018-2019 into 2 groups, withone receiving saline dressings and the other,silver dressings and compared their outcomes. Outcomes were measured in terms of healing by comparing the relative percentages of granulation tissue and slough at various points of time. **Results:**Outcomes were measured over 8 weeks. It was observed that a significant proportion of diabetic foot ulcers showed regression in terms of slough reduction and granulation in patients receiving silver dressings over saline dressings at the end of 8 weeks with a P value of 0.015. There was no significant correlation between the change in bacteriological profile pre- and post-dressing.**Conclusion:**Diabetic foot ulcers being a prevalent health problem, it is of paramount importance to come up with effective treatment methods. Introduction of topical agents such as nanocrystalline silver can help control it.

**Keywords:**Diabetes mellitus,metabolic



## Introduction

Diabetes mellitus (DM) is one of the most important and common metabolic disorders affecting around 5-17% of people in India. The incidence of diabetes mellitus is increasing worldwide; by 2030, it will grow up to 366 million. This estimate occurred because of longer life expectancy and changing dietary habits.Even though there are many complications affecting the person with diabetes, none are more debilitating than those complications involving the foot[1]. Diabetic foot lesions have significant health and socioeconomic implications holding adverse effects on the quality of life of the patient and imposing a heavy economic toll on the patient's family[2].Foot ulcers contribute to the morbidity and mortality of patients with diabetes mellitus. The diabetic patients with foot ulcers require prolonged hospitalisation and carry the risk of limb amputation[3].Foot complications are common in diabetic patients and are considered one of the most expensive diabetes complications to treat [4] People at highest risk of ulceration can easily be identified by meticulous clinical examination of the feet during health education about diabetes complication and during follow-up visits[5]. In developing countries, foot ulcers are one of the most feared and prevalent complications of diabetes as they are a major cause of disability, morbidity, and mortality among diabetic patients, and it has been estimated that 15% of all people with diabetes will have an ulcer at some stage of their life[6].The most important complications of diabetes mellitus are neuropathy and foot ulcer. Features of complications range from simple to complex,including limb amputations and life-threatening infections [7]. Studies show that severity of diabetic foot ulcer is the strongest risk factor for amputation in diabetes patients.. In developed countries, one out of every six people with diabetes will develop an ulcer during their lifetime. The risk is higher in developing countries[8].Risk factors associated with the natural history of foot ulcer in diabetic patients include metabolic or biologic features and the extrinsic characteristics which result from the patient's interaction with his environment. Peripheral neuropathy, peripheral vascular disease, and foot trauma were also reported risk factors in the pathophysiology of foot ulcer[9]. Though preventive strategies have been shown to be cost-effective, diabetic foot ulcers still occur frequently and are a challenge for the individual and for the healthcare system[10].The rapid increase in the incidence of foot ulcer among diabetics requires solid epidemiological knowledge based on high-quality health care services and effective preventive strategies, which must be tailored to the needs of specific groups. Research shows that diabetic foot ulcer is affected by several factors including patient age, socioeconomic status, weight of patient, type of diabetes mellitus, patient habits of foot self-care practice, and the presence of complicated peripheral neuropathy [11]. However, the determinants of diabetic foot ulcer are not the same across different socioeconomic and demographic strata and progress of disease within the institution. Thus, assessing factors affecting diabetic foot ulcer in various areas is very important to prevent the debilitating effect of foot ulcer among diabetes patients. Therefore, this study aims to assess diabetic foot ulcer and risk factors among adult diabetic patients . The finding of this study will help to decrease the occurrence of diabetic foot ulcer and its complication in the area.

**Methods**

The study is a prospective and comparative one, conducted on patients admitted in the Department of general surgery, Kottayam Medical College, from the month of November of the academic

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year 2018 to December 2019. Patients with non-ischemic Wagner grades 1 and 2 ulcer were chosen for the same . 50 patients were included with one half of them receiving nanocrystalline silver dressing and the other half receiving conventional saline dressings. Allocation of patients to either arm was done randomly and unbiasedly on the basis of their patient number, i.e. in the order in which they were admitted under general surgery with alternate patients being allocated to each arm. Those with an even patient number going to group A, and odd patient numbers to group B with A receiving nano-crystalline silver dressings and B receiving saline dressings. Their wounds were kept under follow up for a duration of two months. The patient outcome was measured based on the following

1. Proportion of ulcers that become bacteriologically sterile at the end of the study period
2. Type of bacteria which are most susceptible to the bactericidal action of silver dressing
3. Change in total ulcer area (percentage change)
4. Time to complete healing or to obtain size reduction
5. Degree of slough reduction and appearance of granulation

The patients were followed up once in 2 weeks in the surgical out patient department and wound assessment was carried out by the author. Outcomes were determined based on wound size, change in total area and ulcer characteristics. The size of ulcers were measured using sterile roller gauze, which was then placed over a scale to get the approximate wound area. The proportion of granulation tissue and slough were also measured in the same way. Swabs were taken from the ulcer site during every visit and sent for microbiological profiling and antibiotic sensitivity testing. Follow up of patients was on an OP basis and patients were kept under follow up for a total of 8 weeks. Total 4 visits per patient was carried out.Details of examination were documented in the proforma. The data collected was statistically analyzed with spss17 software.

Inclusion Criteria:

1.Diabetic foot patients with Wagner's grades 1 and 2 diabetic foot ulcers.

Exclusion Criteria:

1.Diabetic foot patients with Wagner's grades 3, 4,5
2.X-ray showing osteomyelitis
3.Doppler showing diffuse atherosclerosis
4.Uncontrolled diabetes mellitus (RBS >500mg/dl with insulin)
5.Immunosuppressed patients-on steroids/immunosuppressant, radiation or chemotherapy
6.Other clinically significant medical conditions that would impair wound healing like renal, hepatic, haematological, neurological, and immunological diseases

**Limitations Expected**

1.Erroneous results due to differences in glycemic control of patients
2.Differences in bacteriological profile of patients, due to variable response for different organisms.

**Results**

Half of the study subjects were randomised to each study group based on the order in which they were admitted

**Table 1:Randomisation of study subjects**

| Group | Number | Percentage |
|---|---|---|
| Silver Dressing | 25 | 50.0 |
| Saline Dressing | 25 | 50.0 |
| Total | 50 | 100.0 |

**Table 2: Percentage of granulation tissue in the wounds at baseline**

| Granulation Tissue-Baseline | Silver Dressing | | Saline Dressing | | P Value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| <20% | 18 | 72.0% | 4 | 16.0% | Chi-Square=18.709<br>DF=3<br>P<0.001 |
| 21-40% | 7 | 28.0% | 13 | 52.0% | |
| 41-50% | 0 | .0% | 7 | 28.0% | |
| 51-60% | 0 | .0% | 1 | 4.0% | |
| 61-70% | 0 | .0% | 0 | .0% | |
| 71-80% | 0 | .0% | 0 | .0% | |
| >80% | 0 | .0% | 0 | .0% | |
| TOTAL | 25 | 100.0% | 25 | 100.0% | |

Among the subjects in group A that received silver dressings, 72% had only less than 20% healthy granulation in their wounds at baseline evaluation And in the second group receiving saline dressings , 52% had 21-40% baseline granulation. This distribution was found to have statistic significance in the outcome.

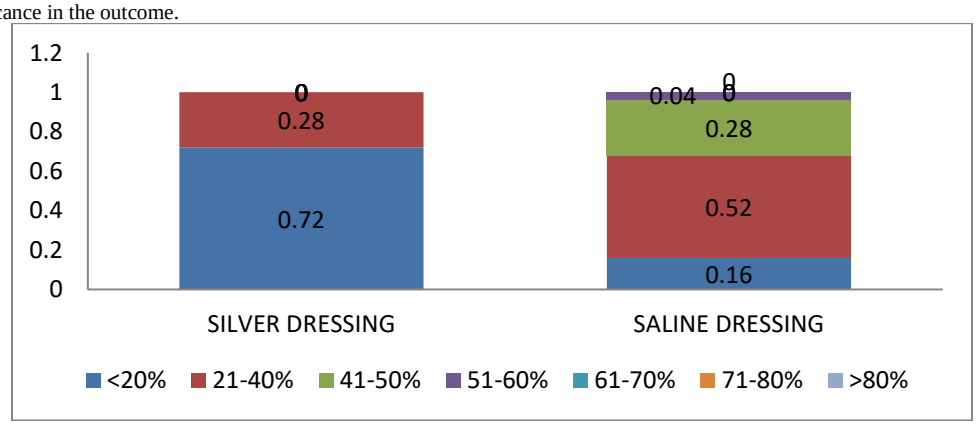


**Fig 1:Silver dressing and Saline dressing**

**Table 3: Percentage of granulation tissue in wounds at the end of 8 weeks**

| Granulation At 8 Weeks | Silver Dressing | | Saline Dressing | | P Value |
|---|---|---|---|---|---|
| | No | % | No | % | |
| <20% | 0 | .0% | 0 | .0% | Chi-Square=7.082<br>DF=3<br>P=0.069 |
| 21-40% | 0 | .0% | 1 | 4.0% | |
| 41-50% | 5 | 20.0% | 12 | 48.0% | |
| 51-60% | 18 | 72.0% | 12 | 48.0% | |
| 61-70% | 2 | 8.0% | 0 | .0% | |
| 71-80% | 0 | .0% | 0 | .0% | |
| >80% | 0 | .0% | 0 | .0% | |
| TOTAL | 25 | 100.0% | 25 | 100.0% | |

At the end of 8 weeks it was observed that 72% of the study subjects in group A had upto 50-60% granulation while only 48% had similar results in the opposite arm

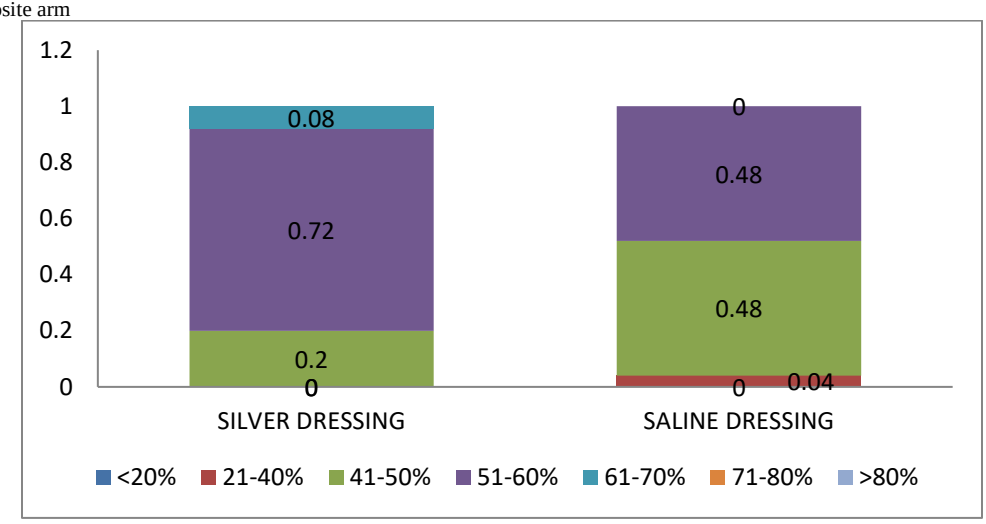


**Fig 2:Silver dressing and Saline dressing**

**Table 4: Table showing the distribution of bacteria in the wound prior to treatment**

| Bacterial Load-Pre Dressing | Silver Dressing | | Saline Dressing | | P Value |
|---|---|---|---|---|---|
| | NO | % | NO | % | |
| Gram Positive | 6 | 24.0% | 5 | 20.0% | Chi-Square=8.808<br>DF=4<br>P=0.066 |
| Gram Negative | 9 | 36.0% | 9 | 36.0% | |
| Mixed | 8 | 32.0% | 3 | 12.0% | |
| Commensals | 1 | 4.0% | 8 | 32.0% | |
| No Growth | 1 | 4.0% | 0 | .0% | |
| Total | 25 | 100.0% | 25 | 100.0% | |

Patients in the group receiving silver dressings and saline dressings were found to have a predominance of gram negative microorganisms in the wound pre-dressing.

**Table 5: Table showing the prevalence of microorganisms in the wound post dressing period**

| Bacterial Load-Post Dressing | Silver Dressing | | Saline Dressing | | P Value |
|---|---|---|---|---|---|
| | NO | % | NO | % | |
| Gram Positive | 0 | .0% | 2 | 8.0% | Chi-Square=26.129<br>DF=4<br>P<0.001 |
| Gram Negative | 0 | .0% | 4 | 16.0% | |
| Mixed | 1 | 4.0% | 11 | 44.0% | |
| Commensals | 10 | 40.0% | 7 | 28.0% | |
| No Growth | 14 | 56.0% | 1 | 4.0% | |
| Total | 25 | 100.0% | 25 | 100.0% | |

**Table 6:Table showing the distribution of slough at the end of 8 weeks**

| Slough-At 8 Weeks | Silver Dressing | | Saline Dressing | | P Value |
|---|---|---|---|---|---|
| | NO | % | NO | % | |
| <20% | 11 | 44.0% | 1 | 4.0% | Chi-Square=17.74<br>DF=3<br>P<0.001 |
| 21-40% | 13 | 52.0% | 12 | 48.0% | |
| 41-50% | 1 | 4.0% | 10 | 40.0% | |
| 51-60% | 0 | .0% | 2 | 8.0% | |
| 61-70% | 0 | .0% | 0 | .0% | |

| | | | | | |
|---|---|---|---|---|---|
| 71-80% | 0 | .0% | 0 | .0% | |
| >80% | 0 | .0% | 0 | .0% | |
| Total | 25 | 100.0% | 25 | 100.0% | |

At the end of 8 weeks it was seen that more than 90% of patients in the group that received silver dressings had less than 40% of slough left, while in the opposite arm , upto 60 percent residual slough was observed. This difference was found to be statistically significant when analysed.

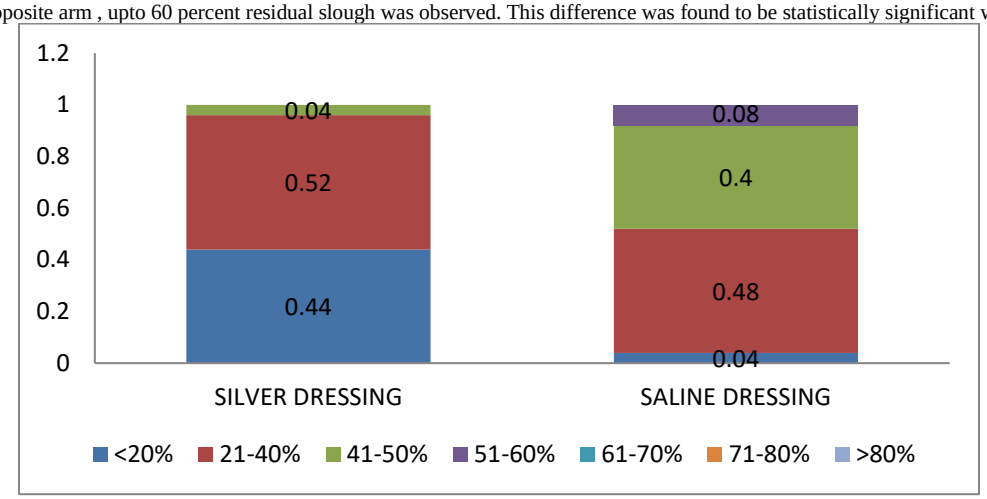


**Fig 3:Silver dressing and Saline dressing**

**Discussion**

This research indicates that nanocrystalline silver dressing is an effective antimicrobial for treating wounds especially burns and chronic wounds in diabetics. In the data obtained from the study described above, it has been observed that silver dressings have been shown to reduce the slough content in diabetic ulcers, as well as increase the rate of granulation tissue formation, in preference to conventional saline dressings. The above data clearly indicates that the proportion of healing is accelerated in the study subjects receiving nanocrystalline silver dressings.The study also shows that the microbiological profile changes towards the end point of the study, favouring no growth with the application of silver dressings. The favourable microbiological profile and the faster wound healing rates as demonstrated by the results of this study, shows the supremacy of silver dressings over conventional dressings.Before application of dressing, cleaning and debridement was carried out for each wound in the opd. This might have also been a contributory factor to the reduction in bacterial load. However statistically it was seen that the application of silver dressings needed to be consistent over a period of 8 weeks at least for the results to be fully evident.In addition to this, the blood sugar levels were also found to be better controlled in the group A that received silver dressings. This might be attributable to the improved wound characteristics in this study group , which decreased the levels of inflammation thus providing better glycemic control in this group.Many studies have shown that nanocrystalline silver reduces the inflammation and facilitates wound healing and is less toxic than other forms of silver dressings due to the slow release of silver onto the wound[12].There have been no features of toxicity of nanocrystalline silver on keratinocytes or fibroblasts, but there is in vitro evidence to suggest so. Thus, clinicians should be cautious in the use of nanocrystalline dressings over reepithelialising and proliferating wounds [12]. Anecdotal evidence from clinical trials, case presentations, and reports suggests that the use of nanocrystalline silver is cost effective, reduces pain levels, and has a longer wear time, thus limiting the frequency of dressing changes. There have been no reports of resistance to nanocrystalline silver dressings; however, physicians should use these dressingsjudiciously, applying them to the appropriate wounds and limiting their use appropriately to prevent the development of bacterial resistance. Practitioners are increasing their use of nanocrystalline silver dressings for wound management either for their antimicrobial or anti-inflammatory properties. More quality clinical research should be conducted in order to direct clinicians in their decision making process in choice of dressings and to provide more evidence for best practices in wound management.During a study conducted in 2000 and 2002, at the Royal Perth Hospital (RPH) Burn Unit, Western Australia, two 'before and after' patient care audits were compared to deduce the efficacy and cost effectiveness of Silvazine(silver sulphadiazine and chlorhexidine digluconate cream) and Acticoat, a new nanocrystalline silver containing dressing product for in-patient treatment of early burn wounds. The main outcome variables measured were: burn wound cellulitis, antibiotic use and cost of treatment. The average length of stay (LOS) in hospital was 17.25 days for the Silvazine group and 12.5 days for the Acticoat group with a difference of 4.75 days. These audits show that Acticoat results in a decreased incidence of burn wound cellulitis, antibiotic use and overall cost compared to Silvazine in the treatment of early burn wounds.A similar study conducted in the Department of Dermatology , Federal Academic hospital in Austria demonstrated the superiority of nanocrystalline silver dressings in breaching the physical barriers and providing better wound healing in wounds infected with MRSA. 67% of all wound observations showed a decrease in the MRSA load with an eradication rate of 11%.The results of a research conducted in the Wound Healing Research Unit of Cardiff University showed that Silver dressings effectively reduced the bioburden of chronic wounds and further supplanted the evidence regarding its effectiveness against MRSA[12]. It follows therefore that there are various properties of a wound that determine its healing rate and thus limb salvage rates in diabetic foot ulcers which pose a prevalent issue in our country, however the use of novel yet simple strategies such as nanocrystalline silver dressings in diabetic ulcers will reduce the time taken for healing as well as improve the microbiological wound profile, which may ultimately improve limb salvage rates.

**Conclusion**

The pathology of Diabetic foot syndrome is complex and microcirculatory blood misdistribution occurs in diabetic foot.The

incidence of diabetic foot ulceration is also increasing worldwide thus increasing the problem scale of the disease necessitating the need for discovery of newer yet technically feasible and commonly applicable methods of wound healing.

This study reveals that topical application of nanocrystalline silver dressings greatly improves the wound characteristics and promotes faster healing as well as improves the glycemic status of diabetic patients.

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