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COMPARATIVE ANALYSIS OF NANOCRYSTALLINE SILVER DRESSING AND SILVER SULPHADIAZINE IN SECOND DEGREE SUPERFICIAL BURN WOUND HEALING: A PROSPECTIVE RANDOMISED STUDY

Plastic Surgery

Samiksha Mehare* Consultant and Assistant Professor, Dept of Plastic Surgery, Army Hospital Research and Referral, New Delhi 110010, India *Corresponding Author

S K Singh MS, Mch, DNB , Dept of Plastic Surgery, Army Hospital Research and Referral, New Delhi 110010, India

Vijay Langer MS, Mch, DNB , Dept of Plastic Surgery, Army Hospital Research and Referral, New Delhi 110010, India

Sandeep Mehrotra MS, Mch, Dept of Plastic Surgery, Army Hospital Research and Referral, New Delhi 110010, India

ABSTRACT

A prospective randomized study was conducted to assess efficacy of two modalities of treatment for second degree superficial burns, namely silver sulphadiazine and nanocrystalline silver dressing with respect to duration of healing, patient comfort and cost.

Methods and Material: All patients presenting to Plastic Surgery department with second degree superficial burns less than 30% from 1st June 2014 to 31st May 2016 were included in the study. Total 130 patients with complete data were evaluated. Patients were followed for an average period of 3 months (Range 3 months to 2 yrs).

Results: Maximum incidence of superficial burns is in 0 -10 years age group. Among superficial burns scalds is the commonest aetiology. Healing is faster in patients treated with silver sulphadiazine. Majority of nanocrystalline silver dressing patients are managed as outpatients and frequency of dressing change is less. Pain score is more in nanocrystalline silver dressing group but difference among two groups is not statistically significant.

Conclusions: This study does not suggest superiority of either of the two groups. Faster wound healing & less pain perception is seen with silver sulphadiazine group. Nanocrystalline silver group needs less frequent dressing change, reducing the morbidity and lesser hospital admission. Wound healing outcome are comparable in both groups.

KEYWORDS

Superficial Burn; Silver Sulphadiazine; Nanocrystalline Silver; Burn wound healing

Introduction

Topical silver as an antimicrobial agent has been used for hundreds of years in wound care (1). There are growing number of silver-containing dressings and topical agents available for treatment of skin wounds. Silver sulphadiazine (SSD) is a commonly available ubiquitous burn care cream, however, it is relatively short-acting, requiring re-application (ideally twice daily,) and is time-consuming and messy to apply and remove (2). Newer dressings are easier to apply with sustained availability of silver, need less frequent dressing changes, and may provide additional benefits such as management of excessive exudate, maintenance of a moist wound environment, or facilitation of autolytic debridement (3). Silver-based dressings are now available as a variety of fibers or polymeric scaffolds impregnated or coated with a silver (Ag) salt or metallic silver (Ag) in nanoparticulate form.

Nanoparticles (NPs) are defined as particles having one or more dimensions in the order of 100 nm or less. Silver NPs (Ag NPs) have been shown to possess unusual physical, chemical and biological properties (4,5,6). Their use is restricted to higher centres, mainly due to perceived high cost.

In India, there have been no studies which compare efficacy of nanocrystalline silver (NCS) dressing with silver sulphadiazine in healing of burn wounds. The aim of this study is to compare conventional silver sulphadiazine cream with nanocrystalline silver therapy in healing of second degree superficial burn wounds.

Material & Methods

A prospective randomised single blinded study was undertaken on all consecutive patients presenting with acute second-degree superficial burns treated at a tertiary referral centre or as an outpatient basis from 1st June 2014 to 31st May 2016. The project was approved by the Institutional Ethical Committee.

All patients with partial thickness burn less than 30% second degree superficial burn wounds were included. Exclusion criteria were first degree burns, more than 30% TBSA, deep burns, patients with gross wound infection, sepsis, co-morbidities (Diabetes, Hypertension, Coronary artery disease, Tuberculosis, Thyroid disorder etc.), patients initially treated elsewhere (usually with SSD that precluded randomisation) and wounds that turned deep during treatment in either group.

Patients were randomised into two groups using computerised random number table and signed informed consent was obtained from the patients or their legal guardians. A detailed history and clinical evaluation and extent of burns was noted. Those with burns more than 20% total body surface area (TBSA) burns were resuscitated with fluids as per Parkland formula. Photographic assessment of wound was done on day zero (before starting treatment), at complete wound healing and three months thereafter.

All patients were administered analgesic (0.1 mg/kg morphine) 10 minutes before dressing according to weight adjusted doses. All wounds were washed with normal saline. Group A patients were managed with silver sulphadiazine (SSD) cream dressing. Uniform layer of cream was applied over burn area followed by secondary dressing consisting of a layer of sterile gamgee pad as sterile securing dressing. In this group dressings were changed daily or more frequently in case of excessive soakage.

Group B patients were managed with nanocrytalline silver (NCS) dressing. Burn area was cleaned with distilled water and dressing sheet was moistened with distilled water; this moist sheet was applied with silvery side facing the wound. It was covered with same secondary dressing same as silver sulphadiazine group. Dressing was inspected after 72 hours if dry & earlier if soakage was observed.

The two study groups were closely monitored on first day, 2 hours after application of dressing, and thereafter on day 7, 14 and 21 for epithelialisation and pain. Pain was assessed 2 hours after dressing by the numeric pain intensity scale described by Houde, R.W. (1982). Pain perception analysis using pain scale was done by adult patient & children more than 10 years on their own whereas for children less than 10 years it was done by parents or observer. Pain Assessment with the "0—10 Numeric" Pain Intensity Scale. The follow up evaluation of the quality of scar was done at 3 months.

For statistical analysis of the study, software SPSS 16.0 was used. The primary outcome, time for full epithelialisation and the secondary outcome of pain and cost were compared between the two groups using Student t test. Other categorical outcomes were compared between the two groups using Chi square test. The p value < 0.05 was considered as

statistically significant.

Results

Among 340 burn patients presenting to burn centre 210 were excluded as per exclusion criteria. One hundred thirty patients of second-degree superficial burns with complete data, were included in study and randomly distributed in either group. Number of subjects in Group A (SSD) was 68 and that in Group B (NCS) dressing was 64. There were 70 males & 60 female patients. The majority of patients suffering from second degree superficial burns were children under 10 years (44%) and then the young active population in age group of 21-30 (25%). Mean age of presentation was 18.53(+/-15.9) years. (Fig 1)

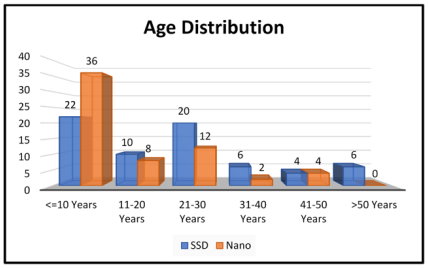

Figure 1- Age Distribution - Maximum incidence – 0 -10 years - Highly Significant (p = <0.001)

Majority of subjects sustained scalds (n=70). (Fig 2) Mean percentage of burns was 6.85% (+/- 7.95%) total body surface area in 130 subjects. Silver sulphadiazine group & nanocrystalline silver dressing group has mean extent of burns as 7.44% (+/-8.57%) & 6.19% (+/-7.10%) TBSA respectively.

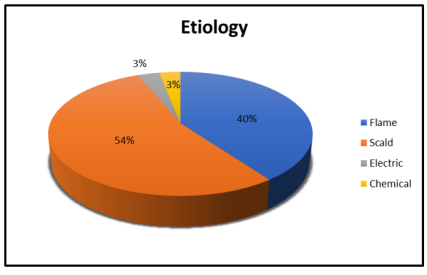

Figure 2 – Etiology of Burns

Fifty five percent patients treated with silver sulphadiazine cream were managed as indoor patients (38 inpatients/68), whereas those treated with nanocrystalline silver dressing were predominantly managed as outpatients (37 outpatients/62) (59.67%) (p=0.05). Mean hospital stay for these groups is comparable, 10.32 (SD+/-7.77) days with silver suplhadiazine and 10.08 (SD+/-5.76) with nanocrystalline dressing. (Fig 3, 4)

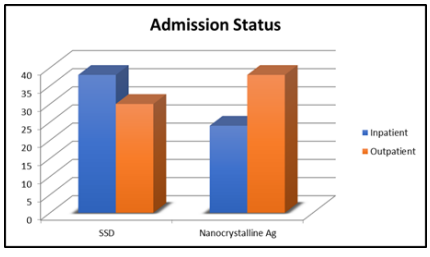

Figure 3 – Admission Status - Majority nanocrystalline silver dressing patients managed as outpatients – Significant (p= 0.05)

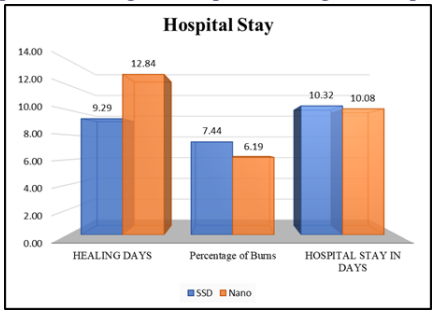

Figure 4 - Hospital Stay

Data suggest that healing was faster in silver sulphadiazine group compared to nanocrystalline group, mean duration being 9.06 (SD+/-4.73) & 12.83 (SD +/- 4.28) days respectively. Faster Healing with Silver sulphadiazine – Highly Significant (<0.001) (Fig 5) Mean number of dressing change in silver sulphadiazine cream & nanocrystalline group were 9.32 (SD+/-4.72) and 3.94 (SD+/-2.57) respectively which was statistically significant. (p < 0.001) (Fig 6).

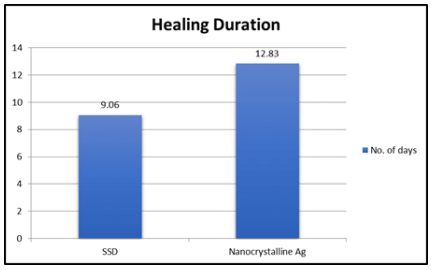

Figure 5 – Duration of Burn Wound Healing- Faster Healing with Silver sulphadiazine – Highly Significant (<0.001)

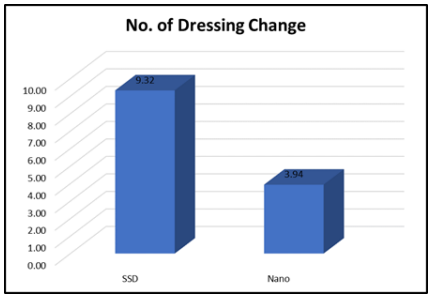

Figure 6 – Frequency of dressing change - Lesser number of dressing change with Nanocrystalline silver dressing – Highly Significant (p < 0.001)

When pain was compared using numerical pain scale, it was found to be more with nanocrystalline silver dressing group on day 1, day 7 and day 14. The difference of pain perception among two groups is not significant (p > 0.05). (Table 1) In all patients healing was complete at end of 3 weeks. None of the patients required secondary grafting. Final outcome at end of three months is same with both dressings.

Table 1 - Pain Score - Difference of pain perception among two groups is not significant.

	TYPE OF DRESSING	N	Mean	Std. Deviation	t-value	p-value
PAIN SCORE D1	SSD	68	6.97	2.73	0.30	0.766
	Nano	62	7.10	2.01		
PAIN SCORE D7	SSD	68	3.03	2.91	1.14	0.256
	Nano	62	3.58	2.57		
PAIN SCORE D14	SSD	68	0.97	2.01	1.04	0.301
	Nano	62	1.35	2.21		
PAIN SCORE D21	SSD	68	0.15	0.85	0.40	0.691
	Nano	62	0.10	0.53		

Cost analysis of dressings revealed that mean cost of SSD per percent burns is 208.35 (+/-240.06) whereas for nanocrystalline dressings it is 743.23(+/-851.82) Rs. (p=0.001). But when total cost (Cost of dressing per % of burns X No. of dressings) was calculated it is not significant (p=0.083). With SSD mean total cost of dressings is 2150(+/-3030.01) Rs. For NCS dressings mean total cost till wound healing 3429(+/-4963.04) Rs. (Fig 7)

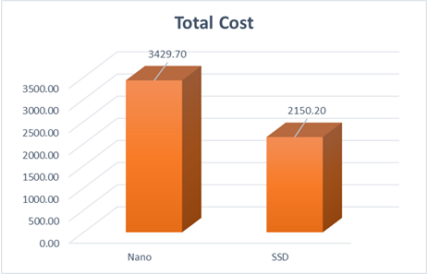

Figure 7 – Cost Analysis – Difference in mean total cost of dressing among two dressings is not significant (p=0.083).

Discussion

Major burn injury is one of the most savage forms of trauma, it causes serious morbidity in the form of significant pain, repeated dressings, prolonged hospitalisation, and an arduous rehabilitative process.

The gold standard in topical burn treatment is silver sulfadiazine. Recent finding, however, indicate that the compound delays the wound healing process (7). In the past decade, renewed interest in silver is due to increased resistance of bacteria to antibiotics and improvements in polymer technology. Nanocrystalline silver dressing was developed in late 1990s to overcome some of the shortcomings of traditional silver dressings.

Nanocrystalline dressing is antimicrobial, simple to apply, with minimal pain on application and does not require to be changed often(8). In present study conventional silver sulphadiazine cream is compared with NCS dressing with regards to healing & patient comfort. Our primary interest was in the outcome results; therefore, most points were allocated to short and long-term outcomes. Short-term outcome results were considered as days of hospital stay, time to re-epithelialization, need for grafting and complications such as infection or pain at dressing changes. Long-term results were in quality of scar formation.

Vloemans et al conducted a study In Netherlands, which states that about 45% of the patients admitted to a Burn Centre are below 17 years of age. Between 1995 and 2007, 2682 children were admitted to a Dutch burn centre. Almost 70% of these children were younger than four years. They suffer from scald burn injuries in over 84% of the cases. (9). Recent studies conducted in Western Australia and the Czech Republic showed similar high frequencies of scald burn injuries in the group of young children (10, 11). Results of this study correlates with all above mentioned studies, Children below 10 years of age constituted 44% of our total subjects and among these children 68% patients had scalds burns.

In an Indian study conducted by B. P. Sarma and N. Sarma (1994), maximum no. of patients was in the age group between 21 – 40 years (12). Studies conducted by Mural Turegan et al and C. N. Malla et al (13,14) showed that maximum number of patients were in the age group 21 – 30 years. These studies include whole spectrum of burns and not second-degree superficial burns only, and may be the reason for different observation.

Dewar et al found that in scalds caused by hot beverages in children, anterior torso was affected in 65%, upper limbs in 51%, head and neck in 39% and legs in 26%. In our study torso was affected in 44% children, while upper & lower limb constituted 39% & 47% respectively (15).

There is a lack of high-quality designed research such as randomized control trials in human studies into superiority of nanocrystalline silver dressings or silver sulphadiazine dressing. In an earlier study in 1998 Tredget conducted a matched paired randomized study to evaluate the efficacy and safety of nanocrystalline silver dressing for burn wound treatment. Thirty patients with symmetrical burns were randomly assigned to be dressed with nanocrystalline silver dressing or silver nitrate solution dressings. They found that the nanocrystalline silver dressing-treated patients had less pain levels initially but the pain levels were comparable with that of the silver nitrate group of patients after 2 hours. They also found that the frequency of dressing changes and incidence of wound sepsis were less in the nanocrystalline silver dressing treated group (16). Contrary to above finding our study concludes that mean pain score was less with silver sulphadiazine than nanocrystalline silver dressing. In our experience when same patient was treated with both modalities at different site, patients were used as their own control. Patients noticed more pain after initial application of nanocrystalline silver dressing than silver sulphadiazine.

Voight presented report that 4.8% of those surveyed used nanocrystalline silver dressing as their principal dressing. They concluded that nanocrystalline silver dressing improved wound healing (17). Dunn in 2004 presented reports from the 2003 European Burns Association meeting of success with the use of nanocrystalline silver dressing on burn patients by several clinicians across Europe. There were reports of improved pain levels, reduction in the frequency of dressing changes, wound exudate and number of surgical procedures (18).

In a randomized control study Varas et al in 2005 examined 14 burn patients pain levels after dressing changes. Patients had 2 areas of burns and were randomly assigned to NCS dressing or SSD cream dressings. Patients were used as their own control. They found that nanocrystalline silver dressing treated wounds were less painful than the silversulfadiazine cream treated wounds (19). Due to small sample size there may be discrepancy between Varas et al findings and this study.

Fong et al in 2005 conducted 2 comparative patient care audits. Patient care audits demonstrated that the NCS dressing treatment group had lower pain levels and had higher levels of feeling of well-being due to lower pain levels and less frequent dressing changes (11). These findings are consistent with this study in terms of less frequent dressing change. However, feeling of wellbeing was not objectively assessed in this study. This study showed average number of dressing change with silver sulphadiazine group and nanocrystalline silver being 9.06 and 3.93 respectively, which was statistically significant.

A retrospective cohort study was performed by Cuttle et al examining 328 SSD treated patients from January 2000 to June 2001 and 241 NCS treated patients from July 2002 to July 2003. The time taken for re-epithelialisation in the NCS dressing group (14.9 days) was significantly less than that for the SSD group (18.3 days), p=0.047(20). Cuttle el al study differs in many aspects like retrospective study, it includes second degree superficial & deep burns, duration of healing with sulphadiazine (18.3 days) verses 9 days in this study. Nanocrystalline healing duration is comparable in both studies.

Cuttle et al states that there were more wounds requiring long term scar management in the Silver sulphadiazine group (32.6%) compared to the Nanocrystalline silver dressing group (29.5%) (20), however this was not significant. In this study healed wound outcome in both groups were comparable. This may be a measure of clinical inaccuracy of determining depth of burns and including deep burns in study. This may skew the final outcome and results of the study.

Very scanty data is available regarding admission status comparing both treatment modalities. Cuttle et al states that with nanocrystalline silver group inpatients are only 18% of the total admissions, with the vast majority of patients treated on an outpatient basis (20), which was consistent with this study's result. This study had 40.32% inpatients in nanocrystalline silver group.

Few articles quote the equivalence of both dressings and none conclude superiority of silver sulphadiazine. In a non-comparative trial, Borsuk et al treated 15 children with a silver-coated nylon dressing (21). The author considered this dressing as effective as other silver containing dressings used for paediatric burns. No conclusion can be drawn as to which silver-releasing dressing would perform better, since no direct comparative studies amongst the different silver containing dressings could be identified. This corresponds with the outcome of the recent Cochrane review on topical silver for preventing wound infection. (22) Cochrane review is one such strong evidence which states that no conclusion can be drawn as to which silver-releasing dressing would perform better.

A study was conducted to assess cost effectiveness of nanocrystalline silver dressing by S. Cox et all which showed clearly saved costs compared to SSD dressing resulted primarily from the decreased number of dressings, and the presumed shorter hospital stay. (23)

Cuttle et all states cost effectiveness of nanocrystalline dressing unlike our study which has comparable cost in both groups. (20) Recent study of 2014 by C. Malic et al financial model illustrated a potential significant cost saving with nanocrystalline silver dressing, primarily as a result of an outpatient model of care. (24)

This study does not suggest superiority of either of the two groups. As per this study faster wound healing was seen with silver sulphadiazine group. Nanocrystalline silver group needs less frequent dressing change, possibly reducing the morbidity and reducing the requirement of hospital admission. Wound healing outcome and scar quality are comparable in both groups. Cost analysis revealed that though cost of

dressing per % of burns is significantly lower in SSD group but total cost till wound healing is comparable.

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