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A CLINICOPATHOLOGICAL COMPARISON BETWEEN SILVER RELEASING DRESSINGS AND CONVENTIONAL POVIDONE IODINE DRESSINGS IN THE MANAGEMENT OF INFECTED WOUNDS.

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ABSTRACT Microscopic Angiogenesis Grading System (MAGS) score is a scoring system which can also be used to assess the healing of the infected wounds. We conducted a clinico-pathological comparison along with MAGS score between silver releasing dressings and conventional dressings using povidone iodine, in the treatment of infected wounds. A prospective, randomized, comparative study was conducted among the patients with infected wound admitted in surgical wards at a tertiary care hospital over a period of one and a half years. A sample of 86 subjects was randomised into two groups. Group A received silver dressing and Group B received povidone iodine dressings. Both groups received oral antibiotics and the routine standard of care was employed for management of the subjects. Presence of exudates, size of wound, MAGS score and bacterial culture were noted at Day 1, 14th, 28th and 42nd day. There significant earlier reduction in size, exudates, MAGS score and bacterial culture in group with silver dressings when compared to conventional dressings.

KEYWORDS :

INTRODUCTION:

Wound healing is a complex dynamic process of replacing devitalised tissue. The process of tissue repair starts as soon as the injury occurs and follows a patterned process[1–4]. Majority of the wounds heal without any incident. But, some wounds turn chronic when the process of healing is disrupted[5,6]. Angiogenesis is one of the most important aspects related to healing in wounds reflecting adequate healing. It may be considered as a measurable target in combating conditions characterized by either poor vascularisation or abnormal vasculature[7–9]. Microscopic Angiogenesis Grading System (MAGS) score is a scoring system developed by Bremm et al[10] in 1972 initially in relation to tumour angiogenesis. However, it takes into account several objective criteria relating also to angiogenesis in a healing wound and thereby facilitates a more justified comparison between modalities when they are used in dressing of such wounds[11]. Based on the this background, the present study had been designed to carry out a clinico-pathological comparison along with MAGS score between silver releasing dressings and conventional dressings most commonly using povidone iodine, in the treatment of infected wounds.

MATERIALAND METHODS:

A prospective, randomized, comparative study was conducted among the patients with infected wound admitted in surgical wards at a tertiary care hospital over a period of one and a half years. All patients with superficial wounds either traumatic or surgical in nature, with controlled diabetes and wound area between 1sqcm-100sqcm were included in the study. The patients with underlying vasculitis, malignant ulcers, arterial diseases, deep burn wounds, tubercular ulcers and patients on immunosuppressive drugs and known allergy to silver were excluded from the study.

A pilot study was conducted in which 5 patients were studied in each group and their mean Microscopic Angiogenesis Grading System (MAGS) score was calculated. At 95 % Confidence levels and 80% power, mean and standard deviations of the MAGS score on follow up, was 56.4 ± 5.4 in silver releasing dressing group and 52.6 ± 6.4 in the povidone iodine dressings group. Based on this a sample size of 86 was decided upon. Randomization of subjects across the group was done by using computer generated numbers. Patients were divided into two groups A and B randomly each with 43 subjects. Wounds of patients in Group A were treated with silver releasing dressings while those in Group B were treated with povidone iodine dressings. Silver foam dressings (Biatain Ag ®) was used which were changed every 7 days. Dressings as per requirement were done in Group B. Both groups received oral antibiotics and the routine standard of care was employed for management of the subjects. Both the groups consisted of patients with or without associated co morbidities such as diabetes.

The outcome was measured in clinical terms as well as objectively using the Microscopic Angiogenesis Grading System (MAGS) score [11] which was calculated for each wound in both groups and a comparison done. The end point of the comparison was a healthy, non infected wound with a MAGS score above 80(if the wound had not completely healed by then). The end of the study period was 42 days (6weeks) from the beginning of the study. Clinical assessment of the wounds was performed at the beginning of each dressing and findings were noted. The wound size, exudates, odour, necrosis, pain and granulation tissue were the parameters assessed. Bacterial culture of the exudates was sent before starting any antibiotics for the patient.

All the data was entered and compiled and analysed using Epi Info version 7.2. The qualitative variables were expressed in terms of percentages and the difference between two proportions was tested using Chi square test or Fisher's exact test. Quantative variables were either expressed in terms of mean and standard deviation or categorised and expressed in percentages. To test the difference between the two means, student't' test was used. All the analysis was 2 tailed and the significance level was set at 0.05.

RESULTS:

We had included 86 study subjects divided equally among Group A and Group B. The mean age of the study subjects was 39.98 ± 16.19 and 35.49 ± 15.08 years in Group A and Group B respectively and there was no significant difference between the proportion of females and males among both the groups. 24.42% and 18.60% subjects in Group A and Group B respectively were diabetics. The most common location of the wound was over the foot followed by the perineal region. In our present study, it was found that on day 1, a total of 82 patients had painful wounds out of which 41 patients were from Group A (47.67%) and 41 were from Group B (47.67%). On day 14 the proportion of painful wounds was more in Group A (19.77%) as compared to Group B (17.44%).However by the 28th day the proportion of patients experiencing pain was less in group A, though the difference was not statistically significant. In our study it was found that all the patients in both groups had presence of exudates on day 1. The proportion of patients with exudates was more in group B on day 14 as well as day 28 and day 42 as compared to Group A, and this difference was statistically significant. All the wounds in both the groups were initially infected and were positive for culture. Most common organism causing wound infection in both the groups was Pseudomonas followed by Staphylococci. However, in wounds treated with Silver releasing dressings, the number of days taken for the culture to become negative was faster as compared with povidone iodine dressings.

The average size of wound in Group A was 21.02 sq. cms, on day 1, 10.88 sq. cms, on day 14, 3.19 sq cms on day 28 and 0.33 sq. cms on day 42 while the average size of the wound in Group B on day 1 was

22.88 sq. cms, on day 14 it was 11.77 sq.cms, day 28 it was 8.21 sq.cms and on day 42 it was 4.09 sq.cms. The average wound size was significantly lower in Group A when compared Group B as seen on day 28 and day 42 follow up ($p<0.001$). In the present study, the average MAGS score on day 1 for group A was 41.79 and group B was 41.58. The MAGS scores were significantly higher in Group A on day 14, day 28 and day 42 when compared with Group B. [Table 1]

Table 1: Wound comparison of the study subjects of both the groups

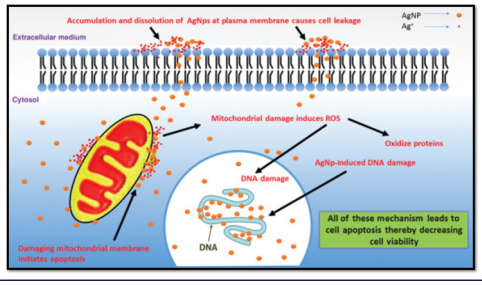
Parameter	Group A n=43	Group B n=43	P value
Pain			
Day 1	41	41	1.000
Day 14	17	15	0.66
Day 28	6	12	0.056
Day 42	2	4	0.20
Exudates			
Day 1	43	43	--
Day 14	5	23	0.004
Day 28	0	15	<0.001
Day 42	0	9	<0.001
Positive bacterial culture			
Day 1	43	43	--
Day 14	4	24	<0.001
Day 28	0	7	0.0013
Day 42	0	6	0.0301
Size of wound			
Day 1	21.02	22.88	0.3632
Day 14	10.88	11.77	0.2700
Day 28	3.19	8.21	<0.001
Day 42	0.33	4.09	<0.001
MAGS score			
Day 1	41.79	41.58	0.72
Day 14	52.21	43.35	<0.001
Day 28	56.06	45.02	<0.001
Day 42	58.67	47.06	<0.001

DISCUSSION:

The wound healing process is not only complex but also fragile, and it is susceptible to interruption or failure leading to the formation of non-healing wounds[2]. Some of the factors that contribute to non-healing wounds are uncontrolled diabetes mellitus, venous or arterial disease, infection, and metabolic and nutritional deficiencies of old age[3]. Since the beginning of medical history topical agents have been used in the management of infected wounds. Silver is one such modality used in the management of wounds. As early as in the 1920's the US Food and Drug Administration accepted colloidal silver as being effective for wound management. Silver ions are highly reactive and affect multiple sites within bacterial cells, ultimately causing bacterial cell death[12–15].

Silver-based wound dressings are often used to prepare the wound for healing. Silver is a broad-spectrum antimicrobial agent that controls yeast, mold, and bacteria, including methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE), when it is provided at an appropriate concentration. It kills microbes on contact through multiple mechanisms of action, such as inhibiting cellular respiration, denaturing nucleic acids, and altering cellular membrane permeability. Silver has low mammalian cell toxicity. It is now known to have potent anti-inflammatory properties, which are dependent on the delivery system. It may be used to maintain a microbe-free, moist wound healing environment[16–19].

Fig. 2 Mechanism of Antibacterial actions of Silver



Following is summary of mechanism of anti microbial activity of silver ionsl6,17

- The cell membrane of bacteria is damaged by the adherence of ionic silver to the membrane, which also leads to interference with several receptors.
- The production of adenosine triphosphate is blocked by the disturbance of bacterial electron transport, caused by ionic silver. This disarranges the cell's energy supply.
- Silver ions have the property, to bind bacterial DNA, which leads to impairment of the cell replication.
- Cytosolic compounds, such as certain nucleotides, proteins, and the amino acid histidine, lose their function of building blocks, due to the formation intracellular insoluble compounds with ionic silver.

Silver preparations in which ionic compounds are present are are silver niterate, silver sulfadizine, silver calcium phosphate, silver chloride, silver carboxy methylcellulose. Nanocrystalline silver and autocatalytic silver coatings are preparations with metallic silver in them——[16–18].

With this background we conducted a prospective randomised study to compare the two agents used in wound care. The mean age of the study subjects was 39.98 ± 16.19 and 35.49 ± 15.08 years respectively in Group A and Group B with almost similar proportion of males and females in both the groups. In relation to a healing wound the best results to a surgeon are in terms of the reduction in the size of wound, reduced exudates and development of healthy granulation tissue; while for the patient it is the reduction in pain, decreased hospital stay and increased mobility as early as possible. In terms of exudates load, our study inferred that after day 14 the proportion of patients with exudates decreased significantly in the group who received dressings with silver releasing agents. A randomised control trail done by Jurczak F et al had concluded that silver dressing was significantly better than the iodine dressing for overall ability of exudates handling and ease of use20**.** Similarly, Munter KC et al conducted a study on comparison between silver foam and the local best practice in chronic wounds with delayed healing and moderate to high levels of exudates and found that after 4 weeks, the silver group also had significantly improved ($p<0.05$) exudates handling, ease of use, odour and pain21. Therefore less time was spent on dressing changes and mean wear time was longer for the silver group ($p<0.05$). Studies done by Lo SF et al and Singh S et al derived similar findings in their studies22[-23].

The reduction in the size of wound in the group with silver releasing dressings was earlier and significantly better from day 14 (2 weeks) when compared to the traditional povidine iodine dressings as mentioned above. A study by Wunderlich U et al used charcoal silver impregnated dressing and found significantly greater epithelialisation and reduction of venous ulcer size ($p<0.05$) as compared with other non silver dressings[24]. About 31.57% of the patients with silver dressing and 10.52% of the patients with non silver dressing had achieved better healing and reduction in the size in their study. Similar findings were confirmed in the studies done by Jorgensen B et al25, Senet P et al26, Singh S et al23 and Lazereth I et al27 in their study substantiating our study in terms of efficacy of silver ion releasing dressings in healing of wounds. Lo SF et al22 conducted a meta analysis of 8 randomised controlled trials of silver dressings versus non silver dressings in the management of non-healing chronic wounds and showed a significant reduction in wound area for the silver dressing group ($p<0.001$). In the study by Münter KC et al21 mentioned above it was concluded that after 4 weeks, median reduction in ulcer area was significantly higher for the silver group than for the control group (47.1% vs. 31.8%; $p<0.05$).

In our study histological assessment of adequate healing was done using the Macroscopic Angiogenesis Grading System (MAGS) score. This is a quantitative method of measuring the histological extent of vascular and endothelial proliferation and was given by Bremm et al10 in 1972. MAGS is based on three parameters.

1. Vasoproliferation
2. Endothelial cell hyperplasia
3. Endothelial cytology

MAGS score is calculated as = KnN+ KeE+ KxX.
N= No of vessels per high power field
E= No of endothelial cells lining cross section of capillary
X= X is given 0-5 points based on the histological appearance of endothelial cells.

Normal endothelial cell	0
Plump clear nucleus	1
Plump clear nucleus with prominent nucleolus	2
Large hyperchromatic nucleus	3
Bizarre endothelial cell	4
Mitotic figure	5

- Kn = constant used to correct for various fields of other microscopes so that they are equal to the magnified area described
- Ke= constant with a value of 3
- Kx= constant with a value of 6.

The MAGS score in a wound can range from 0 to 100.

In the present study, the average MAGS score on day 1 for group A was 41.79 and group B was 41.58. The MAGS scores were significantly higher among Group A on Day 14, Day 28 and Day 42 when compared with Group B. [Table 1]

It would not be out of place to mention some limitations of our study in terms of being a single centre study with a relatively small sample size. Multicenter studies with larger number of subjects would yield a better validation. Nonetheless, this study has highlighted the importance of silver dressings in terms of a histopathological comparison using a tool such as MAGS scores for the first time.

CONCLUSIONS:

With reference to reduction of pain, exudates and bacterial load reduction , the outcomes were better in the group where silver releasing dressing were used as compared to the group where povidine iodine dressings where used. We found a statistically significant reduction of size of the wound in the silver dressing group as compared to the group where traditional method of dressing with Povidone Iodine was employed. The MAGS scores were also significantly higher in the group where silver releasing dressings were used. Thus the superiority of using silver releasing dressings over conventional povidone iodine dressings was validated.

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