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Original research article

A Comparative Study of Effectiveness of Negative Pressure Wound Therapy (NPWT) Versus Standard Chlorhexidine Gauze Dressing in the Management of Post Traumatic Soft Tissue Defects in the Extremities- One Year Hospital Based Randomized Clinical Trial

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Abstract

Introduction: Soft tissue defects are more commonly seen in the extremities following high velocity trauma & occupational injuries posing countless challenges in their management. Early flaps or skin grafts reduce the chance of infections in the soft tissue defects. Both are done after thorough surgical debridement. In some cases wound related and patient related factors won't allow early coverage of these defects. During which, one has to consider alternative methods of managing the soft tissue defects in the primary set up. One of the available modality for managing soft tissue defects in the initial periods is Negative Pressure Wound Therapy. This has been found to have a vast benefit over conventional dressings like tulle grass and others. This present study has been conducted in our hospital which is a tertiary care centre, to evaluate the efficacy of Negative Pressure Wound Therapy (NPWT) in the management of soft tissue defects in the extremities over the conventional method of managing the wounds with chlorhexidine dressing.

Materials and Methods: A randomized clinical trial was carried out in Belagavi Institute of Medical sciences, Belagavi from 1st Nov 2020 to 31st Oct 2021 and required data was collected from the 40 patients who underwent either Negative Pressure Wound Therapy (Group A) or Chlorhexidine gauze dressing (Group B) for post traumatic soft tissue defects in the extremities and the outcome was assessed in terms of formation of healthy granulation tissue, absence of slough/infection, wound retraction after intervention in both the groups

Results: In the present study all forty patients were having unhealthy pale yellow granulation tissue at day 0. At day 5, seventeen out of twenty patients were having healthy red granulation tissue in group A compared to five out of twenty patients in group B. At day 10, the remaining three patients were having healthy red granulation tissue in group A and thirteen out of fifteen remaining patients were having healthy red granulation tissue in group B. At day 15, remaining two patients were having healthy red granulation tissue in group B with p value less than 0.0001 (using chi square test) and this difference was considered to be extremely statistically significant.
Conclusion: Thus, we conclude that rate of formation of healthy red granulation tissue was faster, slough was reduced rapidly and mean surface area of the wound is reduced significantly in the Negative Pressure Wound Therapy, making Negative Pressure Wound Therapy a superior option in the management of patients with post traumatic soft tissue defects in the extremities.

Keywords: Post traumatic soft tissue defect, Negative Pressure Wound Therapy, chlorhexidine gauze dressing, healthy red granulation tissue, slough, reduction of wound area.

Introduction

Soft tissue defects are more commonly seen in the extremities following high velocity trauma. Traumatic soft-tissue defects are not superficial but involve multi-structural tissue damage or loss of tissue when extremities are affected and rarely involve only the skin and the subcutaneous tissue.[1] Various individual and institutional epidemiological studies report the incidence of open fractures to be 11.5 per 100,000 individuals, with an estimated 3.3% of all upper limb and 3.7% of all lower limb and 0.3% of limb girdle, fractures being open. Tibial fractures are open up to 21%, mainly because the soft tissue envelope is thinner when compared to other long bones.[2] Modern advances and super specialities in surgical disciplines can deal with these injuries in a combined and sophisticated manner. Secondary infection of the wound is a significant complication and will lead to complex complications which pose challenges in the line of treatment in the form of increased hospital stay, partial or complete failure of treatment, exposed implants and deep structures like tendons, nerves, and bone.[3,4] Surgical options to reduce the chances of infection of the wounds include early coverage of wound in the form of flaps or skin grafts. These surgical choices are made after thorough debridement. However, some wound related and patient related factors do not permit early coverage of these wounds. In these cases one has to consider alternative methods of managing the soft tissue defects in the primary set up. One of the available modality for managing soft tissue defects in the initial periods is Negative Pressure Wound Therapy. This has been found to have a vast benefit over conventional dressings like tulle grass and others.

Negative-pressure wound therapy (NPWT) was initially described as cupping in 1500 BC.[5] It was named in 1952 as Negative-pressure wound therapy. The modern NPWT equipment came into existence in the 1990's with the use of polyurethane foam and a mechanical vacuum designed by Dr. Louis Argenta and Michael Morykwas of Wake Forest University School of Medicine.[6] This mechanically induce negative pressure removes fluid from the extravascular space, improves circulation in oedematous tissue by lowering capillary afterload and enhances the proliferation of reparative granulation tissue and aids in wound contraction and continues to be advantageous, meritorious in the process of healing of complex wounds and preventing the complications thus decreasing the hospital stay and improving compliance.

In 1950s Chlorhexidine was discovered by the Imperial Chemical Industries, Limited (Manchester, UK) while researching the synthesis of anti-malarial agents.[7,8] Bactigras consists of a gauze fabric impregnated with yellow soft paraffin containing 0.5% chlorhexidine acetate, a potent antimicrobial agent which is active against a wide range of microorganisms. It is strongly bound to cellulose materials, such as cotton or viscose and its antimicrobial activity is reduced in the presence of the blood and pus. Clinical experience with bactigras suggested that the dressing may be of some value in the treatment of non-infected minor burns as a prophylactic agent against the growth of bacteria.

The present study has been conducted in our hospital which is a tertiary care centre, to evaluate the efficacy of negative pressure wound therapy (NPWT) in the management of soft tissue defects in the extremities over the conventional method of managing the wounds with chlorhexidine dressing.

Materials and Methods:
A randomized clinical trial was carried out in Belagavi Institute of Medical sciences, Belagavi from 1st Nov 2020 to 31st Oct 2021 and required data was collected from the 40 patients who underwent either Negative Pressure Wound Therapy (Group A) or Chlorhexidine gauze dressing (Group B) for post traumatic soft tissue defects in the extremities and the outcome was assessed in terms of formation of healthy granulation tissue, absence of slough/infection, wound retraction after intervention in both the groups. Exposed bare bones, cartilages or other vital structures (blood vessels, anastomotic sites, organs or nerves), chronic wounds, post-surgical, dehisced wounds, diabetic and neuropathic ulcer, patients with bleeding disorder or on anticoagulants, wounds with slough which cannot be completely debrided were excluded from the study.

Results:
In the present study all forty patients were having unhealthy pale yellow granulation tissue at day 0. At day 5, seventeen out of twenty patients were having healthy red granulation tissue in group A compared to five out of twenty patients in group B. At day 10, the remaining three patients were having healthy red granulation tissue in group A and thirteen out of fifteen remaining patients were having healthy red granulation tissue in group B. At day 15, remaining two patients were having healthy red granulation tissue in group B with p value less than 0.0001 (using chi square test) and this difference was considered to be extremely statistically significant.

Six out of twenty patients in group A were having slough free wounds compared to thirteen out of twenty patients in group B at day 0. At day 5, ten out of fourteen remaining patients in group A were having slough free wounds compared to four out of seven remaining patients in group B. At day 10, remaining four patients and three patients were having slough free wounds in group A and group B respectively with p value less than 0.0001 (using chi square test) and this difference was considered to be extremely statistically significant.

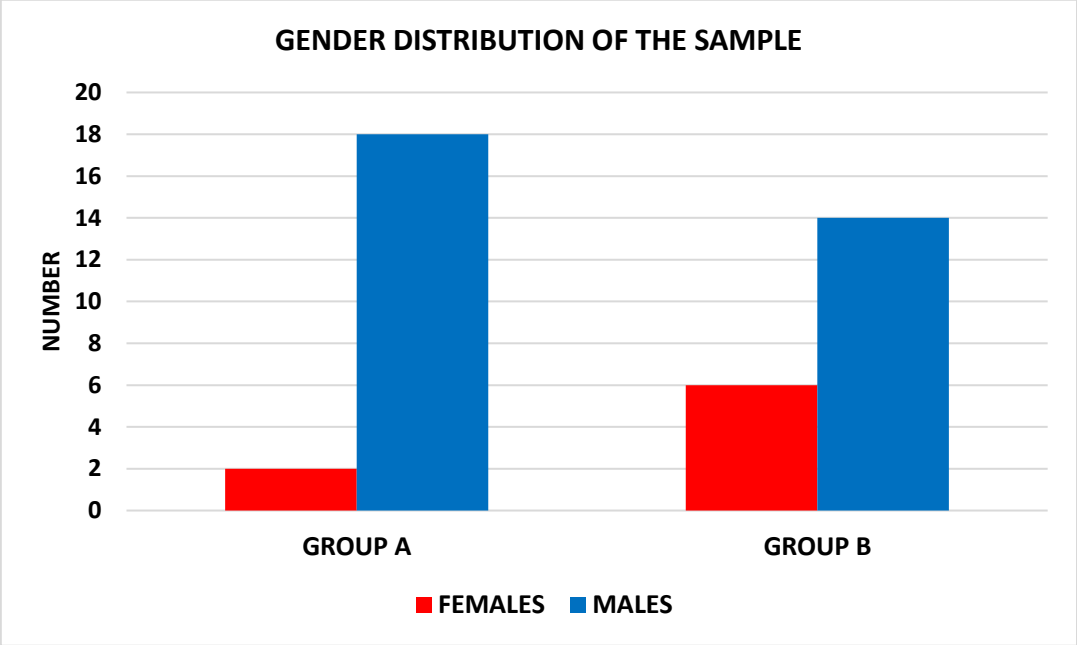
Overall average reduction of wound area of all twenty patients at the end of the treatment was 28.49% (from 81.3375 sq.cm to 58.719 sq.cm) in group A compared to 9.90% (from 52.8865 sq.cm to 47.71 sq.cm) in group B, with p value less than 0.0001 (using student's unpaired t test) and this difference was considered to be extremely statistically significant.
Patients treated in NPWT Group completed treatment earlier than in chlorhexidine gauze dressing group.

Table 1: SEX DISTRIBUTION

	GROUP A		GROUP B	
GENDER	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
FEMALES	2	10.00	6	30.00
MALES	18	90.00	14	70.00
TOTAL	20	100.00	20	100.00

P = 0.113846 (NS) – chi-square test

In the present study 90% of the patients in group A were males compared to 70% in group B. The male to female ratio in group A was 9:1 and in group B, it was 2.33:1. However, this difference was statistically not significant.



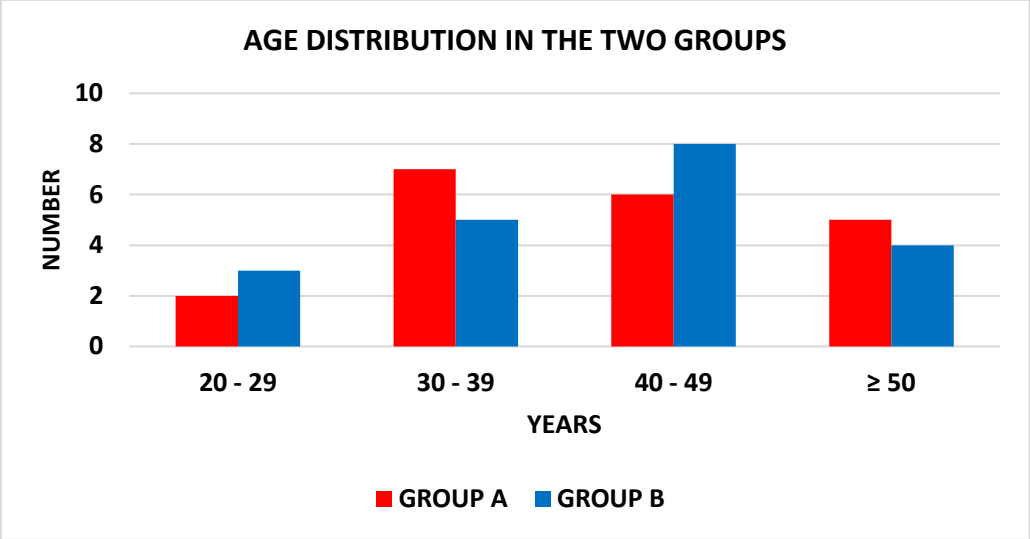
Graph 1: SEX DISTRIBUTION

Table 2: AGE DISTRIBUTION

AGE	GROUP A	PERCENTAGE	GROUP B	PERCENTAGE
20 – 29	2	10.00	3	15.00
30 – 39	7	35.00	5	25.00
40 – 49	6	30.00	8	40.00
≥ 50	5	25.00	4	20.00
TOTAL	20	100.00	20	100.00

P = 0.8181 (NS) – chi-square test

In the present study 10% of the patients in group A were aged between 20 and 29 years compared to 15% in group B, 35% of the patients in group A were aged between 30 and 39 years compared to 25% in group B, 30% of the patients in group A were aged between 40 and 49 years compared to 40% in group B and 25% of the patients in group A were aged above 50 years compared to 20% in group B.



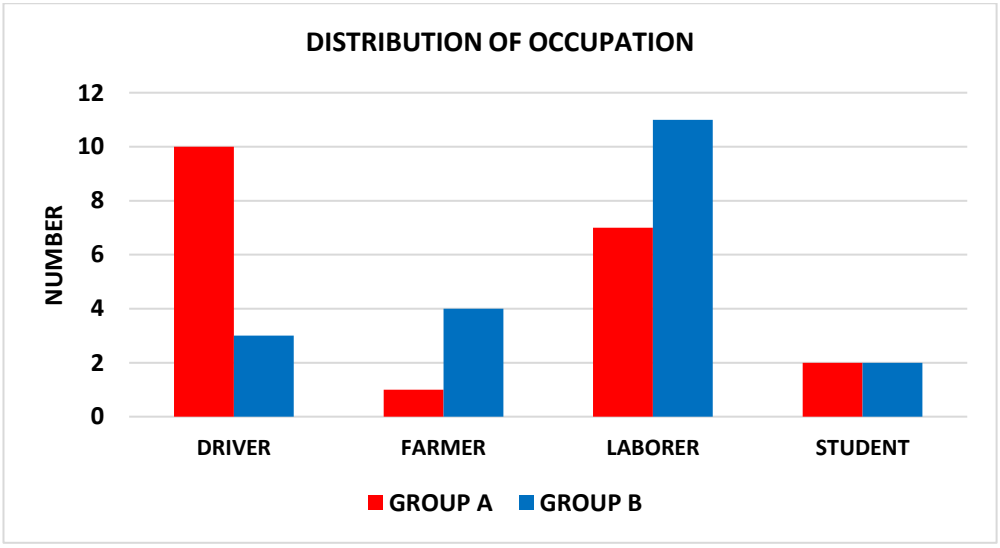
Graph 2:AGE DISTRIBUTION

Table 3: OCCUPATION

	GROUP A		GROUP B	
OCCUPATION	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
DRIVER	10	50.00	3	15.00
FARMER	1	5.00	4	20.00
LABORER	7	35.00	11	55.00
STUDENT	2	10.00	2	10.00
TOTAL	20	100.00	20	100.00

P = 0.0913 (NS) – chi-square test

In the present study 50% of the patients in group A were drivers by occupation compared to 15% in group B, 5% of the patients in group A were farmers by occupation compared to 20% in group B, 35% of the patients in group A were laborers by occupation compared to 55% in group B and 10% of the patients each in group A & group B were students by occupation.

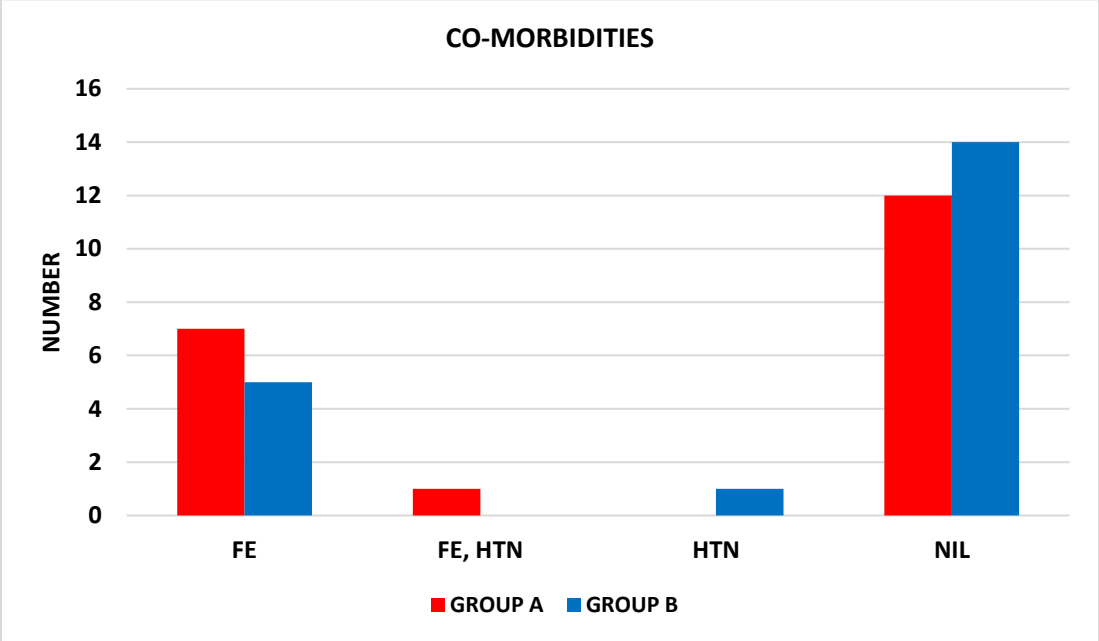


Graph 3: OCCUPATION

Table 4: COMORBIDITIES

	GROUP A		GROUP B	
CO-MORBIDITIES	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
FE	7	35.00	5	25.00
FE, HTN	1	5.00	0	0.00
HTN	0	0.00	1	5.00
NIL	12	60.00	14	70.00
TOTAL	20	100.00	20	100.00

In the present study 35% of the patients in group A were having fracture of bones compared to 25% in group B, 5% of the patients in group A were having fracture of bones and hypertension, 5% of the patients in group B were having hypertension and 60% of patients in group A were not having any co-morbidities compared to 70% in group B.



Graph 4: COMORBIDITIES

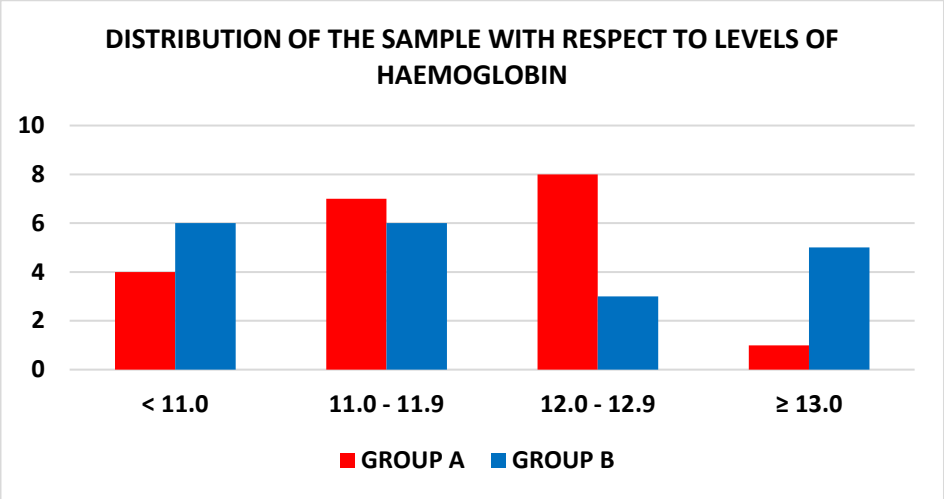
Table 5: HAEMOGLOBIN DISTRIBUTION

	GROUP A		GROUP B	
HAEMOGLOBIN (gm%)	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
<11.0	4	20.00	6	30.00
11.0 - 11.9	7	35.00	6	30.00
12.0 - 12.9	8	40.00	3	15.00
≥ 13.0	1	5.00	5	25.00
TOTAL	20	100.00	20	100.00

P = 0.1437 (NS) – chi-square test

In the present study 20% of patients in group A were having haemoglobin levels below 11 gm% compared to 30% in group B, 35% of patients in group A were having haemoglobin levels between 11gm% and 11.9 gm% compared to 30% in group B, 40% of patients in group

A were having haemoglobin levels between 12gm% and 12.9 gm% compared to 15% in group B and 5% of patients in group A were having haemoglobin levels above 13 gm% compared to 25% in group B.



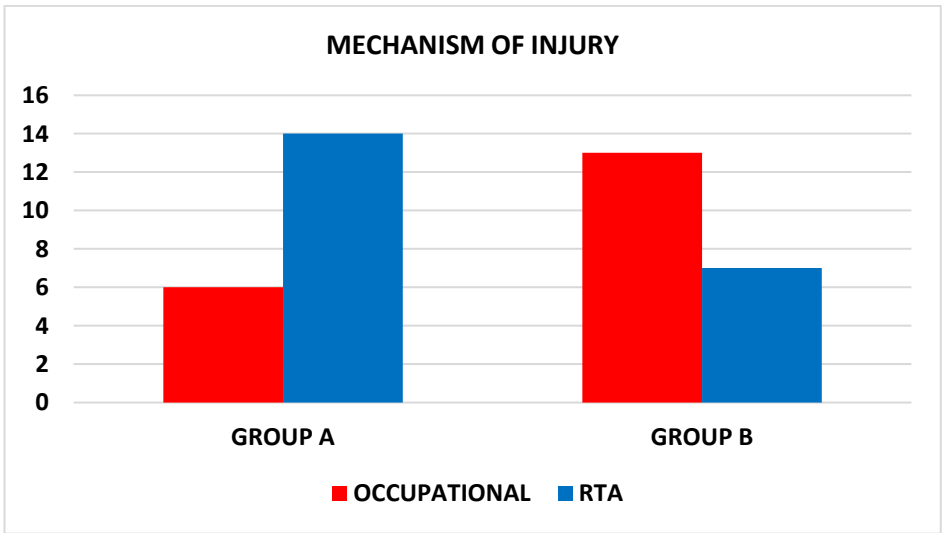
Graph 5: HAEMOGLOBIN DISTRIBUTION

Table 6: MECHANISM OF INJURY

	GROUP A		GROUP B	
MECHANISM OF INJURY	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
OCCUPATIONAL	6	30.00	13	65.00
RTA	14	70.00	7	35.00
TOTAL	20	100.00	20	100.00

P = 0.0266 (significant) – chi-square test

In present study 30 % of patients in group A were having soft tissue defects due to occupational injuries (industrial, agricultural) compared to 65% in group B and 70% of patients in group A were having soft tissue defects due to road traffic accidents (RTA) compared to 35% in group B. This difference was found to be statistically significant.



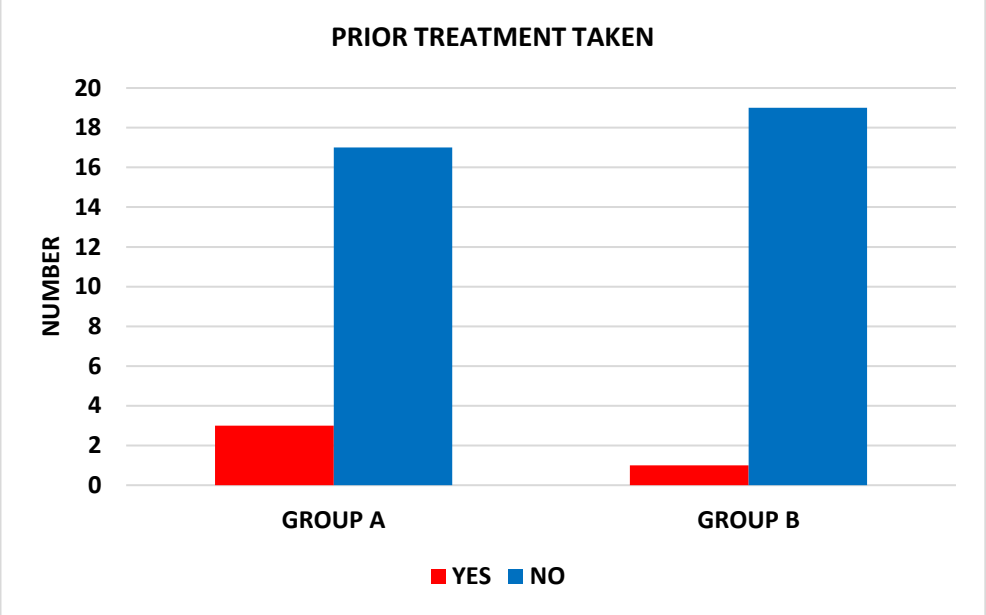
Graph 6: MECHANISM OF INJURY

Table 7: PRIOR TREATMENT

	GROUP A		GROUP B	
PRIOR TREATMENT TAKEN	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
YES	3	15.00	1	5.00
NO	17	85.00	19	95.00
TOTAL	20	100.00	20	100.00

P = 0.2918 (NS) – chi-square test

In our study 15% of patients in group A had taken prior treatment in the form of first aid at local hospitals compared to 5% in group B.



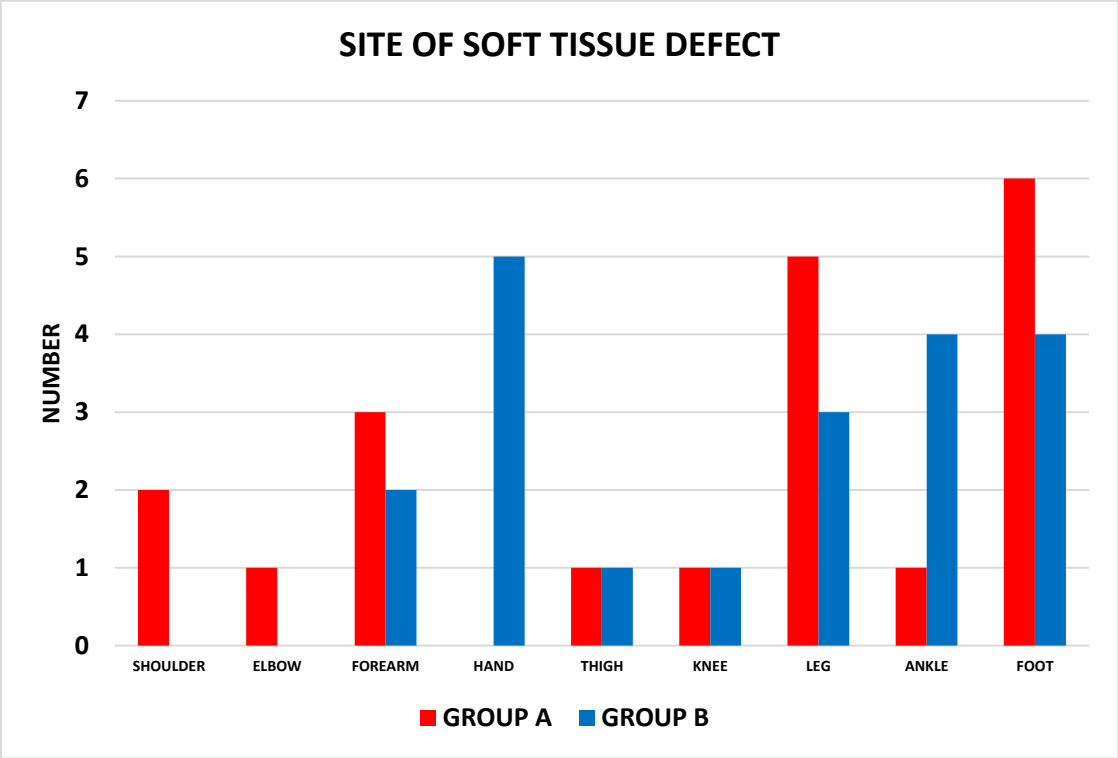
Graph 7: PRIOR TREATMENT

Table 8: SITE OF SOFT TISSUE DEFECT

	GROUP A		GROUP B	
SITE	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
ARM	2	10.00	0	0.00
ELBOW	1	5.00	0	0.00
FOREARM	3	15.00	2	10.00
HAND	0	0.00	5	25.00
THIGH	1	5.00	1	5.00
KNEE	1	5.00	1	5.00
LEG	5	25.00	3	15.00
ANKLE	1	5.00	4	20.00
FOOT	6	30.00	4	20.00
TOTAL	20	100.00	20	100.00

P = 0.1954 (NS) – chi-square test

In the present study 10% of the patients in group A were having soft tissue defects over arm, 5% of patients in group A were having soft tissue defects over elbow, 15% of the patients in group A were having soft tissue defects over forearm compared to 10% in group B, 25% of the patients in group B were having soft tissue defects over hand, 5% of the patients each in group A & group B were having soft tissue defects over thigh, 5% of the patients each in group A & group B were having soft tissue defects over knee, 25% of the patients in group A were having soft tissue defects over leg compared to 15% in group B, 5% of the patients in group A were having soft tissue defects over ankle compared to 20% in group B and 30% of the patients in group A were having soft tissue defects over foot compared to 20% in group B.
However, in the present study 32.5% of the soft tissue defects were seen in upper extremity and 67.5% of the soft tissue defects were seen in lower extremity.



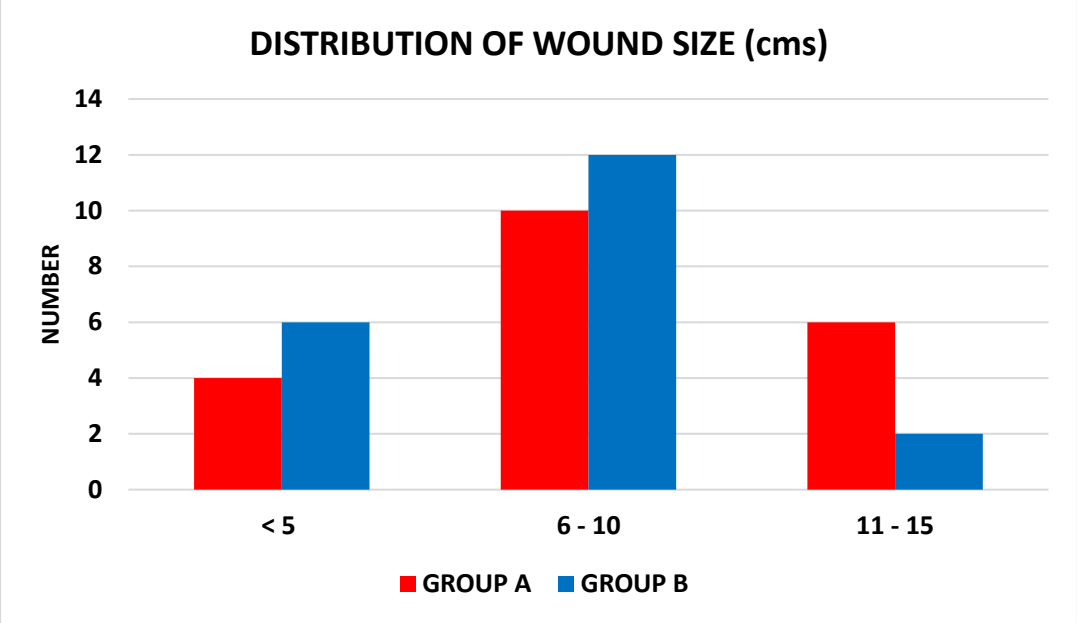
Graph 8: SITE OF SOFT TISSUE DEFECT

Table 9: SIZE OF SOFT TISSUE DEFECT (maximum length/ breadth in cms)

	GROUP A		GROUP B	
SIZE	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
<5 cm	4	20.00	6	30.00
6-10 cm	10	50.00	12	60.00
11-15 cm	6	30.00	2	10.00
TOTAL	20	100.00	20	100.00

P = 0.2754 (NS) – chi-square test

In the present study 20% of the patients in group A were having wound size of <5cm compared to 30% in group B, 50% of the patients in group A were having wound size between 6cm & 10cm compared to 60% in group B and 30% of the patients in group A were having wound size between 11cm & 15cm compared to 10% in group B at the time of admission.



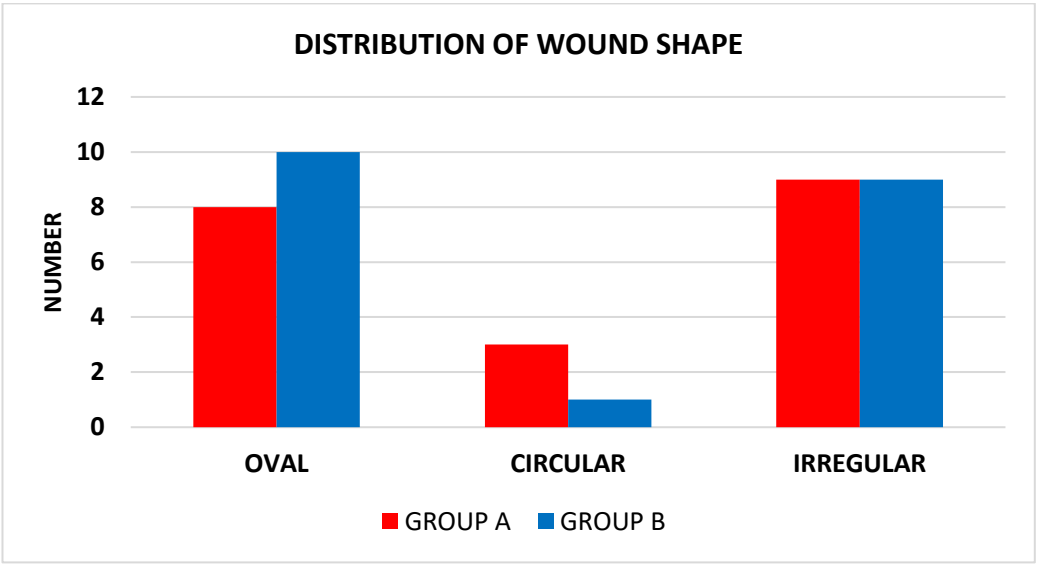
Graph 9: SIZE OF SOFT TISSUE DEFECT

Table 10: SHAPE OF SOFT TISSUE DEFECT

	GROUP A		GROUP B	
SHAPE	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
Oval	8	40.00	10	50.00
Circular	3	15.00	1	5.00
Irregular	9	45.00	9	45.00
TOTAL	20	100.00	20	100.00

P = 0.5427 (NS) – chi-square test

In the present study 40% of the patients in group A were having oval shaped wounds compared to 10% in group B, 15% of the patients in group A were having circular wounds compared to 60% in group B and 45% of the patients in each group A and group B were having irregular wounds at the time of admission.



Graph 10: SHAPE OF SOFT TISSUE DEFECT

Discussion

In the present study all forty patients were having unhealthy pale yellow granulation tissue at day 0. At day 5, seventeen out of twenty patients were having healthy red granulation tissue in NPWT Group compared to five out of twenty patients in chlorhexidine gauze dressing Group. At day 10, the remaining three patients were having healthy red granulation tissue in NPWT Group and thirteen out of fifteen remaining patients were having healthy red granulation tissue in chlorhexidine gauze dressing Group. At day 15, remaining two patients were having healthy red granulation tissue in chlorhexidine gauze dressing Group with P value less than 0.0001 (using chi square test) and this difference was considered to be extremely statistically significant.

In a study conducted on 30 patients by Prabhdeep Singh Nain et. al it was observed that during the first week granulation tissue was absent in 4 patients (26.67%) in Group A (NPWT) and 10 patients (66.67%) in Group B (saline-moistened gauze). It was seen that granulation tissue appeared at 2nd week in three out of four patients (75%) and 4th week in the remaining 1(25%) patient in Group A. The appearance of granulation tissue in patients of Group B was at 2nd, 4th and 5th week in three (30%), 3(30%) and two (20%) patients, respectively. It was also noted that in two (20%) patients granulation tissue remained absent even at the end of observation period. This suggested early appearance of granulation tissue in patients of Group A which was also found to be statistically significant.[10]

In another study conducted on 54 patients by C.M. Moue¨s et. al it was found that in the vacuum-treated Group, 20 patients (69%) showed a healthy, granulating wound bed within 1 week compared to 14 (56%) in the conventionally treated Group. Within the next week, five more patients in the vacuum Group showed a clean, healthy wound bed (cumulative 86%) compared to seven in the conventionally treated Group (84%). In one vacuum-treated patient (3%) wound healing was slow and duration of therapy exceeded 14 days compared to three patients in the conventional Group (12%). Based on the visual aspects in combination with the formation of granulating tissue, healthier wound conditions were observed earlier in Group A compared to wounds in Group B.[9]

In 3rd study conducted on 162 patients by Armstrong DG, Lavery LA, the rate of granulation tissue formation, based on the time to 76-100% formation in the wound bed, was faster in the NPWT Group than in controls (p=0.002).[11]

In our study also it was found that rate of formation of healthy red granulation tissue was faster in the patients of NPWT Group as compared to chlorhexidine gauze dressing Group indicating NPWT is superior in development of red healthy granulation tissue in post-traumatic soft tissue defects in the extremities. This supports the finding that NPWT has a positive effect on promotion of granulation tissue which is indication if improved vascularity.

In the present study, six out of twenty patients in NPWT Group were having slough free wounds compared to thirteen out of twenty patients in chlorhexidine gauze dressing Group at day 0. At day 5, ten out of fourteen remaining patients (71.42%) in NPWT Group were having slough free wounds compared to four out of seven remaining patients (57.14%) in chlorhexidine gauze dressing Group. At day 10, remaining four patients and three patients were having slough free wounds in NPWT Group and chlorhexidine gauze dressing Group respectively and most commonly present organisms in culture were *Staphylococcus aureus* at the time of admission with P value less than 0.0001 (using chi square test) and this difference was considered to be extremely statistically significant. Reduction in slough is indication of

reduction in the burden of nonviable tissue which is a prerequisite for planning definitive coverage of the wound.

As per our awareness after complete search through available and updated literature, there are no studies on reduction of slough in the wound bed between NPWT and conventional dressings and our study is the first to demonstrate such a difference between NPWT and conventional dressing.

In our study it was found that patients of NPWT Group showed rapid reduction in slough compared to chlorhexidine gauze dressing Group. This suggests that NPWT also plays a role in improving vascularity of wound and preventing further cell death.

In the present study, Overall average reduction of wound area of all twenty patients at the end of the treatment was 28.49% (from 81.3375 sq.cm to 58.719 sq.cm) in NPWT Group compared to 9.90% (from 52.8865 sq.cm to 47.71 sq.cm) in chlorhexidine gauze dressing Group with P value less than 0.0001 (using student's unpaired t test) and this difference was considered to be extremely statistically significant.

In a study conducted on 24 patients by Abdullah Etoz, before treatment, the mean area was 109 sq.cm in the NPWT Group and 94.8 sq.cm in control Group. Following therapy, the mean wound surface area decreased by 20.4 sq.cm (109 sq.cm to 88.6 sq.cm) in the NPWT Group, and decreased by 9.5 sq.cm (94.8 sq.cm to 85.3 sq.cm) in the control Group ($P = 0.032$). The difference in the rate of surface area decrease between the Groups was significant. The surface area of wounds in the NPWT Group was reduced more effectively than control Group wounds ($P < 0.05$).[12]

	Study by Abdullah Etoz		**PRESENT STUDY**	
AREA OF AN ULCER (MEAN)	**NPWT Group**	**Control Group**	**NPWT Group**	**Control Group**
BEFORE	109 sq.cm	94.80 sq.cm	81.33 sq.cm	52.88 sq.cm
AFTER	80.6 sq.cm	85.30 sq.cm	58.71 sq.cm	47.71 sq.cm

In another study conducted on 30 patients by Prabhdeep Singh Nain et. Al, the percentage decrease in the wound size was more in patients of Group A (NPWT) as compared to Group B (saline-moistened gauze). The mean decrease in the wound size in patients of Group A was -16.14 ± 13.04 sq.cm and that of Group B was -5.98 ± 14.41 sq.cm. The observation was found to be statistically significant ($P<0.05$).[10]

In 3rd study conducted on 10 patients by Isago T et.al, where the efficacy of topical negative pressure moist dressings was assessed, in pressure ulcers, by comparing the mean rate of reduction of ulcer area and depth before and after application of the dressing. The mean reduction in ulcer depth and surface area were 61.2% and 55.1% respectively. This study clearly shows the efficacy of topical negative pressure dressings in the management of pressure ulcers which are usually resistant to healing by conventional types of wound dressings.[13]

In our study also it was found that the percentage decrease in the wound surface area was more in patients of NPWT Group as compared to chlorhexidine gauze dressing Group indicating NPWT is superior in wound contraction in post-traumatic soft tissue defects in the extremities.

In our study fifteen patients (75%) completed treatment at day 5 in group A compared to five patients (25%) in group B. Four patients (20%) completed treatment at day 10 in group A compared to thirteen patients (65%) in group B. One patient (5%) completed treatment at day 15 in group A compared to two patients (10%) in group B with P value of 0.0064 (using chi square test) and this difference was considered to be highly statistically significant indicating NPWT is superior in the management of post traumatic soft tissue in the extremities and also reduced the hospital stay of patients, reduced dressing changes, reduced nursing time with better patient tolerance, improved patient's quality life and reduced overall cost burden for the patients.

Conclusions

In our study, rate of formation of healthy red granulation tissue was faster in the patients of NPWT group as compared to chlorhexidine gauze dressing group. Overall reduction in slough was faster in NPWT group as compared to chlorhexidine gauze dressing group. Average percentage reduction in the mean surface area of the wound was significantly more in the NPWT group as in comparison to the chlorhexidine gauze dressing group. Thus, we conclude that rate of formation of healthy red granulation tissue was faster, slough was reduced rapidly and mean surface area of the wound is reduced significantly in the Negative Pressure Wound Therapy, making Negative Pressure Wound Therapy a superior option in the management of patients with post traumatic soft tissue defects in the extremities. But further studies with larger population will be needed in the future before NPWT can be added to the wide spectrum of treatment modalities available in the management of post traumatic soft tissue defects and wounds of other etiology.

References

1. U. BÜchler -- Traumatic soft-tissue defects of the extremities; Archives of Orthopaedic and Trauma Surgery Volume 109 issue 6 1990.
2. Court-Brown CM, Rimmer S, Prakash U, McQueen MM. The epidemiology of open long bone fractures. injury 1998; 29(7): 529-34.
3. Bihariesingh VJ, Stolarczyk EM, Karim RB, van Kooten EO. Plastic solutions for orthopaedic problems. Arch Orthop Trauma Surg. 2004;124(2):73-6.
4. Kramhøft M, Bødtker S, Carlsen A. Outcome of infected total knee arthroplasty. J Arthroplasty. 1994;9(6):617-21.
5. Wu A (2016)Chinese fire cupping. http:// www. chinahighlights. com/ travelguide/chinese-medicine/fire-cupping.htm. Accessed 4 July 2016.
6. Dirckx John H. Negative pressure wound therapy. Health Professions Insititute. December 2008:17-18.
7. Lim, K. S. and P. A. A. Kam. "Chlorhexidine--pharmacology and Clinical Applications." Anaesth Intensive Care. 2008 Jul;36(4):502-12.
8. Mathur, Setu, Tanu Mathur, Rahul Srivastava, and Rohit Khatri. "Chlorhexidine: The Gold Standard in Chemical Plaque Control." *National Journal of Physiology, Pharmacy & Pharmacology* 1.2 (2011): 45-50.
9. C.M. Moue¨s, G.J.C.M. van den Bemd, F. Heule, S.E.R. Hovius, Comparing conventional gauze therapy to vacuum-assisted closure wound therapy: A prospective randomised trial, Journal of Plastic, Reconstructive & Aesthetic Surgery (2007) 60, 672-681
10. Prabhdeep Singh Nain, Sanjeev K. Uppal, Ramneesh Garg, Kuljyot Bajaj, Shirin Garg Role of Negative Pressure Wound Therapy in Healing of Diabetic Foot Ulcers, Journal of Surgical Technique and Case Report | Jan-Jun 2011 | Vol-3 | Issue-1.

11. Armstrong DG, Lavery LA, Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial, Lancet. 2005 Nov 12;366(9498):1704-10.
12. Abdullah Etoz, MD, Ramazan Kahveci, Negative Pressure Wound Therapy on Diabetic Foot Ulcers MD,Wounds. 2007;19(9):250-254.
13. Isago T, Nozaki M, Kikuchi Y, Honda T, Nakazawa H. Negative pressure dressings in the treatment of pressure ulcers. J Dermatol 2003 Apr; 30(4): 299- 305.