

A STUDY TO COMPARE THE EFFECT OF NEGATIVE PRESSURE WOUND THERAPY WITH TOPICAL INSULIN APPLICATION ON WOUND HEALING IN DIABETIC FOOT WOUNDS VERSUS NPWT ALONE.

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Abstract :

Background : Diabetic foot wounds affecting either limb is seen in immense numbers on out patient basis in the department of general surgery all over India. They present to the health care professionals in varying general conditions , ranging from a simple wound with adequate granulation tissue which can be managed on OPD basis to v those presenting in septic shock and MODS due to poorly managed wound and systemic control of diabetes mellitus , hence requiring admission. Innovations are being tried with respect to the type of dressings to hasten the formation of granulation tissue, decrease the size of the wound and reduce the foul smelling exudate in diabetic foot wounds. On similar grounds a novel dressing technique using a combination of NPWT and topical insulin has been tried on diabetic foot wounds and its results assessed using accepted criterias.

objectives : To assess the reduction in the size of the wound when a combination of NPWT and topical insulin is used using the BATES - JENSEN WOUND

ASSESSMENT TOOL as compared to plain NPWT on diabetic foot ulcers in Type 2 diabetic patients.

methodology: The present prospective interventional study was done by the Department of Surgery at JSS Medical College and Hospital, Mysuru from July 2019 to December 2021. A total of 96 study patients were enrolled for the study out of which 48 subjects were divided randomly into two groups namely case and control group. Evidence of granulation tissue formation, decrease in the size and depth of the wound, decrease in the amount of exudate, peripheral tissue induration as well as an increase in epithelisation of the wound is assessed by the BATES - JENSEN WOUND ASSESSMENT TOOL on the 5th, 10th and 15th day, using the BATES-JENSEN WOUND ASSESSMENT SCALE. **RESULTS :** Using the Bates Jensen Wound Assessment tool this study showed that the BWAT score which was 43.39 on day 5 in the VAC group reduced to 32.5 on day 15 in the same group whereas the BWAT score which was 41.7 on day 5 in VAC +topical insulin group reduced to 27.1 on day 15, which was found to be statistically significant. **CONCLUSION :** This study has shown that on using NPWT + topical insulin as a dressing method for diabetic foot wounds as compared to NPWT alone there has been significant reduction in the size of the wound, hastening in the process of formation of granulation tissue hence proving that a combination of NPWT + topical insulin is an effective dressing method for diabetic foot wounds.

Key words: Negative Pressure Wound Therapy (NPWT), topical insulin, BATES -JENSEN WOUND ASSESSMENT TOOL (BWAT).

Introduction :

Diabetes Mellitus is an important public health problem and affecting one in every five Indians. The disease burden may double by the year 2030 as per estimated reports. The literature available classifies four different types of diabetes mellitus. Type 2 Diabetes mellitus is the most common of these types and accounts for 90 to 95% of the cases diagnosed. It is characterized by hyperinsulinemia and hyperglycemia due to peripheral insulin resistance.¹

Type 2 Diabetes Mellitus carries both microvascular and macrovascular complications. They include cerebrovascular, cardio – vascular, peripheral arterial disease, retinopathy, neuropathy and nephropathy. Diabetic foot is one of the significant and devastating complications of diabetes and is often defined as a foot affected by ulceration which is associated with neuropathy and/or peripheral arterial disease of the lower limb in a patient with diabetes.²

The literature had shown a prevalence of 4 – 10% and the condition is more frequent in older patients.^{3, 4} The estimates show that, 5% of all patients with diabetes present with a history of foot ulceration, while the lifetime risk of diabetic patients developing

this complication is 15%.^{3,4} The majority (60 – 80%) of foot ulcers will heal, while 10 – 15% of them will remain active and 5 – 24% of them will finally lead to limb amputation within a period of 6 – 18 months after the first evaluation.⁵ Another study showed that the lifetime risk of a diabetic patient developing a foot ulcer can be 25%.⁶ These patients are also at 50% risk of redeveloping the ulcer within the next 3 years. Also, as the diabetic foot ulcers worsen in severity, the possibility of an amputation also increases. Major amputation rates are 5 to 10 times higher in diabetics than in non diabetics. Also, diabetic patients may be unaware of the presence of infections because of peripheral neuropathy and a decreased ability to sense pain.⁷

In this population, infections can progress very rapidly, with significant tissue damage from a combination of delayed presentation and compromised immune function. Vacuum assisted closure is also referred to as micro deformational wound therapy (MDWT) or Negative Pressure Wound Therapy.⁸

This method of wound closure has been used to treat pressure sores, open abdomens, sternal wounds, diabetic foot infections, second degree burns and skin graft recipient sites. Negative Pressure Wound Therapy stabilises the wound environment, by reducing wound edema and bacterial load, improves tissue perfusion and stimulates angiogenesis and growth of granulation tissue.

Insulin has been shown to have a positive effect on wound healing. Insulin like growth factor which is very similar to the hormone insulin, has been shown to promote the proliferation, migration and extracellular matrix excretion by keratinocytes, endothelial cells and fibroblasts and even promote the reformation of granulation tissue.⁹

Various studies have shown that topical application of insulin normalises the cell permeability, promotes vascularisation and enhances phagocytosis. It has also been shown to reduce the exudation from the wound surface, arrest the bacterial growth, decrease tissue hypoxia, reduce edema and greatly reduce the wound healing time and increase wound tensile strength.

Thus there is a strong relationship between the application of topical insulin therapy on accelerating wound healing. There are studies which show that NPWT also causes rapid reduction in wound size and promotes granulation tissue formation .

Objective :

To assess the reduction in the size of the wound when a combination of NPWT and topical insulin is used using the BATES - JENSEN WOUND ASSESEMENT TOOL as compared to plain NPWT on diabetic foot wounds in Type 2 diabetes patients.

Materials and Methods :

The present prospective interventional study was done by the Department of Surgery at JSS Medical College and Hospital , Mysuru from July 2019 to December 2021.

A total of 96 study patients were enrolled for the study out of which 48 subjects were divided randomly into two group namely case and control group. The Obtained sample was from the formula $S = Z^2 pq/d^2$ where = prevalence was 6.75% which is determined by considering the total number of diabetic foot cases admitting under surgery department for a period of 1 year divided by the total number of any surgery cases admitting under surgery department for a period of 1 year and at 5 % margin of error the sample was estimated to be 96.

Inclusion Criteria:

1. Patients more than 18 years of age who are known diabetics or newly diagnosed as diabetic.
2. One or more diabetic foot ulcers without any clinical evidence of osteomyelitis.
3. Patients with diabetic foot wounds, willing for Vacuum assisted closure dressing and those who have given their consent willingly.
4. Patients with diabetic wounds greater than 5 cm in width and greater than 1 cm in depth.
5. Patients willing for regular follow up.
6. Ankle brachial pressure index more than 0.7.
7. Diabetic wounds status post amputation of the affected limb.

Exclusion Criteria :

1. Osteomyelitis of the foot with the ulcer.
2. Patients with various malignancies.
3. Patients having an active systemic infection.
4. Patients who are at a risk of bleeding.
5. Sites where there are large vascular structures
6. Patients not willing for vacuum assisted closure.
7. Patients unable to come for regular follow ups.

The wounds in both the experimental and control group are opened on the 5th, 10th and 15th day and compared using the BATES - JENSEN WOUND ASSESEMENT TOOL.

Under aseptic precautions, after inspecting the wound a thorough betadine and peroxide wash is given and the wound is debrided until fresh bleeding occurs from the wound surface.

First the wound bed is sprayed with insulin (Human Actrapid 1 U/ cm² of wound area) ,allowed to dry for 15 minutes and then covered with sterile gauze. The blood

glucose levels are measured using a glucometer 10 minutes before and 1 hour after the application of topical insulin to ascertain that there are no episodes of hypoglycemia. The wound bed is then covered with sterile sponges cut to the shape of the wound with a 16F ryles tube inserted between the sterile sponges.

The wound is then sealed with sterile polyurethane sheet and confirmed that the whole setting is air tight. The ryles tube is then connected to a wall mounted suction apparatus and the pressure is set at - 125 mm hg and the suction is kept on for 20 minutes to 30 minutes in an hour. The dressing is opened every 5th day and the wound is inspected. Along with this culture is sent from the wound area.

The wound is then assessed in terms of size, depth, granulation tissue formation and percentage of negative culture reports on 5th, 10th and 15th day, using the BATES- JENSEN WOUND ASSESEMENT SCALE.

All patients with diabetic foot ulcers above the age of 18 years, admitted in the JSS HOSPITAL surgery wards for management of the diabetic foot ulcers after fulfilling the inclusion and exclusion criteria were interviewed to obtain a complete sociodemographic and clinical detail. After thorough general, physical and systemic examination along with a thorough wound examination, consent proforma cleared and validated by the expert group is given to the subjects and their valid consent istaken for the test.

Evidence of granulation tissue formation, decrease in the size and depth of the wound ,decrease in the amount of exudate, peripheral tissue induration as well as an increase in epithelisation of the wound is assessed by the BATES - JENSEN WOUND ASSESEMENT TOOL.

A score of 13 according to the BWAT score indicates wound regeneration.

A score of 60 according to the BWAT score indicates wound degeneration.

All demographic data were summarized as proportion, mean, standard deviation,Sensitivity, Specificity, Negative predictive value, Positive predictive value was measured at 95% confidence interval. All measurements were done using SPSS Version 21

Results :

A total of 48 study subjects were enrolled in each group and analyzed for the objective.

Table 1: Social Profile of the study subjects

		VAC n (%)	VAC + Topical insulin n (%)	

Age group	31 – 40 years	0	2 (4.2)	χ^2 value=2.223 df=3 p value =0.527
	41 – 50 years	5 (10.4)	6 (12.5)	
	51 – 60 years	19 (39.6)	17 (35.4)	
	More than 60years	24 (50.0)	23 (47.9)	
Gender	Male	39 (81.2)	37 (77.1)	χ^2 value=0.253 df=1 p value =0.615
	Female	9 (18.8)	11 (22.9)	

This study had shown that majority of the study subjects in VAC and VAC + topical insulin group were aged more than 60 years. There was no statistically significant difference in age between the two groups. About 81.2% of the study subjects in VAC group and 77.1% in the VAC + topicalinsulin group were males. This difference in sex was not statistically significant

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Table 2 : Distribution of Study subjects based on history of Diabetics and other information

		VAC n (%)	VAC + Topical insulin n (%)	
Duration of Diabetes	Mean \pm SD	5.95 \pm 3.77	5.62 \pm 3.1	T= 0.458 p=0.648
Type of Treatment	Insulin	20 (41.7)	26 (54.2)	χ^2 value=1.509 df=1 p value =0.220
	OHA's	28 (58.3)	22 (45.8)	
Mode of onset of ulcer	Post traumatic	27 (56.2)	27 (56.2)	
	Spontaneous	21 (43.8)	21 (43.8)	

Side of the ulcer	Left	23 (47.9)	21 (43.8)	χ^2 value=0.168 df=1 p value =0.682
	Right	25 (52.1)	27 (56.2)	

The mean duration of diabetes in VAC group was 5.95 years and 5.62 years in VAC + topical insulin group. However, this difference was not statistically significant between the two groups. The mode of onset of wound was post traumatic in 56.2% in both the groups. This difference was not statistically significant between the two groups. About 52.1% of the VAC and 56.2% of the VAC + topical insulin study subjects had right lower limb affected which was statistically not significant.

Table 3 : Distribution of Ulcer/Wound dimensions among the study subjects

		VAC	VAC + Topical insulin	
Length	Mean \pm SD	7.17 \pm 2.77	7.23 \pm 3.16	T= 0.103 , P= 0.918
Width	Mean \pm SD	7.48 \pm 2.01	7.02 \pm 2.21	T= 1.061 , P= 0.219
Size (in cm²)	Mean \pm SD	55.35 \pm 28.82	53.33 \pm 33.6	T= 0.361 , P= 0.752
BWAT score	Mean \pm SD	47.12 \pm 2.27	47.12 \pm 2.33	

The mean length of the wound was 7.17 cms in VAC and 7.23 cms in VAC + topical insulin group in this study which was statistically not significant between the two groups. The mean width of the wound was 7.48 cms in VAC and 7.02 cms in VAC + topical insulin study subjects which was statistically not significant between the two groups. The mean size of the wound in VAC group was 55.35 cm² area and 53.3 cm² area in this study. This difference was not statistically significant between the two groups. The mean BWAT score in VAC group was 47.12 and 47.12 in VAC + topical insulin group. This difference was not statistically significant between the two groups at the baseline of the study.

Table 4 : Comparison of the parameters of BWAT scoring

BWAT Parameters	VAC	VAC + Topical insulin	T value	P value, Sig
Depth of wound	3.19 ±0.39	3.18 ± 0.36	0.543	0.589, NS
Edges	3.31 ±0.47	3.35 ± 0.48	0.429	0.669, NS
Undermining	4.04 ±0.85	3.92 ± 0.74	0.769	0.444, NS
Necrotic tissue type	3.79 ± 0.8	3.69 ± 0.88	0.608	0.545, NS
Necrotic tissue amount	3.44 ± 0.5	3.37 ± 0.49	0.618	0.538, NS
Exudate type	3.54 ± 0.5	3.46 ± 0.5	0.811	0.42, NS
Exudate amount	3.42 ± 0.5	3.62 ± 0.49	2.067	0.041, Sig
Surrounding skin colour	4.33 ±0.78	3.44 ± 0.5	0.133	0.895, NS
Peripheral tissue edema	3.44 ±0.50	3.48 ± 0.5	0.406	0.686, NS
Peripheral tissue induration	4.02 ±0.67	4.02 ± 0.82	0.000	1.000, NS
Granulation tissue	3.25 ±0.44	3.46 ± 0.50	2.164	0.033, Sig
Epithelialization	3.48 ± 0.5	3.5 ± 0.50	0.202	0.84, NS

There was no statistically significant difference in parameters of BWAT scoring including Depth, Edges, Undermining, Necrotic tissue, necrotic tissue amount, exudate type, surrounding skin colour, peripheral tissue edema, peripheral tissue induration, and Epithelialization. But there was a statistically significant difference in exudate amount and Granulation tissue between the VAC and VAC + Topical insulin group.

Table 5. Distribution of the study group according to BWAT score at different follow up intervals

BWAT score after dressing (Mean \pm SD)	VAC	VAC + Topical insulin	T value	P value, Sig
Day 5	43.39 \pm 2.26	41.7 \pm 2.3	3.71	0.000, Sig
Day 10	38.73 \pm 2.26	34.85 \pm 2.15	8.587	0.000, Sig
Day 15	32.5 \pm 2.46	27.1 \pm 2.18	11.366	0.000, Sig

The BWAT score at day 5 was 43.39 in VAC group and reduced to 32.5 on day 15. The score was 41.7 on day 5 in VAC + topical insulin group which had reduced to 27.1 on day 15. The difference in BWAT scores were statistically significant at day 5, day 10 and day 15 of follow up.

Table 6. Distribution of the study group according to granulation tissue formation score at different follow up intervals

BWAT score for granulation tissue formation (Mean \pmSD)	VAC	VAC + Topical insulin	T value	P-value, Sig
Day 5	2.25 \pm 0.44	2.46 \pm 0.5	2.164	0.033, Sig
Day 10	1.25 \pm 0.44	1.46 \pm 0.5	2.164	0.033, Sig
Day 15	1.0 \pm 0	1.0 \pm 0	0.000	1.000, NS

The mean granulation tissue formation in VAC group was 2.25 and VAC + Topical insulin group was 2.46 which was statistically significant at 5 days of follow up. The score for VAC group was 1.25 and 1.46 for VAC + Topical insulin group which was also statistically significant at 10 days. The score was 1.0 in both the groups at 15 days of follow up which was not statistically significant.

DISCUSSION :

Diabetes Mellitus is a major public health problem and is affecting one in every five Indians. These studies are scant regarding the combination of NPWT along with topical insulin application and its effect on wound healing when compared to NPWT alone, hence this study was undertaken.

A prospective interventional study was undertaken in the department of general surgery of JSS Hospital, Mysore. In 96 patients, 48 patients were taken into the control group where only plain NPWT was used for diabetic foot wounds and the rest 48 patients were taken into the experimental group where topical insulin application along with NPWT was used for diabetic foot wounds.

Most of the study subjects in this study were aged more than 60 years. There was no statistically significant difference in the age between the two groups ensuring comparability between the two groups. In a study by Stephen et al, the mean age of the control group was 41.56 years and 43.36 years in the intervention group.¹⁰

Majority of the patients with diabetic foot were males in both the groups in this study. Stephen et al also observed similar findings.¹⁰

The mean size of the wound in VAC group was 55.35 cm² area and 53.3 cm² area in this study. In a study by Stephen et al, the mean baseline wound area was 11.78 cm² in normal saline and 9.61 cm² in insulin groups. The decrease in wound area was significant in insulin group than the normal saline group.¹⁰ In a study by Ramarao et al, a significant reduction of mean ulcer area was observed with higher mean percent of reduction (35.19) in topical insulin group than the normal saline group.¹¹ In a study by Goenka et al, the mean ulcer size on day 1 in topical insulin group was 670 mm² and 629 mm² in normal saline group. The rate of healing was 130.2 mm² / week in topical insulin group and 95.1 mm² in normal saline group.¹²

The mean BWAT score in VAC group was 47.12 and 47.12 in VAC + topical insulin group. In a study by Stephen et al, the mean PUSH scores was 10.52 in normal saline group and 10.28 in the insulin group.¹⁰

The mean granulation tissue formation in VAC group was 2.25 and VAC + Topical insulin group was 2.46 which was statistically significant at 5 days of follow up. The score for VAC group was 1.25 and 1.46 for VAC + Topical insulin group which was also statistically significant at 10 days. The score was 1.0 in both the groups at 15 days of follow up which was not statistically significant. The BWAT score at day 5 was 43.39 in VAC group and reduced to 32.5 on day 15. The score was 41.7 on day 5 in VAC + topical insulin group which had reduced to 27.1 on day 15. The difference in BWAT scores were statistically significant at day 5, day 10 and day 15 of follow up. In a study by Stephen et al, the authors used Pressure Ulcer Scale for Healing (PUSH) scores and at day 7, the decrease in the mean PUSH scores in the intervention group was from 10.28 to 8.52.¹⁰

Conclusion :

This study emphasized that when a combination of NPWT and topical insulin is used as a means of dressing in the management of diabetic foot wounds it has shown appreciable results , in terms of faster reduction in the size of the wound as assessed using the Bates – Jensen wound assessment tool , hastening the process of granulation tissue formation and in bringing about negative culture reports .

Thus , this study has shown that although NPWT is a good method for treating diabetic foot wounds without osteomyelitis , on addition of topical insulin prior to application of the VAC dressing there has been a beneficial effect of insulin on the wound and the combination of the two methods has thus resulted in faster rate of wound healing.

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