International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2017): 7.296

Role of Negative Pressure Therapy for Chronic Surgical Wounds

Dr Mayuri Kamble[1], Dr Nitin Chore[2]

[1]Associate Professor, Department of General Surgery, B.J. Govt. Medical College, Pune, Maharashtra, India

[2]Senior Resident, Department of General Surgery, B.J. Govt. Medical College, Pune, Maharashtra, India

1. Introduction

Patients with chronic wounds constitute a significant workload burden for health care organizations. Successful therapy should be based on knowledge of the wound aetiology and the different features of the wound care products available.

Wound management during the early Egyptian civilization resembles current approaches. The Egyptians may have been the first, unknowingly, to employ the "moist wound healing" principle.

Wound healing has a multifactorial etiology. Various treatment modalities have been discovered over the years in forms of different types of wound dressings. Some commonly used dressing agents are povidone iodine, EUSOL, acetic acid, silver sulfadiazine etc. An ideal wound care product in addition to controlling the infection should also protect the normal tissues and not interfere with the normal wound healing [1,2].
Negative pressure has been used as part of the treatment of wounds in the form of various drains since the 1940s [3,4]. The treatment technique for open wounds based on negative pressure was developed in Germany and the United States during the 1990s [5-7].

The treatment is based on evenly distributed local negative pressure applied to the wound surface. The open wound is covered with a separate wound dressing (polyurethane or polyvinyl alcohol) and an air-tight film. The wound dressing is connected by means of a set of suction tubes to a control unit by which the primary negative pressure on the surface of the wound can be adjusted. Most commonly 80–125 mm Hg of negative pressure is used, either continuously or in cycles. The fluid suctioned from the wound is collected into a container in the control unit.

NPWT has been recommended for virtually all kinds of acute and chronic wounds to accelerate healing in pressure wounds, diabetic leg ulcers, lower leg wounds, surgical incision, traumatic wounds, burns, infected wounds, necrotizing fascitis, infected sternal wounds and after skin grafting (KCI marketing brochures and personal communication with company representatives). The duration of the therapy varies from a few days to months, depending on the treatment aim and the nature of the wound. The literature analyzing the mechanisms believed to account for the efficacy of NPWT therapy and the different possible clinical benefits are analyzed in a recent review by Hunter et al. [8].

The data available on the role of NPWT for the management of chronic leg wounds is limited. Therefore, present study was conducted to compare the effectiveness of VAC with conventional dressings in the healing of chronic ulcers.

2. Materials & Methods

Study Design
An open labelled randomised control trial.

Study Population
Patient with chronic wounds of following etiology: diabetic ulcers, pressure ulcers, venous ulcers and pilonidal sinus ulcers.

Sampling Technique and Sample size
Consecutive type of non-probability sampling was used for the selection of study subjects during study duration. All the subjects fulfilling the eligibility criteria were taken for study after informed consent. A total of 120 patients of chronic wounds were divided into 2 study groups as per computer generated random numbers:

Group A: Negative Pressure Wound Treatment (60 patients)

Group B: Conventional Dressing (60 patients)

Statistical Analysis
All the collected data was entered in Microsoft Excel sheet. It was then transferred to SPSS ver. 21 software for statistical analysis. All the Quantitative data was presented as **mean** and **standard deviation** and compared using student's t-test.

Qualitative data was presented as frequency and percentage and analysed using chi-square test (Continuity correction was applied in case of 2x2 contingency tables). P-value of < 0.05 was considered as significant

Inclusion Criteria
1) Patients with chronic ulcers (> 3 months duration).
2) Both gender and age group of 18-70 years.
3) Type of ulcers- diabetic foot ulcers
   - Pressure ulcers
   - Venous ulcers

Exclusion Criteria

1) Any patient who refused to participate in the trial or is biased to a particular modality of treatment after informed consent.
2) Pre-existing Infection
3) Underlying malignancy
4) Unresolved osteomyelitis
5) Coagulopathies
6) Patient allergic to dressing

Equipment

1) Polyuethane foam
2) Closed circuit negative pressure wound therapy system
3) Plastic Drapings
4) Disposable canister

Methodology

A detailed history, clinical examination and relevant investigations were performed in all patients. The institutional ethical committee approved the study.

The Index ulcer was defined as the ulcer with the largest area and a duration of at least three months at the time of inclusion. Size of the Index ulcer was determined by volume of the wound i.e., by multiplying greatest length with greatest width and depth.

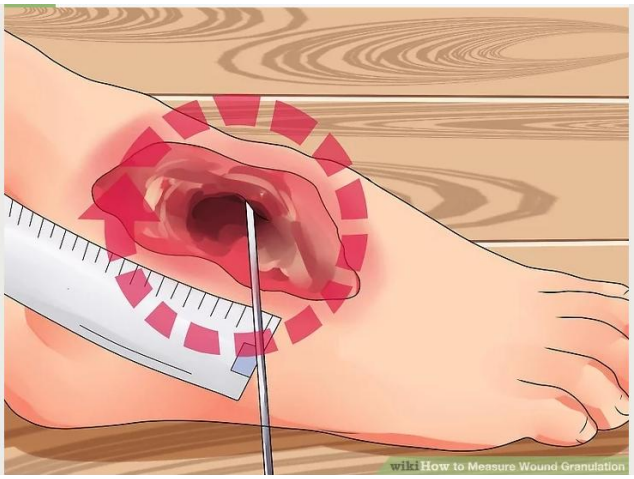
Wounds of all the patients included in the study underwent sharp surgical debridement initially and during subsequent dressing change to remove necrotic tissue and slough. After debridement in the emergency operation theatre, a foam-based dressing was applied over the wounds of the study group patients under all aseptic conditions. The dressing was covered with an adhesive drape to create an airtight seal. An evacuation tube embedded in the foam was connected to a vacuum and sub-atmospheric (negative) pressure was applied within a range of 80–125 mmHg on a continuous basis for 72 hours.

The control group received once daily saline soaked gauze dressing. Oral analgesics were administered to all of the patients at the time of changing the dressing. Standard antibiotic regimens were administered to all patients, which consisted of broad-spectrum antibiotics initially and later guided by the culture sensitivity reports.

Ulcers were treated until the wound was closed spontaneously, surgically or until completion of the 3-week period, whichever was earlier. Blood glucose levels were monitored strictly during treatment and controlled by appropriate doses of insulin. Treatment outcome was assessed in terms of:

- Appearance of granulation tissue at week 1, 2 and 3.
- Wound contraction achieved by week 1, 2 and 3.
- Wound surface area at week 1, 2 and 3.
- Pain by VAS Score at week 1, 2 and 3.
- Days of Hospitalization
- Final outcome – healing by secondary intention or requirement of STSG
- Patient's subjective assessment

Measurement of the wound dimensions (Clock Technique)



In "clock technique", we measure the longest length, width and depth of the wound with the body as an imaginary clock using a ruler measured in centimeters.

The ruler was placed on the widest portion of the width from 3 o'clock to 9 o'clock. This allowed us to measure the width of the wound. When getting the length, the heels are at 12 o'clock and toes at 6 o'clock. The ruler was put over the longest portion of the wound.

At each follow up, wound surface area was measured and percentage of wound contraction was calculated.

Measurement of granulation tissue

The plastic cover of urine bag was split open and the sterile inner part was used to cover the ulcer. The outline of the ulcer was traced out over the cover and area of slough was marked. The cover was then placed on graph paper (with box size: 1 cm^2) and the entire drawing was retraced on graph for measurement. Perimeter was measured in centimetres by running length of a pliable string over the outline. The granulation tissue was calculated by subtracting area covered by slough from total area.

3. Results

Table 1: Distribution of subjects based on Age Group

Age Group (years)	Group		Total
	Conv	NPWT	
≤ 50	22	21	43
	36.7%	35.0%	35.8%
> 50	38	39	77
	63.3%	65.0%	64.2%
Total	60	60	120
	100.0%	100.0%	100.0%
Age (years)	52.8 +/- 12.1	53.61 +/- 11.9	53.38 +/- 12.3
p-value - 1.0			

Mean age of study subjects was 52.8 and 53.6 years in Conventional and NPWT group respectively. The difference was statistically non-significant (p-1.0).

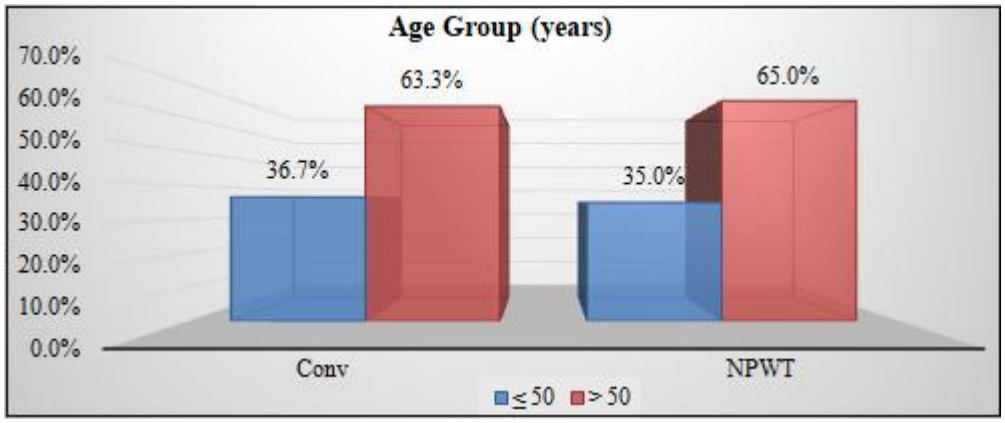


Table 2: Distribution of subjects based on Gender

Sex	Group		Total
	Conv	NPWT	
Female	19	18	37
	31.7%	30.0%	30.8%
Male	41	42	83
	68.3%	70.0%	69.2%
Total	60	60	120
	100.0%	100.0%	100.0%
p-value - 1.0			

Male Preponderance was observed in both groups (68.3% in Conventional and 70% in NPWT group respectively). The difference was statistically non-significant (p-1.0).

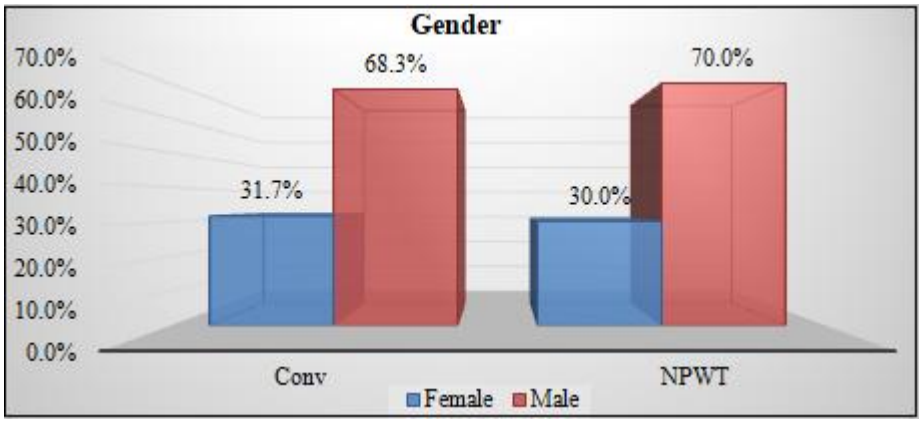


Table 3: Distribution of subjects based on type of Ulcer

Type of Ulcer	Group		Total
	Conv	**NPWT**	
Venous Ulcer	10	9	19
	16.7%	15.0%	15.8%
Pressure Ulcer	3	2	5
	5.0%	3.3%	4.2%
Diabetic Ulcers	43	49	92
	71.7%	81.7%	76.7%
Total	60	60	120
	100.0%	100.0%	60.0%
p-value - 0.647			

Most common type of chronic ulcer observed in present study was diabetic ulcer (76.7%) followed by venous ulcers (15.8%) and pressure ulcers (4.2%). No difference was seen in the study groups on the basis of type of ulcer (p-1.0).

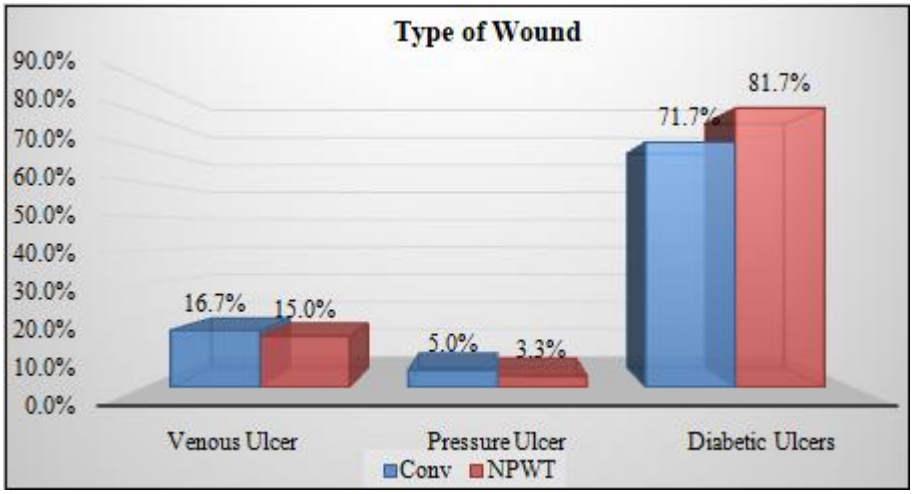


Table 4: Comparison of Groups as per appearance of granulation tissue

Granulation Tissue appearance	Group		Total	p- value
	Conv	**NPWT**		
Week 1	9	28	37	**<0.05**
	15.0%	46.7%	30.8%	
Week 2	38	59	97	**<0.05**
	63.3%	98.3%	80.8%	
Week 3	47	60	107	**<0.05**
	78.3%	100.0%	89.2%	

At the end of 3 weeks, all the cases in NPWT group had granulation tissue as compared to 78.3% cases in conventional group. The difference was statistically significant (p<0.05).

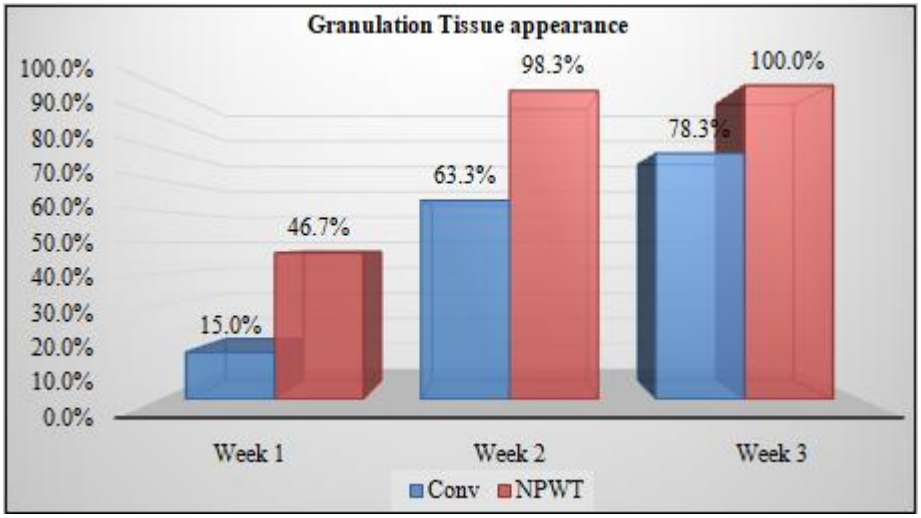


Table 5: Comparison of Groups as per Wound Contraction rate

Wound Contraction (%)	Group	Mean	SD	p-value
Week 1	**Conv**	46.57	20.21	**< 0.05**
	NPWT	58.76	18.12	
Week 2	**Conv**	61.34	19.12	**< 0.05**
	NPWT	77.69	16.83	
Week 3	**Conv**	74.54	17.94	**< 0.05**
	NPWT	90.90	14.41	

The wound contraction rate was significantly faster with NPWT therapy. The difference in the rate of wound contraction was apparent since 1st week and by week 3, mean percentage of wound contraction was 90.9% in NPWT therapy as compared to 74.54% in conventional group patients. The difference was statistically significant ($p<0.05$).

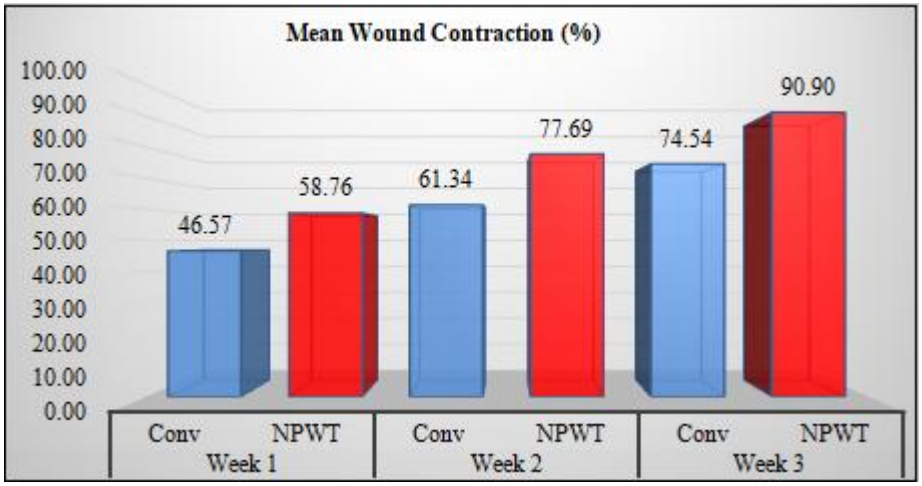


Table 6: Mean comparison of Wound dimensions at each follow up

Wound dimensions (cm^3)	Group	Mean	SD	p-value
After Debridement	**Conv**	142.57	20.21	**0.79**
	NPWT	141.92	18.12	
Week 1	**Conv**	116.54	28.21	**0.06**
	NPWT	84.52	15.12	
Week 2	**Conv**	74.35	12.12	**< 0.05**
	NPWT	51.72	6.83	
Week 3	**Conv**	42.21	7.94	**< 0.05**
	NPWT	24.37	6.41	

Decrease in wound dimensions was significantly faster in NPWT group patients as compared to conventional group. The difference was statistically significant from week 2 ($p<0.05$).

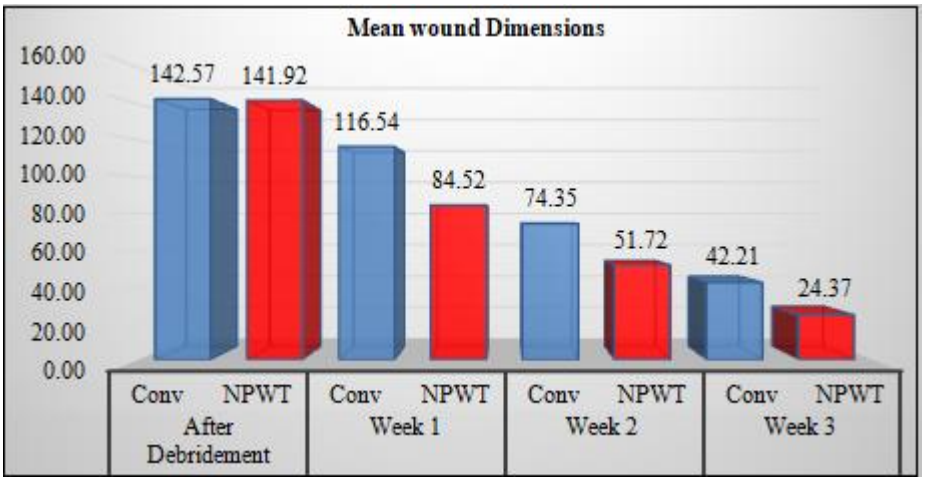


Table 7: Mean comparison of VAS score at each follow up

Pain (VAS Score)	Group	Mean	SD	p-value
Week 1	**Conv**	4.51	1.10	**0.09**
	NPWT	4.07	1.20	
Week 2	**Conv**	4.01	1.09	**< 0.05**
	NPWT	3.22	1.06	
Week 3	**Conv**	3.53	1.12	**< 0.05**
	NPWT	2.38	0.89	

Mean VAS score at week 1, 2 and 3 in conventional group was 4.51, 4.01 and 3.53 respectively while in cases of NPWT, it was 4.07, 3.22 and 2.38 respectively. The difference was statistically significant at week 2 and 3 ($p<0.05$).

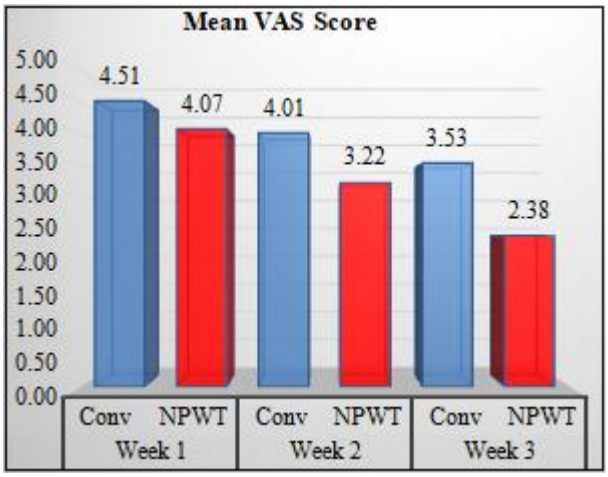


Table 8: Mean comparison of hospital stay between the groups

	Group	Mean	SD	p-value
Hospital Stay	Conv	11.13	5.34	<0.05
	NPWT	17.23	4.32	

Mean hospital stay was significantly more in cases managed by conventional dressing as compared to NPWT (17.23 vs 11.13 days; $p<0.05$).

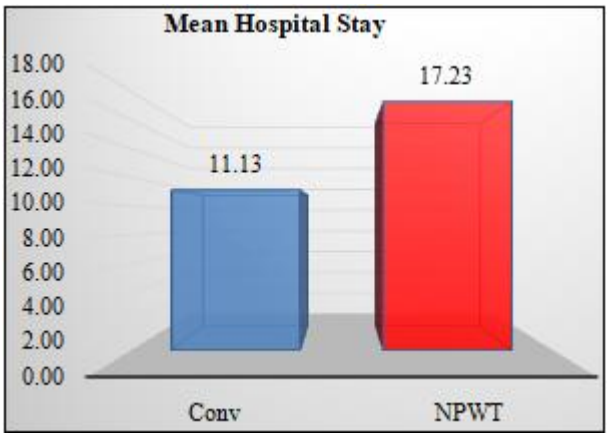


Table 9: Comparison of wound closure technique between the groups

Wound Closure	Group		Total
	Conv	**NPWT**	
Secondary Intention	42	52	94
	70.0%	86.7%	47.0%
STSG	18	8	26
	30.0%	13.3%	13.0%
Total	60	60	120
	100.0%	100.0%	60.0%
p-value <0.05			

Closure by secondary intention was achieved in 86.7% and 70% patients of NPWT and Conventional group while skin grafting was required in 13.3% cases of NPWT group as compared to 30% cases in conventional group respectively.

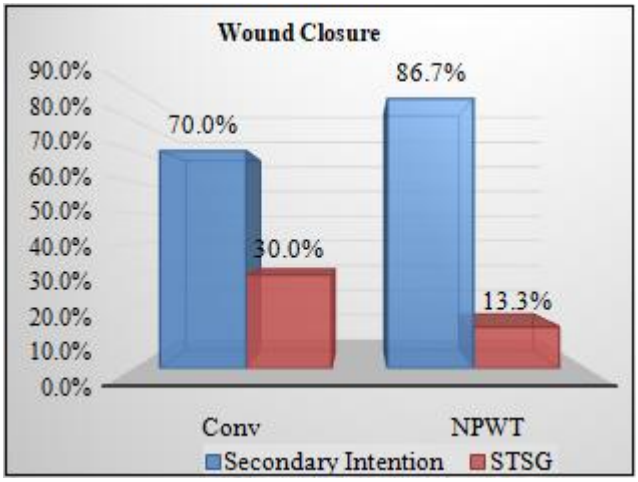
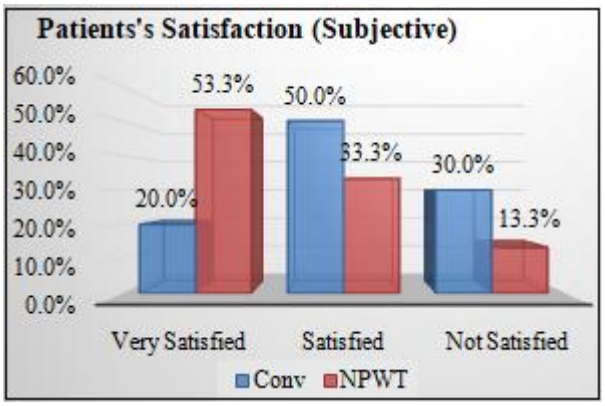


Table 10: Comparison of patient's satisfaction level between the groups

Patients' Satisfaction (Subjective)	Group		Total
	Conv	NPWT	
Very Satisfied	12	32	44
	20.0%	53.3%	22.0%
Satisfied	30	20	50
	50.0%	33.3%	25.0%
Not Satisfied	18	8	26
	30.0%	13.3%	13.0%
Total	60	60	120
	100.0%	100.0%	60.0%
p-value 0.11			

As per the subjective assessment, 86.7% cases of NPWT were satisfied with the procedure as compared 70% cases of conventional dressing. The dissatisfaction among cases of conventional group were primarily due to delayed healing and requirement of STSG.



4. Discussion

Negative Pressure Wound Therapy (NPWT) has been advocated as a novel method in the healing of chronic ulcers

by stimulating the chronic wound environment in such a way that it reduces bacterial burden and chronic interstitial wound fluid, increases vascularity and cytokine expression and to an extent mechanically exploiting the viscoelasticity of periwound tissues. NPWT is generally well tolerated and, with few contraindications or complications, is fast becoming a mainstay of current wound care. But the results of various trials comparing it with conventional wound dressing had equivocal results. Hence, we planned to use NPWT for the treatment of chronic ulcers and compare its results with conventional dressing in terms of wound healing arte and hospital stay.

Demography

Mean age of study subjects was 52.8 and 53.6 years in Conventional and NPWT group respectively.

The incidence being higher age group can be well explained by fact that most of the chronic ulcers are diabetic ulcers, which is a complication of diabetes mellitus. Complications of diabetes increase with age. Also diabetes is disease of mostly elderly. Similar findings of highest incidence being in age group of 45 to 64 years in the National health department survey (N.H.D.S) survey at USA. [9] In another similar study by Lone AM et al. mean age in NPWT group was 53.79 years and in Conventional group was 54.57 years. [10]

Male Preponderance was observed in both groups (68.3% in Conventional and 70% in NPWT group respectively). This was similar to that observed in review of literature by Rieber et al. [11]. India being a male dominated country and lack of medical care given to females may also be a contributing factor. In a study by Lone AM et al. women constituted approximately one third and men around two third of study participant in a NPWT and Conventional group [10].

Wound Characteristics: Granulation tissue & Contraction

Application of negative pressure over the wound bed allows the arterioles to dilate, increasing the effectiveness of local circulation, promoting angiogenesis, which assists in the proliferation of granulation tissue [12].

We observed that patients on NPWT therapy had early appearance of granulation tissue as compared to patients treated by Conventional dressing $p<0.05$). At the end of 3 weeks, all the cases in NPWT group had granulation tissue as compared to 78.3% cases in conventional group. The difference was statistically significant ($p<0.05$). The wound contraction rate was significantly faster with NPWT therapy. The difference in the rate of wound contraction was apparent since 1st week and by week 3, mean percentage of wound contraction was 90.9% in NPWT therapy as compared to 74.54% in conventional group patients. The difference was statistically significant ($p<0.05$).

In a study by Lone AM et al. granulation tissue appeared in 26 (92.85%) patients by the end of Week 2 in NPWT group in contrast to 15 (53.57%) patients by that time in conventional group [10]. Armstrong and Lavery also observed that the use of negative pressure therapy resulted in an increased rate of granulation tissue formation and a higher proportion of healed wounds compared to saline gauze dressings [13]. Eginton MT et al. compared the rate of wound healing with the NPWT Assisted Closure device (NPWT) to conventional moist dressings in the treatment of large diabetic foot wounds. NPWT dressings decreased the wound volume and depth significantly more than moist gauze dressings (59% vs. 0% and 49% vs. 8%, respectively). The study concluded that Negative-pressure wound treatment may accelerate closure of large foot wounds in the diabetic patient [14]. In a study by Moues CM et al., 54 patients were included (NPWT n = 29, conventional n = 25). The authors observed that wound surface area reduced significantly faster with NPWT therapy [15].

Vuerstaek et al. evaluated 60 patients with lower limb venous ulcers, comparing wound treatment with NPWT or moist dressings in a randomized, controlled clinical study. Patients in the NPWT group healed faster (29 days x 45 days, $p<0.01$), also reaching more quickly the time of wound bed preparation (7 days x 17 days, $p<0.01$) [16]. Egemen et al. applied NPWT in 20 patients with venous ulcers and found a rapid preparation of the bed, as well as an optimization of the subsequent integration of the skin graft [17].

Ford et al. [18] conducted a randomized, controlled study with 41 patients with deep pressure ulcers, comparing NPWT with topical healing promoter gels. The mean percentage reduction in ulcer volume was higher in the NPWT group (51.8% vs. 42.1%, $p=0.46$). The authors stated that NPT promotes healing and neovascularization. Ashby et al. [19] conducted a randomized controlled trial in patients with Pressure ulcers grades III and IV, showing superior benefits of NPWT in comparison with moist dressing in regards to rapid development of granulation tissue and wound contraction.

Hospital Stay

In present study, mean hospital stay was significantly more in cases managed by conventional dressing as compared to NPWT (17.23 vs 11.13 days; $p<0.05$). The decreased stay can be attributed to rapid healing and wound contraction rate in cases of NPWT therapy.

In a study by Moues CM et al. [15], patients on NPWTuum therapy had shorter duration of hospital stay as compared to conventional moist dressing. Petzina et al. [84], retrospectively, analyzed 118 patients treated with NPT (n=69) or with conventional therapy (n=49). The group treated with NPT had a tendency of lower hospital stay ($p=0.08$). Assenza et al. [21] in their iterature review affirmed that NPWT accelerated the preparation of the wound, which allowed an earlier reconstruction and reduced the days of hospitalization. Anghel et al. [22] reviewed the evidence for the use of NPWT with instillation, indicating a role for this therapy in helping to reduce hospital stay, number of debridements and treatment costs in patients.

Pain Relief

Mean VAS score at week 1, 2 and 3 in conventional group was 4.51, 4.01 and 3.53 respectively while in cases of NPWT, it was 4.07, 3.22 and 2.38 respectively. The

difference was statistically significant at week 2 and 3 ($p<0.05$).

Meloni et al.[25] in their study also observed that chronic wound ulcers managed with NPWT benefit from significant reduction in the ulcer size, and improvement with pain control in comparison with ulcers treated with traditional gauze dressing. Menzies et al. [26] in their study also reported rapid and significant pain relief with the application of negative pressure wound therapy

Outcome

Closure by secondary intention was achieved in 86.7% and 70% patients of NPWT and Conventional group while skin grafting was required in 13.3% cases of NPWT group as compared to 30% cases in conventional group respectively. As per the subjective assessment, 86.7% cases of NPWT were satisfied with the procedure as compared 70% cases of conventional dressing. The dissatisfaction among cases of conventional group were primarily due to delayed healing and requirement of STSG. The difference was statistically non-significant.

In the study by Lone AM et al. [10] most of the cases required skin grafting owing to large ulcers, the healing by secondary intention was higher in cases of NPWT as compared to Conventional dressing(23% vs 7%). Our observations were consistent with those of Prabhdeep et al. [23] who also reported more cases requiring skin grafting in conventional group. Llanos et al. [24] in their study on traumatic wounds, observed that need for second coverage procedure was less common in the NPWT group (5 [16.7%] vs. 12 [40.0%] patients, p = 0.045).

5. Summary

A hospital based randomized control trial was conducted for a period of one year in the department of surgery of a tertiary care hospital with the aim of studying the efficacy of negative pressure wound therapy in chronic wound ulcers and compare it with conventional method of treatment. A total of 120 patients between age 30-70 years with chronic ulcers (i.e. without infection and ischemia), were randomly divided in two groups: **Group A:** Negative Pressure Wound Therapy and; **Group B:** Conventional Dressing. Following observations were made during the study:

1) Mean age of study subjects was 52.8 and 53.6 years in Conventional and NPWT group respectively. The difference was statistically non-significant (p-1.0).
2) Male Preponderance was observed in both groups (68.3% in Conventional and 70% in NPWT group respectively). The difference was statistically non-significant (p-1.0).
3) Most common type of chronic ulcer observed in present study was diabetic ulcer (76.7%) followed by venous ulcers (15.8%) and pressure ulcers (4.2%). No difference was seen in the study groups on the basis of type of ulcer (p-1.0).
4) At the end of 3 weeks, all the cases in NPWT group had granulation tissue as compared to 78.3% cases in conventional group. The difference was statistically significant ($p<0.05$).
5) The wound contraction rate was significantly faster with NPWT therapy. The difference in the rate of wound contraction was apparent since 1st week and by week 3, mean percentage of wound contraction was 90.9% in NPWT therapy as compared to 74.54% in conventional group patients. The difference was statistically significant ($p<0.05$).
6) Decrease in wound dimensions was significantly faster in NPWT group patients as compared to conventional group. The difference was statistically significant from week 2 ($p<0.05$).
7) Mean VAS score at week 1, 2 and 3 in conventional group was 4.51, 4.01 and 3.53 respectively while in cases of NPWT, it was 4.07, 3.22 and 2.38 respectively. The difference was statistically significant at week 2 and 3 ($p<0.05$).
8) Mean hospital stay was significantly more in cases managed by conventional dressing as compared to NPWT (17.23 vs 11.13 days; $p<0.05$).
9) Closure by secondary intention was achieved in 86.7% and 70% patients of NPWT and Conventional group while skin grafting was required in 13.3% cases of NPWT group as compared to 30% cases in conventional group respectively.
10) As per the subjective assessment, 86.7% cases of NPWT were satisfied with the procedure as compared 70% cases of conventional dressing. The dissatisfaction among cases of conventional group were primarily due to delayed healing and requirement of STSG.

6. Conclusion

Present study concluded that Negative Pressure Wound Therapy appears to be superior compared to conventional dressings in the treatment of chronic wounds in terms of

1) Early appearance of granulation tissue, rapid contraction
2) Decrease in hospital stay.
3) Overall patient satisfaction rate was higher .

We thus recommend use of Negative Pressure Wound Therapy in chronic wound management as first line therapy.

NPWT delivered by VAC system seems to be a safe and effective treatment for complex diabetic foot wounds and could lead to a higher proportion of healed wounds, faster healing rates and potentially fewer re-amputation rates than standard care.

We also recommend further studies with larger sample size to validate our observations in each specific type of chronic wounds viz. venous, diabetic and pressure ulcers.

References

[1] Broughton 2nd G, Janis JE, Attinger CE. The basic science of wound healing. Plastic and reconstructive surgery. 2006 Jun;117(7 Suppl):12S-34S.
[2] Martin P. Wound healing--aiming for perfect skin regeneration. Science. 1997 Apr 4;276(5309):75-81.
[3] Fay MF. Drainage systems. Their role in wound healing. AORN J 1987;46:442e55.
[4] Fox 4th JW, Golden GT. The use of drains in subcutaneous surgical procedures. Am J Surg 1976;132:673e4.

[5] Fleischmann W, Lang E, Russ M. Treatment of infection by vacuum sealing. Unfallchirurg 1997;100:301e4.
[6] Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. Ann PlastSurg 1997;38:553e62.
[7] Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. Ann PlastSurg 1997;38:563e76.
[8] Hunter JE, Teot L, Horch R, Banwell PE. Evidence-based medicine: vacuum-assisted closure in wound care management. Int Wound J 2007;4:256e69.
[9] Armstrong DG, Lavery LA. Diabetic foot ulcers: prevention, diagnosis and classification. Am Fam Physician. 1998;57:1325–32.
[10] Lone, Ali M., et al. "Vacuum-assisted closure versus conventional dressings in the management of diabetic foot ulcers: a prospective case–control study."Diabetic foot & ankle 5 (2014).
[11] Reiber, Gayle E. "Epidemiology and health care costs of diabetic foot problems." The diabetic foot. Humana Press, 2002. 35-58.
[12] Morykwas MJ, Argenta LC, Shelton B, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. Ann Plast Surg. 1997;38:553–62.
[13] Armstrong DG, Lavery LA, Diabetic Foot Study Consortium Negative pressure wound therapy after partial diabetic foot amputation: a multicenter randomized controlled trial. Lancet. 2005;366:1704–10.
[14] Eginton, Mark T., et al. "A prospective randomized evaluation of negative-pressure wound dressings for diabetic foot wounds." Annals of vascular surgery17.6 (2003): 645-649.
[15] Moues, C. M., et al. "Comparing conventional gauze therapy to vacuum-assisted closure wound therapy: a prospective randomised trial." Journal of plastic, reconstructive & aesthetic surgery 60.6 (2007): 672-681.
[16] Vuerstaek JD, Vainas T, Wuite J, Nelemans P, Neumann MH, Veraart JC. State-of-the-art treatment of chronic leg ulcers: a randomized controlled trial comparing vacuum-assisted closure (V.A.C.) with modern wound dressings. J VascSurg . 2006;44(5):1029-37; discussion 1038.
[17] Egemen O, Ozkaya O, Ozturk MB, Aksan T, Orman Ç, Akan M. Effective use of negative pressure wound therapy provides quick wound-bed preparation and complete graft take in the management of chronic venous ulcers. Int Wound J . 2012;9(2):199-205.
[18] Ford CN, Reinhard ER, Yeh D, Syrek D, De Las Morenas A, Bergman SB, et al. Interim analysis of a prospective, randomized trial of vacuum-assisted closure versus the healthpoint system in the management of pressure ulcers. Ann PlastSurg . 2002;49(1):55-61.
[19] Ashby RL, Dumville JC, Soares MO, McGinnis E, Stubbs N, Torgerson DJ, et al. A pilot randomised controlled trial of negative pressure wound therapy to treat grade III/IV pressure ulcers [ISRCTN69032034]. Trials. 2012;13:119.
[20] Petzina R, Hoffmann J, Navasardyan A, Malmsjö M, Stamm C, Unbehaun A, et al. Negative pressure wound therapy for post-sternotomymediastinitis reduces mortality rate and sternal re-infection rate compared to conventional treatment. Eur J Cardiothorac Surg. 2010;38(1):110-3.
[21] Assenza M, Cozza V, Sacco E, Clementi I, Tarantino B, Passafiume F, Valesini L, et al. VAC (Vacuum Assisted Closure) treatment in Fournier's gangrene: personal experience and literature review. Clin Ter. 2011;162(1):e1-5.
[22] Anghel EL, Kim PJ, Attinger CE. A solution for complex wounds: the evidence for negative pressure wound therapy with instillation. Int Wound J . 2016;13Suppl 3:19-24.
[23] Prabhdeep SN, Sanjeev KU, Ramneesh G, Kuljyot B, Shirin G. Role of negative pressure wound therapy in healing of diabetic foot ulcers. J Surg Tech Case Rep. 2011;3:17–22.
[24] S. Llanos, S. Danilla, C. Barraza, E. Armijo, J.L. Piñeros, M. Quintas. Effectiveness of negative pressure closure in the integration of split thickness skin grafts: a randomized, double-masked, controlled trial. Ann Surg, 244 (2006), pp. 700-705.
[25] Meloni M, Izzo V, Vainieri E, Giurato L, Ruotolo V, Uccioli L. Management of negative pressure wound therapy in the treatment of diabetic foot ulcers. World journal of orthopedics. 2015 May 18;6(4):387.
[26] Menzies et al. Portable Negative Pressure Wound Therapy Leading to Rapid Resolution of Pain. J ClinExpDermatol Res 2017, 8:6.