

VACUUM ASSISTED CLOSURE (VAC) THERAPY FOR DIFFICULT WOUND MANAGEMENT

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ABSTRACT

Objective: To show the usefulness of vacuum assisted closure (VAC) therapy for management of difficult wounds.

Study Design: descriptive type of study.

Place and Duration of the study: The study was conducted in the surgical dept of Combined Military Hospital Rawalpindi from September 2002 to February 2003.

Patients and Methods: Fifty two patients were selected through non-probability convenient sampling.

Results: Age ranged from 12 years to 61 years. Out of 52 patients 22% were females while 78% were males. The commonest wound type was traumatic in 68%, diabetic ulcer in 15%, pressure ulcer in 8%, venous ulcer in 7% and radiation ulcers in 2%. The commonest location of wound was lower limb in 42%, foot in 30%, hand in 12%, abdomen in 9% and chest in 7%. Muscle and soft tissues comprised the largest group of wound bed 71%, tendon in 16%, bone in 7% and orthopedic implant in 6%. Out of 52 patients in the study 18% were smokers while 21% had diabetes mellitus. The reduction in wound size at the end of VAC therapy was 68.1%. Granulation tissue formed in 88% of wounds. Duration of VAC therapy ranged from 2 weeks to 5 weeks. The dressing changes ranged from 2 to 12 and mean was 5 dressing changes. Foam odour, pain in-growth of granulation tissue in foam and infection.

Conclusion: Vacuum-assisted closure therapy promotes healing and the formation of healthy granulation tissue.

Keywords: vacuum therapy; vacuum sealing; topical negative pressure therapy; wound closure.

INTRODUCTION

There are over 2.8 million patients with chronic wounds treated at a cost of billions of dollars per year in the United States alone [1]. Wounds and especially chronic, open, nonhealing wounds pose a continual challenge in medicine since the treatment is variable and there are no documented consistent responses. Wound healing is a complex and dynamic process that includes an immediate sequence of cell migration leading to repair and closure. This sequence begins with removal of debris, control of infection, clearance of inflammation, angiogenesis, deposition of granulation tissue, contraction, remodeling of the

connective tissue matrix, and maturation. When wounds fail to undergo this sequence of events, a chronic open wound without anatomical or functional integrity results [2]. Clinically, wounds may be associated with trauma, pressure, venous insufficiency, diabetes, vascular disease, or prolonged immobilization. The treatment of open wounds is variable and costly, demanding lengthy hospital stays or specialized home care requiring skilled nursing and costly supplies. Rapid healing of chronic wounds could result in decreased hospitalization and an earlier return of function. A method that improves the healing process could greatly decrease the risk of infection, amputation, and length of hospital stay, and result in an estimated potential annual savings of a billion dollars of healthcare cost¹. A method that may increase the rate of healing of wounds has recently been introduced. The method

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utilizes a new subatmospheric technique: vacuum-assisted closure (VAC). The VAC technique involves placing a foam dressing into the wound cavity and applying a controlled subatmospheric pressure at 100-200mmHg. The technique removes edema, leading to increased localized blood flow, and the applied forces result in the enhanced formation of granulation tissue [3,4]. This technique aids wound healing by applying localized negative pressure that removes fluid from the wound and stimulates the growth of granulation tissue to obtain closure [3,4]. The technique may be applied to acute, subacute, and chronic wounds [3]. The rapid healing of wounds should not only decrease hospital stay, but may avoid extensive plastic surgery flap closure of some wounds. Patients who are unable to tolerate a surgical procedure should be effectually treated to complete wound closure with minimal pain and suffering at the low cost and hospitalization. Any improvement in wound healing provided by the VAC method could also eliminate the additional morbidity of infection, pain, humiliation, and depression associated with having wounds. The VAC system provides a closed system with dressings that are changed every 72 hours. The objective was to test the ability of the VAC to obtain rapid wound closure.

PATIENTS AND MATERIAL

Study design

This was a descriptive type of study. It was conducted at the surgical department of CMH Rawalpindi. Fifty two patients were selected through non-probability convenient sampling from September 2002 to February 2003. Patient data were collected on a proforma.

Inclusion criteria:

All patients with clean difficult wounds were applied VAC therapy irrespective of age.

Exclusion criteria:

- Malignant ulcers
- Osteomyelitis
- Grossly Infected wounds

- Wounds with slough or devitalized tissue

Procedure Vacuum-assisted closure (vac) therapy

During this study all clean wounds were applied VAC therapy. A piece of foam was cut to the size of the wound and was placed on it, then a perforated tube was put on top of it, again a piece of foam was folded on underlying foam and tube. The whole wound with foam and tube was then covered with a sterile transparent dressing (Op-site). The tube was connected to a common sucker machine and a pressure of 100-200 mm Hg was applied for 20 minutes after every hour.

Dressings were changed after every 72 hours and wound size were measured subsequently. Finally, the method of wound closure and complications were noted.

Data Collection / Variable Selection Procedure

Data was collected utilizing a pre-prepared proforma. Following information was used from the proforma for variable analysis.

Personal information about patient was used to assess age distribution, sex distribution and co-morbid conditions affecting outcome in the study. History and physical examination were utilized for type of wound, location of wounds and bed of wound.

Main outcome measures for the study were effect on wound size, wound granulation tissue appearance over a period of time, any complications and wound closure method. Duration of VAC therapy and dressing changes were also assessed. Relationship between age and the rate of granulation tissue appearance were also noted.

ANALYSIS

A detailed analysis of the data collected was carried out and inference drawn using a computer software SPSS-11. For all variables summary of the data were generated, histograms, scatterplots and graphs were created using Microsoft Excel XP.

RESULTS

A total of 52 patients were selected in this study. All clean wounds were treated by application with vacuum-assisted closure (VAC) technique while all infected wounds were prepared before application of VAC.

Main outcome measures were reduction in the size of wound, frequency of granulation tissue formation, development of any complications and wound closure.

Age Frequency

Age varied from 12 years to 61 years, mean age of study group was 36 years. Majority of patients were in the 20-30 age group.

Sex Distribution:

Out of 52 patients 22% (n=12) were females while 78% (n=40) were males.

Type of Wounds

The commonest wound type was traumatic in 68% (n=35), diabetic ulcer in 15% (n=8), pressure ulcer in 8% (n=4), venous ulcer in 7% (n=4) and radiation ulcers in 2% (n=1) (Figure 1).

Location of wounds:

The commonest location of wound was lower limb in 42% (n=21), foot in 30% (n=16), hand in 12% (n=6), abdomen in 9% (n=5) and chest in 7% (n=4) (Figure 2).

Bed of wound:

Muscle and soft tissues comprised the largest group of wound bed 71% (n=37), tendon in 16% (n=8), bone in 7% (n=4) and orthopedic implant in 6% (n=3) (Figure-3).

Co-morbid conditions:

Out of 52 patients in the study 18% (n=10) were smokers while 21% (n=11) had diabetes mellitus (Figure 4).

Effect on wound size:

The size of wound before application of VAC therapy ranged from 8 cm² to 310 cm² (mean 77 cm² std dev 77 cm²) and after VAC therapy ranged from 5 cm² to 240 cm² (mean 39 cm², std dev 44 cm²). The reduction in wound size at the end of VAC therapy was 68.1% (Figure 5).

Effect on wound granulation:

Granulation tissue formed in 88% (n=46) cases and it was profuse. The results were analyzed by Unpaired Student's t-test which showed highly significant difference in the rate of granulation tissue formation (p< 0.000082). Muscles and soft tissue responded early and profusely while it took sometime for tendons and bones to become covered with granulation tissue. Granulation tissue formed on an average of 11 days (Table 1). A good correlation between age and granulation tissue formation was seen (Figure 6).

Duration of vac therapy:

The duration of VAC therapy ranged from 2 weeks to 5 weeks and mean duration was 3.5 weeks. Majority of patients required 3 weeks of VAC therapy 33% (n=17) and more than 50% (n=38) required 3 or fewer weeks of therapy (Fig.7).

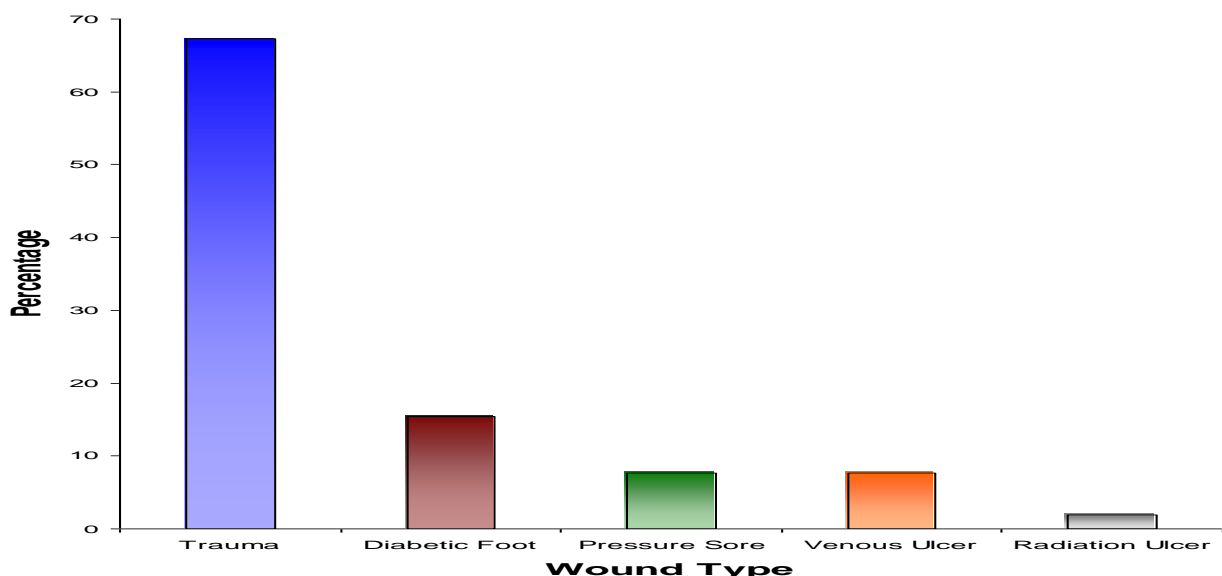


Fig.1: Type of Wounds

Dressing changes

The dressing changes ranged from 2 to 12 and mean was 5 dressing changes. But majority of patients required 4 dressing changes 25% (n=14) and more than 50% (n=35) required 5 or fewer dressing changes (Table-1).

Wound closure technique

Majority of wounds were subsequently closed using a partial thickness skin graft 90% (n=47) while 7% (n=3) were closed by delayed primary closure, 3% (n=1) required a rotation flap (Figure 8).

Complications:

Odour from foam was the commonest complain 27% (n=14), followed by pain in 19% (n=10), bleeding in 12% (n=7), in-growth of granulation tissue in foam in 7% (n=4) and infection in 3% (n=2) (Figure-9).

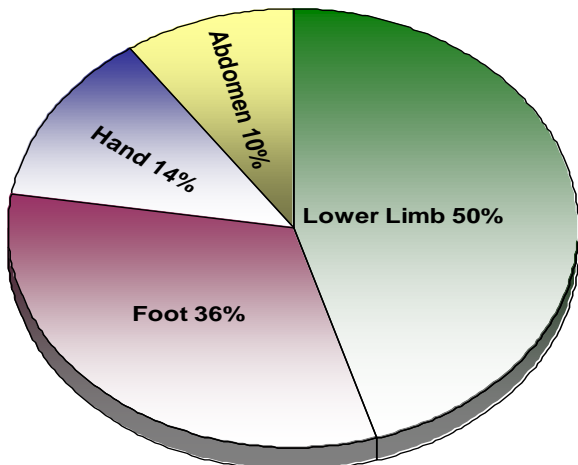


Fig. 2: Location of Wounds

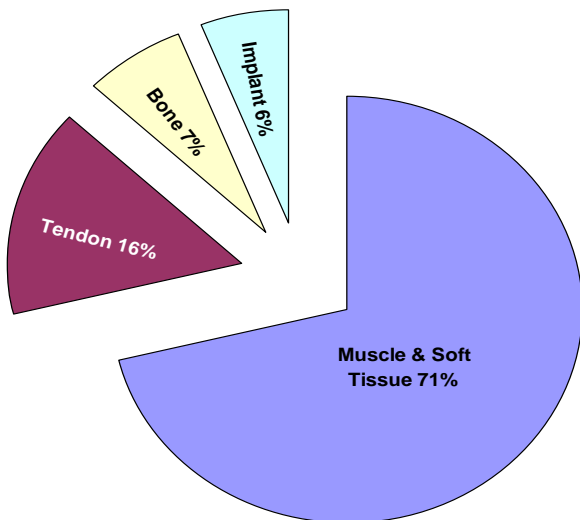


Fig. 3: Bed of Wound

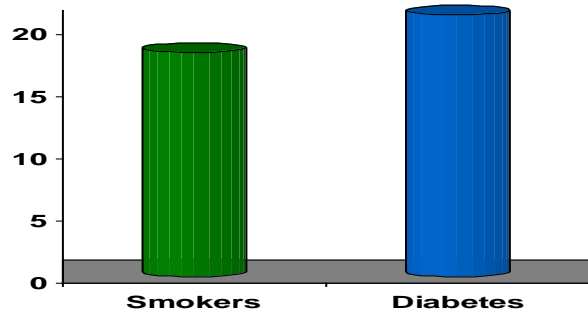


Fig. 4: Co-Morbid Factors

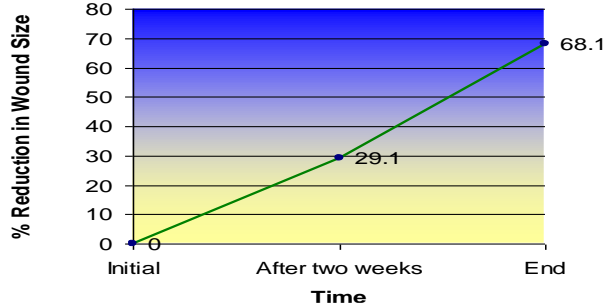


Fig. 5: Reduction in wound size

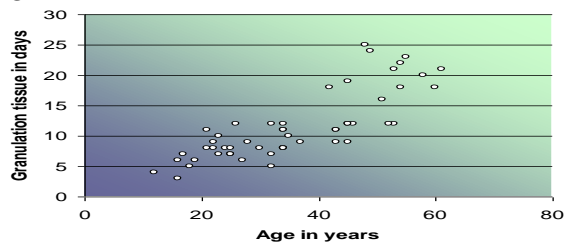


Fig. 6: Relationship between age and Granulation Tissue

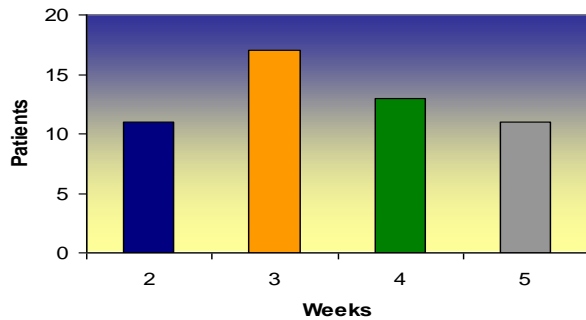


Fig. 7: Duration of Vac Therapy

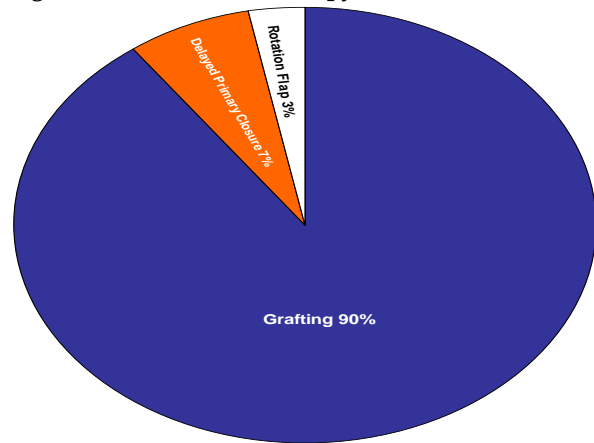


Fig. 8: Wound Closure Technique

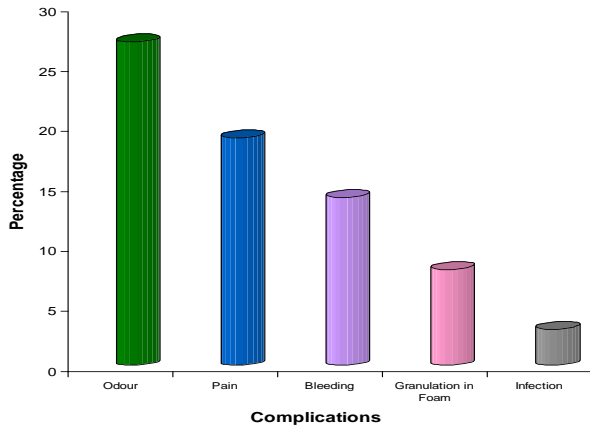


Fig. 9: Complications Frequency

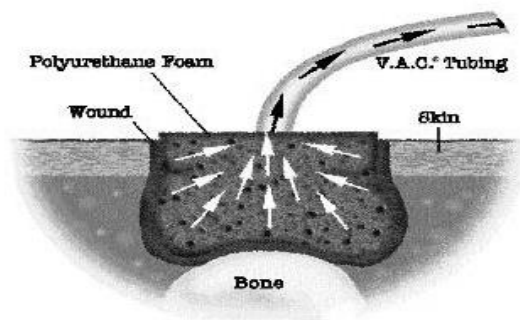


Figure 10: Cross Section Illustrating Mechanism of Vac Therapy

Table-1: Vac Results

Variable	Minimum	Maximum	Mean	Std Deviation
No of weeks on VAC	2	5	3.46	1.056
No of dressing changes	2	12	5.33	2.518
Granulation tissue in days	3	25	11.44	5.564

Table-2: Comparison between the old studies and present study

Study	No of patients	Remarks
Leischmann et al 12	25	Duration=12.7 days, Dressings changes=2.1, Wound closure achieved=25, Complication=1
	313	Duration=16.7 days, Dressing changes=3.1, Wound closure achieved= 97%, complication = 8%
Mullner et al 17	45	Wound closure in 76%, Reduction of diameter in 84% of wounds
Morykwas et al 3	300	Favourable results in 296
Joseph et al 25	18	Reduction in wound volume 78%, Change in depth 66%, Granulation tissue formation 64%
DeFranzo et al 27	75	Wound closure 95%
Smith et al 34	93	Dressing changes 171
Present study	52	Duration 3.5 weeks, Dressing changes=5, Granulation tissue 11.4 days, Wound closure 96%, Complications=3%

DISCUSSION

Development of the vacuum assisted closure technique

The practice of exposing a wound to sub-atmospheric pressure for an extended period to promote debridement and healing was first

described by Fleischmann et al in 1993 [12], following the successful use of this technique in 15 patients with open fractures. They reported that the treatment resulted in "efficient cleaning and conditioning of the wound, with marked proliferation of granulation tissue". No bone infections occurred in any of the patients although one developed a soft tissue infection, which subsequently resolved with further treatment.

In two further papers, Fleischmann and colleagues described the treatment of 25 patients with compartment syndromes of the lower limb [13] and 313 patients with acute and chronic infections of various types [14]. The average duration of the vacuum therapy treatment for the patients with compartment syndrome was 12.7 (4-31) days with 2.1 (1-8) dressing changes per patient. These wounds were subsequently either closed by secondary suturing (n=20) or by skin grafts following partial closure by suturing (n=5). One patient developed a superficial wound necrosis, which healed spontaneously without invasive surgical treatment.

The average duration of vacuum therapy in the treatment of the 313 patients with infected wounds was 16.7 days with an average of 3.1 dressing changes. Of the 203 wounds with acute infections the majorities were subsequently closed by secondary suturing (65.5%) and the remainder by

spontaneous epithelialisation (17.2%), skin grafting (12.3%) or flap transfer (2%). Six patients (3%) died. Infection recurred in 3.9% and was managed using another treatment. Unstable scar formations 1% were treated by free flap transfers.

Further success with topical negative pressure treatment in Germany was reported by Muller [15] following the treatment of 300 patients with infected wounds, and in 1998 Kovacs et al [16] described how 'vacuum sealing' could be used for the treatment of chronic radiation ulcers.

The results of a prospective trial involving 45 patients with soft tissue injuries including sacral pressure ulcers, acute traumatic soft tissue defects and infected soft tissue defects following rigid stabilisation of lower extremity fractures were described by Mullner et al [17]. They reported that in 38/45 patients (84%), the use of the vacuum sealing technique following irrigation and debridement decreased the dimensions of the initial wound, thus facilitating healing time and the eradication of any pre-existing infection.

Banwell et al [18] in his study discusses problems in terms of the delivery, control and maintenance of the required levels of negative pressure.

Vacuum assisted closure: mode of action

In early studies no attempts were made to investigate the physiological basis for the observed clinical effects, or to determine the optimum levels of pressure required. In a seminal paper Morykwas et al [4], addressed both of these issues following a series of animal studies. Deep circular defects, 2.5 cm in diameter, produced on the backs of pigs were dressed with open-cell polyurethane-ether foam with a pore size ranging from 400-600 μm .

In the first series of experiments, a laser Doppler technique was used to measure blood flow in the subcutaneous tissue and muscles surrounding the wounds as these were exposed to increasing levels of negative pressure, applied both continuously and

intermittently. Their results indicated that whilst an increase in blood flow equivalent to four times the baseline value occurred with negative pressure values of 125 mmHg, blood flow was inhibited by the application of negative pressures of 400 mmHg and above. A negative pressure value of 125 mmHg was therefore selected for use in subsequent studies.

The rate of granulation tissue production under negative pressure was determined using the same model by measuring the reduction in wound volume over time. Compared with control wounds dressed with saline soaked gauze, significantly increased rates of granulation tissue formation occurred with both continuous (63.3 +/- 26.1%) and intermittent (103% +/- 35.3%) application of negative pressure.

The observation that intermittent or cycled treatment appears more effective than continuous therapy is interesting although the reasons for this are not fully understood. Two possible explanations were advanced by Philbeck et al [19]. They suggested that intermittent cycling results in rhythmic perfusion of the tissue which is maintained because the process of capillary autoregulation is not activated. They also suggested that as cells which are undergoing mitosis must go through a cycle of rest, cellular component production and division, constant stimulation may cause the cells to 'ignore' the stimulus and thus become ineffective. Intermittent stimulation allows the cells time to rest and prepare for the next cycle. For this reason it is suggested that cyclical negative pressure should be used clinically, although some authors [20,21] suggest that this may follow a 48-hour period of continuous vacuum, which can be applied to exert a rapid initial cleansing effect.

Microbiological studies were also undertaken which involved inoculation of punch biopsy wounds with large numbers of microorganisms. These indicated that, compared with control values, tissue bacterial counts of vacuum-treated wounds decreased significantly after four days [4].

In a final part of the same study using a standard technique, the effect of vacuum therapy was found to increase flap survival by 21% compared with control values [4].

Following these investigations, Morykwas and colleagues postulated that multiple mechanisms might be responsible for these observed effects. In particular, they suggested that removal of interstitial fluid decreases localised oedema and increases blood flow, which in turn decreases tissue bacterial levels. It has since been proposed that the application of sub-atmospheric pressure produces mechanical deformation or stress within the tissue resulting in protein and matrix molecule synthesis [22] and enhanced angiogenesis [23].

Fabian et al [23], using the rabbit ear model, provided further hard evidence for the stimulatory effects of sub-atmospheric pressure on the production of granulation tissue and also demonstrated a trend to enhanced epithelialisation. In experimental partial-thickness burns in pigs, sub-atmospheric pressure was shown to prevent progressive tissue damage in the zone of stasis that surrounds the area of the initial injury. This effect was demonstrable within 12 hours following injury, with treatment times of as little as six hours being sufficient to exert a measurable effect [24]. The authors proposed that removal of oedema fluid containing suspended cellular debris, osmotically active molecules and biochemical mediators, released following the initial injury, may prevent cessation of blood flow (fig.10).

Clinical experiences with VAC

Following these animal studies, the same research group described the clinical use of the VAC in 300 wounds of varying aetiology [3]. These were treated until completely closed or could be covered with a split-thickness skin graft, or were suitable for surgical reconstruction by rotating a flap on to the healthy granulating wound bed. Overall 296 wounds responded favourably to treatment and the authors concluded that

VAC is an extremely efficacious modality for treating chronic and difficult to heal wounds.

Joseph et al [25] conducted a prospective randomized trial of vacuum-assisted closure versus standard therapy of chronic non-healing wound. They randomized 36 chronic non-healing wounds; half into VAC group and half into standard saline soaked gauze dressings. Their results compared final percent change in wound volume over time which was 78% for VAC and 30% for saline soaked gauze dressings ($p=0.038$). The most significant difference in volume was change in depth of 66% for VAC and 20% for saline soaked gauze ($p<0.00001$) followed by the change in width over time ($p=0.02$). There was no change in length between the two groups ($p=0.38$). VAC group of wounds showed granulation tissue formation in 64% of wounds while saline soaked dressings showed inflammation and fibrosis in 81% of wounds. The study concluded that "VAC therapy promotes faster healing rates than standard saline soaked dressings and increases the formation of healthy granulation tissue. The VAC should be applied to chronic, nonhealing wounds, especially those that are deep and complicated."

Mullner et al. [26] conducted a prospective clinical trial from 1994 to 1996 in 45 patients and evaluated the efficacy of a vacuum sealing technique in dealing with sacral pressure ulcers, acute traumatic soft tissue defects and infected soft tissue defects following rigid stabilization of lower extremity fractures. They described that 84% (38/45) of patients on VAC therapy decreased dimensions of the initial wound, thus facilitating healing time and eradication of any pre-existing infection. Wound closure was achieved in 78% (35/45) wounds. They concluded that vacuum sealing technique is an effective option in the management of infected wounds.

DeFranzo et al. [27] used VAC therapy for the treatment of lower extremity wounds with exposed bone. They carried out this study on 75 patients with open wounds of the lower extremity but without osteomyelitis.

They reported a rapid granulation tissue formation, reduction in bacterial count and successful wound closure in 95% (71/75) of cases. They further state that patients formed granulation tissue over challenging areas of bone and tendon exposure, without VAC therapy such patients would require free flap coverage.

Numerous other papers have described the use of VAC in the treatment of a variety of wound types including extensive degloving injuries [28,29] infected sternotomy wounds [21,30,31] and various soft tissue injuries prior to surgical closure [32], grafting or reconstructive surgery [33].

Smith et al [34], in a retrospective review, described the use of VAC over a four-year period in 93 patients who required open abdomen management for a variety of conditions. A total of 171 dressings were applied to the wounds of 38 surgical patients and 55 patients with traumatic injuries. The authors concluded that with careful subsequent management good patient outcomes could be achieved and recommended vacuum assisted closure as the treatment method of choice for open abdomen management and temporary abdominal closure.

Vacuum therapy has also been used in the treatment of donor sites, particularly in areas that are difficult to manage using conventional techniques [35] such as those on the radial forearm [36]. It has been reported that as many as one third of all patients undergoing radial forearm free flaps develop exposed tendon complications and it has been suggested that these individuals may derive particular benefit from the use of VAC therapy [37]. When used as donor site dressings, some authors recommend the use of a low adherent wound contact layer such as Adaptic or paraffin gauze beneath the foam layer [35,36].

Vacuum assisted closure has also been used in conjunction with split thickness skin grafts in the treatment of burns and is claimed to be particularly useful for body sites with irregular or deep contours such as the

perineum, hand or axilla [38,39]. In all these situations the vacuum helps to hold the graft securely onto the wound bed thus preventing pooling of tissue fluid which would otherwise make the graft unstable.

Molnar et al [40] described how they used VAC in conjunction with skin grafts to treat four patients with full thickness loss of the scalp following a burn injury or excision of an extensive carcinoma. Normally, if such wounds cannot be closed with a flap, the outer surface of the skull is removed to obtain punctate bleeding and a skin graft is applied a week or two later once granulation tissue has started to form. Without this delay the graft take is usually very poor, but with the use of VAC it was possible to apply a successful skin graft immediately after the initial operation.

Numerous case histories describing the successful use of VAC in a variety of non-healing or chronic wounds have also been published. These include a recalcitrant below knee amputation wound and a suspected Brown Recluse Spider bite [41], pressure sores [20,42-46], leg ulcers [46], and a group of 30 patients with longstanding wounds that were deemed unsuitable for reconstructive surgery, [26] of whom responded favourably to the treatment [47].

To function correctly, the adhesive membrane applied over the foam wound insert must form an airtight seal with the skin. Obtaining such a seal can be particularly difficult near the anus or vagina or where the surrounding skin is moist. These problems can sometimes be overcome by the use of a hydrocolloid dressing such as Duoderm3, which is first applied around the wound and used as a base for the adhesive membrane.

Some of the practical problems associated with the application of the VAC system have been discussed previously by Greer et al [45], who developed techniques to allow it to be used successfully on sacral pressure ulcers close to the anus and to multiple large ulcers on the lower extremities.

Fabian et al [23] in a well controlled animal study, investigated the possibility that sub-atmospheric pressure might act

synergistically with hyperbaric oxygen (HBO2). They found, however, that although negative pressure increased the rate of healing compared with control values, HBO2 therapy did not offer any significant benefit. The development and use of sub-atmospheric pressures in the management of patients with different types of wounds has been reviewed previously [48].

Cost of treatment

Philbeck et al [19] claimed that the technique was very cost effective in use. In a retrospective study, they compared the treatment costs of VAC with those of a more conventional therapy by comparing the results of an analysis of the healing rates achieved with the vacuum technique with those recorded for similar wounds in a previously published study. Treatment records of 1032 Medicare patients with 1,170 VAC-treated wounds of all types that had failed to respond to previous interventions were reviewed. From these data, the healing rates of patients nursed on a low air loss surface (LAL) with 43 pressure ulcers (stages III and IV) located on the trochanter and trunk were abstracted and compared with previously published values for a comparable group of patients also nursed on a LAL surface and whose wounds were dressed with saline-gauze packs.

Prior to treatment, the VAC dressed wounds averaged 22.2 cm² compared with 4.3 cm² for the saline-soaked gauze wounds. Wounds dressed with VAC closed at an average of 0.23 cm² per day compared with 0.090 cm² for the historical controls. Using these healing rates they calculated that the time to heal a group of patients with wounds 22.2 cm² in area would be 97 days with VAC and cost much less, compared with 247 days with traditional therapy at a much higher cost. Whilst acknowledging all the limitations of their study, the authors concluded that negative pressure therapy is an "effective treatment modality for a variety of chronic wounds" producing healing in certain types of pressure ulcers 61% faster than saline soaked gauze whilst reducing costs by 38%.

Present study

This study was conducted on 52 patients at CMH Rawalpindi. The commonest wound type was found to be of traumatic in 35 patients, diabetic ulcer in 8, pressure ulcer in 4, venous ulcer in 4 and radiation ulcer was present in 1 patient. Majority of patients had a wound on lower limb n=21, foot n=16, hand in n=6, abdomen n=5 and chest in n=4. Bed of wound contained muscle and soft tissue in [37], tendon in 8, bone in 4 and orthopedic implant in 3 wounds. The average duration VAC therapy was 3.5 weeks but more than 50% required less than 3 weeks of therapy with 5 dressing changes per patient. Granulation tissue appearance was found to take at least 11 days and it appeared in 88% of cases. Granulation tissue appeared even in cases with a history of smoking or diabetes. Wound was successfully closed in all patients utilizing different techniques and no significant complication was seen. Overall reduction in wound size was found to be 68%.

A comparison of present study and major studies from literature is given below (table-2)

CONCLUSION

The vacuum-assisted closure is a relatively new technique. It is very effective in promoting healing in acute, subacute and chronic non-healing wounds. It helps by reducing wound size and promoting granulation tissue. It is also effective in promoting granulation tissue on bones devoid of any periosteum, tendons without any paratenon and even bare orthopaedic implants. Many of such patients would have required a plastic surgical procedure but with application of this simple technique it was possible to close these defects with simple partial thickness grafting or delayed primary closure.

This technique needs to be refined as it is operator dependent. An automatic machine is highly desirable for continual application of pressure.

This technique is safe and reliable and should be applied at all peripheral setups where help from plastic surgeons is not available and even at tertiary care hospitals

with such help available as this technique saves a lot of time and money.

REFERENCES

- Hibbs P. The economics of pressure ulcer prevention. *Decubitus* 1989; 2:32-8.
- Lazarus GS, Cooper DM, Knighton DR, Margolis DJ, Pecoraro RE, Rodeheaver G, et al. Definitions and guidelines for assessment of wounds and evaluation of healing. *Arch Dermatol.* 1994; 130: 4:489-93.
- Argenta LC, Morykwas MJ. Vacuum-assisted closure: A new method for wound control and treatment: Clinical experience. *Ann Plast Surg* 1997; 38:6: 563-76.
- 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 Plast Surg* 1997; 38:6:553-62.
- Russell RCG, Williams NS, Bulstrode CJK, editors. *Bailey and Love's Short Practice of Surgery.* London: Arnold Publishers. 2000.
- Lawrence WT, Diegelmann RF. Growth factors in wound healing. *Clin. Dermatol.* 1994; 12:157.
- Cohen IK, Diegelmann RF. Wound Healing. In: Greenfield L. editors. *Surgery: Scientific Principles and Practice.* Philadelphia: Lippincott. 1993: 86.
- Werner S, Smola H, Liao X, Longaker MT, Krieg T, Hofschneider PH, et al. The function of KGF in morphogenesis of epithelium and reepithelialization of wounds. *Science.* 1994; 4: 266: 5186:819-22.
- Andersen DK, editor. *Master Series in Surgery: Advances in Wound Healing and Tissue Repair.* New York: World Medical Press. 1993.
- Border WA, Ruoslahti E. Transforming growth factor b in disease: The dark side of repair. *J. Clin. Invest.* 1992. 901.
- Cushieri A, Steele RJC, Moossa AR, editors. *Essential Surgical Practice.* Arnold Publishers. 2002.
- Fleischmann W, Strecker W, Bombelli M, Kinzl L. Vacuum sealing as treatment of soft tissue damage in open fractures. *Unfallchirurg* 1993; 96: 9: 488-92.
- Fleischmann W, Lang E, Kinzl L. Vacuum assisted wound closure after dermatofasciotomy of the lower extremity. *Unfallchirurg* 1996; 99: 4: 283-7.
- Fleischmann W, Lang E, Russ M. Treatment of infection by vacuum sealing. *Unfallchirurg* 1997; 100: 4: 301-4.
- Muller G. Vacuum dressing in septic wound treatment. *Langenbecks Arch Chir Suppl Kongressbd* 1997; 114: 537-41.
- Kovacs L, Kloppel M, Geishauser S, Schmiedl S, Biemer E. Vacuum sealing: a new and promising regimen in the therapy of radiation ulcers. *Br J Surgery* 1998; 85: 70.
- Mullner T, Mrkonjic L, Kwasny O, Vecsei V. The use of negative pressure to promote the healing of tissue defects: a clinical trial using the vacuum sealing technique. *Br J Plast Surg* 1997; 50: 3: 194-9.
- Banwell P, Withey S, Holten I. The use of negative pressure to promote healing. *Br J Plast Surg* 1998; 51: 1: 79.
- Philbeck TE, Whittington KT, Millsap MH, Briones RB, Wight DG, Schroeder WJ. The clinical and cost effectiveness of externally applied negative pressure wound therapy in the treatment of wounds in home healthcare Medicare patients. *Ostomy Wound Manage* 1999; 45: 11: 41-50.
- Collier. Know-how: A guide to vacuum-assisted closure (VAC). *Nurs Times* 1997; 93: 5: 32-3.
- Tang AT, Ohri SK, Haw MP. Novel application of vacuum assisted closure technique to the treatment of sternotomy wound infection. *Eur J Cardiothorac Surg* 2000; 17: 4: 482-4.
- Morykwas MJ, Argenta LC. Nonsurgical modalities to enhance healing and care of soft tissue wounds. *J South Orthop Assoc* 1997; 6: 4: 279-88.
- Fabian TS, Kaufman HJ, Lett ED, Thomas JB, Rawl DK, Lewis PL, et al. The evaluation of subatmospheric pressure and hyperbaric oxygen in ischemic full-thickness wound healing. *Am Surg* 2000; 66: 12: 1136-43.
- Morykwas MJ, David LR, Schneider AM, Whang C, Jennings DA, Canty C, et al. Use of subatmospheric pressure to prevent progression of partial-thickness burns in a swine model. *J Burn Care Rehabil* 1999; 20: 1: 15-21.
- Joseph E, Hamori CA, Bergman S, Roaf E, Swann NF, Anastasi GW. A prospective, randomized trial of vacuum-assisted closure versus standard therapy of chronic non-healing wounds. *Wounds* 2000; 12: 3:60-67.
- Mullner T, Morkonjic L, Kwasny O, Vecsei V. The use of negative pressure to promote the healing of tissue defects: a clinical trial using the vacuum sealing technique. *Br J Plast Surg* 1997; 50: 3: 194-9.
- DeFranzo AJ, Argenta LC, Marks MW, Molnar JA, David LR, Webb LX, et al. The use of Vacuum-assisted closure therapy for the treatment of lower-extremity wounds with exposed bone. *Plast Reconstr Surg* 2001; 108: 5: 1184-91.
- Meara JG, Guo L, Smith JD, Pribaz JJ, Breuing KH, Orgill DP. Vacuum-assisted closure in the treatment of degloving injuries. *Ann Plast Surg* 1999; 42: 6: 589-94.
- DeFranzo AJ, Marks MW, Argenta LC, Genecov DG. Vacuum-assisted closure for the treatment of degloving injuries. *Plast Reconstr Surg* 1999; 104: 7: 2145-8.
- Obdeijn MC, de Lange MY, Lichtendahl DH, de Boer WJ. Vacuum-assisted closure in the treatment of poststernotomy mediastinitis. *Ann Thorac Surg* 1999; 68: 6: 2358-60.

31. Tang AT, Ohri SK, Haw MP. Vacuum-assisted closure to treat deep sternal wound infection following cardiac surgery. *J Wound Care* 2000; 9: 5: 229-30.
 32. Bauer P, Schmidt G, Partecke BD. Possibilities of preliminary treatment of infected soft tissue defects by vacuum sealing and PVA foam. *Handchir Mikrochir Plast Chir* 1998; 30: 1: 20-3.
 33. Avery C, Pereira J, Moody A, Whitworth I. Clinical experience with the negative pressure wound dressing. *Br J Oral Maxillofac Surg* 2000; 38: 4:343-5.
 34. Smith LA, Barker DE, Chase CW, Somberg LB, Brock WB, Burns RP. Vacuum pack technique of temporary abdominal closure: a four-year experience. *Am Surg* 1997; 63: 12: 1102-7.
 35. Blackburn JH, Boemi L, Hall WW, Jeffords K, Hauck RM, Banducci DR, et al. Negative-pressure dressings as a bolster for skin grafts. *Ann Plast Surg* 1998; 40: 5: 453-7.
 36. Avery C, Pereira J, Moody A, Whitworth I. Negative pressure wound dressing of the radial forearm donor site. *Int J Oral Maxillofac Surg* 2000; 29: 3: 198-200.
 37. Greer SE, Longaker MT, Margiotta M, Mathews AJ, Kasabian A. The use of subatmospheric pressure dressing for the coverage of radial forearm free flap donor-site exposed tendon complications. *Ann Plast Surg* 1999; 43: 5: 551-4.
 38. Schneider AM, Morykwas MJ, Argenta LC. A new and reliable method of securing skin grafts to the difficult recipient bed. *Plast Reconstr Surg* 1998; 102: 4: 1195-8.
 39. Pfau M, Rennekampff HO, Schaller HE. Skin graft fixation by vacuum assisted topical foam dressing. *J Burn Care Rehab* 2000; 21: 1: 1.
 40. Molnar JA, DeFranzo AJ, Marks MW. Single-stage approach to skin grafting the exposed skull. *Plast Reconstr Surg* 2000; 105: 1: 174-7.
 41. Mendez-Eastman S. Negative pressure wound therapy. *Plast Surg Nurs*. 1998;18: 1: 27-9, 33-7.
 42. Deva AK, Siu C, Nettle WJ. Vacuum-assisted closure of a sacral pressure sore. *J Wound Care* 1997; 6: 7: 311-2.
 43. Hartnett JM. Use of vacuum-assisted wound closure in three chronic wounds. *J Wound Ostomy Continence Nurs* 1998; 25: 6: 281-90.
 44. Baynham SA, Kohlman P, Katner HP. Treating stage IV pressure ulcers with negative pressure therapy: a case report. *Ostomy Wound Manage* 1999; 45: 4: 28-32, 34-5.
 45. Greer SE, Duthie E, Cartolano B, Koehler KM, Maydick-Youngberg D, Longaker MT. Techniques for applying subatmospheric pressure dressing to wounds in difficult regions of anatomy. *J Wound Ostomy Continence Nurs* 1999; 26: 5: 250-3.
 46. Mendez-Eastman S. Use of hyperbaric oxygen and negative pressure therapy in the multidisciplinary care of a patient with nonhealing wounds. *J Wound Ostomy Continence Nurs* 1999; 26: 2: 67-76.
 47. Deva AK, Buckland GH, Fisher E, Liew SC, Merten S, McGlynn M, et al. Topical negative pressure in wound management. *Med J Aust* 2000; 173:3:128-31.
 48. Banwell PE. Topical negative care. *J Wound pressure therapy in wound Care* 1999; 8: 2: 79-84.
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