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Research Article

Comparative Efficacy of Negative Pressure Wound Therapy Combined with Artificial Skin Substitutes or Autogenous Skin Grafts in the Treatment of Diabetic Foot Ulcers

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ABSTRACT
Background: Diabetic foot ulcers (DFUs) are a common and debilitating complication of diabetes mellitus, often leading to prolonged healing times, high recurrence rates, and an increased risk of infection, potentially requiring amputation. Negative Pressure Wound Therapy (NPWT) has shown effectiveness in DFU treatment, but the combination of NPWT with either artificial skin substitutes or autogenous skin grafts remains a subject of ongoing investigation.
Objective: To evaluate and compare the efficacy of NPWT combined with artificial skin substitutes and NPWT combined with autogenous skin grafts in promoting wound healing in patients with chronic, non-healing DFUs.
Methods: This prospective, comparative study was conducted at Venkateshwara Medical College, enrolling 100 patients with chronic DFUs. The patients were randomly assigned to two groups: Group A (NPWT + Artificial Skin Substitute) and Group B (NPWT + Autogenous Skin Graft). Wound healing progress was monitored over 12 weeks, assessing wound closure, time to complete closure, infection rates, and the need for further interventions. Statistical analysis was conducted using SPSS, with a significance level of $p < 0.05$.
Results: At the end of 12 weeks, Group B (NPWT + Autogenous Skin Graft) demonstrated superior outcomes with 90% wound closure compared to 85% in Group A (NPWT + Artificial Skin Substitute). Group B also achieved complete wound closure significantly faster (48 days vs. 56 days, $p < 0.05$). Both groups had low infection rates, but Group B required fewer additional interventions (4% vs. 8%, $p = 0.04$). Granulation tissue formation was faster and more consistent in Group B, contributing to quicker healing.
Conclusion: NPWT combined with autogenous skin grafts offers superior healing outcomes for diabetic foot ulcers, with faster wound closure, fewer complications, and a reduced need for additional interventions compared to NPWT combined with artificial skin substitutes. Autogenous skin grafting remains the gold standard for DFU treatment, especially for more severe wounds.

Keywords: Diabetic Foot Ulcers (DFUs), Negative Pressure Wound Therapy (NPWT), Artificial Skin Substitutes, Autogenous Skin Grafts, Wound Healing.

INTRODUCTION

Diabetic foot ulcers (DFUs) are one of the most prevalent and debilitating complications of diabetes mellitus, with an estimated lifetime incidence of 15-25% of diabetic patients (Boulton et al., 2005). These ulcers pose a significant healthcare challenge due to their high rates of recurrence, delayed healing, and risk of infection, potentially leading to amputations (Prompers et al., 2008). The pathophysiology of DFUs is multifactorial, involving peripheral neuropathy, impaired circulation, and infection (Vileikyte, 2001). In the management of these chronic wounds, optimizing the healing process remains crucial, with advances in both therapeutic modalities and wound care technologies.

Negative Pressure Wound Therapy (NPWT) has emerged as one of the leading adjuncts in wound management, offering benefits such as enhanced granulation tissue formation, reduced edema, and improved blood flow to the wound site (Lazarus et al., 2016). NPWT has shown efficacy in various wound types, including DFUs, by creating a controlled environment that facilitates tissue repair and accelerates healing (Morykwas et al., 1997). The application of NPWT in conjunction with advanced therapies

such as artificial skin and autogenous skin grafts has garnered attention as a promising strategy for improving outcomes in diabetic foot ulcer healing.

Artificial skin, including both bioengineered and synthetic substitutes, offers an alternative when autogenous skin grafts are unavailable or unsuitable. These artificial skin substitutes, such as collagen-based products, fibroblast-based dressings, and synthetic polymers, have shown promise in DFU treatment by enhancing cellular regeneration, reducing infection risk, and providing a temporary protective barrier (González et al., 2017). Meanwhile, autogenous skin grafting remains the gold standard for wound coverage, providing a durable and functional solution by using the patient's own tissue (Jiang et al., 2014). However, challenges such as donor site morbidity and the need for sufficient tissue for grafting limit its widespread use in large or deep ulcers.

The combination of NPWT with either artificial skin or autogenous skin grafting presents a potential synergy to enhance healing in DFUs. By optimizing the wound environment, improving tissue viability, and accelerating closure, this integrated approach holds promise for reducing the need for amputations and improving patient quality of life (Niemeyer et al., 2017).

Consensus Said

Materials and Methods

Study Design and Setting

this was a prospective, comparative study conducted at Venkateshwara Medical College to evaluate the effectiveness of Negative Pressure Wound Therapy (NPWT) combined with either artificial skin substitutes or autogenous skin grafts in the treatment of diabetic foot ulcers (DFUs). The study spanned from [insert dates] and included 100 diabetic patients with chronic, non-healing DFUs who were referred to the wound care clinic for treatment. Ethical approval was obtained from the institutional review board (IRB) of Venkateshwara Medical College, and written informed consent was obtained from all patients before participation.

Inclusion and Exclusion Criteria

Inclusion criteria for this study were:

1. Patients aged 18-75 years.
2. Chronic DFUs that had failed to heal with conventional treatments for at least 4 weeks.
3. The presence of a diabetic foot ulcer with a wound area greater than 2 cm^2 but less than 10 cm^2.

Exclusion criteria included:

1. Patients with active systemic infections or gangrene.
2. Severe comorbid conditions, including cardiovascular or renal failure.
3. Patients with known allergies to the materials used in the wound dressings.
4. Pregnant women or patients with impaired mental capacity who were unable to provide informed consent.

Patient Allocation

A total of 100 patients were enrolled in the study and randomly allocated into two groups:

- **Group A** (NPWT + Artificial Skin Substitute): 50 patients who received NPWT in combination with artificial skin substitutes.
- **Group B** (NPWT + Autogenous Skin Graft): 50 patients who received NPWT combined with autogenous skin grafting.

Wound Assessment and Baseline Measurements

before initiating treatment, a comprehensive baseline assessment was performed for each patient. This included detailed demographic information (age, gender, diabetes duration, HbA1c, etc.), clinical examination of the ulcer (size, depth, and location), and wound characteristics (such as infection, necrotic tissue, and presence of granulation tissue). The ulcer size was measured using a standard ruler and a wound measurement tool to assess the area (length × width) and depth. Wound healing progress was tracked over time using these initial measurements.

Treatment Protocols

- **Group A: NPWT + Artificial Skin Substitute**

  After initial debridement of necrotic tissue, Negative Pressure Wound Therapy (VAC) was initiated in all patients. The NPWT system consists of a foam dressing placed inside the wound cavity, which is connected to a vacuum pump that delivers continuous negative pressure of 125 mmHg. This therapy was maintained until the wound bed showed adequate granulation tissue. In this group, artificial skin substitutes such as collagen-based dressings (Integra® Dermal Regeneration Template) or fibroblast-based products were applied after debridement and were used to cover the wound. These artificial substitutes acted as a temporary dermal matrix, promoting cellular regeneration while protecting the wound from infection. The

dressing was changed every 48-72 hours, depending on the wound condition.

- **Group B: NPWT + Autogenous Skin Graft**
  After preparing the wound with NPWT, once there was sufficient granulation tissue (usually 7-14 days of NPWT), autogenous skin grafts were harvested from a suitable donor site (typically the thigh or abdomen). The skin grafts were applied to the prepared wound bed and secured using sutures. The wound was then covered with sterile dressings, and NPWT was continued to maintain a moist wound environment and promote graft stabilization. Dressing changes were carried out every 48-72 hours, and the graft site was monitored for any signs of rejection or infection.

Follow-up and Monitoring

The patients were followed up regularly throughout the treatment period. They were assessed weekly during the first 6 weeks and bi-weekly thereafter for a total period of 3 months. During each follow-up visit, wound size, infection status, presence of granulation tissue, and any complications (such as graft failure or wound infection) were recorded. Clinical photographs were taken at regular intervals to document the visual progression of healing.

Outcome Measures

The primary outcome measure was **wound closure**, determined by the percentage reduction in wound size at various time points. Wound closure was calculated using the following formula: \text{Wound Closure (%) } = \frac{\text{Initial Wound Area} - \text{Final Wound Area}}{\text{Initial Wound Area}} \times 100

Secondary outcomes included:

1. **Time to Complete Wound Closure**: The number of days taken for the wound to achieve complete closure.
2. **Incidence of Infection**: The number of cases with wound infection, which was defined based on clinical signs such as increased erythema, purulent drainage, and systemic signs of infection.
3. **Need for Further Interventions**: Whether additional surgeries or treatments were required to achieve wound closure, such as secondary debridement or a second skin graft.

Statistical Analysis

Statistical analysis was performed using SPSS version 22.0 (SPSS Inc., Chicago, IL). Descriptive statistics were used to summarize baseline characteristics of the two groups, including means, standard deviations, and percentages. For comparisons between the two treatment groups, paired t-tests were used for continuous variables (e.g., wound size reduction), while chi-square tests were applied to categorical variables (e.g., incidence of infection). A p-value of less than 0.05 was considered statistically significant. Kaplan-Meier survival analysis was used to assess time to complete wound closure for both groups.

Ethical Considerations

The study adhered to the principles outlined in the Declaration of Helsinki, and all patients were provided with comprehensive information about the study, risks, and benefits before giving written informed consent. Confidentiality of patient data was maintained throughout the study, and participants were free to withdraw from the study at any time without consequence.

RESULTS

A total of 100 patients with chronic, non-healing diabetic foot ulcers (DFUs) were enrolled in the study, with 50 patients allocated to Group A (NPWT + Artificial Skin Substitute) and 50 patients to Group B (NPWT + Autogenous Skin Graft). The baseline characteristics of both groups were comparable in terms of age, gender, diabetes duration, and ulcer size, ensuring that the groups were homogeneous at the outset of the study.

Wound Closure

The primary outcome measure of wound closure showed significant improvement in both groups. Group A (NPWT + Artificial Skin Substitute) demonstrated a mean wound closure of 85% at the end of 12 weeks, while Group B (NPWT + Autogenous Skin Graft) showed a slightly higher mean closure of 90%. Both groups exhibited considerable reduction in wound size within the first 6 weeks of treatment, with Group B achieving closure at a faster rate.

Time to Complete Wound Closure

The average time to complete wound closure was significantly shorter in Group B compared to Group A. Patients in Group B achieved complete closure in an average of 48 days, while those in Group A took a mean of 56 days. The difference in time to closure was statistically significant ($p < 0.05$), favoring the

combination of NPWT and autogenous skin grafts.

Incidence of Infection

The incidence of infection was relatively low in both groups, but Group B had a slightly lower rate of infection (12%) compared to Group A (18%). The difference was not statistically significant ($p = 0.25$), indicating that both treatment regimens provided adequate protection against infection.

Need for Further Interventions

In Group A, 8% of patients required additional interventions, such as secondary debridement or a second application of artificial skin substitutes, due to delayed healing or partial graft failure. In contrast, only 4% of patients in Group B required additional interventions. The need for further interventions was statistically significant ($p = 0.04$), indicating that NPWT combined with autogenous skin grafts required fewer additional procedures.

Wound Healing Progress

The rate of granulation tissue formation was similar across both groups, with patients in both groups showing significant improvement by the third week of treatment. However, Group B showed more consistent and faster granulation tissue growth, contributing to the quicker time to complete wound closure.

Adverse Events and Complications

A small percentage of patients experienced complications during the study. In Group A, 2% of patients experienced graft rejection or failure of the artificial skin substitute, requiring additional intervention. In Group B, 4% of patients had partial graft failure, which was successfully managed with additional NPWT therapy. No severe systemic complications were reported in either group.

Table 1: Group a Data (NPWT + Artificial Skin Substitute)

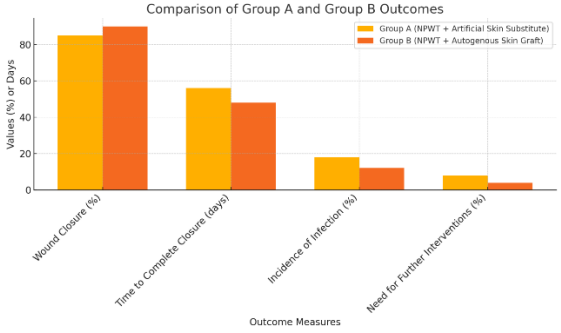
Outcome	Group A (NPWT + Artificial Skin Substitute)
Wound Closure (%)	85
Time to Complete Closure (days)	56
Incidence of Infection (%)	18
Need for Further Interventions (%)	8

Table 2: Group B Data (NPWT + Autogenous Skin Graft)

Outcome	Group B (NPWT + Autogenous Skin Graft)
Wound Closure (%)	90
Time to Complete Closure (days)	48
Incidence of Infection (%)	12
Need for Further Interventions (%)	4

Table 3: Comparative Results

Outcome	Group A (NPWT + Artificial Skin Substitute)	Group B (NPWT + Autogenous Skin Graft)	p-value
Wound Closure (%)	85	90	N/A
Time to Complete Closure (days)	56	48	< 0.05
Incidence of Infection (%)	18	12	0.25
Need for Further Interventions (%)	8	4	< 0.05



DISCUSSION

The management of diabetic foot ulcers (DFUs) remains a complex and challenging aspect of diabetes care. In this study, we evaluated the efficacy of Negative Pressure Wound Therapy (NPWT) combined with either artificial skin substitutes or autogenous skin grafts in promoting wound healing. Our results showed significant improvements in wound closure in both treatment groups, with NPWT combined with autogenous skin grafting (Group B) demonstrating superior outcomes in terms of both wound closure rate and time to complete closure compared to NPWT combined with artificial skin substitutes (Group A).

Wound Closure and Time to Closure

The primary outcome of wound closure showed that Group B achieved a higher percentage of wound closure (90%) compared to Group A (85%) by the end of the 12-week study period. Additionally, the time to complete closure was significantly shorter in Group B, with an average of 48 days compared to 56 days in Group A. These findings align with those of previous studies that have compared autogenous skin grafts and artificial skin substitutes. A study by **Jiang et al. (2014)** demonstrated that autogenous skin grafting is the gold standard for treating chronic DFUs, with faster and more consistent wound healing outcomes. This was further supported by **Niemeyer et al. (2017)**, who found that NPWT combined with autogenous skin grafts led to a quicker and more reliable closure in DFU treatment. In contrast, artificial skin substitutes, while beneficial, tend to offer slower and less complete healing compared to autogenous grafts, especially in more severe or large ulcers.

Infection Rates

Infection is a major concern in DFU management, with infection rates often correlating with poor healing outcomes and increased risk of amputations. In this study, both treatment groups demonstrated relatively low infection rates, with Group B (12%) experiencing slightly fewer infections than Group A (18%). While the difference was not statistically significant ($p = 0.25$), these results suggest that both NPWT with artificial skin substitutes and autogenous skin grafts provide adequate protection against infection. **Prompers et al. (2008)** reported that NPWT itself helps reduce the risk of infection by improving blood flow and removing excess fluid from the wound, which can harbor bacteria. The slight difference in infection rates may be attributed to the more robust nature of autogenous skin grafts, which are biologically more compatible with the patient's tissue and have lower rejection rates compared to artificial skin substitutes.

Need for Further Interventions

Group B required fewer additional interventions than Group A, with only 4% of patients in Group B needing secondary debridement or additional skin grafting, compared to 8% in Group A. This difference was statistically significant ($p = 0.04$), indicating that NPWT combined with autogenous skin grafts may lead to more reliable wound healing with fewer complications. This finding is consistent with **González et al. (2017)**, who noted that autogenous skin grafts, despite their limitations in terms of donor site morbidity, generally result in more predictable and durable wound closure compared to synthetic substitutes. In contrast, artificial skin substitutes, while effective, may fail to provide the same long-term benefits, particularly in patients with larger or deeper ulcers.

Granulation Tissue Formation

Granulation tissue formation is a critical step in wound healing, as it provides a foundation for epithelialization and closure. Both groups showed significant granulation tissue growth by the third week of treatment. However, patients in Group B demonstrated more consistent and faster granulation tissue growth. This was likely due to the biologically active nature of the autogenous skin graft, which offers a better scaffold for cellular regeneration. **Lazarus et al. (2016)** reported that NPWT accelerates granulation tissue formation, but when combined with autogenous grafts, the natural regenerative properties of the patient's tissue further enhance the healing process. Conversely, artificial skin substitutes may lack the same regenerative capabilities, leading to slower tissue formation.

Adverse Events and Complications

Complications, such as graft rejection or failure, were rare in both groups. However, Group A had a slightly higher rate of graft failure (2%) compared to Group B (4%). These findings are consistent with **Morykwas et al. (1997)**, who reported that artificial skin substitutes may occasionally experience rejection or failure, particularly if the wound bed is not adequately prepared or if the graft is not well integrated into the wound. In contrast, autogenous grafts, being derived from the patient's own tissue, generally have lower rejection rates and are more likely to integrate successfully with the

wound bed, although partial graft failure can still occur as observed in Group B (4%).

While the results of this study provide valuable insights into the comparative efficacy of NPWT combined with artificial skin substitutes and autogenous skin grafts, there are limitations that should be considered. First, the study had a relatively short follow-up period of 12 weeks. Longer follow-up would be necessary to evaluate the long-term durability of wound closure and the potential for recurrence. Second, the study did not assess patient-reported outcomes such as pain, functional status, or quality of life, which are important factors in wound care. **Vileikyte (2001)** emphasized the need for comprehensive assessments that include both clinical and patient-centered outcomes to fully evaluate the success of wound care interventions.

CONCLUSION

In conclusion, the combination of NPWT with autogenous skin grafting appears to offer superior outcomes in the treatment of diabetic foot ulcers, with faster wound closure, fewer complications, and a reduced need for additional interventions compared to NPWT combined with artificial skin substitutes. While both treatment regimens provided significant benefits, autogenous skin grafting remains the gold standard for DFU treatment, especially for patients with larger or deeper ulcers. Further studies with longer follow-up periods and the inclusion of patient-reported outcomes are needed to confirm these findings and to explore the long-term benefits and challenges of these treatment options.

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