Title: Treatment of Pressure Ulcers using Biological Skin Substitutes: A Comparison of Type-I Collagen and Amnion/Chorion Membranes

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Background

Pressure ulcers, also known as decubitus ulcers or bedsores, are localized injuries to the skin and underlying tissue resulting from prolonged pressure. They are prevalent in individuals with limited mobility, such as the elderly and those with spinal cord injuries, particularly in long-term care settings. Effective management of pressure ulcers is crucial to prevent complications and improve patient outcomes, includes pressure relief, wound care, and advanced therapies such as bioengineered skin substitutes. Management of pressure sores is crucial due to their association with increased morbidity, healthcare costs, and reduced quality of life. This study aims to evaluate the efficacy of two treatment modalities: Type-I Collagen-based Skin Substitute (HPTC) vs. Dehydrated Human Amnion/Chorion Membrane (dHCAM) in promoting the healing of pressure ulcers. While both products are used in wound management, direct comparative studies evaluating their efficacy in treating pressure ulcers are limited.

MATERIALS AND METHODS

This prospective, randomized, controlled, open label, two parallel group, single-centre clinical trial will be conducted at a tertiary care hospital, in India, specializing in wound care and reconstructive surgery. The study protocol was approved by the Institutional Ethics Committee (Approval Number: AIMS/IEC/012/2025) and pre-registered with the ClinicalTrials.gov (NCT06853210). All procedures will be performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. All participants or guardians will be provided informed consent.

Outcome Measures

Primary Outcome:

a. Percentage Wound Area Reduction.
b. Histopathological Parameters
    i. Vascular Infiltration
    ii. Neo-epithelialization
    iii. Fibroblast Activity
    iv. Capillary Density
    v. Inflammatory Response
    vi. Collagen Deposition

Secondary Outcomes:

a. Complete Wound Closure Rates (defined as 100% epithelialization).
b. Wound Size Progression Over Time – 7 weeks

c. Number of Reapplications
d. Incidence of treatment-related adverse events (e.g., infection, allergic reactions)
e. Quality of Life Improvement
f. Patient Satisfaction Scores

Study Design

Prospective, randomized, controlled, single-centre study with two parallel-group, open-label trial
Duration: 6 weeks of intervention with follow-up for 1 week. Participants will be randomly assigned in a 1:1 ratio to receive either HPTC or dHCAM treatment
Sample Size: 80 patients (40 per arm)

i. Group A: 20 patients receiving HPTC treatment.
ii. Group B: 20 patients receiving dHCAM treatment.

Eligibility Criteria

Inclusion criteria

a. Subjects must be at least 18 years of age or older
b. Presence of a Stage III or Stage IV pressure ulcer, as defined by the National Pressure Ulcer Advisory Panel
c. Ulcer size between 5 cm^2 and 25 cm^2
d. Ulcer duration of at least 4 weeks prior to enrolment
e. The subject must agree to attend the twice-weekly/weekly study visits required by the protocol
f. The subject must be willing and able to participate in the informed consent process
g. Adequate blood supply to the affected area, confirmed by clinical assessment

Exclusion criteria

Potential subjects meeting any of the following criteria will be excluded from enrolment.

a. A subject known to have a life expectancy of <6 months
b. Presence of infection in the ulcer requiring systemic antibiotics.
c. Known allergy to components of HPTC or dHCAM.
d. Participation in another wound care study within the last 30 days.
e. A subject with autoimmune or connective tissue disorders.
f. Women who are pregnant or considering becoming pregnant within the next 6 months and those who are breast feeding.
g. History of autoimmune disease, immunosuppressive therapy, malignancy, or uncontrolled diabetes (HbA1c >10%).

Study treatment

The treatment phase will begin with a series of assessments designed to confirm the patients' continued eligibility. Subjects who continued to meet study inclusion criteria after the screening period were randomized to one of two groups:

1. HPTC
2. dHCAM

Interventions

Wound Preparation - Prior to application, wounds will be debrided to remove necrotic tissue and cleansed with a standard saline solution.

Application Protocol:

a. HPTC Group: Participants will receive standard wound care plus application of HPTC
b. dHCAM Group: Participants will receive standard wound care plus application of dHCAM

All participants will receive standard care measures, including:

a. Regular repositioning to alleviate pressure.
b. Nutritional support to address deficiencies.
c. Management of comorbid conditions.

Randomization and Blinding

Patients will be randomized 1:1 to the HPTC or dHCAM group using a computer-generated randomization sequence. Due to the nature of the interventions, blinding of participants and clinicians is not feasible. However, outcome assessors and data analysts will be blinded to group assignments.

Data Collection and Monitoring

a. Baseline data: Demographics, medical history, ulcer characteristics.
b. Weekly follow-ups: Wound measurements (photographic documentation), assess healing progress, record adverse events and patient-reported outcomes.
c. End-of-Study Visit (Week 5): final wound assessment, collect patient feedback on treatment experience.
d. Data entry and monitoring will be managed using an electronic data capture system.
e. Regular monitoring will ensure adherence to the study protocol and address any compliance issues.

Statistical Analysis

Descriptive statistics for baseline characteristics. Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY). Continuous variables were presented as mean ± standard deviation or median (interquartile range) based on distribution normality assessed by Kolmogorov-Smirnov test. Categorical variables were presented as frequencies and percentages.

Between-group comparisons for continuous variables were performed using independent t-test or Mann-Whitney U test as appropriate. Chi-square test or Fisher's exact test was used for categorical variables. Time-to-event analysis was performed using Kaplan-Meier survival curves with log-rank test. Repeated measures ANOVA was used to analyse wound size changes over time.
Statistical significance was set at $p<0.05$. All analyses were performed on intention-to-treat basis with last observation carried forward for missing data.

Sample Size Calculation
Sample size calculation was based on expected difference in wound closure rates between groups. Assuming 85% closure rate in HPTC group versus 65% in dHACM group, with 80% power and 5% significance level, 38 patients per group were required. To account for 10% dropout rate, 40 patients per group were enrolled.

Study completion
Patients will complete the study 6 weeks after the first treatment visit. In addition, if, patients whose study ulcer closes prior to the 6-week visit will be considered as having completed the study. Complete healing of the study ulcer is defined as 100% re-epithelialization without drainage. At any point during the treatment period, patients can refuse to participate or withdraw from the study without prejudice. If a patient withdraws from the study, their last available wound measurement will be carried forward and used to calculate change in wound size and their final outcome.

Ethical Considerations
i. Approval will be obtained from the Institutional Ethics Committee.
ii. Adherence to the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines.
iii. Informed and written consent will be obtained from all participants.
iv. Adverse events will be monitored and reported.
v. Participants may withdraw at any time without penalty.
vi. Dissemination of Results
vii. Findings will be submitted to peer-reviewed journals and presented at relevant conferences.

Timeline
Recruitment: 1 months
Intervention: 3 months
Data analysis and reporting: 1 months

Potential Implications

This study aims to provide direct comparative data on the efficacy of HPTC versus dHACM in the treatment of pressure sores. The findings could inform clinical decision-making and potentially lead to improved patient outcomes in wound care management of pressure sores.

References:

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