2055

A new fibrin sealant derived from snake venom candidate to treat chronic venous ulcers

Luciana Abbade, PhD, Department of Dermatology of Botucatu Medical School, São Paulo State University Botucatu, São Paulo State, Brazil; Silvia Regina Catharino Sartori Barraviera, PhD, Department of Dermatology of Botucatu Medical School, São Paulo State University Botucatu, São Paulo State, Brazil; Maria Regina Silvares, PhD, Department of Dermatology of Botucatu Medical School, São Paulo State University Botucatu, São Paulo State, Brazil; Rui Seabra Ferreira Junior, PhD, Center for the Study of Venoms and Venomous Animals, São Paulo State University Botucatu, São Paulo State, Brazil; Márcia Tonin Rigotto Carneiro, Unidade de Pesquisa (UPECLIN) Botucatu Medical School, Botucatu, São Paulo Satate, Brazil; Natália Bronzatto Medolago Medolago, Unidade de Pesquisa Clinica (UPECLIN) Botucatu Medical School, Botucatu, Brazil; Benedito Barraviera, PhD, Center for the Study of Venoms and Venomous Animals, São Paulo State University Botucatu, São Paulo State, Brazil

Introduction: Venous ulcer is a health problem of Western countries whose treatment remains a challenge. Among its alternative therapies, there is the commercial fibrin sealant. Since 1993, the Center for the Study of Venoms and Venomous Animals (CEVAP) of São Paulo State University (UNESP), Brazil, have been developing a new fibrin sealant composed of fibrinogen extracted from large animals and an enzyme derived from snake venom.

Objectives: This study assessed the safety and most appropriate dose of the new fibrin sealant for treating the venous ulcers.

Methods: Phase I/II clinical trial was supported by the Clinic of Chronic Ulcers of the Dermatology Service at the Botucatu Medical School, UNESP, where the participants were selected. The present study was approved by the Research Ethics Committee and consent was obtained from each person. The patients were treated with the fibrin sealant, essential fatty acid and Unna's boot during 12 weeks. The following variables were evaluated: primarily, local and systemic adverse events related or not to the product; secondly, determination of the safe dose for the maximum coverage of 60 cm^2; and, finally, assessment of the healing process.

Results: Ten participants were studied, 9 females and 1 male, with ages ranging from 50 to 83 years. Eighteen ulcers were initially diagnosed, their time of appearance ranged from 2 to 60 months and the initial area from 1.5 to 59.6 cm^2. The total dose of sealant used ranged from 6 to 22.8, with an average of 12.8 doses per patient. The appearance of a new ulcer occurred in 5 patients (50%), local pain was reported by 3 patients, 3 cases of myiasis, 2 cases of critical colonization, and one patient was discontinued due to a local infection. Four ulcers showed an increase in their areas (22.2%). The development of new ulcers, as well as the augmentation of 4 of them, was related to the placement of an Unna boot. Systemic adverse events occurred in 2 patients and they were not related to the product. All adverse events were mild, with no severe events. At the end of the process, we had 7 healed ulcers (38.8%) and 7 presented a decrease of their initial areas (33.3%), totalizing 72.1% of the ulcers with significant improvement.

Conclusions: The new fibrin sealant is a safe and clinically promising candidate for treating this type of ulcers. A multicenter clinical trial, phase II/III, with a larger number of participants will be performed to prove the efficacy of the product.

Commercial support: None identified.

2054

Adverse outcomes after major surgery in patients with pressure ulcer: A nationwide population-based retrospective cohort study

Chia-Lun Chou, MD, Department of Dermatology, Shuang Ho Hospital, Taipei Medical University, Taipei, New Taipei City, Taiwan; Chien-Chang Liao, PhD, MPH, Department of Anesthesiology, Taipei Medical University Hospital, Taipei, Taiwan; Woan-Ruoh Lee, PhD, Department of Dermatology, Shuang Ho Hospital, Taipei Medical University, Taipei, New Taipei City, Taiwan

Background and objective: Postoperative adverse outcomes in patients with pressure are not completely understood. This study evaluated the association between preoperative pressure ulcer and adverse outcomes after major surgeries.

Methods: Using reimbursement claims from Taiwan's National Health Insurance Research Database, we conducted a nationwide retrospective cohort study of 17,609 patients with preoperative pressure ulcer receiving major surgery in 2008-2010. With propensity score matching procedure, 17,609 surgical patients without pressure ulcer were selected for comparison. Eight major surgical postoperative complications and 30-day postoperative mortality were evaluated among patients with pressure ulcer of varying severity.

Results: Patients with preoperative pressure ulcer had significantly higher risk than control for postoperative adverse outcomes, including septicemia, pneumonia, stroke, urinary tract infection, and acute renal failure. Surgical patients with pressure ulcer had approximately 2.33-fold risk (95% confidence interval 1.94 to 2.81) of 30-day postoperative mortality compared with control group. The most significant postoperative mortality was found in those with serious pressure ulcer, such as pressure ulcer with local infection, cellulitis, or treatment by debridement or antibiotics. Prolonged hospital or intensive care unit stay and increased medical expenditures were also associated with preoperative pressure ulcer.

Conclusions: This nationwide propensity score—matched retrospective cohort study showed increased postoperative complications and mortality in patients with preoperative pressure ulcer. Our findings suggest the urgency of preventing and managing preoperative pressure ulcer by a multidisciplinary medical team for this specific population.

Limitation: Detailed information on patient sociodemographics, lifestyle, nutritional status and biomedical measurements was not available from the National Health Insurance Research Database. In addition, we could not investigate the impact of severity of pressure ulcer on postoperative mortality.

Commercial support: None identified.

1937

Analysis of the role of *Bacillus oleronius* proteins in the induction of tissue damage and inflammation in ocular rosacea

Fred McMahob, Maynooth University, Maynooth, Ireland; Clair Gallagher, Dublin City University, Glasnevin, Ireland; Martin Clynes, Dublin City University, Glasnevin, Ireland; Finbarr O'Sullivan, Dublin City University, Glasnevin, Ireland; Kevin Kavanagh, Maynooth University, Maynooth, Ireland

Rosacea is a chronic inflammatory dermatosis of the central T-zone region of the face, and the surrounding regions of the eye and its surface. Factors such as alterations in the innate immune response, changes to the vascular network in the skin, the presence of reactive oxygen species within the skin, and neutrophil activation have been suggested as major players in the induction and persistence of the disease. The aim of the work presented here was to examine the response of a transformed corneal epithelial cell line (hTCEpi) to *Bacillus oleronius* proteins, an endosymbiotic bacterium of the Demodex facial mites, as this might give an insight into how exposure to these proteins in vivo leads to the corneal damage characteristic of ocular rosacea. Exposure of corneal epithelial cells to *B oleronius* proteins reduced growth in a dose-dependent manner and this corresponded to decreased rate of cell proliferation and increase in mean generation time of the epithelial cells treated with the *B oleronius* proteins. Through FACS analysis, it was shown that corneal epithelial cells stimulated by Bacillus proteins displayed a halt in the G1/S transition of the cell cycle but did not undergo apoptosis. Corneal epithelial cells exposed to *B oleronius* proteins demonstrated an increase in production and gene expression of interleukin-6 (IL-6) (11.6-fold, $P = .0337$) and IL-8 (7.8-fold, $P = .0378$), and increased expression of the defensins, CCL20 (4.1-fold, $P = .0129$) and S100A7 (5.7-fold, $P = .005$). Elevated expression of genes coding for IL-1β, IL-6, IL-8, and TNF-α was observed in cells exposed to the Bacillus proteins. In addition, matrixmetalloproteinase-9 (MMP-9) production (3.2-fold, $P = .003$) and activity (2.2-fold, $P = .0186$) was elevated. The results presented here indicate that exposure of corneal epithelial cells to *B oleronius* proteins increased the production of MMP-9 and the expression of inflammatory cytokines. The significance of this work lies in the fact that if elevated MMP-9 activity and cytokine production occurs in vivo this could lead to the tissue damage (corneal scarring) and inflammation on the surface of the eye (keratitis) observed in ocular rosacea. The elucidation of the role of *B oleronius* in the induction of ocular rosacea will facilitate the development of more effective and targeted therapies for the control of this disease.

Commercial support: None identified.

1757

Biafine topical emulsion accelerates excisional and burn wound healing in mice

Angelo Landriscina, Montefiore Medical Center, Bronx, NY, United States; Jamie Rosen, Montefiore Medical Center, Bronx, United States; Brandon Adler, Montefiore Medical Center, Bronx, United States; Aimee Krausz, Montefiore Medical Center, Bronx, United States; Tagai Musaev, Montefiore Medical Center, Bronx, United States; Joshua Nosanchuk, MD, Montefiore Medical Center, Bronx, NY, United States; Adam Friedman, MD, Montefiore Medical Center, Bronx, United States

Macrophages play a fundamental role in wound healing; therefore, employing a strategy that enhances macrophage recruitment would be ideal. It was previously suggested that the mechanism by which Biafine topical emulsion improves wound healing is enhancement of macrophage infiltration into the wound bed. The purpose of this study was to confirm this observation through gross and histologic assessments of wound healing using murine full-thickness excisional (n = 80/group) and burn wound models (n = 40/group), and compare to common standards, Vaseline and silver sulfadiazine (SSD), for each wound type respectively. Treatments were administered daily, and each group was evaluated by measurement of relative wound closure and histologic signs of wound healing. Biafine enhanced wound healing in both wound types as compared to control, and surpassed petroleum jelly and SSD in respective wound types. Biafine treatment accelerated wound closure clinically, with near complete closure of Biafine treated excisional wounds by day 10 (94.6%), as compared to 89.6% and 85.3% closure in respective control wounds ($P = .01$), and Biafine treated burn wounds by day 16 (95.7%) as compared to 67.4% closure in SSD-treated wounds and 61.1% closure in control wounds ($P = .001$). In both groups, histology revealed greater epidermal/dermal maturity, granulation tissue formation, and collagen quality and arrangement with biafine treatment as compared to other groups. Using immunohistochemistry, Biafine application was associated with greater macrophage and lower neutrophil infiltration at earlier stages of healing when compared to other study groups. These data provide a biologic mechanism through which Biafine is validated as an appropriate treatment option for both burn and excision wounds.

Supported by a research grant from Valeant Pharmaceuticals North America LLC.