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A novel rapid and selective enzymatic debridement agent for burn wound management: A multi-center RCT

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Abstract

Objectives

Excisional debridement followed by autografting is the standard of care (SOC) for deep burns, but is associated with serious potential complications. Conservative, non-surgical and current enzymatic debridement methods are inefficiently slow. We determined whether a non-surgical option of rapid enzymatic debridement with the debriding enzyme NexoBrid™ (NXB) would reduce need for surgery while achieving similar esthetic and functional outcomes as SOC.

Methods

We conducted a multi-center, open-label, randomized, controlled clinical trial including patients aged 4-55 years with deep partial and full thickness burns covering 5-30% of their total body surface area (TBSA). Patients were randomly assigned to burn debridement with NXB (applied for 4 h) or SOC, which included surgical excisional or non-surgical debridement.

Results

NXB significantly reduced the time from injury to complete débridement (2.2 vs. 8.7 days, $P < 0.0001$), need for surgery (24.5% vs. 70.0%, $P < 0.0001$), the area of burns excised (13.1% vs. 56.7%, $P < 0.0001$) and the need for autografting (17.9% vs. 34.1%, $P = 0.01$). Scar quality and quality of life scores were similar in both study groups as were the rates of adverse events.

Conclusions

Enzymatic débridement with NXB resulted in reduced need for and extent of surgery compared with SOC while achieving comparable long-term results in patients with deep burns.

Trial registration

: Clinical Trials.gov NCT00324311.

Introduction

Burns are common injuries, associated with significant morbidity and mortality often leading to disfigurement and dysfunction due to scarring. Deep partial thickness and full thickness burns are characterized by the presence of necrotic tissue (the eschar) that makes accurate diagnosis of burn depth difficult and contributes to local and systemic complications [1], [2], [3].

Early burn eschar removal (*débridement*) followed by autografting is a cornerstone of modern burn therapy and considered the standard of care (SOC) since it reduces early complications and late sequelae, mainly scarring [1], [2], [3]. At present, most deep burns are surgically debrided in the operating room by excision (*escharectomy*), mainly sequential, tangential excision of thin layers of necrotic tissue until viable, bleeding tissue is reached. While effective, excisional debridement is traumatic, resulting in loss of viable tissue, blood and heat, and requiring specialized surgical personnel and facilities and is often delayed until an accurate diagnosis of burn depth is reached confirming the necessity for surgery [1], [2], [3], [4]. Due to surgical demands, a conservative, "*autolysis*" based, approach is often used where the necrotic eschar slowly macerates under the activity of cellular enzymes, bacteria and antibacterial medications.

Enzymatic and chemical debridement have been proposed in the past to speed the autolytic process and as an alternative to excisional debridement (ED), but present agents are slow, of limited efficacy, and increase the risk of infection by macerating necrotic tissues [5]. We developed a debriding enzyme, NexoBrid™ [1] (NXB), which is mixed with an inert carrier gel, forming a debriding gel dressing (DGD). NXB consists of a lyophilized, partially purified proteolytic protein mixture with increased specific enzymatic activity derived from Bromelain raw material extracted from pineapple plant stems.

Preliminary studies in animals and humans with NXB[2] have suggested that it selectively removes the burn eschar after a single 4 h application resulting in a clean wound bed, reducing the time to complete debridement and need for ED as well as reducing burn induced elevated compartment/interstitial pressures [6], [7], [8], [9], [10], [11]. In partial thickness burns, such debridement leaves behind enough non-injured dermis that can epithelialize spontaneously, decreasing the need for ED and autografting [6], [7], [8], [9], [10]. We have coined this approach in burn care the "Minimally Invasive Modality" or MIM [12]. The current study was aimed at confirming prior preliminary results and determining whether NXB use reduces ED and autografting compared to SOC. We hypothesized that NXB if effective and selective, would reduce the need for and extent of surgery and that the reduction in excision and autografting would not impair long-term outcomes (cosmesis and quality of life) compared with the SOC.

Section snippets

Trial design

This study was a prospective, randomized, multicenter, open-label, controlled, confirmatory, phase 3 clinical trial that was conducted between 2006 and 2009. The study was approved by the institutional review boards of each of the 26 participating burn centers from 13 countries. …

Study population

Patients aged 4-55 years in good health with deep partial and full thickness thermal burns covering between 5 and 30% of their total body surface area (TBSA) hospitalized in specialized burn units/centers were enrolled. …

Patients

Overall, 190 patients were screened and 182 enrolled (Fig. 1) between the years 2006 and 2009. Out of the 182 enrolled, 26 were NXB training patients (the first patient at each site) and 156 patients underwent randomization. The training patients were only included in the safety analysis but were excluded from the efficacy analysis in order to maintain randomization. The study was terminated after pre-planned interim analysis that demonstrated NXB superiority in both co-primary end points. Of …

Discussion

In our study we compared SOC debridement (surgical and/or non-surgical) with a novel, rapid and selective, non-surgical, enzymatic debriding agent (NXB) in patients with deep partial and full thickness burns covering ≤ 30% TBSA. NXB debridement, performed at the patient's bedside, resulted in earlier complete eschar removal consequently reducing the number and area of burns requiring surgical excision. Although full thickness defects still require autografting, because of its selectivity, …

Funding

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Disclosure

MediWound, the producer of DGD under the name of NexoBrid-Debrase funded the trial, which was designed by MediWound and the study group investigators and approved by the European Medicine Agency (EMA). Data was reported by the investigators and analyzed after data base lock by an independent statistician for MediWound, EMA and the primary author. The authors had full access to the data and made the decision to submit the manuscript for publication. All authors contributed to the content of the …

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