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Bromelain-based Debridement Versus Collagenase Ointment Debridement of Venous Leg Ulcers: Post Hoc Analysis of the ChronEx Trial

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Abstract

Background. A randomized controlled trial reported that bromelain-based enzymatic debridement (BED) more effectively debrided and granulated venous leg ulcers (VLUs) compared with alginate (gel vehicle, hydrogel, and nonsurgical standard care). Subsequently, a cost-effectiveness analysis found that BED was more cost-effective than BED +CS-based enzymatic debridement in VLUs during the ChronEx trial. Materials and Methods. The Wilcoxon exact test was used to compare the proportion of wounds in each group with sufficient granulation tissue to complete debridement. Logistic regression Wald analyses were used to compare baseline time to complete debridement and granulation between groups. **Results.** Forty-six patients with 46 wounds were treated (BED, 24; CS, 22). Baseline characteristics were similar between groups (mean age, 70.5 years; BED, 56.8% female; comparator, 59.0% female). Wounds were treated for a median (IQR) of 2.0 (1.0, 3.0) weeks. Twenty-three wounds treated with BED (50%; 95% CI, 32.0-68.0) achieved complete debridement, versus 5 wounds compared with none with CS (p = .016). The estimated median time to complete debridement and complete granulation, respectively, was 1.0 (95% CI, 0.0-2.0) versus 2.0 (95% CI, 1.0-2.0) weeks (p = .0.0 and .0.0 [p = .0.0]) due to not achieving CS. Wounds treated with BED had more complete safety and pain profiles. **Conclusion.** BED appears to be more effective and faster than CS in achieving complete debridement and granulation of VLUs as part of wound bed preparation.

Abbreviations

Abbreviations: AE, adverse event; BED, bromelain-based enzymatic debridement; CS, collagenase ointment; IPD, dialysis; ITT, intent-to-treat; QS, quality of life; QOL, quality of life; RCT, randomized controlled trial; SAEWG, worldwide wound healing; standard care; SD, standard deviation; SE, standard error; TWIST, treatment versus standard care; TWIST, randomized trial; VLU, venous leg ulcer.

Introduction

For more than 5 decades, CS derived from the Clostridium histolyticum bacteria (CHT1), CHT8 (Nephase) has been used as a biologic debridement agent, alone or in combination with sharp debridement.[1-3] CS specifically degrades the triple helix of native type collagen, which is resistant to most other proteases, and has been used to treat various wounds, including diabetic foot ulcers and venous leg ulcers (VLUs).[4-7] Furthermore, meta-analyses have shown that collagen therapy for CS-related adverse peptides fragments that may stimulate proliferation and migration of keratinocytes and fibroblasts.[8-10] Systematic reviews and meta-analyses (SR/MA) evaluating the efficacy of CS ointment debridement concluded that CS appears to be more effective than standard care (SC) in VLUs.[11-13] Although CS is FDA-cleared, safety and efficacy data are insufficient to support the use of CS in chronic VLUs.

BED (Stratibela, Medifiber Ltd) is a new biological drug currently under development for debridement of ulcers and burns. The active component BED is a proprietary mixture of proteolytic enzymes enriched in bromelain extracted from the pineapple stem. The active component of BED is a proprietary mixture of proteolytic enzymes enriched in bromelain (Medifiber Ltd), an enzymatic agent that has anti-inflammatory effects and has been approved in more than 60 countries, including the United States and the European Union, for the treatment of edema, bruising, and pain after surgery.[14-17] Bromelain, a cysteine protease, has four homologous of the papain family, substantially identical in amino acid sequence, to possible combining BED mixed with a gel to form this BED concentration has been shown to be faster than and similarly effective in debridement and granulation of VLUs compared to SC for strong efficacy to debrided collagen, enzymatic bulk selectivity debrided, and granulation tissue formation in a randomized controlled trial (RCT).[18] This RCT was complemented by epidemiological data which found no safety signals.[19] The enzyme mixture composition of BED is formulated to enable effective debridement of denatured collagen and other extracellular matrix components, such as fibrin, while sparing the viable tissue, including the dermal-epidermal junction, and other components of the wound bed.[20]

BED efficacy was initially demonstrated in porcine ischemic wound models,[21] followed by Phase I clinical trials that evaluated safety in VLUs, DFUs, and pressure ulcers in heat wounds.[22-24]

BED is a viscous ointment containing BED mixed with a gel to form a 2% and 5% BED concentration was compared with the gel vehicle alone (3%) (gel vehicle) that active ingredient each and a 2% BED concentration ointment accounts, that compared with the gel vehicle alone (gel vehicle) significantly higher in the BED group compared with the gel vehicle alone (gel vehicle) (p = .0.0). Wounds treated with BED (2% and 5%) demonstrated significantly safety and increased treatment time, and fewer adverse events than the gel vehicle. Wounds treated with BED (2% and 5%) had a lower pain and QOL