Impact of a nitric oxide-generating treatment in diabetic foot ulcers segmented by infection status and wound age: a post-hoc analysis

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Introduction

- Diabetic foot ulcers (DFUs) are a common and serious complication of diabetes, which significantly impact patient's quality of life and pose a substantial burden on healthcare systems[1]
- Nitric oxide (NO) represents a promising therapeutic agent for the management of DFUs, due to its antimicrobial properties and ability to target mechanisms integral to biofilm survival
- A novel wound dressing technology that generates NO, via acidification of nitrite within a superabsorbent dressing, has demonstrated antibiofilm activity *in vitro*[2]
- In a randomized controlled trial (RCT) in DFUs, the population treated with a NO-generating dressing (NOGD) showed statistically significant superiority in percentage area reduction (PAR) and complete healing, over a standard of care (SoC) control population[3]

Objective

To evaluate the impact of NOGD compared with SoC, on DFU healing when segmented by infection status and wound age

Methods

- A post-hoc analysis of the ProNOx 1 randomized controlled trial of a NO-generating wound dressing[3] compared to SoC was performed.
  - The ProNOx 1 study was a multicenter RCT to determine the safety and efficacy of NOGD in diabetic foot ulcers
- Primary objective: to determine the impact of utilization of NOGD on complete wound healing dependent on:
  i. Presence or absence of wound infection/laboratory diagnosed microbial contamination at first enrolment
  ii. Wound age
- The study was conducted in 10 wound care centers in the UK and primary endpoint analysis has been reported by the principal investigators (Edmonds et al, 2018)[3]

Results: Infection/contamination

Infected/contamination DFUs

- 39/75 (52%) and 38/74 (51%) of DFUs were classified as infected/contaminated in the intention to treat (ITT) populations for NOGD and SoC arms, respectively

Healing rates in infected/contaminated DFUs (Fig 1):

- Week 12: 36% vs. 21% for NOGD and SoC arms, respectively Week 16+: 46% vs. 24% for NOGD and SoC arms, respectively, with no further increase at final follow-up

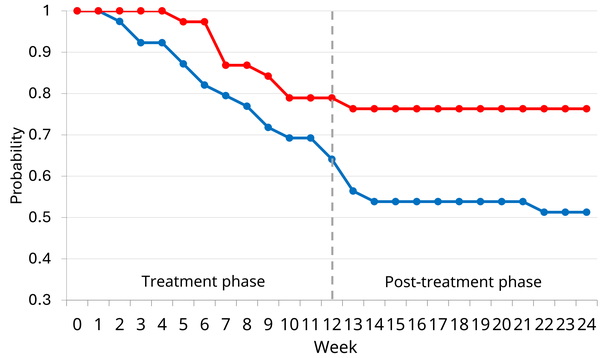

Figure 1. Probability of infected or contaminated DFUs not healing. (●) SoC; (●) NOGD

Results: Infection/contamination

Healing rates in non-infected/non-contaminated DFUs (Fig 2):

- Week 12: 35% vs. 25% for NOGD and SOC arms, respectively
- Week 16+: Healing rates increased further in NOGD arm to 38% at week 16 and 41% at final follow-up, but remained at 25% at week 16 and was 34% at final follow-up in SoC arm

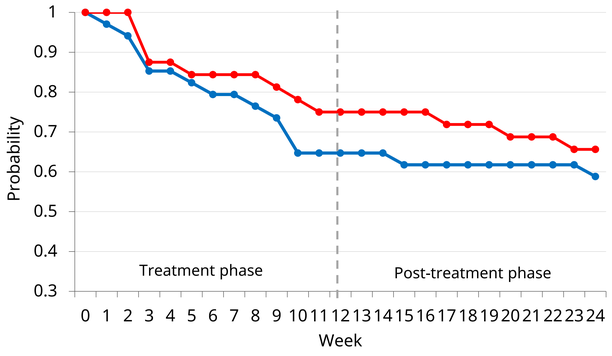

Figure 2. Probability of non-infected/non-contaminated DFUs not healing. (●) SoC; (●) NOGD

Results: Wound age

Healing rates in DFUs ≤12 weeks of age (Fig 3):

- Week 12: 46% vs. 24% for EDX110 and SOC arms, respectively
- Week 16+: Increased in NOGD arm to 54% at 16 weeks and 60% at final follow-up, but only to 28% in SoC arm, with no increase at final follow-up

Healing rates: DFUs >12 weeks of age

- Similar healing rates observed for NOGD and SoC arms (week 12, 26% vs. 31%; week 16, 33% vs. 27%; week 24, 27% vs. 29%)

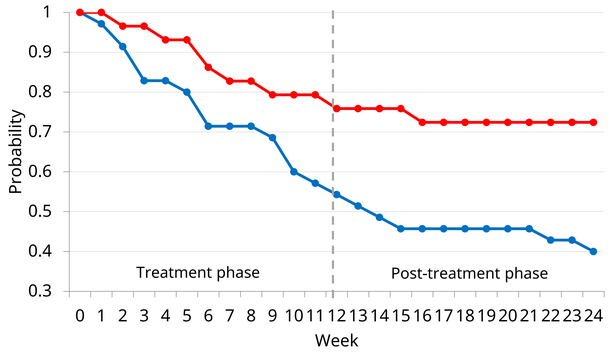

Figure 3. Probability of DFUs ≤12 weeks of age not healing. (●) SoC; (●) NOGD

Results: Infection/contamination & age

Healing rates in infected/contaminated DFUs >12 weeks of age (Fig 4):

- Week 12: 25% vs. 22% for NOGD vs SOC arms, respectively
- Week 16+: Increased further in NOGD arm to 35%, compared to 22% in SoC arm, with no further increase seen at final follow-up

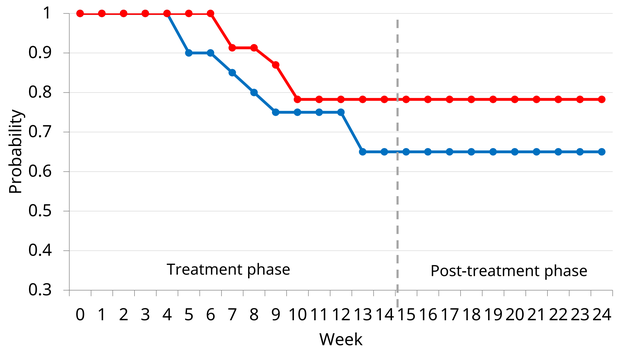

Figure 4. Probability of infected/contaminated DFUs >12 weeks of age not healing. (●) SoC; (●) NOGD

Discussion

- In infected/contaminated wounds, NOGD population out-performed SoC, with 36% of DFUs healed at 12 weeks vs. 21% in the SoC population, rising to 46% vs 24% at 16 weeks
- In wounds ≤12 weeks of age, the effect of NOGD was even more pronounced, with 46% of DFUs healed at 12 weeks, rising to 54% at 16 weeks, and 60% at final follow-up, compared to 24% and 28% in the SoC population
- Limitations: This is a post hoc analysis of an RCT[3] that was not powered to demonstrate clinical superiority of the endpoints described
- Although interesting, further studies are required to substantiate these preliminary observations

Conclusion

This analysis demonstrated the ability of NOGD to improve the DFU healing rate in wounds that were infected/contaminated, and of <12 weeks of age, compared to SoC

1. McDermott et al. Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers. Diabetes Care 2023; 46: 209-221.
2. Waite et al. Activity of a nitric oxide-generating wound treatment system against wound pathogen biofilms. Int J Antimicrob Agents 2018; 52: 338-343.
3. Edmonds et al. Multicenter, randomized controlled, observer-blinded study of a nitric oxide generating treatment in foot ulcers of patients with diabetes: ProNOx1 study. Wound Repair Regen 2018; 26: 228-237.

Presented at the Symposium on Advanced Wound Care (SAWC) Spring, April 30th–May 4th 2025, Grapevine, TX, USA