



*A Randomized, Multi-Center,
Prospective Analysis
of Diabetic Foot Ulcers
treated with TheraGauze™
alone or TheraGauze +
Becaplermin*

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Abstract

This study represents the first randomized, multi-center, prospective study utilizing a moisture regulating dressing for the treatment of diabetic foot ulcers, in conjunction with Becaplermin (Regranex), a topical recombinant growth factor (PDGF bb).

Study subjects (n=32) were randomized to receive either TheraGauze alone or TheraGauze in conjunction with Becaplermin. We found that 46% of the patients in both groups closed within 12 weeks. After 20 weeks, we found that 69% closed with TheraGauze + Becaplermin, and 62% closed with TheraGauze alone. This compares very favorably to historic controls in which only 32% close within 12 weeks, and 45% close in 20 weeks or less. Closure rates, adverse events, and co-variants were also evaluated.

Based on this data, we conclude that moist wound healing with a saline soaked gauze is not enough. Instead, we have demonstrated that Moisture Regulation (i.e. the ability to add or remove moisture as needed) will dramatically improve the rate of wound closure and % of wounds which will go on to close.

Introduction

Moist wound care with saline-saturated gauze has been a cornerstone of local wound care for many years. However, it is also clear that moisture without precise regulation can lead to wounds which become either macerated or desiccated, and this can greatly diminish the capacity for healing.

TheraGauze is an example of the new class of smart dressings which are capable of precise moisture regulation. Thus, TheraGauze is able to add or remove moisture as needed by the wound bed. It's complex microstructure enables it to make fine adjustments across the entire wound surface.

Our purpose was to determine if precise moisture regulation would result in faster closure times by measuring the rate of closure with TheraGauze, with and without Becaplermin. In order to evaluate this effect, a randomized, multi-center clinical trial was designed to evaluate the rate and percentage of wound closure, and compare this value to historic controls using saline moistened gauze.

Hypothesis

We hypothesize that:

- Precise moisture regulation will increase the rate of wound healing,
- Precise moisture regulation will result in a higher percentage of wounds closing, as compared to historic controls with saline moistened gauze,



FIG. 1: Precision moisture regulation is achieved with TheraGauze. This advanced polymer dressing is capable of absorbing or releasing fluids, such as saline, simultaneously and differentially across the wound bed, as needed.

- The ability of Becaplermin 0.01% gel (Regranex) to achieve wound closure will be improved as compared to historic clinical trials previously reported

Materials and Methods

This was a randomized, multi-center clinical trial to determine the effect of precise moisture regulation on the rate and percentage of closure for plantar diabetic foot ulcers. For this study, a total of 32 patients (n=32) were enrolled at 4 sites across the country.

Prior to enrollment, all study subjects signed an informed consent, which was site specific, and was approved by the appropriate central or internal (Northwestern University) IRB committee. Monitoring, treatment randomization, and data collection was performed by Arkios BioDevelopment International, Virginia Beach, VA. Uniformity of training for all principal investigators was also conducted by Arkios. Study patients were drawn from the Investigator's existing patient populations. Two cohorts were utilized, and the resultant data was compared to historic results captured from the literature.

- Group TG +B:** Becaplermin (Regranex) was applied to the wound on a daily basis, along with daily application of TheraGauze moisture regulating dressing as the contact layer.
- Group TG:** TheraGauze alone was applied as the contact layer every other day.

In both groups, the dressings were backed by gauze and wrapped with a gauze roll. Those assigned to the TG + B groups were only permitted to receive Becaplermin for up to 12 weeks. Becaplermin was applied in accordance with the manufacturer's recommendations,

except that TheraGauze was substituted for saline moistened gauze.

In order to qualify for participation in this study, all study subjects were required to satisfy the inclusion and exclusion criteria. Once enrolled, study subjects had a 1 week lead in time prior to initiating treatment. During this time, wound closure had to be less than 50% of the initial surface area. Study subjects were followed for up to 20 weeks. All subjects deemed closed (i.e. wound <0.01cm²) were required to return for confirmation after 1 week.

Data analysis included calculations of wound closure rate and percentage of wounds closed. Kaplan-Meier curves were also calculated. This data was compared to results found from a variety of sources in the literature. Adverse events were also monitored throughout the study.

to an average of 33% closure rate for saline moistened gauze calculated by combining the data from references 1,2,3, and 34% for Bercaplermin 0.01% from reference 5.

%of Wounds Closed @ 12 weeks

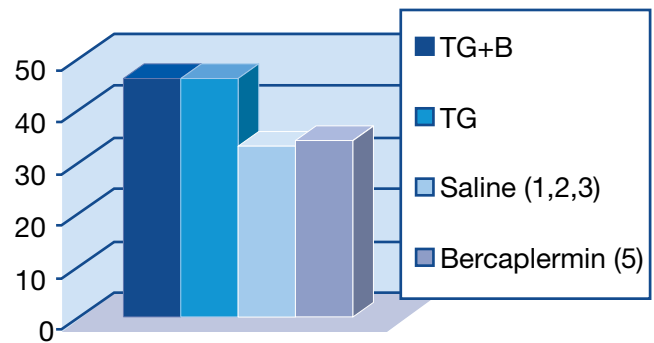


FIG. 2: Historic data for % of wounds closing after treatment with Bercaplermin 0.01% is analyzed after 20 weeks. This information is displayed in Figure 3. Historic value for Bercaplermin 0.01% comes from references 4,5,6. We found that closure rates increased from 32% with normal saline to 69.2% and 61.5% with TG+B and TG, respectively. The difference in closure rates between TG+B and TG was not statistically significant (p=0.53)

%of Wounds Closed @ 20 weeks

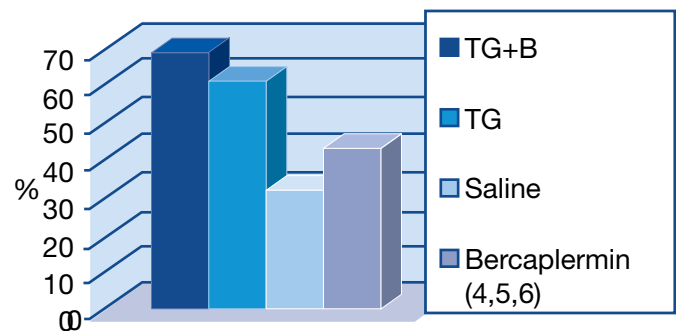


FIG. 3: We also considered the rate of wound closure. This value represents the average number of cm² closure which occurred per week. This figure is important because the rate of wound closure, especially during the initial month of treatment, has been shown to be a reliable measure for predicting which wounds will eventually close and which will not. We calculated the rate of wound closure from historic data based on the average size of the wound at initial treatment and the average time to closure (references 4,5,6). (Figure 4)

Rate of Wound Closure (cm²/week)

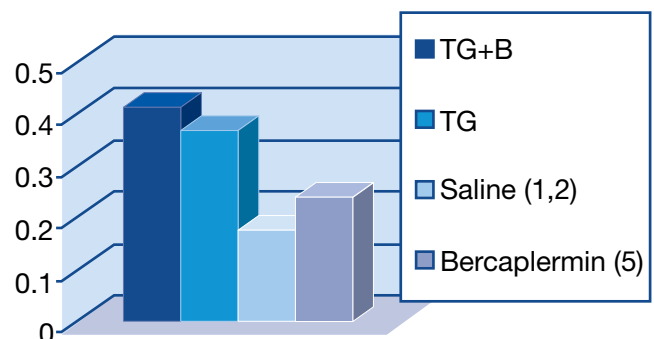


Fig. 4: This figure illustrates the rate of wound closure observed in the TG+B and TG groups, and compares this to values calculated from the literature for the historic controls. We found that the rate of closure was 0.41cm²/week for TG+B, 0.37 for TG, 0.24 for Bercaplermin, and 0.18 for Saline gauze.

Inclusion/Exclusion Criteria

INCLUSION

- Forefoot or midfoot ulcer
- Wagner Grade 1 or 2
- Tolerate off-loading w/ healing shoe, fixed ankle walker, or NWB
- Age 18-70
- IDDM or NIDDM
- HgA1C < 10.0
- Palpable DP and/ or PT pulses
- 1-8cm²

EXCLUSION

- Active Infection
- Exposed Bone
- Osteomyelitis assoc. w/ ulcer
- Purulent discharge
- Cellulitis
- Dorsal ulcers
- Ischemic ulcers
- Evidence of gangrene

Results

In this study, 32 patients (n=32) were enrolled. As of the time of this analysis, data was available on 26 subjects with 4 lost to follow-up before all data could be collected, and 2 had not completed the study at the time of this presentation.

Both cohorts had 13 subjects each, with an average wound size of 5.53cm² (TG+R), and 6.36cm² (TG). There was no statistically significant difference in the size of the wounds between groups (p=0.004).

The % of wounds closed after 12 weeks was compared to historical data for saline-moistened gauze and for wounds treated with Bercaplermin with saline-moistened gauze (Figure 2). The data shows that 46.2% of the wounds close with TG or TG+R. This compares

Discussion

Based on the data presented here, the value of precise moisture regulation can be appreciated. Not only do wounds close more frequently, but they also close more quickly. The value of moist wound healing has been discussed in the literature for years. However, the ability to regulate this moisture content by adding or subtracting fluid from the wound bed, without causing maceration or desiccation, is relatively new in the field of wound management.

TheraGauze represents the first among a new generation of smart dressings which are able to adapt to the needs of a wound on a continuous basis. We believe that by regulating and continuously adjusting the moisture content of the wound, there is a greater period of time where conditions are optimal for wound healing. This change is reflected in the fact that the closure rate is increased by approximately 39.3% in the first 12 weeks, and by nearly 50% over 20 weeks, as compared to good local wound care given in conjunction with saline-moistened gauze.

The mechanism by which TheraGauze regulates wound moisture within the wound margin can be appreciated by examining the electron micrograph (figure 5). Tube-like structures and canals, which are only a few microns in diameter, are able to differentially regulate moisture content across the wound at the cellular level, giving the clinician precise control over the wound field.

Conclusions

In this study, we demonstrated that precise moisture regulation results in an increase in the percentage of wounds closing, and increases the rate of wound progression. This improvement is attributed to the fact that conditions are being continuously optimized.

We demonstrated that there was no statistically significant difference in the rate and percentage of wounds closed, regardless of whether Bercaplermin

was used in conjunction with the precision moisture regulating dressing or the precision moisture regulating dressing was used alone ($p=0.53$).

Although this study clearly demonstrates the benefits of moisture regulation, it was not powered to be the definitive study in this area. Future studies will undoubtedly demonstrate the benefits of this new technology.

We found that the precise moisture regulating dressing directionally appears to outperform Bercaplermin covered with saline soaked gauze in percentage of wounds closed at both 12 and 20 weeks.

Based on the data presented here, it is clear that precise moisture regulation is a powerful tool to help achieve ulcer closure in patients with diabetes. We anticipate that there will be other scenarios where something other than saline will be regulated with a smart dressing as well. The ability to regulate all types of fluid added to the wound bed, such as steroids, antibiotics, and a host of other topical agents, leads us to believe that there could be many custom applications for a dressing such as this.

References

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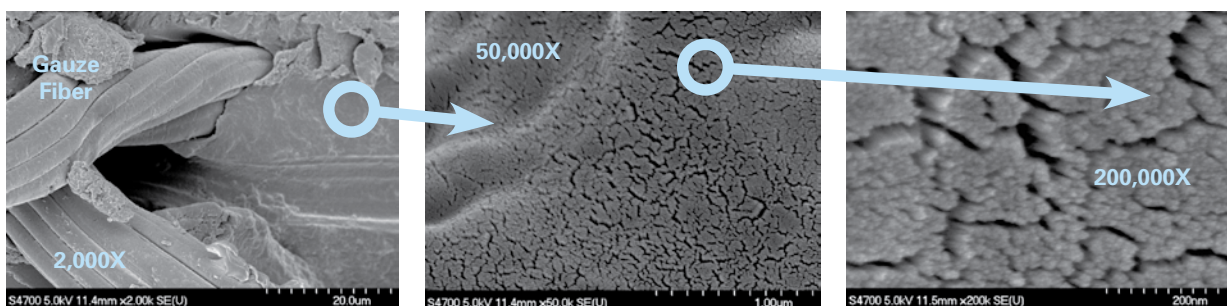


Fig 5: Electron Micrographs illustrate the unique structure of TheraGauze. The polymer dressing appears to be a biomimetic material — it contains a series of tube-like structures and canals which enable the dressing to regulate moisture at the cellular level across the wound interface.