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Patient-Reported Outcomes and Perceptions Following the Use of Compounded Topical Scar/Burn Treatments: Interim Results from an Observational Study

Abstract

Background. In addition to the aesthetic implications, scar tissue can cause pain, tenderness and itching, and can negatively impact quality of life. Though many individuals are impacted by scar tissue, there is no consensus on optimal treatment. The purpose of this study was to determine the effects of two treatment compounds incorporating PracaSil™ and naltrexone on scar size, patient perceptions and related symptoms. This is an interim analysis of an observational survey study involving 31 sites. Methods. Adult patients (ages 18 to 64 years) having scars/burns for a minimum of one month, healed, and not infected, and using one of two formulations of a compounded scar tissue treatment were enrolled. Patients completed surveys assessing scar size, pain at the scar site, itching and interference ratings at visits 1 and 3. Results. Patients (n=109) were predominantly female (n=97) and Caucasian (n=76) and used the treatment compounds over an average duration of 4 months, during which time, no serious adverse events occurred. Most patients (69%) reported noticing a reduction in scar size while using the medications. Patients also reported significant reductions in itching ($p<0.001$) and scar/burn interference with general activity, mood, normal work, relations with other people, sleep and life enjoyment ($p<0.05$ for all). Improvements in well-being were also reported while using the treatment compounds. Conclusions. Preliminary results show that the treatment compounds were safe and may be effective in reducing scar size, itching and interference ratings in adults having scars/burns for at least one month.

Keywords: scars, burns, compounded treatment

Introduction

Scar tissue develops from an overgrowth of fibrous tissue following injury to the skin and represents a natural part of the healing process. Scars restore tissue integrity and can range from asymptomatic fine lines to hypertrophic scars and keloids.[1] In addition to the aesthetic implications, scars can be associated with pain, tenderness, itching, stress and anxiety, and can negatively impact patient quality of life.[2] While scar tissue impacts most individuals, there is no consensus on optimal treatment.[3]

Pharmaceutical compounding is the mixing of active substances and raw materials and enables the tailoring of treatment to patients' individual needs. Compounding also gives clinicians latitude in prescribing optimal dosages of each component of the prescription. A great degree of variability in scar formation exists within patient populations and scar characteristics can depend on genetic predisposition[4] as well as wound site.[5] Thus, the customization of treatment may represent a more effective strategy by addressing these inconsistencies. While much research has focused on various topical, over-the-counter scar/burn treatments including silicone, vitamin E, onion extract and others, fewer studies have investigated the impact of compounded pharmaceutical treatment therapies.[6-8]

Silicones have been studied in the treatment of scars/burns for their hydrating and occlusive properties[6], either isolated or in combination with other components. Pracasil™ is a relatively new scar treatment option containing silicones and pracaxi oil, a plant seed oil used for skin regeneration and healing. To date, no randomized controlled trials have investigated the impact of Pracasil™, either isolated or in combination with other substances, on scar tissue. However, a series of case studies yielded promising results with patients reporting improvements in scar size, severity, color and pain over a duration of 2 days to 3 weeks of usage.[5]

Topical naltrexone is an opioid antagonist shown to enhance wound healing by increasing epithelial proliferation and angiogenesis.[9,10] While previous research has investigated the impact of this opioid antagonist on earlier stages of wound healing (e.g. wound closure)[9-11], studies on the use of naltrexone for scar/burn treatment are sparse. Therefore, the purpose of this ongoing observational study is to investigate the effects of topical compounded scar/burn treatments incorporating Pracasil™, naltrexone and other components on patient – and clinician – reported scar size, symptoms and interference.

Methods

A total of 109 adult patients (ages 18-64 years) having

healed, closed and not infected scar/burn tissue ≥1 month from 31 clinical sites in the United States were enrolled in the study only after being prescribed one of two formulations: Collagenase 200U/gm, Naltrexone 1% 10mg/gm, Aloe Vera freeze-dried 1:200 3 mg/gm in Pracasil Plus gel; or Naltrexone 1% 10 mg/gm, EGCG 1%, Dimethyl Sulfone 5%, Caffeine 1% in Sanare™ gel. Institutional review board approval was obtained in line with the Declaration of Helsinki and all study procedures comply with Good Clinical Practice (GCP) guidelines.

Patients were instructed to apply the topical formulations twice daily and completed surveys at visit 1 and visit 3. Survey 1 included a scar size assessment for the clinician to complete and patient assessments for pain interference with general activity, mood, restrictions (walking, using your hand, arm, lifting, foot, ankle, elbow, wrist, hip, knee), normal work, relations with other people, sleep and life enjoyment and the use of all other over-the-counter and prescription pain medications. Survey 3 included all of the items above along with additional patient questions on whether a reduction in scar size had been noticed, side effects and emotional well-being.

Statistical Analysis

All statistics were done with IBM SPSS Statistics version 19 (IBM, New York, USA). Ordinal data (itching and interference ratings, which were not normally distributed as determined by the Shapiro-Wilk test) were compared using the Wilcoxon Signed Ranks test for paired values. P-value ≤0.05 was considered significant. Categorical data (clinician-reported scar/burn length categories) were compared using McNemar's test for paired values (data not shown). All data are presented as means ± standard deviations.

Results

Patients were predominantly female (89%) and white/Caucasian (70%) ranging in age from 19 to 64 years *(Table 1).* Patients used the topical compounded treatments over an average duration of 128 days. A statistically significant, 69% reduction in the use of pain medications was observed with topical scar/burn compound use (p<0.001) *(Table 2).* No side effects were experienced in ~91% of patients. Of the side effects reported: rash or redness (n = 4); other (n = 4); and skin dryness (n = 2), no serious adverse events occurred *(Table 3).*

A majority of patients (69%) reported reductions in scar size with the use of the topical treatment compounds *(Figure 1).* Patient-reported itching (p<0.001) and scar/burn interference with general activity, mood, normal work, relations with other people, sleep, life enjoyment and limb restrictions all significantly declined from Survey 1 to Survey 3 (p<0.05 for all) *(Figures 2 & 3).* In addition, 88% of patients reported some improvement in scar appearance and 56% reported some improvement in emotional well-being while using the compounds *(Figure 4).* A significant reduction in the percentage of patients with scars above 20 mm at baseline was also reported by clinicians with treatment (p<0.01).

	MEAN ± SD	RANGE
Female/Male (n)	97/12	
Age at Survey 1 (years), n=110	43 ± 10	19 - 64
Race, n=110	White/Caucasian: 76 Hispanic/Latino: 20	Black/African American: 8 Other: 6
Scar/Burn Age (n), n=108	1 month: 12 2-6 months: 14 6-12 months: 9	1-5 years: 30 >5 years: 43
Time between Surveys 1 & 3 (days), n=110	128 ± 245	70 - 170

Table 1. Patient Characteristics. *SD = standard deviation.*

CURRENT MEDICATION USAGE	SURVEY 1 (%, N)	SURVEY 3 (%, N)
Yes	63.1, 65	19.4, 20*
None	36.9, 38	80.6, 83

Table 2. Changes in Pain Medication Use from Survey 1 to Survey 3 (n=103). **P<.001, a 69.3% decrease in medication use.*

SIDE EFFECT	%, N
None	90.7, 98
Rash or redness at scar site	3.7, 4
Other (not specified)	3.7, 4
Skin dryness	1.9, 2

Table 3. Patient-Reported Side Effects from Scar Medication (n=108). *No serious adverse events were reported.*

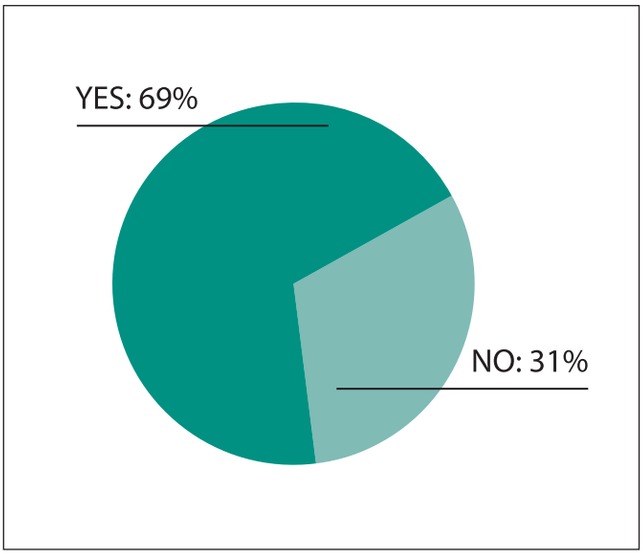

Figure 1. Have you noticed a reduction in the size of the scar since you started the medication? (n=109).

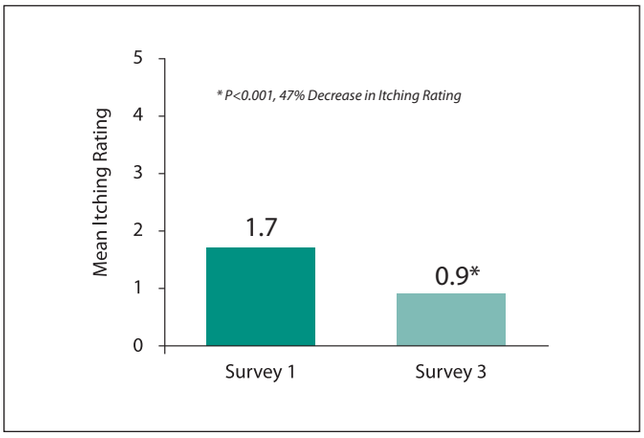

Figure 2. Has there been any itching associated with your scar/burn during the last 7 days? (n=104).

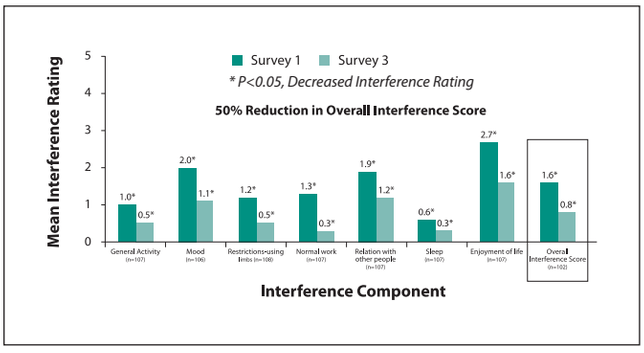

Figure 3. Changes in Scar/Burn Interference Ratings from Survey 1 to Survey 3.

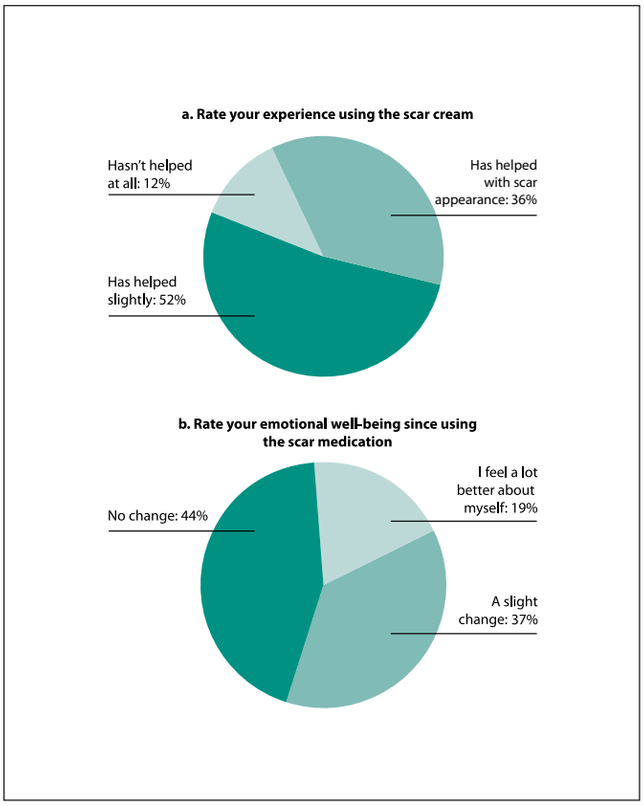

Figure 4. Patient-Reported Observations on Scar/Burn Medication Use at Survey 3 (n=108).

Discussion

Key findings from the current observational investigation were the reductions in pain medication use, scar size, itching and scar/burn interference with the use of the compounded topical formulations. Patients also reported finding the treatment compound helpful and reported no serious side effects from the use of the formulations. Patient-reported scar size reductions were supported by clinician measurements showing a significant reduction in the proportion of patients with largest scars at baseline.

Scarring is a pervasive issue affecting most, if not all individuals. Scar revision surgery has been among the top five reasons for cosmetic surgical procedures in the United States for several years and accounted for 177,000 procedures in 2014.[12] These preliminary results provide support for the use of unique, compounded therapies for scar/burn treatment. The formulations studied in this investigation consisted of components designed to address various areas of scar pathophysiology: PracaSil™, Sanare™, and aloe vera for hydration; Naltrexone, EGCG and caffeine for inflammation; collagenase for breaking down collagen peptide bonds; and dimethyl sulfone for promoting collagen fiber flexibility.

Though studies have explored the efficacy of compounded scar/burn treatment therapies, this is the first evidence to support the use of these specific compounds incorporating PracaSil™, naltrexone and collagenase, three substances that have received little attention among previous studies. PracaSil™ is a mixture of silicones with pracaxi oil, which is derived from Amazonian Pentaclethera macroloba trees. Pracaxi oil has been used for postpartum stretch marks, bacterial infections and snake bites and has been shown to accelerate wound closure in various wound models.[13-15] The potential benefit of PracaSil™ may be due to the anti-inflammatory properties of its fatty acid content as well as its hydrating properties.

Naltrexone, an opioid receptor antagonist incorporated into both treatment compounds has previously been shown to improve the healing process when used in earlier stages of wound healing for wound closure.[9-11] Our preliminary results show that naltrexone is also beneficial when incorporated later in the wound healing process improving both scar appearance as well as symptoms.

In scar/burn treatment, some studies emphasize clinician observations and do not include patient accounts of changes in scar appearance.[16,17] Duality can sometimes exist between physician and patient determinations of success, especially within the field of plastic surgery. Given the highly subjective nature of the impact of scars/burns, it is important to emphasize patient-reported outcomes in the determination of treatment success or failure. A strength of the current study is the focus on patient-reported outcomes with the use of the topical formulations.

This study is not without its limitations. This was an observational study and thus, it cannot be definitively concluded that the beneficial effects were attributed solely to the treatment compounds. There was no inclusion of an objective measure of scar characteristics such as texture/smoothness, color, intensity and depth/height. We also did not isolate the effects of each unique treatment compound on scar size and symptoms. This practical approach in simply observing patients after having been prescribed either of these compounds was feasible and although lacking in some controls, sets a good foundation

for future controlled trials which delineate the effects of specific compounded scar/burn therapies.

Conclusion

Scar formation is a complex process subject to multiple factors including ethnicity and wound type and location.[7] Given the intricacies and individual variability of the healing process, a tailored approach to treatment is a sensible option. These preliminary results suggest that two uniquely compounded scar/burn treatment therapies are safe and well-tolerated and may reduce patient-reported and clinician-measured scar size as well as scar/burn interference and itching. ■

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Conflict of interest: Dr. ED Harris is a consultant to Clarity Research and Consulting, LLC. Dr. HJ Visser has received honoraria from Clarity Research and Consulting, LLC. Dr. S. Hunter has no financial conflicts of interest to disclose. D. Dietze received payment from Clarity Research for the data analysis for the current investigation. P. Hurwitz is President of Clarity Research and Consulting, which received funding from the pharmacies listed above. This study was funded by the following pharmacies: Advantage Medical and Pharmacy, Hattiesburg, MS, USA, Advantage Medical Infusion, Hattiesburg, MS, USA, Annie's Apothecary, Boerne, TX, USA, Annie's Apothecary, Kerrville, TX, USA, Boothwyn Pharmacy, Boothwyn, PA, USA, Cypress Compounding Pharmacy, Houston, TX, USA.