

Results of a non-invasive protocol for healing leg ulcerations in sickle cell anemia utilizing non-contact ultrasound and bilayered living cell therapy

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BACKGROUND

Leg ulcers, a late complication in adult sickle cell patients, have healing rates 16 times lower than comparable venous ulcers. The pathophysiology of these ulcers involves multiple poorly understood mechanisms. Venous incompetence and venous hypertension are known contributing factors. Many modalities have been utilized to achieve healing including successful use of bilayered living cell therapy* (BLCT) in a longstanding sickle cell ulcer. BLCT efficacy in longstanding venous leg ulcers is reported as 47% closure at 24 weeks as compared to 19% closure without BLCT.

Sickle cell ulcers are usually characterized by adherent fibrin slough requiring wound bed preparation.

PURPOSE AND HYPOTHESIS

Non-contact non-thermal ultrasound was employed to débride adherent fibrin slough which characterizes sickle cell ulcers. Additionally, non-contact non-thermal ultrasound decreases bioburden, increases neo-angiogenesis and granulation tissue formation. It has additionally been shown to reduce pain in chronic painful wounds including sickle cell ulcers. Bilayered tissue equivalents have been shown to assist in healing of a sickle cell ulceration in a case report and we postulated that employment of this modality after preparation of the wound with MIST ultrasound would result in improved healing outcomes. Additionally, we postulated that a noninvasive protocol for treating such ulcerations would be feasible and efficacious.

*Apligraf™ is a registered trademark of Organogenesis, Inc

**MIST Therapy® is a registered trademark of Celleration, Inc.

MATERIALS AND METHODS

Our protocol was initiated with compression along with non-contact ultrasound** 3 times weekly for at least 5 treatments for debridement, bacterial clearance, and neo-angiogenesis. Curettage of remaining slough and concurrent application of BLCT when wound healing trajectory plateaued.

Topical antimicrobial therapy was employed prior to bilayered cell therapy using cadexomer iodine or silver alginate containing dressings.

Non-contact non-thermal ultrasound was provided utilizing a commercially available unit according to the manufacturer's recommendation for treatment duration based on wound size. (Celleration, Inc.)

Bilayered living cell therapy was employed with commercially available tissue units applied according to the manufacturer's recommendations. (Organogenesis, Inc)

Compression therapy was accomplished utilizing multilayered wraps reapplied after each ultrasound treatment and after application of bilayered cell therapy.

The outcomes were retrospectively reviewed from the standard patient charting, measuring and photography employed in our clinic.

No patients were treated with concurrent blood product therapy despite anemia documented in all patients.

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RESULTS

Four patients with recalcitrant sickle cell ulcerations were treated accordingly. Hgb ranged 8.3-10.4; transfusions were not utilized. Pretreatment average ulcer duration was 16 months (range 9-22) and size ranged 0.54-51cm². Average healing time was 16 weeks (range 8-28) following BLCT. One to five BLCT applications occurred. Three patients healed without recurrence. Two recurrent episodes in one patient resolved with fewer applications of BLCT for closure. Two recalcitrant ulcers showed rapid healing with non-contact ultrasound alone.

	Patient age (yrs)	Ulcer age prior to initiation of protocol	Ulcer size cm ²	Ultrasound duration (weeks/ treatments)	Apligraf applications #	Weeks to closure from initiation of MIST protocol treated without BLCT	Weeks to closure from initial BLCT
Patient 1a (right)	54	68 weeks	33	56/131*	2	N/A	13
Patient 1b (left)	54	68 weeks	7	14/34*	0	14	N/A
Patient 2	27	88 weeks	51	11/25*	5	N/A	28
Patient 2 recurrence 1	28	3 weeks	27	2/5	2	N/A	12
Patient 2 recurrence 2	28	1 week	2	2/5	2	N/A	21
Patient 3	29	40 weeks	14	16/39*	1	N/A	8
Patient 4	34	36 weeks	.54	1/3	0	1	N/A

*patient did not fully comply with 3 times weekly treatment



CONCLUSIONS

Our noninvasive protocol for treatment of longstanding sickle cell anemia associated ulceration utilized compression therapy, wound preparation with non-thermal non-contact ultrasound (MIST), curettage, and BLCT (Apligraf). It was effective in closure of longstanding ulcerations in an initial series of patients. 80% of chronic sickle cell ulcers treated with our protocol healed within 24 weeks as compared to a RCT in which 47% of venous ulcers of greater than 1 year duration healed within 24 weeks. We believe wound bed preparation with non-contact ultrasound and curettage to remove fibrin slough proved essential prior to BLCT. Our protocol was well tolerated resulting in reduction of fibrin slough, pain reduction, closure of the wounds and durability of healing.