

Treatment of recalcitrant diabetic foot ulcers using trichloroacetic acid

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BACKGROUND: Despite using different treatment modalities, treatment of diabetic foot ulcer is still a very important challenge. In this case series, we report successful treatment of 6 patients with resistant diabetic ulcers using topical application of trichloroacetic acid (TCA). **METHODS:** Six patients with type 2 diabetes mellitus received standard treatment for 6 weeks. TCA 70% was applied to the periphery of the ulcer while TCA 50% was applied to the center of the ulcer every week until the first significant reepithelialization was observed. **RESULTS:** All wounds in all 6 treated patients were improved after a mean duration of 7.5 ± 0.83 weeks. In fact, significant reductions were observed in the areas and infection scores of the ulcers. **CONCLUSIONS:** The range of improvement efficacy ranged from 68.6% to 100% with no complications after 1, 2, and 3 months of follow-up. The observed efficacy of TCA on diabetic ulcer healing is due to production of granulation tissue and epithelial cells.

KEYWORDS: Diabetes; Ulcer; Trichloroacetic Acid

BACKGROUND

Ulcers of the lower extremities are regarded as serious complications of diabetes. This complication is usually caused by peripheral neuropathy or vascular insufficiency. Foot ulcer may affect at least 15% of diabetic patients throughout their life.^[1] These ulcers are considered as one of the main causes of hospitalization and limb amputation in diabetic patients.^[2] Diabetic foot ulcers due to neuropathy may predispose patients to infection and osteomyelitis.^[3] Electrical stimulation with heat laser, cold laser, and growth factors such as becaplermin as well as other routine treatments including off loading, debridement, and control of infection has also shown to be promising in the treatment of these types of ulcers.^[4] Obtaining wound closure is the primary goal in the treatment of diabetic foot ulcers. Management of the foot ulcer depends on its grade, stage and vascularity, and the presence of infection. Although many various topical medications and gels are advised for ulcer treatment, few have proved to be more efficacious than current dressings.^[5]

Trichloroacetic acid (TCA) solution is known as an appropriate treatment for some cutaneous lesions such as pigmentation disorders, early facial rhytids, atrophic scars, and leishmaniasis lesion.^[6-8]

TCA is able to penetrate dermal layer up to mid-dermis and results in destruction of epidermal lesions up to the epidermal adnexa.^[8,9]

The aim of this report was to assess the efficacy of topical TCA 50% in the treatment of diabetic foot ulcer.

METHODS

This study evaluated 6 patients with type 2 diabetes mellitus and refractory foot ulcer. During 2011, all patients had been regularly visited by a team composed of an orthopedist, dermatologist, infectious disease specialist, and cardiologist at Ulcer Clinic of Skin Disease and Leishmaniasis Research Center, Isfahan, Iran. Ankle brachial index (ABI) was determined in dorsalis pedis and tibialis posterior arteries as a comprehensive physical examination for assessing vascular setting in patients. Normal values of ABI were considered to range from 0.91 to 1.30. Ratios of < 0.91 or > 1.30 were considered as indicative of peripheral arterial disease (PAD).^[10]

All patients received standard treatment of diabetic ulcer including antibiotics, debridement, and glucose control. Off-loading was also performed by referring the patients to a podiatrist who advised special fitting shoes and total contact cast (TCC) for

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each patient based on their foot pressure points. Education plan on ulcer management was also included.^[11] Appropriate antibiotics were administered when needed.

Despite implementation of standard treatment for 6 weeks, none of these patients showed signs of improvement and were referred to the Ulcer Clinic of Skin Disease and Leishmaniasis Research Center to be considered for treatment with TCA.

After completing patient records, informed consents were taken. The ulcers were photographed under the same conditions using a digital camera (Canon, Iso400 D) every week. The width, length, depth, and area of ulcers were also determined by Pictzar software (version 5.05.2) before and 8 weeks, and 1, 2, and 3 months after treatment.

The stage and grade of the wounds were defined according to table 1.^[12] Wound infection scores are also presented in table 2.^[13,14] The improvement efficacy was analyzed according to percent of difference in ulcer area before and after treatment.

Method of the treatment

After area defatting with alcohol, using cotton applicators, TCA 70% and TCA 50% were applied to the periphery and the center of ulcers, respectively. The ulcers were then covered by normal saline and sterile gauze. The dressing was changed every day until a week. All other routine treatments and evaluations were applied for all patients.

This procedure was repeated every week until the first significant reepithelialization was observed. The patients were followed monthly for 3 months.

RESULTS

This study included 6 (1 female and 5 male) patients with the mean age of 56.0 ± 13.7 years. All 6 ulcers healed completely after 7.50 ± 0.83 weeks.

Demographic data, wound characteristics, and ulcer improvement of patients with diabetic foot ulcers are presented in tables 3 and 4.

The first case was a 51 year-old man with a 15-year history of diabetes and an ulcer with an area of 1.585 cm² (stage B, grade 1) on the dorsal surface of his left second toe since 6 months before the study. After 8 weeks of treatment, the width, length, area, and depth of his ulcer reduced. In this patient, the ulcer was completely reepithelialized and healed. Wound infection score was 4 at the first visit but decreased to 0 after 8 weeks. The improvement efficacy was 97.2%.

The second case was a 57 year-old man with a history of diabetes for 18 years. He had had a foot ulcer on the left plantar area since 6 months prior to the study. The area of the wound was 4.186 cm² (stage B, grade 1) on the first visit. The width, length, area, and depth of ulcer were decreased 6 weeks after the application of TCA 50% and new pink tissue (skin) was grown in from the edges and as islands on the ulcer surface. Wound infection score was decreased from 6 at the first visit to 1 after 6 weeks. The improvement efficacy was 68.6% (Figure 1).

Table 1. University of texas wound classification system

Stage	Grade 0	Grade 1	Grade 2	Grade 3
A	Preulcer or postulcer lesion No skin break	Superficial ulcer	Deep ulcer to tendon or capsule	Wound penetrating bone or joint
B	+ Infection	+ Infection	+ Infection	+ Infection
C	+ Ischemia	+ Ischemia	+ Ischemia	+ Ischemia
D	+ Infection and ischemia	+ Infection and ischemia	+ Infection and ischemia	+ Infection and ischemia

Table 2. Diabetic foot ulcer wound infection score that was used to evaluate an infected wound (based on the system from Knighton et al, as modified by Pecoraro et al).

Parameter	0	1	2	3
Purulent drainage	Absent	Present
Nonpurulent drainage (serous, sanguinous)	Absent	Mild: pink, barely perceptible	Moderate: pale red, defined edges	Severe
Erythema	None	Mild	Moderate	Severe: red to dark red
Induration	None	Mild	Moderate	Severe
Tenderness (sign)	None	Mild	Moderate	Severe
Pain (symptom)	None	Mild	Moderate	Severe
Local warmth (relative to uninfected contralateral foot)	Same	Mildly increased	Moderately increased	Severely increased

NOTE. Each of the 7 parameters was scored from 0 to 3, then all of the scores were added to generate a total wound infection score

Table 3. Demographic data and wound characteristics of patients with diabetic foot

Diabetic patients	Age (yrs)	sex	Duration of diabet	Duration of ulcer	Location of ulcer	ABI*	Staging of ulcer	Grading of ulcer
Case 1	51	Male	15 yrs	6 months	Dorsal surface of left second toe	0.92	B	1
Case 2	57	Male	18 yrs	6 months	Left plantar area	0.86	B	1
Case 3	68	Male	7 yrs	7 months	Dorsal surface of right forth toe	1.20	B	1
Case 4	31	Female	19 yrs	4 months	Left first toe	1.00	B	1
Case 5	64	Male	20 yrs	2 yrs	Right plantar area	0.90	B	2
Case 6	65	Male	6 yrs	9 months	Left plantar area	1.00	B	2

* Ankle Brachial index (ABI)

Table 4. Ulcer improvement of patients with diabetic foot before and after treatment

Diabetic patients		Before treatment	After treatment	Diabetic patients		Before treatment	After treatment
Case 1	Length× Width (cm)	1.88×1.11	1.2×0.28	Case 4	Length× Width (cm)	0.87×0.31	0×0
	Ulcer area (cm2)	1.585	0.331		Ulcer area (cm2)	0.259	0
	Ulcer depth (mm)	0	0		Ulcer depth (mm)	0.2	0
	Wound infection score	4	0		Wound infection score	5	0
Case 2	Length× Width (cm)	1.28×4.46	4.46×0.5	Case 5	Length× Width (cm)	2.14×1.01	1.23×0.37
	Ulcer area (cm2)	4.186	1.317		Ulcer area (cm2)	1.846	0.286
	Ulcer depth (mm)	1	0		Ulcer depth (mm)	2.5	1.5
	Wound infection score	6	1		Wound infection score	7	2
Case 3	Length× Width (cm)	0.78×0.56	0×0	Case6	Length× Width (cm)	1.56×0.59	0×0
	Ulcer area (cm2)	0.281	0		Ulcer area (cm2)	0.716	0
	Ulcer depth (mm)	0.5	0		Ulcer depth (mm)	2	0
	Wound infection score	4	1		Wound infection score	6	0



Figure 1. Treatment of diabetic foot ulcer before and after TCA

The third case was a 68 year-old man with a 7-year history of diabetes. An ulcer of 0.281cm² (stage B, grade 1) had developed on the dorsal surface of his right fourth toe 7 months prior to the study. In this patient, the width, length, area, and depth of ulcer reduced 8 weeks after TCA treatment and the ulcer was covered with epithelium. Wound infection score was 4 at the

first visit and 1 after 8 weeks. The improvement efficacy was 100%.

The fourth case was a 31 year-old woman with 19 years history of diabetes. Her ulcer was located on the left first toe, started 4 months before the study, and had an area of 0.259 cm² (stage B, grade 1). The width, length,



Case 4: Before treatment



Case 4: After 7 weeks of treatment

Figure 2. Treatment of diabetic foot ulcer before and after TCA

area, and depth of ulcer reduced after 7 weeks and new epithelium was formed. Wound infection score decreased from 5 at the first visit to 0 after 7 weeks. The improvement efficacy was 100% (Figure 2).

The fifth case was a 64 year-old man with a 20-year history of diabetes. He had an ulcer of 1.846 cm² (stage B, grade 2) on the right plantar area for 2 years. The width, length, area, and depth of the ulcer area reduced after 8 weeks of TCA treatment and new granulation tissue was formed. Wound infection score was 8 at the first visit but decreased to 2 after 8 weeks. The improvement efficacy was 84.6%.

The sixth case was a 65 year-old man with a 6-year history of diabetes and an ulcer of 0.716 cm² (stage B, grade 2) on the left plantar area since 9 months before the study. After 8 weeks of treatment, the width, length, area, and depth of his ulcer reduced and it was completely reepithelialized. Wound infection score was 6 at the first visit and 0 after 8 weeks. The improvement efficacy was 100%.

There were palpable dorsal pedal pulses in these 6 patients.

DISCUSSION

TCA is an established peeling agent commonly used for superficial and medium depth peel.^[15,16] While depth of peel depends on TCA concentration, high concentrations can be safely used since TCA is a self-neutralizing agent and is not thus absorbed in the circulation.^[17]

The suggested mechanism of chemical materials for wound repair and scars is the acceleration of cellular regeneration in the dermal and epidermal areas following induction of inflammation. TCA peeling is an appropriate method for treatment of cutaneous leishmaniasis, actinic keratosis, and photoaging.^[9] In deep ulcers, application of caustic materials can possibly give better results and cellular regeneration is accelerated as 2 weeks after TCA treatment.^[8]

TCA is able to promote necrotic coagulation of cells throughout extensive protein denaturation. It therefore causes death of structural cells. TCA concentration affects the depth of necrosis, i.e. medium level concentrations of TCA, such as 35% to 50%, can penetrate across the superficial papillary and mid-reticular dermis. Cy-

tologically atypical keratinocytes will be carried away by the epidermis and superficial dermis slough and will be compromised by dermal connective tissue after several days. By second use of TCA, the wound is repopulated by deep follicular epithelium and is healed. The skin is thus rejuvenated by generation of new connective tissue.^[18]

The histological effects of TCA peels are generated by a thickened, homogenized band of dermal collagen that is filled by the cytologic and architectural normalization of the epidermis.^[19]

The efficacy of TCA in increasing collagen I and III and elastic fibers has also been postulated.^[20,21] The observed efficacy of TCA in treatment of diabetic ulcer is due to production of granulation tissue and epithelial cells.

In this report, all wounds in the 6 treated patients were improved after a mean duration of 7.50 ± 0.83 weeks. In facts, significant reductions were observed in their areas and infection scores. The improvement efficacy ranged from 68.6% to 100% with no complications after 1, 2, and 3 months of follow up.

The results of this study may suggest a new convenient method for treatment of resistant, well-selected, diabetic ulcers. As the healing of long-standing diabetic foot ulcers depends on various factors such as aging, glucose control, off-loading, infection control, and life style, more detailed studies should be designed considering these factors before making any firm therapeutic conclusion.

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