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Limb salvage in extensive diabetic foot ulceration—a preliminary clinical study using simple debridement and herbal drinks

糖尿病人患嚴重足部潰瘍可避免截肢－使用清創術和草藥飲料的初步臨床研究

Diabetic patients frequently suffer from foot ulcer. In spite of the advances in treating many complicated diseases, amputation is usually the 'cure' for diabetic foot ulcer. Diabetic foot ulcer was treated in this study using Chinese herbal medicine and simple debridement as an alternative to amputation. Limb salvage was successful in 35 of 40 legs. These results encourage continuing research into the treatment of diabetic ulcer using Chinese herbal medicine.

糖尿病患者往往患有足潰瘍。縱使現今醫學可以治癒很多複雜的疾病，但截肢仍然是糖尿病足部潰瘍的一種療法。本研究使用中草藥和簡單的清創術替代截肢來治療糖尿病足潰瘍。在40條足潰瘍病腿中，有35條不需截肢。這些結果為使用中草藥治療糖尿病足潰瘍的研究帶來鼓勵。

Key words:
Diabetic foot;
Drugs, Chinese herbal;
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Introduction

A common complication among elderly patients suffering from diabetes mellitus is ulceration of the foot. Ulcers form as a result of minor trauma to the toes, often already compromised by peripheral neuropathy and/or vascular insufficiency. Such ulcers heal poorly due to these predisposing factors, as well as to the susceptibility to infection, and advanced age. Frequently, the ulcers enlarge, reducing the likelihood of healing. Spread of infection may lead to sepsis, while the ulcers also adversely affect control of the diabetic state.[1]

In spite of attempts to heal the ulcers, conservative and local treatments often fail. Amputation becomes inevitable when repeated treatment failure occurs. Limited amputations, such as metatarsal, mid-foot, or Chopart/Lisfranc type amputations may be appropriate. Due to the unsatisfactory vascular and neuropathic states, however, stump healing is a frequent problem.[2] In many orthopaedic units, the experience of poor stump healing in foot level amputations has prompted surgeons to rely on below-knee amputation as the standard practice. It has been argued that given that the use of a below-knee prosthesis is simple and straightforward, below-knee amputation should be preferred.[3] Unfortunately, even with below-knee amputations, primary stump healing is not guaranteed. Skin flap problems are common among diabetic patients and re-amputations sometimes become mandatory.[4]

Further questions also remain to be answered. Does amputation improve the elderly diabetic patients' well-being? Do elderly patients use leg prostheses well?[5] Elderly patients are often more limited in their daily activities. Even if they could manage a prosthesis well, they may prefer to retain the lower limb which, though not normal, may be adequate and preclude the fitting of an artificial limb.[6]

Chinese herbalists have long been credited with the ability to preserve the limb in situations of severe distal ulcerations. Herbalists are not capable of modern surgical intervention. Instead, they focus on the process of healing the ulcers without considering the alternative of amputation.[7]

The Shanghai Institute of Integrated Western and Chinese Medicine incorporates a section for the treatment of vascular diseases. This section uses a protocol of ulcer management consisting of simple daily surgical removal of dead tissue, while promoting healing through the use of a number of herbal drinks. The authors paid a visit to the institute in 1998, and convinced by the logic of the management and the outcomes, applied the same philosophy and methodology to the treatment of diabetic patients with foot ulcers.

Subjects and methods

Patients selected were diabetic patients with one or more foot ulcers, who were admitted to the orthopaedic ward because of ulcers or gangrene of the toe. Inclusion and exclusion criteria for the study are outlined in Box 1.

The Shanghai group had found that, irrespective of the size of the ulcer, the soft tissues—that is, the fat, tendinous and ligamentous tissues below it—underwent extensive necrosis, which extended well beyond the ulcer edges. The direction of extension of necrosis followed the tendons and joint capsules. Thorough removal of necrotic tissue, not only at the ulcer bed, but well beyond the ulcer boundary, was therefore required to heal the diabetic ulcers.[8]

Box 1. Inclusion and exclusion criteria

Inclusion criteria
(1) Ulcer or gangrene for more than 3 weeks;
(2) Lack of improvement with treatment at clinics, including local dressings and infection control;
(3) At least one of three peripheral pulses (dorsalis pedis, posterior tibial, and peroneal) in the vicinity of the ankle palpable;
(4) Non-smoker;
(5) Full consent given by patient and next of kin; and
(6) Patient advised to receive amputation

Exclusion criteria
(1) Total absence of peripheral pulses in the vicinity of the ankle;
(2) Unstable diabetic state; and
(3) Medically unfit because of cardiac, pulmonary, or other disease

Box 2. Herbal drink to strengthen muscle and control swelling (托毒生肌湯)： ingredients

Radix astragali (生黃芪)	20 g
Rhizoma atractylodis marcocephala (白朮)	9 g
Radix stephaniae tetrandrae (漢防己)	9 g
Radix polygoni multiflori (制首烏)	9 g
Radix rehmanniae (生地)	9 g
Radix smilax china (菝葜)	9 g

Box 3. Herbal drink to promote regeneration (芪味地黃湯)： ingredients

Radix rehmanniae (生地)	12 g
Fructus corni (山茱萸)	9 g
Rhizoma dioscoreae (山藥)	9 g
Cortex moutan (牡丹皮)	6 g
Rhizoma alismatis (澤瀉)	6 g
Rhizoma smilacis glabrae (茯苓)	6 g
Radix astragali (黃芪)	20 g
Fructus schisandrae (五味子)	6 g

In this study, treatment consisted of limited, repeated debridement completed daily without anaesthesia. Pain was minimal because of peripheral neuropathy. At the same time, herbal drinks were given to the patients. Two types of herbal drink were used—the first one was given when local circulation needed to be improved, and the second when granulations failed to appear. The first herbal preparation contained raw huang-chi (生黃芪) as the main ingredient (Box 2), while in the second preparation, huang-chi (黃芪) was the main component (Box 3). According to traditional Chinese medicine principles, the first preparation was to effect the strengthening of muscle and the control of swelling; the second preparation was given to promote regeneration.

Meanwhile, diabetic control was maintained using standard medical means. Similarly, infection control was achieved through the use of broad-spectrum antibiotics according to antibiotic sensitivities. Liver and renal function was assessed at 2-weekly intervals.

Since the ulcers (with or without gangrene of the toe) were unlikely to heal spontaneously, small pieces of split skin grafts were applied. Skin grafting had two advantages: firstly, closing down the area of ulcer exposure, and secondly, inducing an effective shrinkage of the ulcer size. Local anaesthesia was adequate for the skin-taking procedure because of the limited amount of skin graft required.

Results

From July 1999 to October 2000, 30 patients (with 40 ulcerated feet in total) were recruited into the study. Biographical and clinical data of the patients enrolled are shown in Table 1.

Table 1. Biographical and clinical patient data

Feature	Patients No. (%)
Sex	
Male	16 (53.3)
Female	14 (46.7)
Age (years)	
50-60	7 (23.3)
61-70	17 (56.7)
≥71	6 (20)
Affected foot	
Unilateral	20 (66.7)
Bilateral	10 (33.3)
No. of ulcers	
1	31 (77.5)
2	6 (15)
3	3 (7.5)
Gangrenous toe(s)	
0	17 (56.7)
1	5 (16.7)
2	5 (16.7)
3	2 (6.7)
4	1 (3.3)
Duration of ulcers before treatment (weeks)	
2	5 (16.7)
3	2 (6.7)
4	12 (40)
8	8 (26.7)
>8	3 (10)
Blood sugar level	
Well controlled	27 (90)
Poorly controlled	3 (10)
Ulcer infection	
Mild	20 (66.7)
Moderate	7 (23.3)
Septicaemia	3 (10)
Hypoaesthesia	
Mild	3 (10)
Moderate	12 (40)
Severe	15 (50)

Table 2. The vascular state and ulcer debridement

Vascular state	Patients No. (%)
Peripheral pulses	
Post-tibial artery pulse absent	20 (66.7)
Dorsalis pedis artery pulse absent	10 (33.3)
Both absent	7 (23.3)
Skin circulation (based on warmth, blanching, and turgor)	
Mildly ischaemic	13 (43.3)
Moderately ischaemic	12 (40)
Severely ischaemic	5 (16.7)
Ulcer debridement	
3-5 times	7 (23.3)
6-8 times	15 (50)
>8 times	8 (26.7)

Vascular state and ulcer debridement

Vascular state, as determined by Doppler stethoscope, and ulcer debridement are shown in Table 2.

Skin grafting

As soon as healthy granulations appeared on the ulcer, split skin grafting was considered and 'stamp-grafts' were taken under local anaesthesia. Healthy looking areas were grafted while unhealthy parts were left for further granulation formation. The number of times skin grafting was undertaken is summarised in Table 3.

Duration of healing

The duration required for healing was determined as the time between commencement of ulcer treatment and the termination of wound care and dressing. Of 35 feet rescued from amputation, 27 feet took less than 10 weeks to heal, five took 11 to 16 weeks, and three between 17 and 30 weeks (Table 4).

Herbal treatment

The first herbal preparation (2 packets per day) was given at the initiation of ulcer treatment. Once early signs of granulation were evident, the second preparation (2 packets per day) was also commenced. Adverse hepatic and renal function effects were not seen. When healthy granulations appeared, herbal treatment was discontinued. Three patients developed mild diarrhoea when the dosage was halved; there was no discontinuation of treatment. Clinically, improved local circulation, that is, improved skin warmth and colour was observed in all successful cases 2 to 5 days after treatment commenced.

Final outcome

Thirty-five legs were rescued from amputation by ulcer healing (Figs 1 and 2). Five of the 40 legs ($P<0.05$) in 30 patients required amputation due to the lack of a

Table 3. Skin grafting

Skin grafting	No. of feet
No skin grafting	2
Toe amputation alone	11
Once	16
Twice	6
Three times	3
Four times or more	2

Table 4. Duration of healing for 35 feet rescued from amputation

Duration (weeks)	Mean no. of weeks	No. of feet
5-10	7	27*
11-16	13	5
17-30	22	3

* $P<0.05$

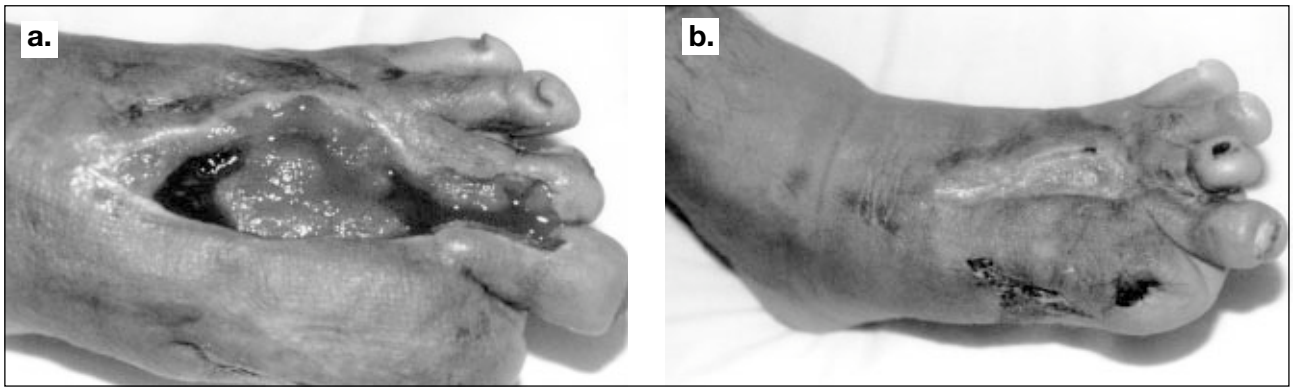

Fig 1. Foot ulcer before herbal treatment (a) and after herbal treatment (b)

Fig 2. Healed ulcer after herbal treatment and skin grafting
Note that in spite of the loss of toes, the foot retained the middle portion and weight-bearing ability

favourable response. Three did not show any sign of improvement, while in two others, infection proved a problem despite the use of antibiotics. Amputations occurred within 3 weeks of initiating limb salvage treatment. There was one death, of a Buddhist monk who refused any form of major surgical intervention. Case numbers were too small to allow correlation between the degree of control of diabetes and antibiotic use.

Discussion

Diabetic control is a relatively straightforward practice. Complications of diabetes are plentiful, however. Diabetic foot ulcers develop as a result of vascular insufficiency, neuropathy and infection, and sadly, quite frequently result in the sacrifice of the affected leg.

The treatment method followed in this study was recommended by an experienced group of Chinese physicians endeavouring to preserve affected legs in preference to amputation. They did not have the surgical facilities available to undertake amputation, or have an effective prosthetic service. Over many years of treating patients with diabetic ulcers, these physicians made the important observation of 'ligamento-necrosis', a Chinese term specially coined to describe the necrotic tissues within tendons and ligaments, underlying an ulcer and extending well beyond the apparent ulcer edges. They advocate gradual, thorough removal of these dead collagen tissues, without which normal granulation tissues would not appear and ulcers would not heal. This observation was not made during typical diagnosis and management of diabetic ulcers but might explain the frequent failure to achieve ulcer healing in diabetics.[7] The method recommended for necrotic tissue is repeated thorough debridement without anaesthesia. This allows clearance of the necrotic tissues, while leaving the local vascular state undisturbed. In contrast, modern surgeons are currently accustomed to undertaking procedures including radical debridement under general anaesthesia. This latter approach may remove unwanted tissues, but the radical process invariably induces further damage to the local vasculature, which does not facilitate ulcer healing. Moreover, necrosis of ligamentous tissues beyond the ulcers appears to be a progressive process, which does not cease after radical ulcer debridement.

The consumption of herbal preparations appeared to produce improvement in the local circulation in this study, as exemplified by improved warmth and colour of the toes. Granulation tissue formation at the ulcer bed was also noted as a sign of improvement. Such improvements would undoubtedly initiate quicker healing of the ulcers. When skin grafting was considered suitable to hasten the process, healthy granulation did allow earlier application.

Limb salvage was successful in 35 of 40 legs, in 30 patients. Five legs eventually required amputation in spite of repeated limited debridement and consumption of herbal preparations. Neither improvement in local circulation nor granulation formation was observed in three cases, while increasing infection was apparent

in the remaining two. These results indicate that treatment with a combination of repeated 'piecemeal' debridement and herbal drinks was able to rescue 87% of legs condemned for amputation due to non-healing diabetic ulcers.

At the time of preparing this preliminary report, further research is planned. The clinical effects of the herbal preparations require study using objective assessments of local circulation, histological changes in the granulation tissues, and histochemical changes in neuropathic state. The herbs should also be analysed biochemically, to identify important components that may lead to favourable responses in circulation, granulation formation, and possible improvements in immunological state. This follows the standard investigation approach in modern research on alternative medicine using herbs. The planned study—an evidence-based, double-blinded, randomised trial with placebo controls—should overcome shortcomings of the preliminary observations compiled in this report.

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