A randomised controlled trial on the effectiveness of an advanced wound dressing used in Iran

• **Objective:** To compare the wound healing rate and incidence of infection in wounds treated with either a bioactive dressing (containing hydrophilic mucopolysaccharide, chitosan) or conservative treatment (gauze).

• **Method:** Eighty-five patients with diabetic foot ulcers, pressure ulcers or leg ulcers were randomised to receive either the bioactive study dressing (n=33 patients, 45 wounds) or the control dressing (n=52 patients, 53 wounds) for 21 days. Wound size, stage where appropriate and the presence of infection were recorded at each dressing change. Thirty-one of these 85 patients dropped out of the study during the three-month post-treatment follow-up, when wound size and grade were assessed on a monthly basis. Data were therefore analysed on 54 patients, of whom 32 (34 wounds) were in the treatment group and 22 (26 wounds) in the control group.

• **Results:** In the control group, four pressure ulcers healed, but the remaining wounds all deteriorated and became infected, requiring antibiotics. In contrast, in the treatment group 29/34 wounds healed completely, and none became infected; the remaining five wounds healed during the follow-up period. The difference between the two groups in the number of wounds that healed was statistically significant ($p<0.001$), as was that for the number of healed pressure ulcers $p<0.05$.

• **Conclusion:** Use of a moist bioactive wound dressing significantly increased the healing rate when compared with the traditional dressings used in the participating hospitals. This will in turn bring significant cost savings.

• **Declaration of interest:** This study was sponsored by ChitoTech.

chronic wounds; infection; cost-effectiveness; bioactive dressings; gauze

Pressure ulcers are a serious and expensive medical problem, imposing a major burden on health-care systems in all countries. It has been estimated that 1.2–2.7% of all patients develop stage II or greater pressure ulcers while in hospital.[1,2] If stage I pressure ulcers are added to this, the figure rises to 5.4%.[3] However, in every country the occurrence of pressure ulceration is different.

Diabetic foot ulceration is increasing worldwide, with 15–20% resulting in amputation, further increasing the burden on health-care resources.[4,5]

Many developing countries still use traditional dressings such as gauze. However, advanced dressings are more likely to promote healing in chronic wounds. The Iranian company ChitoTech produces advanced wound dressings containing the biomaterial chitosan (hydrophilic mucopolysaccharide) and polysaccharide alginate. These dressings, which are suitable for all exudate levels, are produced in different forms, including transparent films, sprays, gels, impregnated pads and powder for cavity and tunnelling wounds. An impregnated pad contains alginate and the rest of the dressings comprise chitosan. As part of our application to the Iranian Ministry of Health for a licence for these dressings, we conducted the first randomised controlled trial to investigate their effectiveness.

Materials and method

Between 2004 and 2006, all inpatients in five major teaching hospitals in Tehran (Shariati Hospital, Imam Khomeini Hospital, Loghman Hospital, Sina Hospital and Imam Hossein Hospital) with pressure ulcers, diabetic foot ulcers and leg ulcers, regardless of the aetiology, wound size and depth, were eligible for recruitment. Exclusion criteria were:

- Pregnancy
- Addiction to cigarettes, alcohol and narcotics, including opium
- Immunocompromising conditions.

Ethics committee approval was obtained, and all patients gave written informed consent.

Patients were randomised to receive either the moist bioactive dressing (treatment group) or a traditional dressing in the form of gauze, bandage and adhesive tapes (control group).

Randomisation was concealed, but patients were

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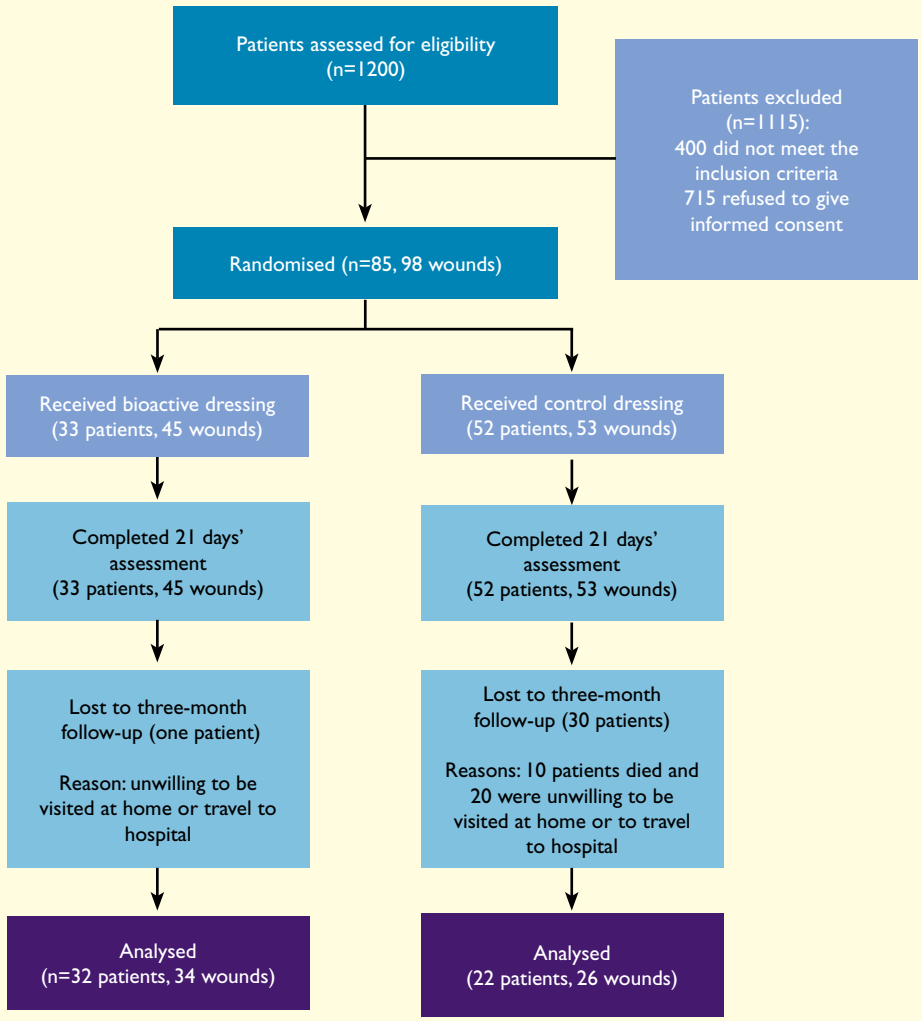
Fig 1. Flow of participants through the trial



allocated to the two groups in an alternating sequence.

The study was blinded, with the two dressings having similar packaging.

Baseline data included the wound aetiology, duration, location, size and stage, presence of infection, as well as the patient's gender, age, weight and comorbidities.

Wounds in the treatment group were irrigated with normal saline and, depending on the wound type and grade, a suitable form of the dressing was applied. The wound was then covered with a non–adherent pad and fixed with a polyurethane adhesive. Patients with heavily exuding wounds had their dressings changed every other day, and those with medium or low exudate had dressing changes every four days.

Patients in the control group received standard wound care in accordance with the hospitals' protocol. Wounds were irrigated with normal saline and covered with gauze secured with a bandage and adhesive tape. Dressings were changed once or twice daily, depending on the exudate level.

Wounds in both groups were debrided as required. None of the patients in either group were offered pressure relief, compression therapy or offloading.

The following were assessed at dressing changes:

- Wound size — photographs of the wound were scanned, and the exact length and width were calculated using AutoCAD 2000 software
- Wound grade — assessed using the National Pressure Ulcer Advisory Panel (NPUAP) classification scale for pressure ulcers, and the Wagner scale for diabetic foot ulcers
- Presence of infection — all wounds were swabbed if they showed clinical signs of infection. Wounds

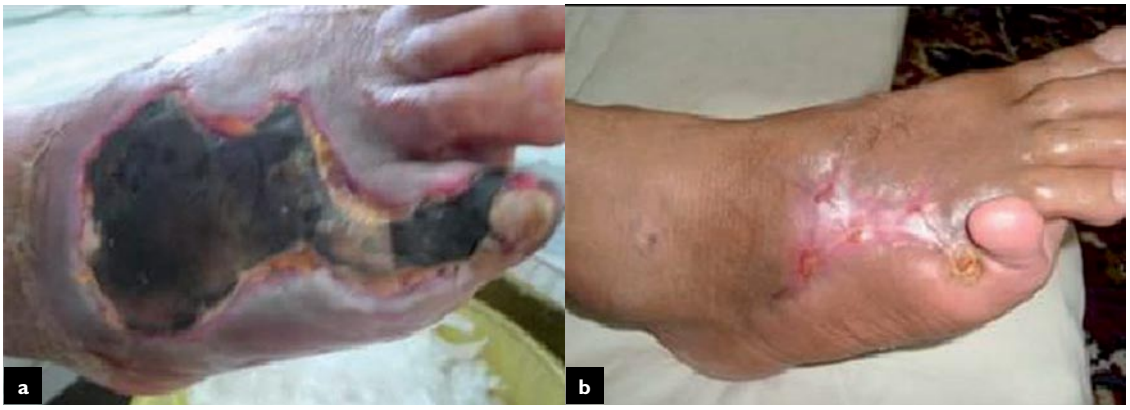


Fig 2. Diabetic foot ulcer in a 65-year-old patient in the treatment group: baseline (a) and after 58 days (b). Amputation had been recommended before entry into the study

were considered infected if the bacterial bioburden exceeded 10^5 colony forming units [CFU]/ml. However, if beta-haemolytic streptococcus was present, 10^3 CFU/ml was the indicator of infection.

The treatment period for both groups was 21 days, during which patients could be discharged from hospital at the physician's discretion.

Patients were then followed up for three months, with monthly visits either in the hospital or at home at which the wound size and grade were assessed. Use of the bioactive dressing was stopped after 21 days, and patients in both groups were treated with antibiotics, if required, and gauze.

The primary outcome measures were the rate of wound healing and presence of infection.

Data were analysed using analysis of variance (ANOVA) and chi-square test, using SPSS software. A p value of <0.05 was considered significant. The power is between 1.5 and 2 for a sample size (number of wounds) of 65.

Results

A total of 1200 patients were eligible for inclusion, but of these 1115 did not meet the exclusion criteria or withheld consent. Eighty-five patients (98 wounds) were therefore enrolled: 33 patients (45 wounds) were randomised to the treatment group and 52 patients (53 wounds) to the control group. However, of these 85 patients, 31 (38 wounds) either died or dropped out during the three-month follow-up period, and so were excluded from the data analysis. This left 32 patients (34 wounds) in the treatment group and 22 patients (26 wounds) in the control group. Fig 1 illustrates the flow of patients through the study.

The sample comprised 25 females and 29 males, with a comparable male:female ratio in the two groups. The mean age in the control and treatment groups was 41.2 and 45.8 years respectively. The mean age for entire sample was 43.42 ± 5.08 years.

Many patients were admitted because of traumatic injuries, generally resulting from falls in older patients and road traffic accidents. Comorbidities included cardiovascular disease, heart disease and diabetes. In many cases, pressure ulcers developed during the hospital stay. Unfortunately, exact figures for these are not available.

Wound types were also comparable between the two groups at baseline. Of the 26 wounds in the control group, 12 were pressure ulcers, eight were leg ulcers and six were diabetic foot ulcers. Of the 34 wounds in the treatment group, 16 were pressure ulcers, 12 were leg ulcers and six were diabetic foot ulcers. The mean wound size for the sample as a whole was 14.13 ± 2.3cm (length) x 8.24 ± 1.92cm (width). The mean wound duration was 21.5 ± 6.2 days.

Control group

During the 21-day study period, four pressure ulcers healed; three were stage I and one was stage II at baseline. However, the NPUAP stage increased progressively in the remaining eight ulcers from I to II and from III to IV. Five of the six diabetics foot ulcers increased from Wagner stage II to IV and the remaining ulcer from stage II to III. The mean area of the eight leg ulcers increased from 19.58cm^2 (5.41 x 3.62) at baseline to 58.50cm^2 (10.41 x 5.62).

All wounds were colonised ($<10^5$) at baseline. During the study 24 wounds became infected ($>10^5$ CFU/ml), with polymicrobial growth; an additional two wounds revealed beta-hemolytic streptococcus ($>10^3$ CFU/ml). All of these patients received antibiotics.

None of the patients in this group were discharged before day 21.

Treatment group

During the 21-day study period, 29 wounds healed completely, but five wounds in three patients (two stage IV pressure ulcers, one stage IV diabetic foot ulcer and two leg ulcers) did not heal completely during the treatment period, although the two pres-

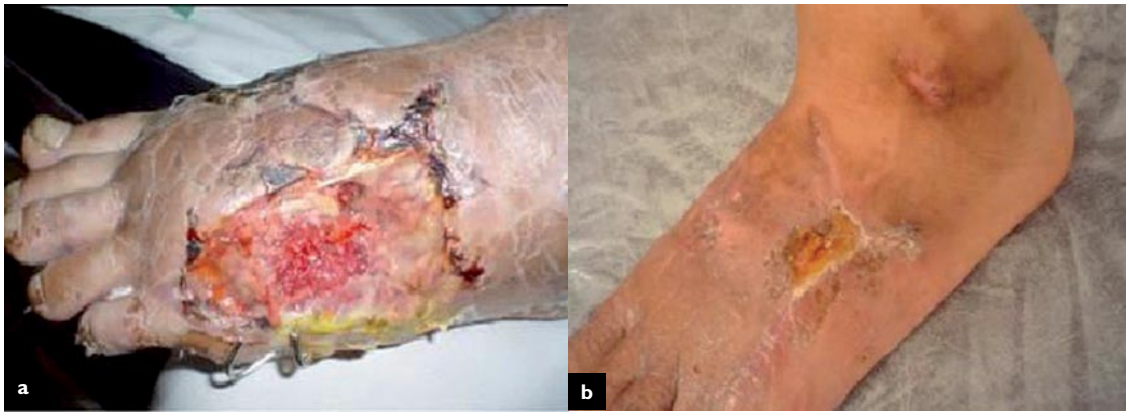


Fig 3. Wound caused by a crush injury with associated metatarsal fractures in a patient in the treatment group: baseline (a) and after 37 days (b)

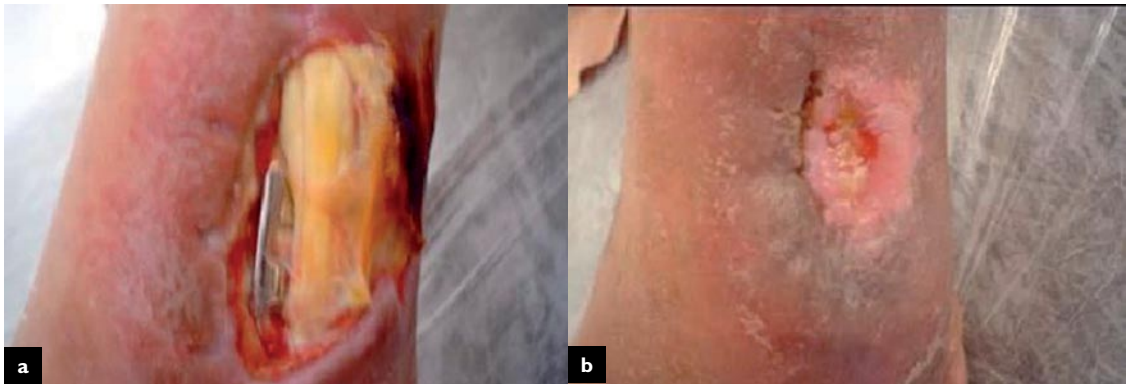


Fig 4. Dehisced wound following fixation of tibial fracture in a 58-year-old man in the treatment group: baseline (a) and after 60 days (b)

sure ulcers did reduce slightly in size. The mean area of the two leg ulcers decreased from 30.26cm^2 (7.12 x 4.25) at baseline to 11.98cm^2 (5.19 x 2.31) on day 21. However, the five wounds reported above did heal during the three-month follow-up period.

All 34 wounds in the treatment group were colonised at baseline. However, none became infected and the signs of colonisation disappeared as healing progressed.

All patients in the treatment group were discharged before day 21.

Overall findings

Twenty-nine wounds (85%) in the treatment group healed completely by day 21 versus four (15%) in the control group. This difference was statistically significant ($p<0.001$). The difference in healing rates between the two groups for pressure ulcers was also statistically significant ($p<0.05$).

Figs 2–5 show clinical examples of the healing achieved with the bioactive dressing.

Discussion

The most difficult aspects of chronic wounds are the prolonged healing times, risk of infection, deterioration of the patient's general health and weakening of the immune system, which can increase morbidity and even result in death.

This study demonstrated that use of a moist bioactive wound dressings decreased the length of hospital stay, and so would have, in turn, reduced hospital costs. Furthermore, in many cases it avoided the need for grafting or a flap.

All of the wounds treated with the advanced dressing healed faster than those treated with gauze in the control group, and unlike them none developed an infection.

While advanced wound dressings are commonly used in western countries, some practitioners in developing countries are still hesitant to stop using traditional methods of wound managements such as gauze.

However, we estimate that, despite their higher unit cost, the use of advanced dressings would save the Iranian national health-care system approximately US$ 140 million a year as a result of shorter hospital stays, a reduced need for antibiotics and surgical debridement, and fewer amputation. In addition, the economy as a whole would benefit as patients would be able to return to work earlier.

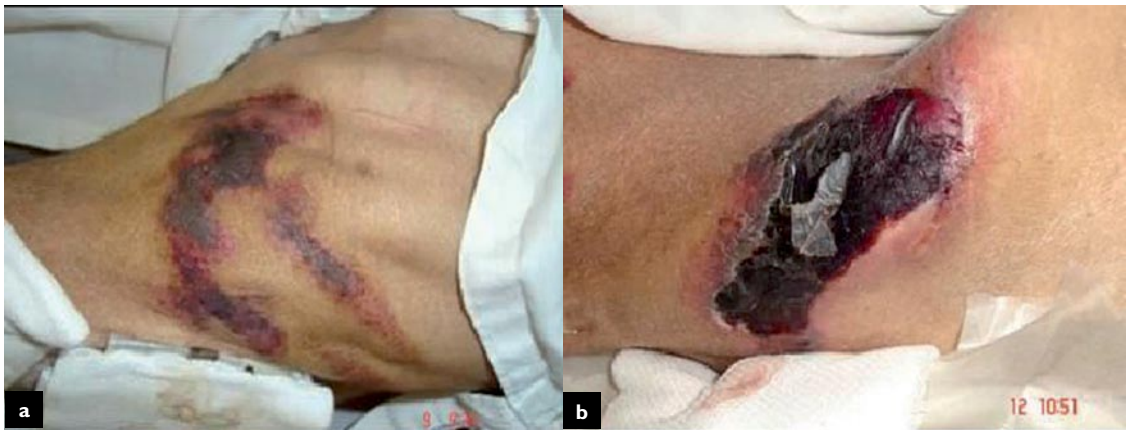


Fig 5. Stage I pressure ulcer in a 40-year-old patient in the control group: baseline (a) and following deterioration during the study (b)

The psychological benefits for the patient are beyond calculation.

Although this was a double-blind study, some of the patients invited to participate in the trial had already observed for themselves the marked benefits of the bioactive dressing before entry.

As a result, a large number (over 500) refused to participate for fear that they might be randomised into the control group.

Study limitations include the difference in size between the two groups, the short study period, inadequate blinding and the large drop-out rate in the follow-up period.

We selected a 21-day study duration as we wanted to avoid the prolonged use of gauze in the study design.

Conclusion

This study aimed to demonstrate that advanced methods of wound management are more effective in treating chronic wounds than gauze.

Advantage of this modern approach to wound include the:

- Acceleration in the wound-healing process
- Reduction in the length of hospital stay
- Reduced need for antibiotics
- Faster return to work.

Modern approach to wound management is gaining momentum in many countries and the present study exhibited that moist bioactive wound dressings would significantly reduce the duration of wound healing and consequently reduce the burden on the health care system. ■