Evidence of effectiveness needed to justify diabetic foot ulcer dressing choices

Sirs,

We thank Timmons and Chadwick (2010) for their comments on the large and detailed randomised trial we recently reported and in which we sought a difference between three dressing products (Aquacel [ConvaTec, Middlesex], Inadine, N-A [both Johnson & Johnson Medical, Berkshire]) in the routine management of foot ulcers (Jeffcoate et al, 2009). We found no difference in effectiveness, although Aquacel was more expensive. Constructive criticism of published work is always welcome and they raise some points for debate.

How representative was the population?

Timmons and Chadwick claim that our selection criteria meant that we excluded many who form "a large percentage of cases in clinical practice". We disagree.

The principal difficulty encountered in the design of any randomised controlled trial is the need to address the balance between rigorous selection of the population to maximise scientific precision, and the study of a more inclusive population that has greater relevance to general clinical practice. This is especially true when the number of participating centres is relatively small, as in this case.

The people invited to take part in our study were as representative of routine outpatient clinical practice as they possibly could be. It is true that we excluded those with severe peripheral arterial disease (ankle–brachial pressure index <0.7), as well as those being considered for revascularisation, because each would have been a significant confounder. We also excluded those with active infection at recruitment. We did not, however, exclude those who had undergone previous revascularisation, nor did we withdraw those who developed infection during the course of the trial.

Inappropriate use of trial dressings for different ulcers?

Timmons and Chadwick also comment on the implications of applying Aquacel to wounds without excessive exudate, and of applying non-absorbent (primary) dressings (such as N-A and Inadine) to wounds that were more moist. They suggest that the use of N-A in exuding wounds may explain the high withdrawal rate in that group. If so, it makes no sense that they add "Inadine is also non-absorbent and its use [in exuding] wounds could have resulted in similar problems". It could have done, but it did not; the withdrawal rate in the Inadine group was the lowest of the three.

There was absolutely no discernible difference in healing between the three products – no matter what the level of exudate. Timmons and Chadwick imply that we mistakenly exercised judgment when they report that an observed lack of difference between groups was "not considered statistically significant". This is misleading: the difference in question was not statistically significant.

It is also worth adding that we have found no statement in the current ConvaTec literature on either Aquacel or Aquacel Ag that specifies that they should be reserved for exuding wounds.

Should all dressing changes have been undertaken by healthcare professionals?

We refute the suggestion that all dressing changes that took place during the trial should have been undertaken by trained healthcare professionals. While this may be appropriate in a study of efficacy, it is not appropriate in one of effectiveness – because this is not what happens in clinical practice. Moreover, relatives and carers who opt to undertake dressing changes will often do it with equal, if not greater, skill than many a

healthcare professional. It should be noted that there was considerable variation between centres regarding the proportion of dressing changes being undertaken by healthcare professionals (from 22% to 82%), but there was no difference between centres in outcome. We do not agree that the involvement of non-professionals in dressing changes "throws doubt on the conclusions".

Choice of endpoint

The main difficulty to be addressed in the design of any trial of this type – and especially a comparison of interventions for a complex clinical condition such as diabetic foot ulceration, in which the response to management can be slow and uncertain – is the choice of primary endpoint. The effect of a dressing product on healing (which was our primary endpoint) can be diluted or masked by a number of other factors.

In designing such a trial, researchers make a choice between a short-term, surrogate, endpoint (such as wound-bed appearance or cross-sectional wound area) with an increased chance of reflecting any action of the intervention being studied, and a long-term outcome (such as healing) that is of greater relevance to clinical practice. The difference in endpoints is, once again, the difference between studies of efficacy (attempting to see if an intervention might work in clinical practice) and effectiveness (to see if it actually does). The study in question was specifically planned with the latter in mind.

The choice we made

We did our best to design a robust study despite the acknowledged, but largely inescapable, difficulties imposed by trial design in this sort of work. Our principal findings were that, in a relatively unselected population with diabetic foot ulcers, there was no difference between the three products in healing by either 12 or 24 weeks, in speed of healing, in incidence of secondary infection or of any other adverse outcome. The only differences that were observed between groups were that the use of N-A was associated with less pain (although this may have been an effect of chance, resulting from analysis of multiple secondary outcomes) and of cost (Aquacel was significantly more expensive).

Consensus

Our principal conclusion, however, was that new, and generally more expensive, interventions should not be adopted in routine clinical practice without convincing evidence of effectiveness. It is unfortunate that dressings and applications are usually marketed as devices, rather than medicines, because there is no requirement for the manufacturer to demonstrate effectiveness of a device, only safety. In this respect, we were pleased that Timmons and Chadwick concluded their commentary by stating that "dressings manufacturers [should] carry out clinically relevant studies prior to the launch on new dressings". Ultimately, therefore, we wholeheartedly agree with each other. ■

Yours sincerely,

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Jeffcoate WJ, Price PE, Phillips CJ et al (2009) Randomised controlled trial of the use of three dressing preparations in the management of chronic ulceration of the foot in diabetes. *Health Technol Assess* **13**: 1–86, iii-iv

Timmons J, Chadwick P (2010) Right product, right wound, right time? *The Diabetic Foot Journal* **13**: 62–6