Antimicrobial silver versus non-adherent dressings for venous leg ulcers: the VULCAN trial

A prospective randomised controlled trial and economic modelling of antimicrobial silver dressings versus non-adherent control dressings for venous leg ulcers: the VULCAN trial

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Executive summary

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Executive summary

Background

Venous leg ulcers are a major health problem and result in considerable costs and morbidity for health services. Despite a lack of clinical evidence of cost-effectiveness, the use of dressings containing antimicrobials has become commonplace for venous leg ulcers, with a particularly rapid rise in the adoption of new silver-donating antimicrobial dressings.

Objectives

The objective of this study was to examine the effectiveness and cost-effectiveness of antimicrobial silver-donating dressings for venous leg ulcers compared with simple non-adherent (also known as low-adherent) dressings, both used beneath compression bandaging.

The aims were to:

- Collect cost and outcome data through a randomised controlled clinical trial of silver-donating antimicrobial dressings versus non-antimicrobial low-adherent control dressings applied to venous ulcers.
- Collect data from an observational arm of the study regarding treatment, clinical outcomes and costs of the management of venous leg ulcers.
- Carry out an economic analysis alongside the clinical trial to estimate the cost-effectiveness of antimicrobial dressings for venous leg ulcers.
- Develop a cost-effectiveness model of venous ulceration and to populate this with data from the trial and published literature.
- Examine the cost-effectiveness of using antimicrobial dressings in different circumstances and with differing sets of assumptions.
- Document current routine practice regarding the use of antimicrobial agents in the treatment of venous ulcers.

Methods

Design

The study was a pragmatic, prospective randomised controlled trial (RCT) and cost-effectiveness analysis of antimicrobial silver-donating dressings versus low-adherent control dressings beneath compression bandaging in the treatment of venous leg ulcers.

Setting

This was a multicentre study that recruited patients in primary and secondary care services in two areas, in the north and south of England.

Participants

Participants were consenting patients with active venous ulceration of the lower leg that had been present for a period of greater than 6 weeks.

Interventions

Patients were randomised to receive either silver-donating dressings or low-adherent dressings without any antimicrobial substances (control dressings), applied beneath compression bandages or hosiery. The choice of dressing within the two groups was left to clinician preference. Evaluation was by clinical assessment, supplemented by evaluation of quality of life and cost-effectiveness.

Main outcome measures

The primary outcome measure was complete ulcer healing at 12 weeks in the index limb. Secondary measures were costs and resource use, quality-adjusted life-years (QALYs), cost-effectiveness, time to healing, and recurrence rates at 6 months and 1 year.

Results

Recruitment was slower than anticipated due to encountering organisational, cultural and bureaucratic obstacles. In total, 304 participants were recruited to the clinical trial. A total of 213 were recruited to the RCT and 91 to the observational arm. Within the RCT, 107 were randomised to silver-donating antimicrobial dressings and 106 to the control dressings. There were no significant differences ($p > 0.05$) between the two groups for the primary outcome measure of proportion of ulcers healed at 12 weeks (59.6% for silver and 56.7% for control dressings). The overall median time to healing was also not significantly different between the two groups ($p = 0.408$).

A total of 24 patients had recurrent ulcers within 1 year: the recurrence rates of 11.6% ($n = 11$) for the antimicrobial and 14.4% ($n = 13$) for the control dressings were not significantly different.

Mean utility valuations for both the EuroQol 5 dimensions (EQ-5D) and Short Form 6 dimensions (SF-6D) showed no statistically significant differences between the groups at 1, 3, 6 or 12 months. In comparison with the control group, the antimicrobial group had an incremental cost of £97.85 and an incremental QALY gain of 0.0002, giving an incremental cost-effectiveness ratio for the antimicrobial dressings of £489,250. Cost-effectiveness modelling of the results of the RCT showed, for the base-case model, that only included variables that were predictive of healing antimicrobial dressings were not cost-effective. Sensitivity analysis where dressing type was forced (i.e used as a predictive variable regardless of statistical significance) into the model, and a small benefit in utility that was assumed to occur at the point of healing, resulted in a small average incremental benefit for the antimicrobial dressings. However, this was not sufficient to justify the additional cost and there remained a high probability that the treatment was not cost-effective.

Conclusions

The key finding of this study was that there was no significant difference in either primary or secondary end points between the use of antimicrobial silver dressings and the control group of low-adherent dressings. The cost analysis showed a significantly higher cost for those treated with antimicrobial dressings. Cost-effectiveness modelling showed antimicrobial dressings to be dominated by inert dressings, with there being no difference in clinical outcomes and a higher cost associated with the antimicrobial dressings.

Antimicrobial dressings have been widely adopted without positive clinical evidence and our surveys suggested that silver-donating antimicrobial dressings have become widely used. If this reflects national practice then the implication is that the National Health Service (NHS) could be spending several million pounds on dressings each year with no evidence of clinical benefit.

Implications for health care

The results of this trial have the following implications for health care:

- The evidence suggests that there are no significant benefits in ulcer healing from using silver antimicrobial dressings beneath compression therapy.
- The use of less expensive low- or non-adherent dressings is recommended in preference to antimicrobial silver dressings.
- The results suggest that there is no indication for the regular use of antimicrobial dressings in general in promoting the healing of venous ulcers.
- The finding of very widespread use of silver-donating dressings, shown by this trial not to be cost-effective, should stimulate the NHS to encourage and facilitate recruitment of patients to large, well-designed studies of new technologies before it disseminates in an uncontrolled way.
- This trial has illustrated a number of the bureaucratic, organisational and cultural obstacles to research, which need to be addressed centrally, for improved development of cost-effective services in the long term. In particular, effective mechanisms for engaging frontline clinical staff with the NHS research agenda are urgently required.

Recommendations for future research

The following are recommendations are made:

- The development of a disease-specific quality of life measure for venous ulcer patients that

can be used in economic evaluation would be an advantage for future studies.
- The differences in healing rates between the two geographical areas of this study have implications for future research. They emphasise the need for very clear descriptions of epidemiology, treatment methods and the experience of staff engaged in compression bandaging; and they suggest an advantage to multicentre studies in different geographical areas, to produce results which can reasonably be generalised to the population as a whole.
- It is recommended that research into new treatments for leg ulcers includes mathematical modelling to establish the potential value of further clinical trials, and to assist in appropriate trial design prior to undertaking large and expensive clinical trials.
- This study has not addressed the problems of ulcers that fail to heal after 12 weeks of compression, or the problem of patients who are unable to tolerate compression. It is uncertain whether antimicrobial dressings might have any advantages in either of those situations.
- Uncertainty also remains about the diagnosis of 'infection' in leg ulcers which might be relevant to the use of antimicrobials. These are complex areas for research, but more information would be useful to guide clinical practice.
- Further studies are needed into how clinicians make decisions regarding dressing type and, in particular, the influence of sales representatives as sources of evidence and guidance.

Trial registration

This trial is registered as ISRCTN72485131.

Publication

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 02/10/02. The contractual start date was in July 2004. The draft report began editorial review in August 2008 and was accepted for publication in April 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

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