

A series of systematic reviews to inform a decision analysis for sampling and treating infected diabetic foot ulcers

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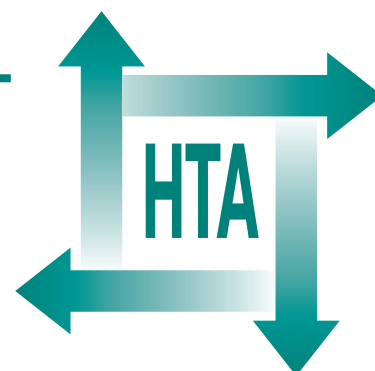
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Executive summary

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Executive summary

Background

Around 6% of people with diabetes have a foot ulcer or have a history of one. Diabetic foot ulcers (DFUs) are associated with increased mortality, illness and reduced quality of life. Diagnosing infection in DFU accurately and administering antibiotics may be important as infection can lead to amputation. However, using antimicrobial agents inappropriately could be costly, and lead to increased bacterial resistance. This review concentrates on the diagnosis of infection and the management of DFUs with antimicrobial agents.

Objectives

The objectives of this study were:

- To review systematically the evidence on the performance of diagnostic tests used to identify infection in DFUs and of interventions to treat infected DFUs.
- To use estimates derived from the systematic reviews to create a decision analytic model in order to identify the most effective method of diagnosing and treating infection and to identify areas of research that would lead to large reductions in clinical uncertainty.

Methods

Data sources

Electronic searches were made of 19 databases covering the period from inception of each database to November 2002. In addition, handsearches of book chapters, conference proceedings, a journal and bibliographies of retrieved studies were carried out. Internet searches were also made.

Study selection

Studies that dealt with the following areas were selected.

Diagnosis

Studies of the diagnosis of infection in people with DFUs or venous leg ulceration where a reference standard was compared with an alternative assessment.

Effectiveness

Randomised controlled trials (RCTs) or controlled clinical trials (CCTs) of the effect of microbiological analysis or antimicrobial agents in people with DFUs.

Cost-effectiveness

Economic evaluations of eligible interventions studied in which costs and effectiveness were synthesised.

Modelling

Economic or decision analytic models in which the progress of patients with DFUs was described in sufficient detail to allow replication of the model.

Data extraction

Quality checklists and data extraction forms for each study design were completed by one reviewer and checked by a second. Interviews were held with experts to inform gaps in the evidence.

Data synthesis

Studies were described in a narrative review. The structure of a decision analytic model was derived for two groups of patients in whom diagnostic tests were likely to be used.

Results

Diagnosis

Three studies investigated the performance of diagnostic tests for infection on populations including people with diabetic foot ulcers. One study investigated the performance of clinical assessment, another investigated the performance of punch biopsy versus wound swab and quantitative analysis and the third compared quantitative and semi-quantitative wound swabs in people with chronic wounds, including DFUs, for the identification of infection. These studies, all of which looked at identifying infection in chronic wounds, found that:

- There was no evidence that single items on a clinical examination checklist were reliable in identifying infection in DFUs.
- Wound swabs performed poorly against wound biopsies.
- Semi-quantitative analysis of wound swabs may be a useful alternative to quantitative analysis.

For the three diagnostic studies few people with DFUs were included, so it was not possible to tell whether diagnostic performance differs for DFUs relative to wounds of other aetiologies.

Effectiveness

Twenty-three studies investigated the effectiveness ($n = 23$) or cost-effectiveness ($n = 2$) of antimicrobial agents for DFU. Eight studied intravenous antibiotics, five oral antibiotics, four different topical agents such as dressings, four subcutaneous granulocyte colony stimulating factor (G-CSF), one evaluated oral and topical Ayurvedic preparations and one compared topical sugar versus antibiotics versus standard care.

The majority of trials were underpowered and were too dissimilar to be pooled. There was no strong evidence for recommending any particular antimicrobial agent for the prevention of amputation, resolution of infection or ulcer healing. Topical pexiganan cream may be as effective as oral antibiotic treatment with ofloxacin for the resolution of local infection.

Ampicillin and sulbactam were less costly than imipenem and cilastatin, a growth factor (G-CSF) was less costly than standard care and cadexomer iodine dressings may be less costly than daily dressings.

Decision analytic model

A decision analytic model was derived for two groups of people, those for whom diagnostic testing would inform treatment – people with ulcers which do not appear infected but whose ulcer is not progressing despite optimal concurrent treatment – and those in whom a first course of antibiotics (prescribed empirically) have failed. There was insufficient information from the systematic reviews or interviews with experts to populate the model with transition probabilities for the sensitivity and specificity of diagnosis of infection in DFUs. Similarly, there was insufficient information on the probabilities of healing, amputation or death in the intervention studies for the two populations of interest. Therefore, we were unable to run the model to inform the most effective diagnostic and treatment strategy.

Conclusions

Implications for healthcare

The available evidence was too weak to be able to draw reliable implications for practice. This means that, in terms of diagnosis, infection in DFUs cannot be reliably identified using clinical assessment. This also has implications for determining which patients need formal diagnostic testing for infection, whether empirical treatment with antibiotics (before the results of diagnostic tests are available) leads to better outcomes, and identifying the optimal methods of diagnostic testing. With respect to treatment, we do not know whether treatment with systemic or local antibiotics leads to better outcomes or whether any particular agent is more effective. Limited evidence suggests that both G-CSF and cadexomer iodine dressings may be less expensive than 'standard' care, that ampicillin/sulbactam may be less costly than imipenem/cilastatin, and also that an unlicensed cream (pexiganan) may be as effective as oral ofloxacin.

Implications for research

Questions to be answered are:

- What characteristics of infection in people with DFUs influence healing and amputation outcomes?
- Does detecting infection prior to treatment offer any benefit over empirical therapy?
- If detecting infection offers clinical benefit, then what are the most effective and cost-effective methods for detecting infection, e.g. clinical assessment, wound swabbing or wound biopsy and microbiological analysis, or novel techniques such as electronic nose/tongue and polymerase chain reaction analysis?
- What are the relative effectiveness and cost-effectiveness of antimicrobial interventions for DFU infection, e.g. combinations of broad-spectrum antibiotics, larval therapy, growth factors and topical agents/dressings?

Publication

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NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts. Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 01/05/02. The contractual start date was in July 2002. The draft report began editorial review in June 2004 and was accepted for publication in August 2005. 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.

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