Systematic review of the effectiveness of preventing and treating *Staphylococcus aureus* carriage in reducing peritoneal catheter-related infections

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**Executive summary**

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**Objectives**

The objectives of this review were to determine the clinical effectiveness and cost-effectiveness of alternative strategies for the prevention and eradication of *Staphylococcus aureus* carriage in patients on peritoneal dialysis (PD). The aim was to prevent, or reduce, the frequency of peritonitis. The review does not cover treatment of peritonitis itself.

**Background and intervention**

In chronic renal failure, dialysis is used to replace the kidneys’ function in removing impurities and unwanted products of metabolism from the blood. Peritoneal dialysis is a form of ambulatory dialysis in which fluid is fed into the abdominal cavity via a catheter through the abdominal wall. The fluid collects the substances normally excreted by the kidney. After an interval the fluid is drained out again.

The main complication of peritoneal dialysis in the short term is infection of the peritoneal cavity, peritonitis. In the longer term, recurrent episodes of peritonitis can impair diffusion across the peritoneal membrane, so that peritoneal dialysis is no longer feasible, which means that patients have to attend hospital for haemodialysis, usually three times per week.

One of the organisms which cause peritonitis is *Staphylococcus aureus*. It can colonise parts of the body without symptoms, but may cause infection where the peritoneal catheter passes through the skin of the abdomen. These are known as exit-site infections. It may also contaminate the tip of the catheter. In both situations, peritonitis may be a consequence.

Various measures have been used to try to prevent or eradicate colonisation, in the hope that this will prevent, or reduce, the frequency of peritonitis. These include antiseptics and antibiotics. The antibiotics can be applied locally or given systemically, by mouth.

*S. aureus* can develop resistance to commonly used antibiotics, and is then known as methicillin-resistant *Staphylococcus aureus* (MRSA).

**Epidemiology**

End-stage renal failure can be a consequence of a number of diseases, the commonest being glomerulonephritis, diabetes, renal vascular disease, pyelonephritis and polycystic kidney disease.

**Methods**

Electronic searches were undertaken to identify published and unpublished reports of randomised controlled trials (RCTs) and systematic reviews evaluating the effectiveness of preventing and treating *S. aureus* carriage on peritoneal catheter-related infections. The main databases searched were MEDLINE (1966–2005), EMBASE (1980–2005), CINAHL (1982–2005), BIOSIS (1985–2005), Science Citation Index (SCI) (1980–2005), MEDLINE Extra (6 January 2006), Cochrane Library (Issue 4 2005), Database of Abstracts of Reviews of Effectiveness (December 2005) and HTA Database (December 2005). The quality of the included studies was assessed and data synthesised. Where data were not sufficient for formal meta-analysis, a qualitative narrative review looking for consistency between studies was performed.

**Results**

**Number and quality of studies and summary of benefits**

Twenty-two trials were found. These fell into several groups: the first split is between prophylactic trials, aiming to prevent carriage, and trials which aimed to eradicate carriage in those who already had it; the second split is between antiseptics and antibiotics; and the third split is between those that included patients having the catheter inserted before dialysis started and people already on dialysis. Many of the trials were small or short-term. The quality was often not good by today’s standards. The body of evidence suggested a reduction in exit-site infections but this did not seem to lead to a significant reduction in peritonitis, although to some extent this reflected insufficient power in the studies and a low incidence of peritonitis in them.
Costs
The costs of interventions to prevent or treat *S. aureus* carriage are relatively modest. For example, the annual cost of antibiotic treatment of *S. aureus* carriage per identified carrier of *S. aureus* was estimated at £179 (£73 screening and £106 cost of antibiotic). However, without better data on the effectiveness of the interventions, it is not clear whether such costs are offset by the cost of treating infections and averting changes from peritoneal dialysis to haemodialysis.

Cost-effectiveness
Although treatment is not expensive, the lack of convincing evidence of clinical effectiveness made cost-effectiveness analysis unrewarding at present. However, consideration was given to the factors needed in a hypothetical model describing patient pathways from methods to prevent *S. aureus* carriage, its detection and treatment and the detection and treatment of the consequences of *S. aureus* (e.g. catheter infections and peritonitis). Had data been available, the model would have compared the cost-effectiveness of alternative interventions from the perspective of the UK NHS, but as such it helped identify what future research would be needed to fill the gaps.

Conclusions
The importance of peritonitis is not in doubt. It is the main cause of people having to switch from peritoneal dialysis to haemodialysis, which leads to reduced quality of life for patients and increased costs to the NHS. Unfortunately, the present evidence base for the prevention of peritonitis is disappointing; it suggests that the interventions reduce exit-site infections but not peritonitis, although this may be due to trials being in too small numbers for too short periods.

Recommendations for research
The study identified key research questions that need to be addressed. These are given below.

- What is the natural history of carriage of *S. aureus*? What are the links between carriage and exit-site infection, and between exit-site infection and peritonitis? What factors predict carriage?
- Is the problem mainly with MRSA, with methicillin-sensitive *Staphylococcus aureus* (MSSA) being relatively harmless?
- Does decolonisation work, or is recolonisation rapid?
- Apart from antibiotic and antiseptic use, what other options for reducing peritonitis are there? Would more training help?
- Should measures to eradicate carriage be intermittent or chronic; antiseptics versus antibiotics?
- Is vaccination worth revisiting?
- Given the common use of mupirocin in renal units, research into that drug and resistance to it should be a priority.

Trials are needed with larger numbers of patients for longer durations.

Publication
The Health Technology Assessment (HTA) programme, now part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the costs, effectiveness and broader impact of health technologies 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 research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the ‘National Knowledge Service’.

The HTA Programme is needs-led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, the public and consumer groups and professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Secondly, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Thirdly, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer-reviewed by a number of independent expert referees before publication in the widely read monograph series *Health Technology Assessment*.

**Criteria for inclusion in the HTA monograph series**

Reports are published in the HTA monograph series if (1) they have resulted from work for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

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 05/29/01. The contractual start date was in September 2005. The draft report began editorial review in May 2006 and was accepted for publication in February 2007. 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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