Types of urethral catheter for reducing symptomatic urinary tract infections in hospitalised adults requiring short-term catheterisation: multicentre randomised controlled trial and economic evaluation of antimicrobial- and antiseptic-impregnated urethral catheters (the CATHETER trial)

R Pickard,[1] T Lam,[2] G MacLennan,[3] K Starr,[2,3] M Kilonzo,[4] G McPherson,[3] K Gillies,[3] A McDonald,[3] K Walton,[5] B Buckley,[6] C Glazener,[3] C Boachie,[3] J Burr,[3] J Norrie,[3] L Vale,[3,7] A Grant[8] and J N'Dow[2]*

[1]Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK
[2]Academic Urology Unit, University of Aberdeen, Aberdeen, UK
[3]Health Services Research Unit, University of Aberdeen, Aberdeen, UK
[4]Health Economics Research Unit, University of Aberdeen, Aberdeen, UK
[5]Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK
[6]Department of General Practice, National University of Ireland, Galway, Ireland
[7]Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK
[8]Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK

*Corresponding author

Executive summary

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Executive summary

Background

Minimisation of health-care-associated infections, particularly within hospitals, is a key aspect of patient safety initiatives in many countries with well-developed health systems such as the UK. Catheter-associated urinary tract infection (CAUTI) is the second most common cause of hospital-acquired infection, and its prevention is therefore an important part of these initiatives. Urethral catheterisation remains a highly prevalent intervention in the care of patients admitted to hospital, particularly for elective surgical procedures, with approximately 15–25% of the 14.5 million patients admitted to NHS England hospitals being catheterised at some point during their stay. The risk of CAUTI is mainly related to the duration of catheterisation, occurring at a rate of 5% per day. This means that, assuming an average duration of catheterisation of 3 days, about 435,000 patients are likely to be affected in the English NHS each year, although most episodes are symptomless. One putative method of reducing CAUTI risk is to use catheters containing antimicrobial agents that inhibit bacterial contamination of the urethra and bladder. Two such devices are available to the NHS: a silver alloy-coated latex (natural rubber) catheter utilising the antiseptic properties of silver ions and a nitrofurazone-impregnated silicone plastic catheter utilising the antimicrobial action of nitrofurazone. This research was commissioned by the UK government National Institute for Health Research Health Technology Assessment programme to investigate whether either of these two devices would be clinically effective and cost-effective in reducing CAUTI risk in the UK NHS.

Objectives

The research set out to determine whether or not the use of antimicrobial catheters in people who undergo short-term urethral catheterisation as part of their routine care in UK NHS hospitals would result in a lower rate of symptomatic UTI compared with standard urethral catheters, and whether or not they would be cost-effective for use in the UK NHS.

Our initial hypothesis was that use of either antimicrobial catheter would result in a 30% relative reduction in the rate of antibiotic-treated symptomatic CAUTI occurring at up to 6 weeks following catheter insertion compared with the control of standard catheter use.

Two pragmatic comparisons of equal importance were made:

- antimicrobial-impregnated silicone catheter (nitrofurazone) compared with standard polytetrafluoroethylene (PTFE)-coated latex catheter
- antiseptic-coated hydrogel latex catheter (silver alloy) compared with standard PTFE-coated latex catheter.

Methods

Adults undergoing urethral catheterisation with an anticipated duration of between 1 and 14 days were identified in 24 UK NHS hospitals. Exclusion criteria were an expected duration of catheterisation of > 14 days or < 1 day, having undergone a urethral procedure in the last 7 days, the need for catheterisation by a non-urethral route, allergy to catheter materials, the presence

of a microbiologically confirmed symptomatic urinary tract infection (UTI) and inability to give informed consent. Those fulfilling the relevant criteria were invited to participate by local clinical research staff and consented for randomisation. Eligible and consented participants were randomised to one of the three trial interventions: silver alloy-coated catheter, nitrofurazone-impregnated catheter or standard PTFE catheter.

Baseline data were collected from each participant by completion of a case report form, patient-completed questionnaire and microbiological examination of a urine sample. The primary clinical effectiveness outcome was the occurrence of at least one UTI, defined as the presence of participant-reported symptoms and clinician prescription of antibiotic drug for a UTI at any point up to 6 weeks after randomisation. The primary economic outcome was the incremental cost per UTI avoided. Outcome data were collected by local trial staff during hospital stay; participant questionnaire and case report form at 3 days following catheter removal; participant diary at 1 and 2 weeks after catheter removal; and participant questionnaire at 6 weeks after randomisation. Collection of primary outcome data was completed when necessary by telephone contact with the participants or communication with their general practitioner. Microbiological examination of a urine sample was performed at baseline and at 3 days after catheter removal. Data collected included UTI symptom questionnaire, European Quality of Life-5 Dimensions (EQ-5D), antibiotic use, use of health service resources over the 6-week trial period, and microbiological report of urine specimens at baseline and 3 days after catheter removal. The primary economic analysis was based on a decision-analytical model, which compared the three catheters in terms of both NHS costs and quality-adjusted life-years (QALYs), based on responses to the EQ-5D. A within-trial cost-effectiveness analysis and cost–utility analysis were also performed. For both economic evaluations, stochastic and deterministic sensitivity analyses were performed to address uncertainty caused by heterogeneity in the patient population.

Results

We randomised a total of 7102 participants recruited from 24 sites over a 40-month period, from July 2007 to September 2010. The main reason for catheterisation was perioperative monitoring. About 74% of participants in all of the three groups received antibiotics at the time of catheterisation, principally to prevent infection relating to the surgical procedure. The median (interquartile range) duration of catheterisation was 2 (1–3) days in all three groups. Data from a total of 6394 (90%) participants were included in the final analysis: 2153 participants were randomised to nitrofurazone, 2097 to silver alloy and 2144 to control. Over 90% of participants received the allocated catheter, with most errors resulting from insertion of a standard-type catheter rather than a silver alloy or nitrofurazone one. Baseline characteristics were well matched across the three groups. For the intention-to-treat analysis, we were successful in confirming participant-reported antibiotic prescription for UTI through participants' clinical records and in obtaining primary outcome data on all except one non-responder (in whom we assumed no UTI occurred).

In terms of the primary outcome, 228/2153 (10.6%) participants in the nitrofurazone group, 263/2097 (12.5%) of those randomised to silver alloy and 271/2144 (12.6%) in the control group experienced at least one symptomatic UTI in the 6 weeks after randomisation. Absolute risk differences [mean (97.5% confidence interval (CI)] were –2.1% (97.5% CI –4.2 to 0.1) in the nitrofurazone group and –0.1% (97.5% CI –2.4 to 2.2) in the silver alloy group. These proportions resulted in an odds ratio (OR) (97.5% CI) for benefit of nitrofurazone catheters in reducing CAUTI of 0.82 (97.5% CI 0.66 to 1.01; $p = 0.037$) and for silver alloy of 0.99 (97.5% CI 0.81 to 1.22; $p = 0.92$). The direction and size of effect were not changed by adjustment for age, sex,

comorbidity or antibiotic use prior to catheterisation. There was no evidence of interaction with the variables of participant age, duration of catheterisation or centre.

For secondary outcomes of benefit, the rate of symptomatic antibiotic-treated CAUTI associated with a positive urine culture at 6 weeks was 69/2153 (3.2%) in the nitrofurazone group, 105/2097 (5.0%) in the silver alloy group and 99/2144 (4.6%) in the control group. Absolute risk differences (97.5% CI) were –1.4% (97.5% CI –2.7% to –0.1%) in the nitrofurazone group and 0.4% (97.5% CI –1.2% to 1.9%) in the silver alloy group. The OR (97.5% CI) for risk was 0.68 (97.5% CI 0.48 to 0.99; $p = 0.017$) in the nitrofurazone group and 1.02 (97.5% CI 0.78 to 1.52; $p = 0.55$) in the silver alloy group.

In terms of harms [OR (97.5% CI)], nitrofurazone-impregnated catheters were associated with greater participant-reported discomfort during catheter use [1.34 (97.5% CI 1.13 to 1.60)] and catheter removal [1.77 (97.5% CI 1.51 to 22.07)].

The planned within-trial cost-effectiveness analysis was limited by implausible estimates from trial data for the likely differences in length of stay, the main driver of costs and cost-effectiveness. Therefore, the pre-planned decision model-based analysis was taken as the primary economic analysis. The price of the catheters used in the trial was £0.86, £5.29 and £6.46 for standard PTFE, nitrofurazone and silver alloy types, respectively. In the base-case analysis, use of nitrofurazone catheters was least costly to the NHS, with PTFE and silver alloy catheters costing, on average £7.00 and £12.00 more, respectively. On average, the nitrofurazone catheter was also slightly more effective so an incremental cost per QALY [incremental cost-effectiveness ratio (ICER)] was not calculated. Nitrofurazone catheters had an approximately 70% chance of being cost saving and an 84% chance of having an ICER of < £30,000, the willingness-to-pay threshold typically suggested by the UK National Institute for Health and Clinical Excellence. Silver alloy catheters had an approximately 0% chance of being cost-effective at all threshold values between £0 and £50,000. As the trial population was heterogeneous in terms of underlying health condition, alternative analyses were performed considering more homogeneous subgroups. The results of these analyses were similar to those of the base case. The main driver of the difference in cost and cost-effectiveness was potential differences in length of stay between the trial arms. A further analysis excluding length of stay data resulted in PTFE being the least costly option, with the ICER against nitrofurazone being £28,600. It should be noted that this result was driven by small differences in QALYs, which may not be important clinically or appreciable by patients.

Conclusions

Silver alloy-coated catheters are unlikely to be effective at reducing CAUTI risk in terms of the pre-set minimum clinically important difference, with the best estimate of clinical effectiveness being close to no difference and the surrounding CI not including the hypothesised relative risk reduction in comparison with standard catheters. Silver alloy-coated catheters were also not considered to be cost-effective at the unit price considered in the analysis for short-term use in the UK NHS. The best estimate for reduction in CAUTI achieved by nitrofurazone-impregnated catheters was less than the prespecified minimum clinically important difference, and the surrounding CI included zero. The trial results therefore give no evidence that use of this catheter could achieve this level of clinical effectiveness. Participants reported greater discomfort of use with nitrofurazone catheters. Model-based health economic analysis suggested that nitrofurazone-impregnated catheters might possibly be cost-effective for use in the UK NHS, although there was a high degree of uncertainty surrounding this finding related to the plausibility of parameter estimates regarding length of stay and change in health-related quality of life.

In summary, in this trial the lack of evidence found to support the use of silver alloy catheters for short-term catheterisation at their current unit price will influence decisions regarding their continued use for this indication. Nitrofurazone catheters were also ineffective against symptomatic CAUTI but did show some antimicrobial activity for secondary bacteriological outcomes. Any benefit may be offset by increased discomfort from their use and concerns regarding indiscriminate antimicrobial use. Clinicians and managers will have to weigh up these factors to plan any change in practice in terms of use of nitrofurazone-impregnated catheters.

Implications for research

Research is required to determine the minimum clinically important difference in terms of CAUTI prevention so that the benefit of antimicrobial catheter devices can be judged against alternative interventions.

Methods are required to detect within-trial quality-of-life benefits and associated changes in length of stay when the intervention under test is a subsidiary part of overall treatment plans.

The short duration of catheterisation for many patients means that further research is required to identify alternative methods of bladder drainage.

Alternative antimicrobial additives, catheter designs and mechanisms of release of agents from catheter materials should be explored to maximise benefit of such interventions.

Trial registration

This trial is registered as ISRCTN75198618.

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Publication

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NIHR Health Technology Assessment programme

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 05/46/01. The contractual start date was in February 2007. The draft report began editorial review in October 2011 and was accepted for publication in March 2012. 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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