Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antisepsis to prevent surgical site infection

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The objective was to examine the clinical and economic impact of chlorhexidine compared with iodine for preoperative skin antisepsis in surgical patients for the prevention of surgical site infections. The authors concluded that chlorhexidine was more effective than iodine and reduced the number of surgical-site infections; it was more expensive, but resulted in overall cost savings. The methods were valid and the available evidence was synthesised in an appropriate meta-analysis, which enhances the validity of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to examine the clinical and economic impact of chlorhexidine compared with iodine for preoperative skin antisepsis in surgical patients for the prevention of surgical-site infections.

Interventions
Two preparations of chlorhexidine were considered: a 113g bottle of 4% chlorhexidine and single-use applicators of a 2% chlorhexidine gluconate and 70% isopropyl alcohol solution. The comparator was a 118mL 7.5% povidone-iodine surgical scrub.

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a decision-analytic model. The authors stated that the perspective of the hospital was adopted.

Effectiveness data:
A literature review was undertaken by searching the website of the Agency for Healthcare Research and Quality (AHRQ) and electronic databases, such as the Cochrane Library, MEDLINE, and EMBASE for systematic reviews, meta-analyses, or randomised controlled trials (RCTs) on the two interventions. The inclusion and exclusion criteria were reported and nine RCTs were found. Heterogeneity between these trials and the quality of their evidence were considered and a fixed-effect meta-analysis was used to synthesise the clinical endpoints. The rate of surgical-site infection and the rate of positive skin culture after application were the key inputs for the model.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The rate of surgical-site infection and rate of positive skin culture after application were the outcomes of the clinical analysis.

Cost data:
The economic analysis included two main categories: the costs of the antiseptic agents and the costs of treating a surgical-site infection. The resource use data and costs were from a review of all surgical cases at the Hospital of the University of Pennsylvania during the fiscal year 2007. The treatment costs included patient, operating, and procedure rooms; the physician, physical therapy, nursing, and technician personnel; and the reagents for laboratory tests, tubes and stoppers, slides, and imaging materials. All costs were in US dollars ($) and the price year was 2009.

Analysis of uncertainty:
One- and two-way sensitivity analyses were carried out on the probability of a reduction in infection with chlorhexidine compared with iodine and the incremental cost of an infection compared with no infection. The range for the former input was from the literature, while the range for the latter input was from a systematic review performed at the authors' institution. Variations in the incremental cost for chlorhexidine were considered.

Results
Compared with iodine, chlorhexidine reduced the risk of surgical-site infection (adjusted RR 0.64, 95% CI 0.51 to 0.80). There was a significant decrease in the risk of a positive skin culture after application of chlorhexidine (adjusted RR 0.44, 95% CI 0.25 to 0.56).

The economic analysis showed that switching from iodine to single-use chlorhexidine resulted in a cost saving of $16 per surgical case, which produced annual cost-savings of $349,904 for the authors' institution. These cost-savings were maintained if the reduction in surgical-site infection was over 10% (25% in the base case). The results were generally robust in all alternative scenarios that were considered in the sensitivity analysis and when increasing the number of applicators.

Switching from iodine to bottled chlorhexidine produced even greater cost-savings ($26 per patient; $568,594 per annum in the authors’ institution). These base-case results were robust in the sensitivity analyses.

Authors' conclusions
The authors concluded that chlorhexidine was more effective than iodine for preoperative skin antisepsis and reduced the number of surgical-site infections; it was more expensive, but resulted in overall cost savings. Further studies were needed to assess which preparation of chlorhexidine is most effective.

CRD commentary
Interventions:
The authors justified their selection of the comparators and they appear to have been appropriate. Iodine was the usual antiseptic in the operating theatre, while chlorhexidine was the new agent, which had advantages over iodine, but was more expensive.

Effectiveness/benefits:
A systematic search of the literature was used to identify the relevant sources of data and this was a valid method. The sole inclusion of head-to-head clinical trials should ensure the validity of the clinical evidence, given their robust design. The key details of the patient populations and clinical outcomes of the trials were reported and an appropriate meta-analysis was used to pool the clinical data. The authors considered the heterogeneity between trials, using appropriate statistical tests. Publication bias was investigated in a regression analysis and some bias was found in the risk of a positive skin culture after application. The authors judged the quality of the data sources, using a valid instrument that assessed randomisation, blinding, and patient retention; in general, moderate quality was observed. Intermediate clinical outcomes were used to assess the impact of the interventions on the patients’ health and these will not permit comparisons with the benefits of other health care interventions.

Costs:
The cost categories were consistent with the perspective of the hospital. A hospital database was used to derive both the resource quantities and the unit costs, but the details were not reported separately. These data were representative of the authors' context and a large sample of patients. The price year was implicitly reported, which will allow reflation exercises in other time periods. The cost estimates were treated deterministically, but alternative estimates were considered in the sensitivity analyses.
Analysis and results:
The results were clearly presented for both preventive strategies, but the costs and benefits were not synthesised and a cost-consequences analysis was conducted. The superior clinical and economic profiles of chlorhexidine mean it would have dominated iodine, if a cost-effectiveness ratio had been calculated. The uncertainty was considered in selected inputs for the model and the overall uncertainty was not assessed. The results appear to be specific to the authors’ setting and it is unclear whether they can be transferred to other settings.

Concluding remarks:
The methods were valid and the available evidence was synthesised in an appropriate meta-analysis, which enhances the validity of the authors’ conclusions.

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