Abstract:

Background: Clinical trials show that antimicrobial-impregnated central venous catheters reduce catheter-related bloodstream infection in adults and children receiving intensive care, but there is insufficient evidence for use in newborn babies.

Objectives: The objectives were (1) to determine clinical effectiveness by conducting a randomised controlled trial comparing antimicrobial-impregnated peripherally inserted central venous catheters with standard peripherally inserted central venous catheters for reducing bloodstream or cerebrospinal fluid infections (referred to as bloodstream infections); (2) to conduct an economic evaluation of the costs, cost-effectiveness and value of conducting additional research; and (3) to conduct a generalisability analysis of trial findings to neonatal care in the NHS.

Design: Three separate studies were undertaken, each addressing one of the three objectives. (1) This was a multicentre, open-label, pragmatic randomised controlled trial; (2) an analysis was undertaken of hospital care costs, lifetime cost-effectiveness and value of information from an NHS perspective; and (3) this was a retrospective cohort study of bloodstream infection rates in neonatal units in England.

Setting: The randomised controlled trial was conducted in 18 neonatal intensive care units in England.

Participants: Participants were babies who required a peripherally inserted central venous catheter (of 1 French gauge in size).

Interventions: The interventions were an antimicrobial-impregnated peripherally inserted central venous catheter (coated with rifampicin-miconazole) or a standard peripherally inserted central venous catheter, allocated randomly (1 : 1) using web randomisation.

Main outcome measure: Study 1 – time to first bloodstream infection, sampled between 24 hours after randomisation and 48 hours after peripherally inserted central venous catheter removal. Study 2 – cost-effectiveness of the antimicrobial-impregnated peripherally inserted central venous catheter compared with the standard peripherally inserted central venous catheters. Study 3 – risk-adjusted bloodstream rates in the trial compared with those in neonatal units in England. For study 3, the data used were as follows: (1) case report forms and linked death registrations; (2) case report forms and linked death registrations linked to administrative health records with 6-month follow-up; and (3) neonatal health records linked to infection surveillance data.

Results: Study 1, clinical effectiveness – 861 babies were randomised (antimicrobial-impregnated peripherally inserted central venous catheter, n = 430; standard peripherally inserted central venous catheter, n = 431). Bloodstream infections occurred in 46 babies (10.7%) randomised to antimicrobial-impregnated peripherally inserted central venous catheters and in 44 (10.2%) babies randomised to standard peripherally inserted central venous catheters. No difference in time to bloodstream infection was detected (hazard ratio 1.11, 95% confidence interval 0.73 to 1.67; p = 0.63). Secondary outcomes of rifampicin resistance in positive blood/cerebrospinal fluid cultures, mortality, clinical outcomes at neonatal unit discharge and time to peripherally inserted central venous catheter removal were similar in both groups. Rifampicin resistance in positive peripherally inserted central venous catheter tip cultures was higher in the antimicrobial-impregnated peripherally inserted central venous catheter group (relative risk 3.51, 95% confidence interval 1.16 to 10.57; p = 0.02) than in the standard peripherally inserted central venous catheter group. Adverse events were similar in both groups. Study 2, economic evaluation – the mean cost of babies' hospital care was £83,473. Antimicrobial-impregnated peripherally inserted central venous catheters were not cost-effective. Given the increased price, compared with standard peripherally inserted central venous catheters, the minimum reduction in risk of bloodstream infection for antimicrobial-impregnated peripherally inserted central venous catheters to be cost-effective was 3% and 15% for babies born at 23-27 and 28-32 weeks' gestation, respectively. Study 3, generalisability analysis – risk-adjusted bloodstream infection rates per 1000 peripherally inserted central venous catheter days were similar among babies in the trial and in all neonatal units. Of all bloodstream infections in babies receiving intensive or high-dependency care in neonatal units, 46% occurred during peripherally inserted central venous catheter days.

Limitations: The trial was open label as antimicrobial-impregnated and standard peripherally inserted central venous catheters are different colours. There was insufficient power to determine differences in rifampicin resistance.

Conclusions: No evidence of benefit or harm was found of peripherally inserted central venous catheters impregnated with rifampicin-miconazole during neonatal care. Interventions with small effects on bloodstream infections could be cost-effective over a child's life course. Findings were generalisable to neonatal units in England. Future research should focus on other types of antimicrobial impregnation of peripherally inserted central venous catheters and alternative approaches for preventing bloodstream infections in neonatal care.

Trial registration: Current Controlled Trials ISRCTN81931394.

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Reference:

Gilbert R, Brown M, Faria R, Fraser C, Donohue C, Rainford N, Grosso A, Sinha AK, Dorling J, Gray J, Muller-Pebody B, Harron K, Moitt T, McGuire W, Bojke L, Gamble C, Oddie SJ. Antimicrobial-impregnated central venous catheters for preventing neonatal bloodstream infection: the PREVAIL RCT. Health Technol Assess. 2020 Nov;24(57):1-190. doi: 10.3310/hta24570. PMID: 33174528.