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Perioperative antibiotics in pediatric cardiac surgery: protocol for a systematic review

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Abstract

Background: Post-operative infections in pediatric cardiac surgery are an ongoing clinical challenge, with rates between 1 and 20%. Perioperative antibiotics remain the standard for prevention of surgical-site infections, but the type of antibiotic and duration of administration remain poorly defined. Current levels of practice variation through informal surveys are very high. Rates of antibiotic-resistant organisms are increasing steadily around the world.

Methods/design: We will identify all controlled observational studies and randomized controlled trials examining prophylactic antibiotic use in pediatric cardiac surgery. Data sources will include MEDLINE, EMBASE, CENTRAL, and proceedings from recent relevant scientific meetings. For each included study, we will conduct duplicate independent data extraction, risk of bias assessment, and evaluation of quality of evidence using the GRADE approach.

Discussion: We will report the results of this review in agreement with the PRISMA statement and disseminate our findings at relevant critical care and cardiology conferences and through publication in peer-reviewed journals. We will use this systematic review to inform clinical guidelines, which will be disseminated in a separate stand-alone publication.

Study registration number: PROSPERO CRD42016052978C

Keywords: Healthcare-associated infections, Pediatrics, Cardiac surgery

Background

Description of the problem

Post-operative infections in pediatric cardiac surgery remain an ongoing clinical challenge. The burden of disease has a wide range, dependent on the case series examined, ranging from approximately 1 to 18% in children with delayed sternal closure [1–4]. There are many factors that contribute to increased risk of infection, including overall acuity, age, delayed sternal closure, steroid use, and length-of-stay in ICU [5–8]. The presence of infection is associated with worsened outcomes and increased costs [9].

Antibiotic use in the perioperative period are well-established adjuncts to reducing the incidence of infection [10]; however, the nature, timing, and duration of administration remain undetermined. Further, in the context of increasing attention to antimicrobial resistance predicated upon the overuse of antibiotics, addressing this issue is timely [11].

Description of the intervention

Antibiotic prophylaxis for surgical procedures is a well-established practice that reduces surgical-site infections. By preventing translocation of bacteria from the skin, antibiotic prophylaxis reduces the rate of post-operative infections in all types of procedures, from clean to dirty. As a clean procedure, pediatric cardiac surgeries should have a lower risk for infection; however, given the severity of illness and prolonged stays in intensive care, infections remain an ongoing challenge.

Antibiotic prophylaxis in pediatric cardiac surgery takes numerous forms. Regimens vary greatly, from single-dose prophylaxis to continuing antibiotics until all chest tubes and central venous catheters have been removed [10]. In children with delayed sternal closure, antibiotic regimens vary again, from 48 h of antibiotics to antibiotics continuing until chest closure has been achieved. Further, the type of antibiotic used varies; although, this is primarily contingent upon the endemic organisms present in specific institutions, i.e., vancomycin for high rates of MRSA.

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Why is it important to conduct this review

Given the issue of antimicrobial resistance and a focus on antimicrobial stewardship in critical care, the varied rates of post-operative infections, and the incredibly diverse regimens used for antibiotic prophylaxis, it is timely to systematically review the literature to determine the optimal strategy to prevent infections in critically ill children. Further, data guidance from adult-specific randomized trials are less relevant to children, given the very different physiology and infectious risks in the two cohorts [12, 13].

Research question

Is a shortened course of perioperative antibiotics in children undergoing cardiac surgery as safe as a prolonged course of perioperative antibiotics?

Methods and analysis

Criteria for selecting studies

Types of studies

We will include all controlled observational studies (case-control or cohort) and randomized trials, excluding case reports or case series, with no restrictions based on language or quality. We will only include papers published after 1990, given the large changes in practice since that point in time in pediatric cardiac surgery.

Types of participants

The population of interest is children (<18 years) undergoing open heart surgery.

Types of interventions

The interventions examined include any systemic antibiotic regimen used for the prevention of infection in children having undergone cardiac surgery. We will include studies that report the nature (drug, duration) of antibiotics administered. We will exclude studies that exclusively report antibiotics used for the treatment of established infections. We will exclude studies that exclusively report on the preoperative use of decolonization regimens.

Types of outcome measures

We will include studies that report the incidence of infection, as defined by the individual studies. Other outcomes of interest include, if reported: length-of-ICU-stay, mortality, cost of care, antibiotic-associated adverse events, and presence of antibiotic-resistant organisms (as defined by individual authors).

Search methods

We will perform a search of the following databases for relevant studies: MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL). The peer-reviewed MEDLINE search strategy is included in Additional file 1, with similar searches with adapted keywords for other databases. To locate in-process and unpublished studies, we will also search trial registries, ClinicalTrials.gov and the World Health Organization's International Clinical Trial Registry Platform (WHO ICTRP), from 2014 to 2017.

We will screen reference lists of included studies and relevant reviews for eligible articles. We will also manually screen conference proceedings from 2014 to 2017 for the following scientific meetings: Society of Critical Care Medicine, Pediatric Cardiac Intensive Care Society, Society of Thoracic Surgeons, American Heart Association, and World Congress of Pediatric Cardiology and Cardiac Surgery.

Search results will be exported to the EndNote X7 citation manager program. Preliminary scoping searches have been performed and no randomized trials have been found.

Study records

Pairs of two reviewers will independently screen titles and abstracts using a pretested electronic screening form (www.covidence.org), including any article for full-text review unless both reviewers exclude. Pairs of two reviewers will then independently screen all full-text articles using specific eligibility criteria through this platform, resolving disagreements by consensus, and reporting a Cohen's k for full-text eligibility screening.

Data collection

Teams of two reviewers will perform data extraction independently and in duplicate using data collection forms through Covidence, collecting information pertaining to the study design, patient characteristics, intervention (and comparator, if applicable), and clinical outcomes. Interventions will include specifying the antibiotic used, doses (if available), the duration of use, and specific reasons for altering these practices. Outcomes will include a primary outcome of incidence of nosocomial infection (as defined by the individual paper), mortality, duration of mechanical ventilation, and duration of intensive care unit stay. Conflicts will be resolved through discussion.

Risk of bias assessment

For observational studies, we will use the risk of bias tools for cohort and case-control studies developed by the Clinical Advances Through Research and Information Translation (CLARITY) group at McMaster university [14, 15]. These tools evaluate the selection of groups, the adequacy of assessment of prognostic factors, the assessment of exposures and outcomes, and the similarity of co-interventions between groups. We will assess the overall quality of data for our primary outcome using the GRADE approach.

Summarizing data and treatment effect

Given the expected heterogeneity of the study designs, we will not perform a meta-analysis. We will provide quantitative summaries where available of relevant treatment effects of different antibiotic treatment durations of individual studies, with tabular results of included studies.

Subgroup analysis and investigation of heterogeneity

Subgroup overviews will be performed for children with delayed sternal closure. Given the absence of a planned meta-analysis, quantitative subgroup analysis will be deferred.

Discussion

Perioperative infections are a common cause of postoperative morbidity in this high-risk population. Optimizing the antibiotic regimens for these children is a frequent clinical conversation that is woefully understudied despite its widespread practice. As a comparative effectiveness program, we aim to determine the best method to prevent infections, without increasing the adverse effects of antibiotics such as increasing resistance and individual adverse effects.

Ethics and dissemination

We did not require ethics approval for this study. We will report this review in accordance with the PRISMA statement [16]. This protocol has been registered at the PROSPERO database (CRD42016052978C) and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) guidelines (see Additional file 2) [17]. There is no specific funding attached to this systematic review. We will disseminate our findings by producing clinical guidelines, as well as conference presentations and publication in a peer-reviewed journal.

Additional files

Additional file 1: Search Strategy, filename: Appendix 1. (DOCX 84 kb)

Additional file 2: PRISMA-P Checklist, filename: PRISMA-P 2015 checklist antibiotics. (DOCX 37 kb)

Abbreviations

CLARITY: Clinical advances through research and information translation; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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Availability of data and materials

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Authors' contributions

VA, AB, RF, and SM contributed to the design and conduct of the study and reviewed the manuscript. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

Ethical approval and consent to participate

Not applicable.

Publisher's Note

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