Parenteral vs oral antibiotics in the prevention of serious bacterial infections in children with Streptococcus pneumoniae occult bacteremia: a meta-analysis


Authors' objectives
To determine whether parenteral antibiotics are superior to oral antibiotics in preventing serious bacterial infections in children with Streptococcus pneumoniae occult bacteraemia.

Searching
MEDLINE was searched from 1966 through 1996 for articles published in the English language. Bibliographies of articles retrieved were reviewed.

Study selection
Study designs of evaluations included in the review
Articles containing a series of children with Streptococcus pneumoniae bacteraemia treated as out-patients were included if they divided the patients either prospectively or retrospectively into parenteral and oral treatment groups and included a description of all patients on follow-up to determine whether serious bacterial infection was present. Articles were excluded if either an oral treatment or parenteral treatment group was absent. Reasons were given for exclusion of studies.

Specific interventions included in the review
Parenteral and oral antibiotics were studied. Parenteral antibiotics included: intra muscular ceftriaxone (50 or 75 mg/kg); and ceftriaxone, ampicillin, penicillin, ampicillin/sulbactam where dose and delivery method was not stated. Oral antibiotics included the following: amoxycillin 60mg/kg and dose not stated; amoxycillin/clavulanate 40mg/kg and dose not stated; trimethoprim-sulphamethoxazole; cefaclor; erythromycin/sulpha; and cefixime. Antibiotics therapy was initiated at the time the blood culture was obtained.

Participants included in the review
Children with Streptococcus (S) pneumoniae occult bacteraemia (defined as well-appearing, with no major focus of infection, recovery of S pneumoniae from a blood culture on initial physician visit) were studied. Excluded from analysis were the following children: immunocompromised; serious bacterial infection present at initial presentation; no antibiotics were administered; child was judged ill-appearing or the Yale observation score > 10; or child underwent lumbar puncture. Reasons were given for excluded cases.

Outcomes assessed in the review
Outcomes included meningitis and serious bacterial infection defined as pneumonia, meningitis, soft-tissue infection, bone or joint infection. The following were excluded from the definition of serious bacterial infection: persistent bacteraemia, persistent fever, otitis media, bronchitis, and sinusitis.

How were decisions on the relevance of primary studies made?
Retrieved articles were independently analysed by 3 senior authors for adherence to inclusion criteria. Disagreements were resolved by consensus.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Three authors independently determined the number of eligible children and the outcome of children meeting entry.
criteria. Disagreements were resolved by consensus. The author of one study was contacted for unpublished data.

Methods of synthesis
How were the studies combined?
Pooled odds ratios (OR) were calculated for the risk of meningitis and serious bacterial infection in children who received oral and parenteral antibiotics.

How were differences between studies investigated?
Woolf's chi-squared test was used to assess heterogeneity.

Results of the review
Two prospective series (214 children) and 2 retrospective studies (297 children) were included.

290 (57%) received oral antibiotics and 221 (43%) received parenteral antibiotics.

Meningitis developed in 2 (0.7%) of those receiving oral antibiotics compared to 2 (0.9%) receiving parenteral antibiotics (P = 0.699). Pooled OR also showed no statistical difference between treatment groups: OR = 0.67 (95%CI: 0.1, 5.1). Heterogeneity chi-squared = 0.389, P = 0.824.

Serious bacterial infections developed in 10 of those receiving oral antibiotics compared to 5 receiving parenteral antibiotics (3.4% vs 2.3%; P = 0.467). Pooled OR also showed no statistical difference between treatment groups: OR = 1.48 (95%CI: 0.5, 4.3). Heterogeneity chi-squared = 0.169, P = 0.919. The study had > 80% power to detect a 5% absolute difference in rates of meningitis and serious bacterial infection between groups (alpha = 0.05).

Authors’ conclusions
The rates of serious bacterial infection and meningitis did not differ between children who were treated with oral and parenteral antibiotics. The extremely low rate of complications observed in both groups suggests no clinically significant differences between therapies.

CRD commentary
The aims and inclusion criteria were defined. Methods used to select primary studies and extract data were described. Reasons were given for exclusion of studies and cases. Heterogeneity was statistically assessed and the power of the study was estimated. The discussion included mention of the following: rationale for strict patient inclusion criteria; lack of standard time or protocol for repeating blood cultures in any included studies; impossibility of comparing rates of persistent bacteraemia between treatment groups; lack of assessment of validity of primary studies; and publication bias.

By limiting the literature search studies published in the English language and retrieved in one database, other relevant studies may have been omitted. Validity was not assessed and there was no attempt to examine baseline differences that may have influenced outcomes between treatment groups. Fuller details of primary studies such as methods used to select patients would have been welcome. Methods used to ascertain outcomes were not described. Neither duration of therapy nor follow-up period were stated.

There did appear to be a low complication rate in participants but in view of the lack of validity assessment and unrandomised design of the primary studies the conclusion of no difference between oral and parenteral antibiotics cannot be considered supported.

Implications of the review for practice and research
Practice: The authors consider that clinicians should re-evaluate the need for and efficacy of empiric antibiotic therapy in preventing sequelae of occult bacteraemia.
Research: The authors do not state any implications for research.

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