Meta-analysis of trials of prophylactic antibiotics for children with measles: inadequate evidence
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Authors' objectives
To assess whether prophylactic antibiotics should be given to all children with measles in communities with a high (more than 1%) fatality rate.

Searching
MEDLINE was searched from 1966 to 1995 using the terms 'measles' plus either 'antibiotic', 'penicillin', 'sulphonamide', 'prospective studies' or 'RCT'. Additional studies were obtained by examining results of previous handsearches of studies of pneumonia in children, in all the journals in the University library from 1935 to 1946.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) comparing routine antibiotic prophylaxis with no antibiotic or with selective antibiotic treatment.

Specific interventions included in the review
Prophylactic antibiotics including sulphanilamide, sulphanilamide derivative, sulphathiazole, chlortetracycline, procaine penicillin, benzathine, tetracycline. No doses or duration of treatment were stated.

Participants included in the review
Children with measles admitted to hospital in Glasgow, London, New York and India. The age limits varied across the studies from under 4 to under 10 years.

Outcomes assessed in the review
The number of children who died or developed either pneumonia or sepsis was assessed. Pneumonia was undefined or diagnosed clinically or by X-ray.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Validity was assessed on the basis of method of randomisation, blinding and withdrawals. The author does not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined numerically to give the percentage of all children in the control, compared with the antibiotic prophylaxis group, who died or who developed pneumonia or sepsis. The studies were combined to give exact common odds ratio (OR) for mortality rates. Only one paper mentioned withdrawals.
How were differences between studies investigated?

Exact test for homogeneity. There were few details in the articles and the small sample size meant that the cause of heterogeneity could not be determined. Two studies with an unusually high mortality rate in the controls were excluded from the sensitivity analysis of the rates of pneumonia and sepsis.

Results of the review

Six RCTs (1,304 children) were included.

Exact test for homogeneity in the development of pneumonia and sepsis showed heterogeneity across studies (P<0.00005). Fourteen of the 681 children receiving antibiotics developed pneumonia or sepsis compared to 34 of the 623 controls. After excluding the 2 studies with an unusually high mortality rate in the controls, studies were homogeneous (p=0.833). These 2 studies reported more complications in the controls than in the antibiotic group (14 versus 1%). The remaining 4 studies gave the incidence of sepsis or pneumonia as 2% in the antibiotic group and 3% in the control group. There was no evidence that the mortality was lower when antibiotics were given routinely rather than selectively or not at all; exact common OR was 4 (95% confidence interval: 0.5, 101.6).

Authors' conclusions

In view of the poor quality of these studies, any inferences must be tentative. The studies provide no evidence that routine antibiotic results in a lower mortality than either no antibiotic treatment or selective treatment when complications develop.

CRD commentary

The search strategy was limited to one database plus a selective handsearch. The studies, as stated by the author, are of poor quality and include children of varying age ranges, are from a mix of populations, have unblinded diagnosis of the outcomes assessed, no definition of what constitutes measles, do not consider withdrawals, have either insufficient details of randomisation or were not truly randomised, and are from the period 1939 to 1967. Some of the antibiotics studied would not be currently recommended for use in children. It is unclear why the studies with high complication rates are excluded from separate consideration. The results obtained today using different antibiotics, plus vitamin A, and with the availability of measles vaccine may differ from those obtained from these studies.

Implications of the review for practice and research

Good quality RCTS in developing countries, using the antibiotics currently available in a regime that includes vitamin A and the availability of measles vaccine, would be required to assess the effectiveness of prophylactic antibiotics in reducing the mortality rate and the development of pneumonia and sepsis in children, in communities with a high-case fatality rate.

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