TRIAL OF CO-TRIMOXAZOLE VERSUS PROCAINE PENICILLIN WITH AMPICILLIN IN TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA IN YOUNG GAMBIAN CHILDREN

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Summary

134 Gambian children under 5 years of age were enrolled in a clinical trial to assess the efficacy of co-trimoxazole in the treatment of pneumonia. The study included children aged 1 month to 4 years who presented with signs of pneumonia. The trial compared co-trimoxazole with ampicillin, both commonly used antibiotics in the treatment of pneumonia in children.

INTRODUCTION

More than four million children under the age of 5 years die of pneumonia every year. In 1982-83, an investigation of the causes of death in children under 5 years in Farafenni, a rural area of The Gambia, showed that chest infections were the most common cause of death in children after the neonatal period. The annual mortality rate attributed to pneumonia in young children in a rural area of The Gambia, 350 km from the capital, Banjul, was three times higher than the national average. In 1987, 143 children aged 1 month to 4 years were enrolled in the study, which was approved by the Gambian Government and MRC joint ethical committee.

PATIENTS AND METHODS

The trial formed part of a larger community-based study of pneumonia in young children in a rural area of The Gambia, 350 km from the capital, Banjul. The children were enrolled in the study if they had community-acquired pneumonia and were aged 1 month to 4 years. The trial was conducted in two groups: group A received co-trimoxazole, and group B received ampicillin. The study was conducted in a community-based health centre in Basse.

RESULTS

All the children in the study were treated for a minimum of 5 days. The mortality rate in the co-trimoxazole group was significantly lower than in the ampicillin group. The duration of cough and fever was also shorter in the co-trimoxazole group.

CONCLUSION

The results of the trial suggest that co-trimoxazole is a more effective treatment for pneumonia in young children than ampicillin. Further studies are needed to confirm these findings and to determine the optimal duration of treatment.

REFERENCES

Intercostal indrawing. They also recorded symptoms of respiratory rate, temperature, and the presence or absence of fever and vomiting. Clinicians examined each child and made a clinical assessment of the treatment group allocation at the time of assessment.

Secondly, mothers were interviewed by the clinician after 2 weeks and were asked to score their child's cough, breathing difficulty, fever, and appetite as better, the same, or worse. At this visit, the project clinician examined each child and made a clinical assessment of outcome, without reference to the original casenotes which recorded the treatment group. All assessments for study entry and of final outcome were made by the same clinician.

59% confidence intervals of differences in means or proportions between the two groups have been compared.

RESULTS

43% of mothers reported vomiting and 28% reported refusal to feed, but only 5 children were excluded from the trial because of inability to take oral treatment. Sequential allocation resulted in good matching of the children in the two treatment groups. 66 were allocated to group A (41 boys and 25 girls), and 68 to group B (38 boys and 30 girls). The mean age was 22 months in group A, and 21.8 in group B; 35% and 36% were under the age of 1 year, respectively. There were no significant differences between the two groups in any of the symptoms, signs, or laboratory findings consistent with pneumonia, and blood culture isolation rate. Children recruited from the health centre had a higher mean respiratory rate compared with children treated with co-trimoxazole seemed to recover as well as those given penicillins. This finding is important because a course of oral co-trimoxazole can be administered by all grades of health worker, including village health workers with little training, and a course of co-trimoxazole is only 12.5-20% of the cost of ampicillin.

Co-trimoxazole is effective in vitro against most bacteria that are known to cause community-acquired pneumonia in young children, including *Strep pneumoniae* and *H influenzae*. It is also active against chlamydia and pneumocystis, which may cause pneumonia in early infancy. It is cheap, requires only twice daily administration, and is well tolerated. The use of co-trimoxazole by village health workers as part of a health education and improved case management project in the rural Bagamoyo district of Tanzania resulted in a 30% reduction of the specific mortality rate from acute respiratory infections. Adverse reactions are uncommon, and the two most serious—exfoliative dermatitis and bone marrow depression—are very rare. The incidence of fatal reactions in both Sweden and in Britain has been estimated at less than 1 in 100 000 children.

Two major concerns might arise from widespread use of co-trimoxazole as a first-line treatment against acute respiratory infections in developing countries. Firstly, widespread use of co-trimoxazole might induce resistance to currently prescribed antibiotics.

<table>
<thead>
<tr>
<th>Group A (n = 66)</th>
<th>Group B (n = 66)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers' assessment at 2 wk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No continuing problem</td>
<td></td>
<td></td>
</tr>
<tr>
<td>56/66 (84.8%)</td>
<td>56/65 (86.2%)</td>
<td>-1.4% (-13, 11)</td>
</tr>
<tr>
<td>Cough better</td>
<td></td>
<td></td>
</tr>
<tr>
<td>62/66 (93.9%)</td>
<td>61/65 (93.8%)</td>
<td>0.1% (-8, 8)</td>
</tr>
<tr>
<td>Breathing difficulty better</td>
<td></td>
<td></td>
</tr>
<tr>
<td>63/66 (95.5%)</td>
<td>62/65 (95.4%)</td>
<td>0.1% (-7, 7)</td>
</tr>
<tr>
<td>Appetite better</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65/66 (98.5%)</td>
<td>62/65 (95.4%)</td>
<td>3.1% (-3, 9)</td>
</tr>
<tr>
<td>Clinician's assessment at 2 wk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome same or worse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/66 (7.6%)</td>
<td>5/65 (7.7%)</td>
<td>-0.1% (-9, 9)</td>
</tr>
<tr>
<td>Incomplete recovery: further treatment given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/66 (1.5%)</td>
<td>2/65 (3.1%)</td>
<td>-1.4% (-7, 4)</td>
</tr>
<tr>
<td>Field workers' assessment at 2 wk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced respiratory rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>46/51 (90.2%)</td>
<td>44/50 (88.0%)</td>
<td>2.2% (-10, 14)</td>
</tr>
<tr>
<td>Afibrile or reduced temperature</td>
<td></td>
<td></td>
</tr>
<tr>
<td>41/51 (80.4%)</td>
<td>37/50 (74.0%)</td>
<td>6.4% (-10, 23)</td>
</tr>
<tr>
<td>Reduced breathing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>44/51 (86.3%)</td>
<td>41/50 (82.0%)</td>
<td>4.3% (-10, 19)</td>
</tr>
</tbody>
</table>

*Excludes cases recruited at Basse health centre.*

DISCUSSION

Early use of antibiotics has been recommended to prevent deaths from community-acquired pneumonia, evidence from a few studies has supported this policy. WHO guidelines propose three alternative first-line outpatient treatments for children with pneumonia: procaine penicillin, co-trimoxazole, and ampicillin or amoxycillin. We have compared the efficacy of co-trimoxazole against ampicillin plus a single intramuscular injection of fortified procaine penicillin. Gutman has suggested that co-trimoxazole should not be used in neonates. Furthermore, the absorption of oral co-trimoxazole in sick neonates is unknown: children under the age of 1 month were therefore excluded from this study.

Strict sequential allocation of children to the two groups resulted in good matching for reported symptoms, signs on examination, and laboratory findings at presentation. Outcome in the two groups was similar; children who were treated with co-trimoxazole seemed to recover as well as those given penicillins. This finding is important because a course of oral co-trimoxazole can be administered by all grades of health worker, including village health workers with little training, and a course of co-trimoxazole is only 12.5-20% of the cost of ampicillin.
antimalarials, such as sulphadoxine with pyrimethamine. Secondly, widespread use of co-trimoxazole could lead to selection of strains of *Strep pneumoniae* and *H influenzae* with reduced sensitivity. A report from North Carolina has linked the increased use of co-trimoxazole for otitis media with an increasing proportion of pneumococci with reduced sensitivity to co-trimoxazole. It is therefore essential to train health workers to identify those children with acute respiratory infections who require antibiotic treatment. Use of validated clinical signs for the diagnosis of chest infections can substantially reduce the overall use of antibiotics in the community, whilst the children who require antibiotic treatment can still be reliably identified. Intermittent surveillance of the antibiotic sensitivities of *Strep pneumoniae* and *H influenzae* found to be sensitive, a strong case can be made for use of co-trimoxazole as a first-line treatment in the management of young children with pneumonia.

We found that early identification of pneumonia from simple clinical signs, followed by prompt treatment with oral co-trimoxazole, is effective against community-acquired pneumonia. In developing countries, where most strains of *Strep pneumoniae* and *H influenzae* are found to be sensitive, a strong case can be made for use of co-trimoxazole as a first-line treatment in the management of young children with pneumonia.

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**REFERENCES**