Review: Antibiotics have no effect on diarrhea and increase bacteriologic relapse in salmonella intestinal infection


Question
What are the effects of antibiotics in salmonella intestinal infection?

Data sources
Studies were identified by using MEDLINE (1980 to 1997) with the search terms diarrhea and salmonella, The Cochrane Library, BIDS Science Citation Index, African Index Medicus, LILACS, and bibliographies of identified articles and by contacting experts.

Study selection
Studies of oral antibiotics in symptomatic or asymptomatic patients who had stool cultures positive for salmonella were selected if they had outcomes of duration of illness, diarrhea, or fever; presence of diarrhea or fever; extraintestinal tract infections; or persistence of salmonella on stool culture. Exclusion criteria were infections with Salmonella typhi, S. paratyphi, S. choleraesuis, and S. bongori.

Data extraction
Trial design, patient characteristics, interventions, and outcomes.

Main results
13 randomized and 2 pseudorandomized controlled trials that included 855 patients (43% infants and children, 93% with symptomatic salmonella infection) studied norfloxacin, cotrimoxazole, ampicillin, ciprofloxacin, neomycin, chloramphenicol, amoxicillin, and fleroxacin. Studies varied in duration of treatment (1 to 14 d) and follow-up (5 d to 6 mo). Antibiotics had no effect on presence of diarrhea (3 studies); clinical failure at the end of therapy (6 studies) (Table); or duration of illness (4 studies), diarrhea (4 studies), or fever (2 studies). Although patients who were receiving antibiotics had fewer salmonella-positive cultures after 2 to 7 days, more patients who were receiving antibiotics than those who were receiving placebo had positive cultures after 3 weeks. Meta-analysis showed that patients who received antibiotic treatment had an increased risk for bacteriologic relapse after 1 to 3 negative cultures (8 studies) (Table) and for adverse effect (10 studies, P < 0.05).

Conclusions
In patients with salmonella intestinal infection, antibiotics do not reduce clinical failure or duration of diarrhoea, illness, or fever. They do increase risk of bacteriologic relapse and adverse effect.

Antibiotics vs control for patients with salmonella infection

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Weighted event rate</th>
<th>Control</th>
<th>RRR (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>31%</td>
<td>41%</td>
<td>20% (-18 to 45)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>19%</td>
<td>23%</td>
<td>27% (-3 to 49)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Bacteriologic relapse</td>
<td>23%</td>
<td>4%</td>
<td>267% (21 to 1007)</td>
<td>5 (3 to 102)</td>
</tr>
</tbody>
</table>

Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article. Follow-up was 5 days to 6 months.

Commentary
In North America, it is commonly taught that enteric infections caused by nontyphoidal salmonella do not require antibiotic treatment because these infections are usually self-limited. Furthermore, many antibiotics prolong the period during which salmonella are carried in the gastrointestinal tract. In other parts of the world, various strategies are used to manage salmonella enteritis on the basis of the belief that intervention has potential benefit and causes little harm.

The diagnosis of salmonellosis is seldom known when the decision to treat diarrhea is made. Because most patients with suspected bacterial diarrhea do slightly better with antimicrobial agents than with placebo (1), it is unclear whether treatment should be stopped or continued if salmonella is cultured from the stool.

As shown by this study, the prospect of performing a meta-analysis to examine the effect of treatment for enteric salmonellosis is overwhelming because of the heterogenous nature of the patients, treatments, and infections studied. Sirinavin and Garner address the issue of antibiotics for patients who have salmonella detected in the stool. Salmonella enteritis is more likely to be severe and to lead to metastatic infection in infants and patients with serious immunodeficiency than in other populations. Because most patients included in this meta-analysis were at low risk for complications, these results cannot be generalized to high-risk groups, such as infants, the elderly, and immunocompromised persons.

This study reaffirms the lack of significant benefit of antibiotics in uncomplicated salmonella enteritis and supports the belief that such intervention prolongs bacterial carriage.

When the risk for complications of salmonella gastrointestinal infection is high, antibiotic treatment is often recommended; however, the benefit, most effective antibiotic, and optimal duration of treatment remain to be determined.

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Reference