Rifampicin therapy in *Escherichia coli* gastroenteritis

YEHEZKEL NAVEH
M.D.

ABRAHAM FRIEDMAN
M.D.

The Department of Paediatrics 'B', Rambam University Hospital,
The Abba Khoushi Medical School, Haifa, Israel

Summary
Eight infants aged 2–4 months suffering from gastroenteritis associated with enteropathogenic *Escherichia coli* were treated with rifampicin. Seven of them had serotype 0125 : B15 and the eighth had serotype 0126 : B16. One of them had septicaemia due to *E. coli* 0125 : B15. Five cases were initially treated with antibiotics and chemotherapeutic agents to which *E. coli* was shown to be sensitive but without results. Rifampicin was effective in curing gastrointestinal signs and eradicating the bacilli in seven of eight infants. The drug was given in a dose of 15–25 mg/kg/day divided into two equal parts, for 7 days in most of the cases. No untoward side effects were observed clinically in any of the cases. Our experience should encourage the use of this agent in controlling outbreaks of gastroenteritis caused by enteropathogenic *E. coli*.

GASTROENTERITIS is still one of the commonest diseases affecting children under the age of 2 years. Among the principal bacterial causes of gastroenteritis of infancy, enteropathogenic *E. coli* (EEC) plays an important role. It can cause disease by at least two mechanisms: elaboration of a cholera-like enterotoxin, and shigella-like intestinal epithelial penetration (Du Pont et al., 1971). EEC were isolated from the faeces of 16% of patients with diarrhoea aged under 2 years (Ironside, Tuxford and Heyworth, 1970) and from the faeces of 16% of infants with diarrhoea aged under 4 months (Moffet, Shulenberger and Burkholder, 1968).

Outbreaks of gastroenteritis associated with EEC are frequent phenomena which may prove disastrous and may cause anxiety to paediatricians responsible for infants' nursery, maternity units and paediatric wards. Treatment of those infants is difficult and the mortality rate may be as high as 24% (Jacobs et al., 1970). Despite the frequency of such outbreaks, the place of antibiotics in managing those infants remained controversial (Coetzee and Leary, 1971; Ironside, 1973).

Recently, we had the occasion to treat eight infants suffering from gastroenteritis due to EEC with rifampicin and our findings are reported.

Material
Eight infants aged 2–4 months (Table 1) suffering from gastroenteritis due to EEC were treated with rifampicin 15–25 mg/kg/day divided into two equal parts. A few of them were admitted for vomiting and diarrhoea and the majority were cross-infected with EEC in the paediatric ward. There were no cases of extraintestinal infections.

With the exception of patient CR, stool cultures of all infants and blood culture of patient PT yielded growth of EEC serotype 0125 : B15, which showed identical sensitivity patterns, with discs, being resistant to chloramphenicol, streptomycin, sulphonamides, ampicillin sodium and carbenicillin, but sensitive to nitrofurantoin, neomycin sulphate, cephalothin sodium, kanamycin sulphate, polymyxin B sulphate, colistin sulphate, gentamicin hydrochloride, trimethoprim-sulphamethoxazole and rifampicin. Serotype 0126 : B16 was isolated from stool specimen of patient CR and showed a similar sensitivity except for being also resistant to neomycin sulphate. Five patients, AA, PT, OI, HT and CR were put on antimicrobial drugs to which *E. coli* was shown to be sensitive before rifampicin therapy, but without results.

Results
Dramatic response of the diarrhoea was achieved in seven out of eight infants after administering rifampicin for 2–4 days. These infants were able to maintain hydration without addition of intravenous fluids after 2–3 days. Patient AA showed some improvement during the first few days but full recovery, however, was not achieved. Eradication of EEC from the stool was obtained in seven out of eight patients during the course of treatment, few days after cessation of the diarrhoea. No untoward side effects were observed.
TABLE 1. Clinical data of the patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (months) and sex</th>
<th>Weight (kg)</th>
<th>Clinical signs</th>
<th>Antimicrobial drugs</th>
<th>Daily dosage per kg b.w.</th>
<th>Duration of therapy (days)</th>
<th>Cessation of diarrhoea after (days)</th>
<th>Negative cultures obtained after (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>2, F.</td>
<td>3-8</td>
<td>vomiting, diarrhoea and dehydration</td>
<td>furazolidone (O)</td>
<td>10 mg</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>gentamicin (i.m.)</td>
<td>4 mg</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>rifampicin (O)</td>
<td>20 mg</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT</td>
<td>2, F.</td>
<td>3-0</td>
<td>vomiting, diarrhoea, dehydration and fever</td>
<td>furazolidone (O)</td>
<td>10 mg</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>gentamicin (i.m.)</td>
<td>3-5 mg</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>rifampicin (O)</td>
<td>25 mg</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OI</td>
<td>2, F.</td>
<td>4-2</td>
<td>vomiting, diarrhoea and dehydration</td>
<td>chloramphenicol (O)</td>
<td>100 mg</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>colistin (O)</td>
<td>200,000 µm</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>gentamicin (i.m.)</td>
<td>3-8 mg</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>cephalothin (i.v.)</td>
<td>100 mg</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>rifampicin (O)</td>
<td>18 mg</td>
<td>7</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>HT</td>
<td>3, F.</td>
<td>4-4</td>
<td>vomiting, diarrhoea, dehydration and fever</td>
<td>colistin (O)</td>
<td>200,000 µm</td>
<td>10</td>
<td></td>
<td></td>
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<tr>
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<td></td>
<td></td>
<td>cephalothin (i.v.)</td>
<td>100 mg</td>
<td>14</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>gentamicin (i.m.)</td>
<td>3-8 mg</td>
<td>7</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>rifampicin (O)</td>
<td>17 mg</td>
<td>7</td>
<td>3</td>
<td>6</td>
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<tr>
<td>SN</td>
<td>4, M.</td>
<td>4-4</td>
<td>vomiting, diarrhoea, dehydration and fever</td>
<td>chloramphenicol (O)</td>
<td>60 mg</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>rifampicin (O)</td>
<td>17 mg</td>
<td>10</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>YG</td>
<td>2, F.</td>
<td>3-0</td>
<td>vomiting, diarrhoea, and dehydration</td>
<td>rifampicin (O)</td>
<td>25 mg</td>
<td>7</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>GN</td>
<td>4, M.</td>
<td>6-0</td>
<td>vomiting, diarrhoea, and dehydration</td>
<td>rifampicin (O)</td>
<td>20 mg</td>
<td>6</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>CR</td>
<td>3, M.</td>
<td>5-0</td>
<td>vomiting and diarrhoea</td>
<td>colistin (O)</td>
<td>200,000 µm</td>
<td>6</td>
<td>2</td>
<td>4</td>
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<td></td>
<td></td>
<td>rifampicin (O)</td>
<td>15 mg</td>
<td>7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

b.w. = body weight; O = oral; i.m. = intramuscular; i.v. = intravenous.

Discussion

The recommended antimicrobial therapy for EEC gastroenteritis consists of various agents, namely neomycin, colistin, furazolidone, nalidixic acid and gentamicin. The ability of EEC to acquire resistance to neomycin and several other antibiotics by transfer of R factors resulted in the death of eleven infants in the Teesside epidemic (Lancet, 1968). This is the first paper concerning the treatment of EEC gastroenteritis with rifampicin and which provides the paediatrician with an alternative drug. Rifampicin was administered subsequent to failure with the other antibiotics. It was given alone and not in combination with any other chemotherapeutic agent. Use of rifampicin enabled us rapidly to control a small outbreak of *E. coli* 0125 : B15 enteritis and to prevent cross-infection from other infants. Failure of rifampicin in patient AA could have been the result of secondary intestinal damage caused by prolonged and uncontrollable diarrhoea which preceded EEC superinfection. Although we succeeded in eradicating *E. coli* bacillus from AA's stool specimens and improving her condition for a few days, her diarrhoea relapsed, but she was no longer a source of infection. Somewhat longer courses were given to patient AA because of failure of response, to patient PT because of EEC septicaemia and to patient SN because of continued positive stool cultures.

The efficacy of this bactericidal drug, its tolerance by small infants, its excellent absorption by the inflamed intestine, and its broad spectrum would make it a useful preparation in infectious diarrhoea caused by EEC, salmonellae (Bessudo, Duarte and Bucio, 1972) and shigellae (Naveh and Friedman, 1973).

We agree with Drucker et al. (1970) and Coetzee and Leary (1971) regarding the need of systemic antimicrobial therapy in EEC enteritis at least for those patients who suffer from diarrhoea for more than a few days. Systemic therapy is imperative in order to improve the clinical condition of the patient, to prevent the complication of septicaemia as was the case in patient PT and to avoid the danger of the spread of the disease. Rifampicin, being orally administered, is preferable to intramuscularly injected gentamicin, bearing in mind that we are dealing with small infants. Rifampicin also has the double effect of eliminating EEC in the gastrointestinal tract and other body tissues which might be invaded by this microorganism.

Although the number of patients reported in this paper is small for drawing definite conclusions, we
feel that the results obtained justify further trials of this antibiotic in EEC gastroenteritis.

Acknowledgment
We wish to thank Dr David Merzbach, Ph.D., Head of Department of Bacteriology, Rambam University Hospital, Israel, for providing the laboratory results, and Ciba Ltd, Basel, Switzerland, for supplying Rimactane.

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Yehezkel Naveh and Abraham Friedman

*Postgrad Med J* 1974 50: 707-709
doi: 10.1136/pgmj.50.589.707

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