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Correspondence to Dr M J Robinson, Department of Paediatrics, St Thomas's Hospital, Lambeth Palace Road, London SE1 7EH.

Brucellosis treated with rifampicin

J LLORENS-TEROL AND R M BUSQUETS

Department of Paediatrics, Universidad Autónoma de Barcelona, and Hospital Nuestra Señora del Mar, Barcelona, Spain

SUMMARY 14 children, aged between 15 months and 14 years, with brucellosis were treated with oral rifampicin only (20 mg/kg per day) for 3 weeks. Laboratory diagnosis depended on blood culture (positive for *Brucella melitensis* in 11 of the cases), serum agglutination, complement-fixation test, and Coombs's test. Response was good in each child, with fever clearing between the 2nd and 8th day. 2 children relapsed, but one relapse was probably a reinfection from contaminated cheese. Both children were given a further course of treatment (rifampicin and co-trimoxazole) which was successful. Despite the reasonably good results with rifampicin alone, it is advisable to combine the drug with co-trimoxazole when treating brucellosis.

In Spain, brucellosis is still endemic and constitutes a major public health problem.¹ Treatment of this infection has been unsatisfactory,² despite the use of such drugs as sulphonamides and streptomycin, and broad spectrum antibiotics—such as chloramphenicol, chlortetracycline, oxytetracycline.³⁻⁴

Rifampicin is a broad spectrum antibiotic with potent antibrucellar activity *in vitro*. It has been reported to be effective in the treatment of experi-

mental brucellosis.⁵ Rifampicin is rapidly absorbed by the bowel to give high plasma levels, spreading widely through the body. Because of its neutral molecule it penetrates into the interior of cells and so reaches the reticuloendothelial system, where the brucellar organisms persist, thus causing relapses and chronic illness.⁶

Materials and methods

We have studied 14 cases of brucellosis in children (9 boys and 5 girls); their ages ranged between 15 months and 14 years. Most came from country areas: 9 from villages, 2 from suburban areas, and only 3 from the city. Except in three cases, the source of infection was almost certainly attributable to the consumption of contaminated milk or cheese.

The variety of symptoms (Table 1) was wide. Fever was present initially, often associated with articular and muscular pains. Sweats and weakness were present in half of the children, but not necessarily together. The fever sometimes took an undulant form, but was more often a constant low fever. Splenomegaly was observed in 11 patients and hepatomegaly in 9.

A clinical diagnosis of brucellosis was made in

Table 1 Initial symptoms in 14 children with brucellosis

Symptoms	Children	
	No.	%
Fever	14	100
Arthralgia and myalgia	10	71
Sweats	7	50
Weakness	7	50
Abdominal pain	4	28
Arthritis	4	28
Headache	3	21
Vomiting	2	14
Rash	2	14

only 7 children. The others had initially been diagnosed before admittance to hospital as acute arthritis (2), typhoid fever (2), purpura (1), and fever of unknown origin (2). Diagnosis of brucellosis was dependent on the results of the investigations shown in Table 2.

Blood cultures were made in the Castañeda double medium with both Albimi broth and agar slant. Three tests for brucellar serum antibodies were carried out: an agglutination test using *Brucella abortus* strain 19 as antigen, a complement-fixation test, and the antiglobulin (Coombs's) agglutination test. This standard method for the serodiagnosis with the 3 tests increases the likelihood of diagnosis and shows how far the illness has progressed.⁷

Treatment. We used rifampicin alone (20 mg/kg per day) given twice daily by mouth and always before meals, for a period of 21 days. Before starting the study it had been agreed to adopt the following conditions: (1) initially severe forms to be excluded; (2) rifampicin to be stopped (changing to tetracycline, sulphonamides, and streptomycin) if fever persisted after 12 days; (3) treatment to be changed if blood culture should be positive in the second week or if the patient's condition worsened. In the event, treatment with rifampicin was not stopped for any of these reasons.

Results

Clinical improvement occurred in all the patients, with fever clearing between the 2nd and 8th day of treatment. Other clinical signs disappeared some days later, except in 2 children with arthritis who took several months to recover completely.

Slight increase in the erythrocyte sedimentation rate, moderate anaemia, and leucopenia were regularly noted at the start, but disappeared between the 8th and 15th day of treatment. Blood culture before treatment was positive in 11 (78%) cases; in all, it became negative in the second week of treatment.

Relapses. All the patients were followed up. This gave us the opportunity to study two relapses which occurred 3 and 7 weeks after treatment had been stopped. One patient developed an acute arthritis, and in the other the typical clinical picture of acute brucellosis recurred. In both cases blood culture was again positive. The first of these was probably due to the fact that treatment had been stopped without due attention being paid to the child's residual arthritis. The second case was perhaps a reinfection rather than a relapse, because the child continued to eat cheese made from goat's milk, despite our warnings. In both cases, full recovery followed a 21-day course of rifampicin and cotrimoxazole.

Discussion

We found rifampicin to be reasonably effective when used as the sole drug in the treatment of acute brucellosis, 85% of the children being cured by a 21-day course of the drug. It is easy to administer, and side effects are minimal. Furthermore, because of its ability to penetrate the reticuloendothelial system, where the brucellar organisms lodge, relapses and chronic forms of the disease are fewer.

Table 2 Initial blood culture and serology

Case	Age (years)	Sex	Length of illness	Blood culture	Agglutination test	Complement-fixation test	Coombs's test
1	11	M	2 months	<i>B. melitensis</i>	1/80	1/320	1/5120
2	12	F	7 days	<i>B. melitensis</i>	1/640	1/320	1/2560
3	12	M	30 days	<i>B. melitensis</i>	1/160	1/1280	1/2560
4	14	F	4 months	<i>B. melitensis</i>	1/80	1/80	1/1280
5	8	M	22 days	Negative	1/320	1/80	1/2560
6	10	F	30 days	Negative	1/40	1/1280	1/2560
7	6	M	6 days	<i>B. melitensis</i>	1/320	1/160	1/1280
8	11	F	30 days	<i>B. melitensis</i>	1/320	1/1280	1/640
9	13	M	2 months	<i>B. melitensis</i>	1/160	1/1280	1/640
10	1	M	15 days	Negative	1/160	1/320	1/1280
11	3	M	45 days	<i>B. melitensis</i>	1/160	1/80	1/640
12	10	M	15 days	<i>B. melitensis</i>	1/1280	1/1280	1/2560
13	10	F	45 days	<i>B. melitensis</i>	1/5120	1/2560	1/5120
14	2	M	3 months	<i>B. melitensis</i>	1/80	1/640	1/1280

Despite these results with rifampicin alone, we think that brucellosis should not be routinely treated with only one antibiotic. We suggest that rifampicin should be combined with co-trimoxazole as currently the most effective treatment.⁸

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Correspondence to Professor J Llorens-Terol, Department of Paediatrics, Hospital Nuestra Señora del Mar, Paseo Marítimo de la Barceloneta, Barcelona 3, Spain.