

THERAPY OF INFANTILE GASTRO-ENTERITIS WITH CHLORAMPHENICOL AND NEOMYCIN

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In a trial conducted by the Medical Research Council of Great Britain, sulphonamides and chloramphenicol were found to be the drugs of choice in the treatment of 'non-specific' gastro-enteritis.¹ At Baragwanath Hospital, chloramphenicol was shown to be the most effective drug in the treatment of intestinal shigella and salmonella infections, while sulphonamides, oxytetracycline, and oral streptomycin were relatively ineffective.^{2,3} However, since chloramphenicol is potentially toxic and recent *in vitro* tests³ suggested that neomycin would be almost as good as chloramphenicol in the treatment of shigellosis and better than chloramphenicol in the treatment of salmonellosis, we decided to compare these 2 drugs in a clinical trial.

Neomycin was first isolated by Waksman and le Chevalier at Rutgers University in 1949.⁴ It is water-soluble and has a bactericidal action on many Gram-positive and Gram-negative bacteria. It is highly toxic when given parenterally causing auditory and renal damage.⁵ However, when given orally very little is absorbed and the action is almost entirely a topical one. This antibiotic has been used quite extensively before operations on the colon

and rectum⁶ for suppressing intestinal organisms, and is the antibiotic of choice in the suppression of intestinal organisms in hepatic failure.⁷ It has also been used in the treatment of pathogenic *B. coli* infection of the bowel. Wheeler and Wainerman⁸ had excellent results when using it to treat infants affected with chloramphenicol-resistant *B. coli* and there are several other reports of good results with the use of neomycin in the treatment of pathogenic *B. coli*.^{9,10}

There is little information on the efficacy of neomycin in the treatment of shigella and salmonella infections. Ponce de Leon¹¹ reported that neomycin was successful in the treatment of 15 children with shigellosis. He reported no untoward effects. Rogers *et al.*¹² found it useful in the treatment of *Shigella sonnei* dysentery but found it unsuccessful in the treatment of salmonella carriers.

The comparative lack of information on neomycin in shigella and salmonella infections and its impressive results *in vitro* against these infections prompted us to set up a clinical trial contrasting neomycin with chloramphenicol in the treatment of diarrhoeal disorders in general and shigellosis and salmonellosis in particular.

MATERIAL AND METHODS

The trial was carried out in the summer of 1958-1959 in the emergency ward at Baragwanath Hospital where we treat children with severe diarrhoea who require intravenous fluid therapy. Altogether 353 children, all under 3 years of age, were treated in the survey. On admission, rectal swabs were taken for bacteriological examination and all patients were given routine intravenous therapy and other supportive treatment. Alternate patients were given neomycin or chloramphenicol in doses of 40-50 mg. per lb. body-weight per 24 hours. Treatment commenced immediately after the rectal swab had been taken and therefore several days before it was known whether the patient was suffering from an infection with shigella or salmonella organisms. Intravenous therapy was continued until the patients were rehydrated and able to retain a maintenance diet. Where deterioration of the condition occurred on this treatment, patients were transferred to the routine wards for further resuscitative measures.

The result of treatment in the groups was judged by the number of deaths, continued deterioration on treatment necessitating transfer to the routine wards, and relapses after discontinuation of intravenous therapy. All patients on whom follow-up investigations could not be carried out and all cases complicated by severe malnutrition were excluded from the trial.

RESULTS

Of the 353 patients (Table I), 28 suffered from salmonellosis, 49 from shigellosis (33 *S. flexneri*, 14 *S. sonnei*, 1 *S. boydii*, and 1 *S. schmitzii*) and the remaining 276 from 'non-specific' acute diarrhoea.

Of the 28 patients suffering from salmonellosis, 12 were in the group treated with neomycin and 16 in the group treated with chloramphenicol; 8 of the 12 treated with neomycin (67%) and 12 of the 16 treated with chloramphenicol (75%) made uncomplicated recoveries.

TABLE I. RESULTS OF CHLORAMPHENICOL AND NEOMYCIN THERAPY IN 'NON-SPECIFIC', SHIGELLA, AND SALMONELLA ENTEROCOLITIS

Organism	Treatment	Total cases	Uneventful recovery	Deaths	Relapses	Transfers to routine wards
'Non-specific' 276 cases	Chloramphenicol	143	118 (83%)	1	5	19
	Neomycin	133	107 (80%)	1	2	23
Shigella 49 cases	Chloramphenicol	22	18 (82%)	0	2	2
	Neomycin	27	16 (59%)	0	0	11
Salmonella 28 cases	Chloramphenicol	16	12 (75%)	0	1	3
	Neomycin	12	8 (67%)	1	0	3
		353				

Of the total of 49 patients suffering from shigellosis 27 were treated with neomycin and 22 with chloramphenicol; 16 of the 27 treated with neomycin (59%) and 18 of the 22 treated with chloramphenicol (82%) made uncomplicated recoveries. Of the 276 patients suffering from 'non-specific' diarrhoea, 133 were treated with neomycin and 143 with chloramphenicol; 107 of the 133 treated with neomycin (80%) and 118 of the 143 treated with chloramphenicol (83%) recovered uneventfully.

DISCUSSION

In this investigation into the treatment of children with

severe gastro-enteritis, 14% of cases suffered from shigellosis and 8% from salmonellosis; 22% in all. In 2 previous investigations at Baragwanath Hospital,^{2,13} the combined incidence of shigella and salmonella infections in severe gastro-enteritis was 29% in the first investigation and 35% in the second, and it has been estimated that, in actual fact, these organisms are the infecting agents in as many as 50% of cases. In all investigations here shigellosis is approximately twice as common as salmonellosis.

This investigation suggests that chloramphenicol and neomycin are of approximately equal value in the treatment of salmonella and non-specific enteritis. From previous *in vitro* studies we had anticipated that neomycin might have been more effective than chloramphenicol in the treatment of salmonellosis, but it is probably not surprising that this was not so. It is known that a proportion of cases with salmonella enteritis have a septicaemic phase and we have obtained positive blood cultures in such cases, particularly where there is associated purpura.¹⁴ Neomycin is not absorbed from the bowel and is therefore ineffective in salmonella septicaemia.

In the treatment of shigella infections of the bowel, this investigation suggests that chloramphenicol is of greater value than neomycin. Chloramphenicol has also been shown to be of greater value than previously-tested antibiotics in shigella infection and would therefore appear to be the antibiotic of choice in the treatment of shigellosis in our community.

SUMMARY

In previous investigations at Baragwanath Hospital, chloramphenicol proved better than sulphonamides, oxytetracycline and streptomycin in the treatment of intestinal shigella and salmonella infections in children.

In the present investigation, neomycin, which had previously shown very promising results *in vitro* against these organisms, was contrasted with chloramphenicol in the treatment of infantile gastro-enteritis.

The 2 antibiotics were equally effective in 'non-specific' gastro-enteritis and salmonella infections. Chloramphenicol, however, appeared to be better in shigella dysentery.

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