THE TREATMENT OF SALMONELLOSIS IN INFANTS AND CHILDREN WITH PAROMOMYCIN ('HUMATIN')

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A significant number of infants and children with salmonellosis fail to respond to antibiotics, and the treatment of the condition must be regarded as unsatisfactory.[1-3] The difficulty of assessing the effects of therapy has been discussed in a previous paper.[1] Too often a particular antibiotic has been credited with producing excellent results when there has been no bacteriological control. Although patients may improve clinically, whatever treatment is employed, a large number of salmonella infections are not eradicated and the victims continue to excrete the organisms in the stool for undetermined periods.

Paromomycin is a new antibiotic, isolated from a strain of streptomyces, with a wide range of bactericidal and bacteriostatic activity against gram-positive and gram-negative bacteria.[4] Because of its nephrotoxic action when administered parenterally it is given only by mouth, since it is said not to be absorbed from the gastro-intestinal tract. The dosage is 50 mg. per kg. per day in divided doses, at 6 - 8 hour intervals, for up to 7 days. Coles *et al.*,[5] using paromomycin, were able to clear salmonellae from the stools in 5 out of 10 patients. In each case the organism was sensitive to paromomycin.

This paper presents the results of a trial of treatment with paromomycin in a group of children aged 1 month - 8 years who were suffering from intestinal salmonella infection.

MATERIAL AND METHOD

Positive salmonella cultures were obtained from stool examination immediately before the administration of paromomycin in 18 patients. The age, admission diagnosis, salmonella typing and sensitivity tests are given in Table I. No sensitivity tests were carried out against paromomycin. The majority of the children (15 out of 18) were under the age of 2 years.

Only 2 patients had had no previous treatment. The rest had been treated with sulphonamides, penicillin or broad-spectrum antibiotics for varying lengths of time before therapy with paromomycin was begun (Table I).

Paromomycin suspension was given in an average dosage of 27 mg. (variation 15 - 50 mg.) per lb. body weight over 24 hours. The duration of therapy varied from 6 to 11 days.

Patients were regarded as cured only if 3 or more consecutive rectal swabs or stool cultures were negative for salmonella.

RESULTS

Three or more consecutive rectal swabs or stools negative to culture were obtained in 8 (44%) of the 18

TABLE I. DATA OF 18 PATIENTS TREATED WITH PAROMOMYCIN HUMATIN)

Name	Age (months)	Admission diagnosis	Pre-humatin treatment	Salmonella type	Sensitivity tests of culture*						Humatin (mg./lb./24 hrs.)	Duration of treatment (days)	Outcome
					Chloromycetin	Neomycin	Streptomycin	Terramycin	Sulphonamides	'Kantrex'			
J.S.	3	Respiratory-tract infection	'Terramycin' 5 days	C1	+	+	+	+		+	43	8	F
B.S.	3	D + V	'Chloromycetin' 5 days Neomycin 4 days	UI	−	+	−	−	−	+	50	7	F
M.N.	60	Anorexia	Nil	E1	+	+	+	+	−	+	35	7	F
J.F.	96	Acute nephritis	Procaine penicillin	C2	+	+	+	+	−	+	20	11	ST
C.H.	24	D + V	Procaine penicillin } 5 days Sulphadiazine }	UI	+	+	+	−	−	+	20	7	F
D.H.	2	D + V	Chloromycetin 6 days, terramycin 5 days		+	+	+	−	−	+	45	7	F
K.A.	10	D	Chloromycetin 5 days	B	+		+	+			20	7	F
E.O.	14	D + pulmonary TB	Chloromycetin 5 days, then streptomycin and novobiocin 7 days	UI	+		+	+			16	7	F
S.S.	4	D	Chloromycetin 8 days	UI	+		+	+			25	6	F
C.V.	3	D + V	Chloromycetin 7 days	C1	+		+	+			20	7	F
P.I.	11	D + V Kwashiorkor	Sulphadiazine Procaine penicillin 6 days	C2	+		+	+			15	6	ST
L.S.	7	Bronchopneumonia	Terramycin 7 days	E & B	+		+	+			25	6	ST
S.L.	6	D + V	Chloromycetin 5 days	C1	+		+	+			30	7	ST
H.W.	6	D	Sulphadiazine 5 days	C1	+		+	+			25	7	F
T.J.	2	D	Chloromycetin 9 days	UI	+		+	+			30	10	ST
J.L.	21	Respiratory-tract infection	Chloromycetin 7 days Neomycin 6 days	UI	+	+	+	+	−	+	20	7	ST
C.S.	1	Haemolytic disease	Nil								25	7	ST
W.vH.	±36	Asthma	Nil								25	7	ST

* All the salmonellae were insensitive to penicillin, erythromycin and novobiocin.
D = diarrhoea, D + V = diarrhoea and vomiting, UI = unidentifiable, ST = successful therapy, F = failure—persistence of infection.

patients following paromomycin therapy (Table I). The rest of the patients (55·6%) therefore proved resistant not only to paromomycin, but also to the antibiotics previously employed.

Although no definite conclusion can be drawn from this small series, it seems that the dosages employed had no effect on the number of patients cleared of salmonella (Table II).

TABLE II. EFFECT OF PAROMOMYCIN DOSAGE

	Dosage (mg./lb./24 hours)		
	20	20-24	25+
Cleared of salmonella	1	2	5
Salmonella still present on culture ..	1	3	6
Total	2	5	11

In the majority of children the diarrhoea and vomiting had subsided by the time therapy with paromomycin was commenced. Without knowledge of the positive culture for salmonella they would have been regarded as 'cured'.

No side-effects, such as diarrhoea or nausea, and no evidence of staphylococcal or mycotic superinfection were noted in this series.

DISCUSSION

In the present series 55·6% of cases proved resistant to therapy with paromomycin. The results are therefore in agreement with Coles *et al.*,[5] who with a paromomycin dosage of 40 mg. per lb. body weight per day reported bacteriological clearance of the gastro-intestinal tract for salmonella in 50% of their cases. This comparison with their results and the evidence presented in Table II both suggest that the dosage employed has no material effect on the clearance of salmonella from the gastro-intestinal tract.

All the children in the present series, with the exception of two who were untreated, were also resistant to therapy with sulphonamides and broad-spectrum antibiotics. Salmonella may, furthermore, be cultured only on the 4th or subsequent rectal swab or stool culture, so that patients regarded as cleared from salmonella in the present series, may still have harboured salmonella in the gastro-intestinal tract. This would tend to make the results even more disappointing.

SUMMARY

Eighteen patients with salmonella infection of the gastro-intestinal tract were treated with paromomycin.

The results in the age group studied were disappointing, negative rectal swabs and stool cultures being obtained in only 8 children.

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REFERENCES

1. Heese, H. de V. (1960): S.Afr. Med. J., **34**, 785.
2. Woodward, T. E., Smadel, J. E. and Levy, H. E. (1950): J. Clin. Invest., **29**, 87.
3. Korns, R. F. and Albrecht, R. M. (1951): J. Lab. Clin. Med., **38**, 617.
4. Coffey, G. L., Anderson, L. E., Fisher, M. W., Galbraith, M. M., Hillegras, A. B., Kohberger, D. L., Thompson, P. E., Weston, K. S. and Ehrlich, J. (1959): Antibiot. and Chemother., **9**, 730.
5. Coles, H. M. T., MacNamara, B., Mutch, L. and Holt, R. J. (1960): Lancet, **1**, 944.