A Comparison between Oral Pivampicillin and Ampicillin in Children with Bronchopneumonia

J. G. PRINSLOO, A. CICORIA, R. G. ROBINSON, N. F. LAUBSCHER

SUMMARY

Pivampicillin and ampicillin were compared, in 30 children suffering from acute bronchopneumonia, as regards intestinal absorption, liver function tests and clinical response.

No significant differences were found in the clinical response or liver function tests of the two groups. Enteral absorption of pivampicillin was significantly better than that of ampicillin. It is concluded that pivampicillin should be theoretically superior to ordinary ampicillin in the oral treatment of infections due to ampicillin-sensitive micro-organisms.

S. Afr. Med. J., **48**, 2627 (1974).

The absorption of ampicillin administered orally is relatively poor. When taken by mouth the quantity excreted in the urine averages only 35% - 45% of that found after a comparable intramuscular dose.[1] For maximal effectiveness of ampicillin, intramuscular or intravenous injection would appear to be preferable. The availability of an ampicillin derivative with improved enteral absorption would thus be an asset, especially in children, since the indications for parenteral administration would then decrease. Pivampicillin, the pivaloyloxymethyl ester of ampicillin, is claimed to be well absorbed from the gastro-intestinal tract and is rapidly hydrolysed to ampicillin in the body by serum and tissue enzymes.[2]

A trial in young children was deemed worth while in order to evaluate the absorption, clinical efficacy and possible side-effects of pivampicillin in comparison with ampicillin.

PATIENTS AND METHODS

Thirty children between 1 and 3 years of age, admitted to hospital with acute bronchopneumonia, were studied. The clinical diagnosis was confirmed roentgenologically. Subjects were included in the study only if no antibiotics had already been given for their present illness and if no signs of measles, tuberculosis or whooping cough were evident. Critically ill patients were also excluded, these children being treated by parenteral administration of antibiotics. Patients were allocated at random to either the pivampicillin or ampicillin regimen.

Blood samples were collected before antibiotic administration for the determination of ampicillin levels to exclude the possibility of previous intake. Haemoglobin estimations, white blood cell counts, and the levels in the serum of total proteins, albumin, urea, electrolytes and SGOT were also determined.

The pivampicillin used was not the hydrochloride, which may cause oesophageal irritation, but the free pivampicillin base. After reconstitution, 5 ml of pivampicillin syrup contained 125 mg pivampicillin base. After a 2-hour fast, patients were given a *stat* dose by mouth of 250 mg of either ampicillin or pivampicillin as a syrup. They were fasted for a further 2 hours, then blood specimens were taken for the determination of ampicillin levels. Blood for ampicillin assays was centrifuged within 30 minutes of collection. The serum was kept frozen until estimations were done. The technologist was unaware of the group allocation of the patients.

In each group the respective antibiotic was continued for 10 days. Both ampicillin and pivampicillin syrup were given in a dosage of 125 mg every 6 hours. The patients' bodyweight values were recorded daily and they were observed for vomiting, skin rashes or other adverse reactions. Blood specimens were collected again after 10 days to repeat the estimations done on admission.

RESULTS

The mean values of the parameters determined are presented in Table I. The average blood concentration of ampicillin 2 hours after the loading dose of 250 mg ampicillin or its molar equivalent of pivampicillin can be seen from Table II. On admission, and before antibiotic administration, all the serum ampicillin levels were less than 0,1 μg/ml, indicating no immediate previous intake. The variables presented in Table I did not differ significantly between the 2 groups, neither on admission nor after 10 days ($P>0,05$—Hotelling's t-test). The 2 groups were thus comparable with respect to these parameters.

There were also no significant differences between the levels of total serum protein, serum albumin, haemoglobin, SGOT or blood urea from admission to recovery (after 10 days) within the same group ($P>0,05$—Wilcoxon

Department of Paediatrics, University of Pretoria, and Kalafong Hospital, Pretoria
J. G. PRINSLOO, M.MED. (PAED.), M.D.
A. CICORIA, M.B. CH.B.

South African Institute for Medical Research, Johannesburg
R. G. ROBINSON, F.I.M.L.T.

National Research Institute for Mathematical Sciences, CSIR, Pretoria
N. F. LAUBSCHER, D.SC.

Date received: 14 August 1974.

TABLE I. MEAN VALUES FOR AGE, BODY WEIGHT AND BLOOD CONSTITUENTS MEASURED IN PIVAMPICILLIN AND AMPICILLIN GROUPS

	Pivampicillin N = 15				Ampicillin N = 15			
	On admission		After 10 days		On admission		After 10 days	
Age (months)	23,60				18,46			
Body weight (kg)	10,17	(1,920)	10,86	(2,249)	9,30	(2,095)	9,73	(2,038)
Haemoglobin (g/100 ml)	11,35	(0,952)	11,33	(1,298)	10,85	(1,601)	10,55	(1,755)
Total serum protein (g/100 ml)	7,07	(0,727)	7,22	(0,888)	6,77	(0,772)	6,84	(0,518)
Serum albumin (g/100 ml)	3,91	(0,746)	3,83	(0,286)	3,68	(0,591)	3,76	(0,473)
White blood cells (per mm^3)	14 320	(7 333)	11 865	(6 623)	10 8?0	(3 491)	10 190	(2 346)
SGOT (mU/ml)	19,53	(11,529)	20,53	(5,377)	18,80	(5,238)	18,73	(5,430)
Blood urea (mg/100 ml)	34,64	(12,380)	39,20	(14,830)	32,73	(10,210)	38,93	(16,500)
Blood uric acid (mg/100 ml)	6,74	(3,348)	4,47	(2,369)	5,66	(2,723)	4,37	(1,708)
Serum Na (mEq/L)	138,6	(2,898)	137,93	(3,554)	138,3	(3,063)	136,47	(2,642)
Serum K (mEq/L)	4,68	(1,150)	4,86	(0,532)	5,02	(0,606)	4,95	(0,501)
Serum total bicarbonate (mEq/L)	17,52	(4,608)	17,10	(3,817)	16,66	(4,096)	16,97	(2,997)

Standard deviations are given in brackets.

TABLE II. AVERAGE SERUM AMPICILLIN LEVELS WITH STANDARD DEVIATIONS IN THE TWO GROUPS

Pivampicillin (μg/ml)	Ampicillin (μg/ml)
7,53*	3,50*
(SD = 3,57)	(SD = 2,50)

* Highly significant difference ($P<0,01$ — Mann-Whitney U-test).

matched-pairs signed-ranks test). There was therefore no evidence of adverse effects on liver function as judged by SGOT levels or total serum protein and albumin levels. The apparent slight increase in serum urea levels was not significant, and could have resulted from high protein feeds and tissue catabolism due to the pulmonary inflammatory process not yet completely resolved after 10 days.

In the pivampicillin group, the mean serum level of ampicillin (7,53 μg/ml) was more than twice as high as the mean level in the ampicillin group (3,50 μg/ml), the differences being highly significant ($P<0,01$—Mann-Whitney U-test). Slight diarrhoea occurred in 2 patients of each group for approximately one day only, while 1 patient in each group vomited for a period of about one day. No untoward reactions were encountered in any other patients. All the patients recovered, and in both groups fever had subsided within 4 days of the initiation of therapy.

CONCLUSION

It may be concluded that absorption of pivampicillin was considerably better than that of ampicillin. Consequently, pivampicillin should theoretically be superior to ordinary ampicillin in the oral treatment of infections due to ampicillin-sensitive micro-organisms.

We wish to thank Messrs Merck, Sharp and Dohme for the supply of pivampicillin (Alphacillin).

REFERENCES

1. Kunin, C. M. (1967): Ann. N.Y. Acad. Sci., **145**, 282.
2. Von Daehne, W., Frederiksen, E., Gundersen, E., Lund, F., Morch, P., Petersen, H. J., Roholt, K., Tybring, L. and Godtfredsen, W. O. (1970): J. Med. Chem., **13**, 607.