Clinical features on admission

Clinical feature	No of cases
Dilated pupils	6
Visual hallucinations	6
Oropharyngeal dryness	5
Disorientation	4
Delirium	3
Paranoia	3
Ataxia	3
Tachycardia*	3
Raised systolic blood pressure†	3
Fever	2
Exaggerated tendon reflexes	2
Anxiety	2
Flushed appearance	1
Euphoria	1
Drowsiness	1
Amnesia	1

*Pulse rate >100 per min.
†>140 mm Hg.

salicylate, 1 to 4 mg (0·5 to 1 mg in children), by slow intravenous injection every one to two hours, and repeated doses may be required; but we did not find it necessary to use this drug in our cases. Sedation should be with parenteral diazepam or chlormethiazole and not with phenothiazines, which may intensify the toxicity of the psychosis on account of their antimuscarinic activity.[2]

Intoxication by datura is common in the USA, where it is used by adolescents and young adults as a legal and readily available hallucinogen.[3] Recently attention has been drawn to the increasing reports from Britain of abuse of strammonium-containing asthma remedies.[4] An account of thorn-apple (*D strammonium*) poisoning in Australia emphasises the existence of a cult in one community, with devotees using the drug to achieve altered states of consciousness.[5] This apparently began with the wide circulation of a paperback, *The Teachings of Don Juan*,[6] in which the use of hallucinogenic plants is extolled and the preparation of extracts from datura detailed. This book is readily available in libraries and bookshops throughout Britain and is constantly in demand. Several cases of poisoning in children in West Cornwall has resulted in local action to cut down datura trees. Other natural and over-the-counter sources of the antimuscarinic drugs remain, however, and will be liable to abuse.

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(*Accepted 29 December 1978*)

Mecillinam in enteric fever

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British Medical Journal, 1979, **1**, 586-587

Summary and conclusions

Twelve consecutive patients with enteric fever entered a trial of 14 days' treatment with mecillinam. Only three patients became afebrile within three days; four continued unimproved with fever and toxaemia for seven to nine days, when treatment was changed to chloramphenicol with good results. In one case the fever did not settle until the 13th day, and five days later the patient had a clinical relapse.

Although all organisms recovered were fully sensitive to mecillinam, this drug is not an effective or consistent treatment for enteric fever.

Introduction

Preliminary studies[1-3] indicated that mecillinam, a new β-lactam amidinopenicillanic acid antibiotic, may be an important alternative to chloramphenicol for enteric fever. We have carried out a trial of this drug on 12 patients and report our results.

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Patients and methods

Twelve consecutive patients with enteric fever and aged 9-37 years were studied (see table). Blood, stool, and urine were cultured on admission, blood cultures being repeated if fever persisted despite treatment. Eight patients had typhoid fever and four paratyphoid fever. In all but one case the clinical diagnosis was confirmed by isolation of the organism from the blood. In the remaining patient (case 7) it was based on the typical illness with positive stool and urine cultures and a highly suggestive Widal test result. This patient had a double infection with *Salmonella paratyphi A* and *B*. Mecillinam was given initially by intramuscular injection in 10 patients and in the event of a satisfactory clinical response changed to oral pivmecillinam. Two patients who were not unduly ill received oral treatment throughout. The planned duration of treatment was 14 days. Full blood counts, liver function tests, and measurement of serum urea and electrolyte concentrations were carried out before, during, and after treatment in most cases.

Results and comments

Defervescence is generally accepted as the best indication of response to a drug in enteric fever. With chloramphenicol this is usually achieved within two to five days.[4] In our series (table) only three patients (cases 1, 6, and 8) showed a prompt response and became afebrile within this period. A further four patients (cases 3, 7, 10, and 12) were afebrile in six to eight days. Four patients (cases 2, 4, 9, and 11) continued unimproved with fever and toxaemia for seven to nine days; the treatment was then changed to chloramphenicol, and the fever settled in two to four days. In case 5 the toxaemia improved but the fever did not settle until the 13th day, and five days later the patient suffered

Clinical and bacteriological details and results of treatment in 12 patients with enteric fever given mecillinam.

Case No	Age and sex	Pretreatment bacteriology	Pretreatment duration of fever (days)	Dose (six-hourly)	Results of treatment
1	28 M	*S paratyphi A* (blood, faeces)	5	800 mg IM by mouth	Afebrile on third day
2	19 F	*S typhi* (blood, faeces)	5	800 mg IM	Changed to chloramphenicol after seven days, then afebrile in two days
3	9 M	*S typhi* (blood, faeces)	2	400 mg IM/by mouth	Afebrile on eighth day
4	37 F	*S paratyphi B* (blood, faeces)	7	600 mg IM	Changed to chloramphenicol after eight days, then afebrile in two days
5	10 F	*S typhi* (blood, faeces)	6	400 mg IM	Temperature not settled till 13th day, then relapsed after five days
6	36 M	*S typhi* (blood, faeces)	14	600 mg IM/by mouth	Afebrile on third day
7	15 F	*S paratyphi A* and *B* (faeces, urine)	14	400 mg by mouth	Afebrile on eighth day
8	30 M	*S typhi* (blood, faeces)	11	400 mg by mouth	Afebrile on day treatment began
9	23 F	*S typhi* (blood, urine)	8	400 mg IM	Changed to chloramphenicol after nine days, then afebrile in four days
10	23 F	*S paratyphi B* (blood, faeces)	10	400 mg IM	Afebrile on sixth day
11	13 M	*S typhi* (blood, faeces)	10	800 mg IM	Changed to chloramphenicol after nine days, then afebrile in 48 hours
12	19 M	*S typhi* (blood)	12	800 mg IM	Afebrile on seventh day

IM = Intramuscularly.

a clinical relapse. All the organisms appeared to be fully sensitive to mecillinam by the disc-diffusion method. No evidence of persisting bacteraemia was found in any of the treatment failures, and where the organisms could be recovered from the stools they remained fully sensitive to mecillinam. Five patients (cases 2, 3, 7, 9, and 10) had positive stool cultures in the immediate post-treatment phase, but all had several negative stool and urine cultures by the third month. No adverse side effects of the drug were noted in any patient.

In the Birmingham trial[1 2] 13 out of 15 patients responded satisfactorily to mecillinam, and the mean duration of fever was five days. Limson[3] reported a mean duration of 4·8 days in 10 patients treated with the oral drug. We cannot explain why our results are at variance with these. The dose of mecillinam could not have been a factor, as we generally used a higher dose regimen than the other workers. The clinical picture of enteric fever varies greatly from mild and self-limiting to severe, and the severity of illness could well have been a factor accounting for the varying response in our series. All our treatment failures had a severe form of the disease, and those who responded had relatively milder illnesses. It would have been interesting to know the days of defervescence in the individual patients in the Birmingham series, and it may be relevant that in Limson's series the patient who showed the slowest response had more severe clinical manifestations.

We originally intended to continue the trial on larger numbers of cases, but the results in these 12 patients showed clearly that mecillinam is not a highly effective or consistent treatment for enteric fever, and so we did not feel justified in continuing to use it.

We thank Leo Laboratories for supplying mecillinam and pivmecillinam.

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(*Accepted 9 January 1979*)

ONE HUNDRED YEARS AGO This case of recovery from leprosy was brought before the Royal Medical and Chirurgical Society as an instance of complete arrest of the progress of true leprosy. There was still paralysis of one ulnar nerve, and many patches of skin were deficient in sensation, and there were permanent changes in the eyes. In other respects, however, the cure was complete, and the patient enjoyed excellent health. The subject of the case had been under the author's observation for twenty-seven years. She was a Jewess, born of parents who had lived only in England, of a family in which no leprosy taint existed. At the age of thirty-two, she went to live in Jamaica; and twelve years later, she returned, the subject of leprosy in a severe form. The tubercular and the anaesthetic symptoms were present in combination; areas of skin were dusky and devoid of sensation; one ulnar nerve was paralysed, and the face was covered with tuberous folds of indurated skin. She was for some time under treatment at the Hospital for Skin-Diseases, then an in-patient under Dr Addison at Guy's, and lastly at Moorfields. For the last twenty years, she had considered herself well. The author [Mr Jonathan Hutchinson] expressed his belief that the cause of recovery was the change of residence, and the element of importance in this the change of diet, and especially cessation from the use of fish. He did not believe that mere climatic influences, air, etc, had any share in the result; for leprosy prevailed under the most various conditions.

The President questioned whether Mr Hutchinson's condemnation of fish was borne out by facts. In Norway, where fish was much used, leprosy prevailed only in certain districts. Certain monastic orders also lived chiefly on fish, and yet he was not aware of the prevalence of leprosy among them. The disease was also widely spread in the middle ages, in districts where fish could not have been easily attainable.—Dr Gilbart Smith had seen many cases of leprosy in the parts about the Delta of the Nile. It was a very common opinion that it arose from eating fish that had been exposed to the rays of a tropical sun.—Mr C Macnamara said that leprosy existed among the tribes of the Himalaya mountains, who ate very little fish; while the disease was not met with among the residents near the Volga and Don, who used much fish. The inhabitants of the Sandwich Islands were free from leprosy until the immigration of Chinese in 1836, since which time it had prevailed extensively. There had also been a case in an European resident in Queensland, where there had been an immigration of Chinese. In this case, filariae were found in the blood, and leprosy would probably be found to be connected with the presence of these organisms.—Mr Hutchinson said that the connection of fish-diet with leprosy was a question of much detail, on the consideration of which there was not now time to enter. He would, however, say that he believed it was not so much the amount of fish as its quality that was important. A small quantity of bad fish would probably produce the disease, especially when it was taken from water of a high temperature. In Norway, leprosy did not prevail in Bergen, except among the poor; the water there was comparatively warm, being exposed to the Gulf-Stream. At Christiania, where the water was cold, there was no leprosy. Again, leprosy was met with in those parts of the coast of the Mediterranean to which fish was largely supplied.—Sir Joseph Fayrer said that, if bad fish produced leprosy, the inhabitants of British Burmah ought to be very liable to the disease, but they were not. It was the universal belief in India that leprosy was not due to the use of fish as food. (*British Medical Journal*, 1879.)