

BRITISH MEDICAL JOURNAL

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We may return unduly long letters to the author for shortening so that we can offer readers as wide a selection as possible. We receive so many letters each week that we have to omit some of them. Letters must be signed personally by all their authors. We cannot acknowledge their receipt unless a stamped addressed envelope or an international reply coupon is enclosed.

Intravenous N-acetylcysteine: the treatment of choice in paracetamol poisoning?

SIR,—Our attention has been drawn to the article by Dr L F Prescott and others (3 November, p 1097), not least by its arresting title. We have long been resigned to this type of "question-begging" caption in the popular and more sensational press; but we must confess to some surprise at the adoption of this device in your journal, when we had adhered to the belief that in a scientific paper the facts should be presented impartially for the enlightened and discriminating reader to draw his own conclusions. You must forgive us, then, for putting the question mark in the heading of this letter.

It happens that we have detailed information on 132 patients with acute paracetamol poisoning treated with oral methionine, the details of which have been presented elsewhere.¹ All of them on admission had plasma concentrations of the drug above a line joining semilogarithmic plots of 200 mg/l at 4 hours and 70 mg/l at 12 hours—that is, those who prognostically, on the basis of the figures in a previous paper by Prescott *et al.*,² should have been destined for severe hepatotoxicity. Of these, 96 were given the oral methionine within 10 hours of ingestion and none died from hepatic failure (see accompanying table). Seven did suffer severe liver damage (aspartate transaminase > 1000 IU/l), but six of these patients had extremely high paracetamol levels (> 300 mg/l at 4 hours and > 75 mg/l at 12 hours).

When, on the other hand, the administration of the oral methionine was delayed beyond 10 hours from the time of paracetamol

ingestion severe hepatic damage did ensue in 17 of these 36 patients, the outcome in this group being similar to that observed in the 57 patients studied retrospectively by Dr Prescott and his colleagues who had received supportive therapy only. So, as with other specific antidotes for this condition, including intravenous N-acetylcysteine, the time interval still seems to be critical. We do suggest therefore that, to judge from our results, oral methionine—as distinct from the intravenous methionine with which Dr Prescott and his colleagues drew their comparisons—is just as effective as intravenous N-acetylcysteine in the treatment of acute paracetamol poisoning.

So there remains the question of adverse reactions and toxicity. Dr Prescott and his colleagues, in their present paper, claim that

"frequent vomiting has been described with oral methionine" and cite a particular report,³ which on scrutiny refers to a single patient—who, it happens, survived quite satisfactorily despite the vomiting. In our series of 132 patients, 16% did vomit prior to the first dose of methionine, though only 5% continued to do so after the antidote; two of the patients among these did develop severe liver damage, possibly because they failed to absorb sufficient of the protective agent. It would seem reasonable therefore to give intravenous N-acetylcysteine rather than an oral preparation to all patients who vomit intractably.

Again, Dr Prescott and his colleagues say that methionine may be toxic. In this context they quote four references. On perusal one

Incidence of hepatic and renal damage in patients poisoned with paracetamol treated with methionine, cysteamine, and N-acetylcysteine

Treatment group	No of patients	No (%) with severe liver damage (AST > 1000 IU/l)	No (%) with acute renal failure	No (%) of deaths
Within 10 hours:				
Oral methionine	96	7 (7)	1 (1)	0
Oral N-acetylcysteine ²	49	8 (17)	0	0
Intravenous cysteamine ⁴	23	0	0	0
Intravenous N-acetylcysteine (Prescott <i>et al.</i> , present study)	62	1 (2)	0	0
After 10 hours:				
Oral methionine	36	17 (47)	2 (5)	2 (5.5)
Oral N-acetylcysteine ²	51	23 (45)	0	0
Intravenous cysteamine ⁴	13	8 (62)	1 (8)	1 (8)
Intravenous N-acetylcysteine (Prescott <i>et al.</i> , present study)	38	20 (53)	3 (15)	1 (5)
Supportive measures (Prescott <i>et al.</i> , present study)	57	38 (58)	6 (17)	3 (6)