combination of haloperidol with promethazine for rapid tranquillisation may not be the most cost-effective or the most efficacious even when resources are poor.

Alexander *et al* used the Clinical Global Impression Scale to rate aggression and violence. We feel that use of more aggression-specific measures, such as the Overt Aggression Scale (Coccaro *et al*, 1991), which assesses different aspects of aggression and its severity, would have generated more specific results.

Alexander *et al* also showed that the combination injection produces sedation quicker than intramuscular lorazepam. However, this finding should be viewed with caution because the lorazepam group included more patients with mania, more patients with substance misuse or already on benzodiazepines (who could have developed tolerance to benzodiazepines) and more patients with marked or severe illness (which would necessitate a higher dose of medication to control aggression and violence). Together these factors might have contributed significantly to the results.

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Authors' reply: We thank Drs Ranjan and Chandra for their considered response to our article. Although we acknowledge variations in prescribing practice, we know of at least two other centres nearby (the Institute of Mental Health and the Government Hospital, Chennai) that use the haloperidol–promethazine combination for rapid tranquillisation; the monthly combined out-patient attendance of the three centres is also greater than 9000.

Our wider survey of drug formularies, including the source of Ranjan and Chandra, and local pharmacies reveals that the price of injectable haloperidol (5 mg/ampoule) ranges between Rs 4.00 and Rs 5.50; that of promethazine (50 mg/ampoule) between Rs 3.00 and Rs 7.00; and that of lorazepam (4 mg/ampoule) between Rs 7.00 and Rs 15.00. We therefore reiterate our contention that the haloperidol–promethazine mix is cheaper than (even reduced doses of) haloperidol and lorazepam.

We agree that the Overt Aggression Scale would have generated more specific results. However, the outcomes for this pragmatic trial were not chosen to generate specific results; they were chosen by the doctors and nurses of the emergency rooms to be of clinical utility. From the reaction we have already had to this study these outcomes do seem acceptable and welcome to others.

We acknowledge that there were nine more people with mania, six more misusing substances and five more already on benzodiazepines in the lorazepam arm than in the comparison arm. There is no indication, however, that the integrity of the randomisation procedure was compromised, as such chance imbalances could occur in the absence of stratification. It is unlikely that these imbalances account for the findings, as the difference in the numbers of people 'clinically improved' between the two interventions at 15, 30, 60 and 120 min were 31, 25, 20 and 14, respectively, and in numbers 'asleep' 40, 47, 35 and 14.

Although recommended by important review articles and guidelines, we have found only four randomised studies in which a total of 80 people received the combination of haloperidol and lorazepam (Arana *et al*, 1986; Battaglia *et al*, 1997; Bieniek *et al*, 1998; Subramaney *et al*, 1998). None of these studies reports useful data on time to tranquillisation/sleeping; most report scale-derived data that are difficult to interpret clinically. For such limited data to direct practice at the two largest psychiatric centres in India, as well as many other places, would seem imprudent. The effects of haloperidol plus promethazine, we would still suggest, are better proven than other prevalent approaches. Recent influential guidelines in the UK have noted this and the sister study (TREC Collaborative Group, 2003) to be the only large trials of high methodological quality in this area (National Collaborating Centre for Nursing and Supportive Care *et al*, 2004).

Certainly the study and others like it need to be repeated so that the evidence upon which we treat people at this vulnerable time is robust. Practice on lesser evidence is surely unethical.

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Limitations of rapid tranquillisation trial

In their excellent paper Alexander *et al* (2004) systematically conducted a comparison trial of intramuscular lorazepam and haloperidol–promethazine in violent or agitated patients. The authors utilised a prospective follow-up design and used proper diagnostic assessment measures, thus taking care of most of the

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