Correspondence

Comparison of IV salbutamol with IV aminophylline in severe acute asthma

Sir,

In a double-blind comparative study of children with acute asthma, Hambleton and Stone (*Archives*, 1979, 54, 391) showed that IV salbutamol and aminophylline were equally effective when given during the first 24 hours.

The optimal use of theophylline requires a dosage regimen that maintains the serum concentration within the therapeutic range of 10-20 mg/l (Jenne *et al.*, 1972; Weinberger and Bronsky, 1974). Hambleton and Stone used a loading dose of 4 mg/kg followed by 0.6 mg/kg per hour. In a recent study (Selvig *et al.*, 1979), despite a bigger loading dose of 5 mg/kg in slightly older children (aged 8-15 years), therapeutic values were reached in only 62% of them and maximum serum concentration in each case was in the lower half of the range. A more suitable loading dose would have been 7.5 mg/kg, which is tolerated by most children, with average serum concentrations in the middle of the range (Weinberger, 1978). Furthermore, the infusion rate of 0.6 mg/kg per hour is much lower than the 0.85 mg/kg per hour recommended to maintain therapeutic serum concentrations in children less than 9 years (Hendeles and Weinberger, 1979).

The similar clinical effect shown by Hambleton and Stone when aminophylline dosage was subtherapeutic suggests to us that a different conclusion might have been reached had a therapeutic dose of aminophylline been used.

References

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Drs Hambleton and Stone comment:

We note the criticism about the dose of aminophylline and make the following comments. The assertion that therapeutic efficacy will be achieved when serum theophylline is 10-20 mg/l is based on the use of oral

theophylline compounds in the prophylaxis of *perennial* asthma (Jenne *et al.*, 1972; Weinberger and Bronsky, 1974). Weinberger *et al.* (1976) gave data on *acute asthma* in children and evaluated the dosages necessary to maintain the above level. However, their paper did not indicate how effective their regimen was in terms of producing relief from asthma. Turner-Warwick (1957) studied acute wheezing in adults, and judged the appropriate serum levels simply from reports from patients on the subjective relief of symptoms after oral theophylline compounds. Selvig *et al.* (1979) studied serum theophylline levels after a single IV dose of aminophylline, and recommended a loading dose of 6 mg/kg but gave no information about maintenance treatment. Weinberger (1978) recommended a loading dose of aminophylline 5 mg/kg, and although he suggested 7.5 mg/kg in some children he pointed out that this dose would be toxic in others. Weinberger (1978) and Hendeles and Weinberger (1979) recommended 0.8 mg/kg per hour and 0.85 mg/kg per hour respectively as maintenance therapy, but gave no indication that these doses were necessary for relief of symptoms in *acute* asthma. They recommended that serial theophylline estimations should be carried out for patients individually, which is the ideal *modus operandi*.

In a double-blind trial such as ours, serum theophylline estimations during treatment are precluded. Pierson *et al.* (1974) used virtually the same dosage regimen as we did, and produced objective evidence that this was effective in acute asthma. In routine practice we have also found this regimen effective and so adopted it for the trial, being confident that there would be no side effects. It also facilitated the pharmaceutical preparation of our ampoules for the double-blind design, having regard to the dosage of salbutamol. We feel our results support those of Pierson *et al.* (1974) by providing objective evidence that this regimen is effective in acute asthma. The assertion that our dose of aminophylline is subtherapeutic is not justifiable. It is possible that a higher dose might have been more effective, but another double-blind trial would be necessary to establish this point.

References

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