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Paracetamol suppositories: a comparative study

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SUMMARY Paracetamol suppositories in two different bases were given to children who had fever after operations. Plasma concentrations and the effect on temperature were compared. There was a significant correlation between peak plasma concentrations and maximum drop in temperature. A lipophilic base produced better results than a hydrophilic base.

Paracetamol given orally is standard treatment for fever. A problem arises, however, with children with impaired consciousness or who have nausea or vomiting. Until recently aspirin suppositories have met this need.[1] Although there have been no reports of Reye's syndrome associated with aspirin given rectally, it would seem prudent to avoid it. Many studies have documented the efficacy of paracetamol given orally for the treatment of fever.[2] Although clinical studies have shown that paracetamol given rectally is also effective, there is little information about its pharmacokinetics in children.[3]

Patients and methods

Twenty eight children recovering from cardiac operations were studied. Their ages ranged from 2 months to 8·3 years. All patients received the drug on the first day after operation. Initially 18 children were given 15–20 mg/kg paracetamol in a hydrophilic base as a single dose. The mean (SD) initial temperature in this group was 38·9 (0·6)°C. After review of the results a further 10 patients were given the same dose in a lipophilic base. The mean initial temperature in this group was 39·1 (0·7)°C.

Blood was taken at 0, 30, 60, 120, and 180 minutes for measurement of paracetamol concentrations. One ml of blood from the intravenous line was placed in a lithium heparin container and refrigerated until assayed. Plasma paracetamol concentrations were measured by a modified enzymatic technique on a Cobas Fara analyser as described by Kenny and Ward.[4] Rectal and peripheral temperatures were recorded routinely for each patient. The study protocol was approved by the hospital ethics and research committees.

Results

The plasma paracetamol concentrations achieved by the two preparations are shown in fig 1. There were significant correlations between the peak plasma paracetamol concentration and the maximum decrease in temperature achieved, the values for the

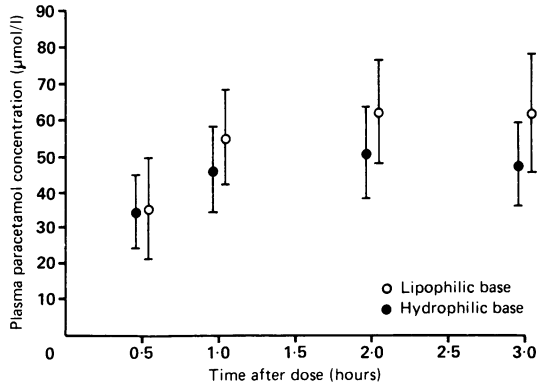

Fig 1 *Mean (SEM) plasma paracetamol concentrations.*

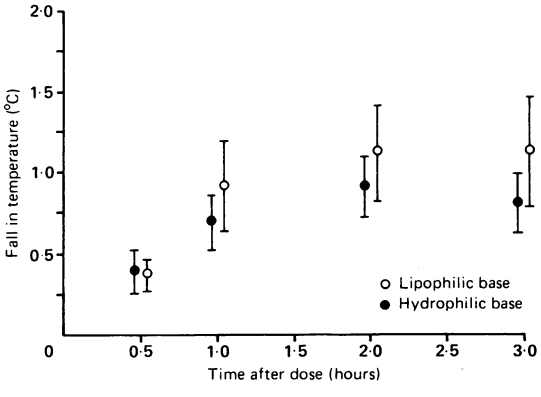

Fig 2 *Mean (SEM) fall in temperature after paracetamol suppositories had been given.*

lipophilic base and the hydrophilic base being 0·63 and −0·56, respectively.

The peak plasma concentrations achieved by paracetamol in a lipophilic base were significantly higher than in the group receiving the hydrophilic preparation ($p<0·03$, Wilcoxon rank sum test) despite variation in the time taken to achieve these concentrations. The maximum decrease in temperature achieved by the paracetamol in the lipophilic base was also significantly greater ($p<0·037$, Wilcoxon rank sum test) but once again this occurred at varying time intervals (fig 2). In those who received paracetamol in a hydrophilic base the mean drop in temperature was −1·0°C (range −0·4 to −1·7°C). The temperature rose again between three and four hours later. In the second group (who received paracetamol in a lipophilic base), the mean decrease in temperature was −1·5°C (range −0·6 to −2·2°C); this reduction in temperature lasted longer.

Discussion

Studies in adults have shown that maximum plasma concentrations after oral paracetamol are reached within 15 to 120 minutes, depending on the time since the last meal. The reported time for peak plasma concentrations to be reached after rectal administration was significantly longer with a range of 60 to 240 minutes.[5] Our results compare favourably with these reports.

The formulation of the base has been shown to have a profound effect on the adsorption of poorly soluble drugs such as paracetamol. Other studies have documented the superiority of triglyceride bases in increasing rectal absorption of paracetamol.[6]

We found no correlation between the age of the patient and either peak plasma concentration or maximum drop in temperature.

Although there was a wide range and considerable overlap in both the plasma paracetamol concentrations and the reductions in temperature achieved at the various time intervals, the lipophilic based paracetamol proved to be superior on average producing higher peak plasma concentrations and a better therapeutic response. We realise, however, that this conclusion can be criticised on the basis that the two groups of patients were not randomised.

Clinical trials have confirmed the efficacy of rectal paracetamol in children. We believe that paracetamol suppositories are effective in reducing fever whenever an alternative to oral medication is required.

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