

Short reports

Rectal aspirin—absorption and antipyretic effect

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SUMMARY Rectal acetylsalicylic acid was given to 14 children who had undergone open heart surgery. The effect on their temperatures was similar whether 15–30 or 30–50 mg/kg was given. Either dose was more effective than no treatment. The greatest fall in temperature occurred after 4 or 5 hours. Rectal aspirin in a triglyceride base is effective in lowering postoperative temperature. It should also be of use in treating other fevers. A dose of 20–25 mg/kg is suggested.

There are several reasons for raised temperatures in postoperative patients apart from infection. Fluid restriction after some types of surgery, and endogenous pyrogen release by leucocytes are two reasons for such pyrexia. However, there is no evidence that this pyrexia plays any beneficial role in aiding the inflammatory response. On the contrary, the increased metabolic rate resulting from raised body temperature may increase the stress to the patient. It is reasonable therefore to attempt to reduce such pyrexia, particularly after major surgery.

Aspirin is an effective antipyretic, and is better and more comfortable than tepid sponging (Hunter, 1973). There are conflicting reports concerning the usefulness of rectal aspirin (Samelius and Åström, 1958; Nowak *et al.*, 1974), and anyway they concentrated on the urinary recovery of salicylate in healthy subjects, rather than on the clinical effectiveness of rectal aspirin.

This trial was carried out with the following aims: (1) to assess the effect of rectal aspirin in lowering temperature after cardiac surgery; (2) to determine the duration of action of a single rectal dose; (3) to determine a weight-related dose for rectal aspirin; (4) to assess the safety of rectal aspirin.

Patients and method

19 children aged between 3 and 14 years who had undergone open heart surgery were studied. All had arterial and venous cannulae and a pulmonary artery temperature probe in place. Acetylsalicylic

acid in a triglyceride base was given as a single dose into the rectum. Suppositories contained either 150 or 300 mg aspirin. Seven of the 19 children were given between 15 and 30 mg/kg, the mean dose being 23 mg/kg. Seven children were given between 30 and 50 mg/kg, with a mean dose of 44 mg/kg. The remaining 5 children were used as controls. 1 ml blood was obtained before and then hourly for 7 hours after the suppositories had been inserted. Pulmonary artery and peripheral temperature were recorded throughout the trial.

No patient developed a clinically obvious infection for 72 hours after the trial. Serum salicylate was measured using the method of Keller (1947), modified for use in an ABA-100 analyser.

Results

The serum salicylate levels, attained after different doses are shown in Fig. 1. The greatest levels were reached 3 or 4 hours after administration. There was very little fall-off in serum levels up to 7 hours after administration. Levels achieved at any time after the higher dose were almost twice those attained after the lower dose, although the two

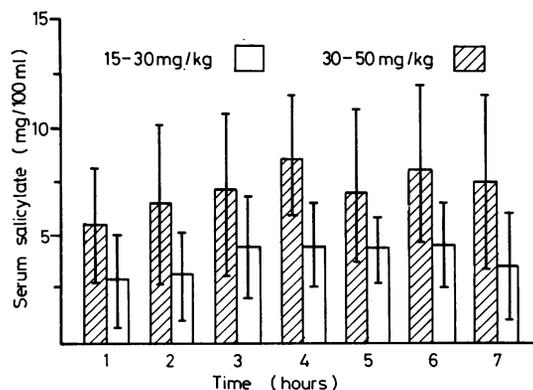


Fig. 1 Serum salicylate levels (mean \pm SD) after rectal acetylsalicylic acid.

groups overlapped. The highest serum level reached in any patient was 14 mg/100 ml (1.0 mmol/l), 6 hours after insertion of the suppositories. Low serum levels were achieved initially in 2 patients whose core-peripheral temperature gradients were more than 8°C for the first 3 hours of the trial.

The temperature pattern in the three groups is shown in Fig. 2. The mean temperature at the time of administration was somewhat lower in those who received the smaller dose, but throughout the period of observation the temperatures between the three groupings overlapped. The temperatures in those who received no aspirin tended to remain constant. Both groups who received rectal aspirin showed a fall in mean temperature of 0.9–1.0°C. The lowest mean level was reached after 4 hours in the low-dose group and after 5 hours in the high-dose group.

All subjects retained the suppositories throughout the trial, and in no patient did rectal bleeding occur.

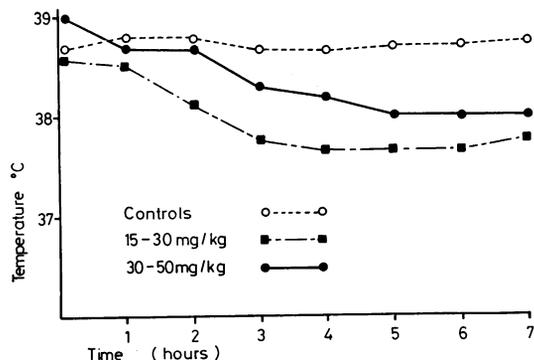


Fig. 2 Temperature pattern after rectal aspirin.

Discussion

The peak serum level after oral salicylate is reached after 2 hours (Lowenthal *et al.*, 1970). The peak level after rectal administration occurs later. When a rapid antipyretic effect is sought, the oral route should be used. However, when temperature reduction is not urgent, or in cases where the patient is vomiting or is unable to swallow, the rectal route is a useful alternative. The delay in attaining a peak serum level after rectal administration reduced the incidence of side effects (Borg *et al.*, 1975).

Results reported by Parrott (1971) suggest that the mucosa of the entire gastrointestinal tract has the same absorption characteristics for aspirin. The suppository base used is one factor that may influence absorption from the rectum (Samelius and Åström, 1958; Gibaldi and Grundhofer, 1975). The trigly-

ceride base used in this trial has a melting point of between 33.5 and 35.5°C and a hydroxyl value below 2, and thus it is appropriate to use it for rectal acetylsalicylic acid administration as long as the rectal temperature is above 33.5°C.

The retention time influences the amount of aspirin absorbed (Nowak *et al.*, 1974). In all subjects in the present study the suppositories were retained throughout the 7 hours, thus a large percentage is likely to have been absorbed.

The overall rate of absorption in the 14 patients was good, although there was individual variation. This was particularly pronounced in the 2 patients with large core-peripheral temperature gradients. It is probable that these 2 had rectal vasoconstriction while the large gradient persisted, resulting in very slow absorption.

The doses used in this trial were higher than those recommended for oral administration. However, the maximum serum level reached in any patient was well below the toxic level. The LD 50 of rectal acetylsalicylic acid in rats is 790 ± 27 mg/kg (Coldwell and Boyd, 1966); the doses used in the present trial were well below this amount.

The optimum serum salicylate level for temperature reduction is not known. The level possibly depends on the aetiology of the pyrexia, and the sex and age of the patient. There is probably individual variation in the response to a given salicylate level.

Our results suggest that 3–5 mg/100 ml is as effective as a level of 5–10 mg/100 ml in post-operative pyrexia. This may be the result of an equal effect on prostaglandin levels in the hypothalamus by any serum salicylate level below about 15 mg/100 ml. It is of interest that this level is lower than that needed for an anti-inflammatory or an analgesic effect. Also, the wide range of apparently effective levels is of interest in view of the large variations in plasma levels attained after a given oral dose of salicylate (Bardare *et al.*, 1978). It thus may be reasonable to recommend a dose on a 'per kilogram' basis in spite of the variation in plasma levels after oral rectal salicylate.

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Thrombocytosis in low birthweight infants

A physiological phenomenon in infancy

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SUMMARY Prematurity has traditionally been connected with thrombocytopenia, although this is unlikely to be associated with prematurity itself but rather with serious illnesses in such infants. Platelet counts were measured in 117 healthy preterm infants with birthweights <2000 g, who were followed up from 2 weeks to 6 months. In this series the platelet counts were high compared with those in previous reports, and also compared with what is considered normal for term infants. The 95% range was between 160 and $675 \times 10^9/l$, with a median value of $375 \times 10^9/l$. The data suggest that thrombocytosis is a phenomenon related to prematurity.

There have been conflicting reports on platelet counts in preterm infants during the first weeks of life and little information about platelet counts after 2 months. Medoff (1964) found low values in infants with birthweights <1700 g, as did Kaplan and Klein (1962). Aballi *et al.* (1968) reported considerably higher values with a mean value $>200 \times 10^9/l$ at 1–2 days and $>300 \times 10^9/l$ at 2 weeks and at one month in a large series of 300 premature infants. They excluded 10% of the infants because they were ill or subsequently died, and concluded that the abnormally low values in earlier reports might be associated with serious illnesses which result in thrombocytopenia. Evidence of illness was also found in many premature infants who had low

platelet values (Oztalay and Beard, 1963). Abnormally high values have been reported in connection with haemolytic anaemia due to vitamin E deficiency (Ritchie *et al.*, 1968). Melhorn and Gross (1971) found platelet counts of between 400 and $450 \times 10^9/l$ in 10 infants with anaemia, reticulocytosis, and low levels of serum vitamin E concentration who were aged 6–8 weeks. The platelet count subsequently decreased when the infants were treated with oral vitamin E.

The purpose of this study was to establish the platelet counts in preterm infants who were followed longitudinally and for a sufficiently long time to exclude any sick infant; iron and vitamin E deficiency was prevented by giving daily supplements.

Subjects and methods

At age 2 weeks a group of 125 healthy preterm infants with birthweights between 1050 and 2000 g was studied (Lundström *et al.*, 1977). None then had had exchange transfusion, but 7 had transfusions later and so were excluded. One infant with hereditary spherocytosis was also excluded. Thus the study group comprised 117 infants who were tested at 2 weeks and then each month until aged 6 months, on average five times per infant. Gestational age according to amenorrhoea ranged from 27 to 40 weeks (mean 32 weeks); the average birthweight was 1650 g.