Study of antipyretic therapy in current use

JOHN HUNTER

From the Royal Children's Hospital, Parkville, Melbourne, Australia

Hunter, J. (1973). Archives of Disease in Childhood, 48, 313. Study of antipyretic therapy in current use. Several commonly used antipyretic therapies were compared in a series of 67 children. All regimens were more effective than exposure alone. Paracetamol and aspirin were comparable in antipyretic effect and superior to tepid sponging alone. The addition of tepid sponging to paracetamol therapy did not further improve the antipyretic response.

The effectiveness and value of antipyretic therapy in children remains controversial (Done, 1959; Cone, 1969; Smith, 1970). In particular, the relative merits of drug therapy and tepid sponging are largely untested. This study was undertaken to assess the relative efficiency of various antipyretic regimens in use at the Royal Children's Hospital, Melbourne.

Materials and methods

67 children aged between 6 months and 5 years presenting to the casualty department of the Royal Children's Hospital with a fever greater than 39.5 °C rectally (39.0 °C orally) were studied. Patients were excluded if either gastroenteritis or dehydration was present, or if antibiotics were considered necessary at the time of the study. 9 children were excluded for failing to achieve a response or to complete the 4-hour period of observation as defined in the method; 1 child was excluded after a febrile convulsion had occurred during the course of the study.

The patients were unclothed to the 'napkin' area and were randomly distributed into 5 treatment groups (Table I). The groups were comparable with respect to sex, age, presenting temperature, and aetiology of fever. A single dose of antipyretic agent was used in

TABLE I

Treatment regimens

(1) Placebo
(Dose $2\frac{1}{2}-5$ ml)
(2) Aspirin
(Dose range 5-12 mg/kg)
(3) Paracetamol
(Dose range 5-10 mg/kg)
(4) Paracetamol plus tepid sponge
(Dose range 5-12 mg/kg)
(5) Tepid sponge alone

Received 11 August 1972.

accord with that recommended by the hospital pharmacopoea. The temperature of the water used for sponging was regulated to 30 °C. The children were observed for a period of 4 hours, or until a *response*, defined as a temperature drop of 1.5 °C, had occurred. During the period of the study the children were in a controlled environment with a temperature of 21 °C to 22 °C and a relative humidity of 50% to 55%. Observations, including temperature, pulse, respiration rate, and evidence of discomfort (shivering, crying, restlessness, etc.), were made half-hourly during the study. Temperatures were measured rectally except in four 5-yearold children whose temperatures were measured orally.

Results

The results of the study are shown in Table II. The placebo group was withdrawn after 6 patients had failed to show any significant response. The remainder of the trial was randomized again on the basis of the remaining treatment groups.

The paracetamol, aspirin, and paracetamol plus tepid sponging regimens all produced significant effects compared with the control placebo group (P = 0.001, 0.005, and 0.001, respectively). Tepid sponging alone produced a significant effect but not at the level of the other treatments (P = 0.05). The data were analysed using a χ^2 2×2 contingency table. A comparison of the treatment regimens indicated that the addition of tepid sponging to paracetamol failed to produce any significant difference in the rate of response compared with paracetamol alone.

The average rate of temperature fall in the respective treatment groups is shown in Table III. Aspirin and paracetamol are again shown to be similar in antipyretic effect, with a slightly earlier onset with paracetamol (Eden and Kaufman, 1967; Colgan and Mintz, 1957). Tepid sponging

John Hunter TABLE II

Percentage of patients responding* during treatment Duration of treatment (hr) Total Treatment groups (no.) retained in study ł 1 11 2 2ł 3 3į 4 (1) Placebo (6) 0 0 0 0 0 0 0 0 0 (2) Aspirin (12) 83% 0 8% 33% 66% 75% 83% 83% 83% 16% 15% 53% 100% (3) Paracetamol (12) 100% 0 83% 100% 0 **60**% 100% (4) Paracetamol plus tepid sponge (13) 84% (5) Tepid sponge (14) 65% 0 7% 29% 43% 65% 65% 65% 65%

*Response defined as a fall in temperature of 1.5 °C.

TABLE III	
Rate of fall of temperature after treatment	(°C)

Treatment	Time (hr)			
	1	1	11	2
Paracetamol	0.6	1.1	1.5	1.6
Aspirin	0.4	0.8	1.2	1.5
Tepid sponge Tepid sponge plus	0.4	0.8	1.1	1.0
paracetamol	0.2	1.0	1.6	1.8
Placebo	0.1	0.6	0.2	0.2

alone is less effective, and the addition of tepid sponging to paracetamol produces little benefit.

Discussion

The management of children with fever is based primarily on the elucidation and treatment of the underlying cause. The role of antipyretic therapy in such children is aimed at reducing the ever present risk of a febrile convulsion. Some criticism of the use of antipyretic therapy has been proposed, based on the possible role of fever in assisting body defence mechanisms, the value of fever as a diagnostic sign, and the allergic or toxic reactions that may occur with the use of antipyretic drugs (Done, 1959). Currently, there is no evidence confirming a beneficial effect of fever in aiding the complement or antibody systems, though an effect on phagocytosis has been shown in vitro (Ellingson and Clark, 1942). The value of fever as a diagnostic sign in younger children must be balanced against the risk of febrile convulsions. The role of intermittent prophylactic antipyretic therapy for children who have had a previous febrile convulsion has been questioned (Mackintosh, 1970). The failure of this form of therapy appears to be largely due to the often brief interval between the onset of fever and the development of febrile convulsion. Others, however, commend the use of antipyretics with the onset of fever, possibly in addition to anticonvulsants, if there is a prior history of febrile convulsions (Millichap, Aledort, and Madsen, 1960).

Several methods for reducing fever have been recommended, including the use of rest, exposure, sponging with cooling solutions, and antipyretic drug therapy (Giesel, 1961; Fruthaler, and Tilden, 1964). This study has shown that rest, coupled with exposure, provides no significant drop in temperature. To increase the evaporative heat loss, sponging with a number of fluids has long been used as a simple method of temperature control. It has been suggested that the use of iced water or alcohol in water is superior to sponging with tepid water, though associated with more patient discomfort (Steele et al., 1970).

This study has suggested that sponging is less efficient as an antipyretic measure than antipyretic drug therapy, and that the combination of sponging with an antipyretic drug produces no additional benefit. Paracetamol is preferred to aspirin in children under the age of 2 years because of its lesser toxicity, particularly with overdosage (Goodman and Gilman, 1965).

I thank Dr. L. E. G. Sloan, Medical Director, Royal Children's Hospital, for enabling me to undertake this study, Sister Jane Altman and her staff for assistance in its performance, Mr. J. Williams for advice with statistics, and Dr. A. S. McNeish for help in preparation of the manuscript.

REFERENCES

- Colgan, M. T., and Mintz, A. A. (1957). A comparative antipyretic effect of N-acetyl-p-aminophenol and acetylsalicylic acid. Journal of Pediatrics, 50, 552.
- Cone, T. E. (1969). Diagnosis and treatment: children with fevers. *Pediatrics*, 43, 290.
 Done, A. K. (1959). Uses and abuses of antipyretic therapy.
- Pediatrics, 23, 774.
- Eden, A. N., and Kaufman, A. (1967). Clinical comparison of three antipyretic agents. American Journal of Diseases of Children, 114, 284.

Fruthaler, G. J., and Tilden, T. (1964). Management of hyper-

pyrexia in children. Postgraduate Medicine, **35**, 643. Giesel, L. O. (1961). Fever control in the office and the home. Pediatric Clinics of North America, **8**, 73.

Goodman, L. S., and Gilman, A. (1965). The Pharmacological

Basis of Therapeutics. Macmillan, New York.
 Mackintosh, T. F. (1970). Studies on prophylactic treatment of febrile convulsions in children. *Clinical Pediatrics*, 9, 283.

Millichap, J. G., Aledort, L. M., and Madsen, J. A. (1960). A

critical evaluation of therapy of febrile seizures. Journal of Pediatrics, 56, 364.

Smith, D. S. (1970). Fever and the pediatrician. Journal of Pediatrics, 77, 935.

Steele, R. W., Tanaka, P. T., Lara, R. P., and Bass, J. W. (1970). Evaluation of sponging and of oral antipyretic therapy to reduce fever. Journal of Pediatrics, 77, 824.

Correspondence to Dr. J. Hunter, The Children's Hospital, Ladywood Middleway, Birmingham BI6 8ET.

The following articles will appear in future issues of this journal:

Review article: Sugar-induced diarrhoea in children. By M. Gracey and V. Burke.

Congenital syphilis and glomerulonephritis with evidence for immune pathogenesis. By J. Wiggelinkhuizen R. O. C. Kaschula, C. J. Uys, R. H. Kuijten, and J. Dale.

Bronchial lability in cystic fibrosis. By G. Day and M B. Mearns.

Reserve albumin binding capacity, salicylate saturation index, and red cell binding of bilirubin in neontal jaundice. By D. Bratlid.

Serum and red cell folates, and serum vitamin B_{12} in protein calorie malnutrition. By M. Khalil, A. Tanios, M. Moghazy, M. K. Aref, S. Mahmoud, and M. el Lozy.

Vitamin E and haemolytic anaemia in premature infants. By S. S. Lo, D. Frank, and W. H. Hitzig.

Long-term prognosis of children with ulcerative colitis. By K. M. Goel and R. A. Shanks.

Massive diastematomyelia without cutaneous dysraphism. By C. B. Sedzimir, J. R. Roberts, and J. V. Occleshaw