PEDIATRIC NEUROLOGY BRIEFS
A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

Vol. 17, No. 7 July 2003

SEIZURE DISORDERS

DO ANTIPYRETICS PREVENT FEBRILE CONVULSIONS?

A frequently held opinion that antipyretic medications may prevent febrile seizures (FS) in at risk children was investigated by pediatricians at Queen Mary's Hospital, Sidcup, Kent, UK. The results of four previously published controlled studies were reviewed. One randomized, placebo controlled trial found paracetamol (acetaminophen), with or without diazepam, to be ineffective in the prevention of FS during subsequent fevers. A second randomized trial comparing the antipyretic effectiveness of paracetamol, administered at regular intervals (group 1) versus only at the time of fever (group 2), in children presenting with a FS found that early recurrences of FS (within the first 24 hours) were similar in the two groups. A third randomized, double-blind, controlled study using ibuprofen in children at risk of FS found similar recurrence rates in antipyretic and placebo treated patients. In a fourth study, an open trial, the risk of FS recurrence was similar in at risk patients offered either ibuprofen or paracetamol at times of fever. It is concluded that the results of these 4 studies and the findings in a recently published review of 12 randomized controlled trials of paracetamol show no convincing evidence that antipyretics prevent FS. The prescription of paracetamol in a child at risk of FS may be expected to provide symptomatic relief but should not be recommended as a preventive of FS. (El-Radhi AS, Barry W. Do antipyretics prevent febrile convulsions? Arch Dis Child 2003;88:641-642). (Respond: Dr A Sahib El-Radhi, Quen Mary's Hospital, Sidcup, Kent, UK).

COMMENT. The height of the body temperature is a measure of the febrile seizure threshold and an important determinant of the induction of febrile seizures (Millichap JG. Febrile Convulsions, New York, Macmillan, 1968). Laboratory studies support the

PEDIATRIC NEUROLOGY BRIEFS (ISSN 1043-3155) © 2003 covers selected articles from the world literature and is published monthly. Send subscription requests ($65 US; $68 Canada; $75 airmail outside N America) to **Pediatric Neurology Briefs - J. Gordon Millichap, M.D., F.R.C.P.-Editor,** P.O. Box 11391, Chicago, Illinois, 60611, USA.
The editor is Pediatric Neurologist at Children's Memorial Hospital and Northwestern University Medical School, Chicago, Illinois. PNB is a continuing education service designed to expedite and facilitate review of current scientific information for physicians and other health professionals. Fax: 312-943-0123.

conclusions regarding the ineffectiveness of antipyretic agents in the prevention of FS. Aspirin and acetaminophen fail to retard the rate of temperature rise induced by radiotherm diathermy in animals, and large toxic doses of aspirin lower the threshold convulsive temperature and exacerbate experimental FS. (Millichap, 1968). Antipyretics in therapeutic doses facilitate heat loss and relieve discomfort associated with fever but do not retard temperature rise and have no proven anticonvulsant effect. Heat production is not inhibited by salicylates, but heat dissipation is augmented by increased peripheral blood flow and sweating. (Goodman LS, Gilman A. Eds. The Pharmacological Basis of Therapeutics, 5th ed, New York, Macmillan, 1975;p327). Numerous studies have shown comparable antipyretic efficacy for aspirin and acetaminophen (ASAP) in febrile children (Wilson JT. In: Febrile Seizures, eds Nelson KB, Ellenberg JH, New York, Raven Press, 1981;pp231-239). Maximum antipyresis for rectal suppositories of ASAP occurs at 2.5 to 4 hours, and efficacy of both oral and rectal ASAP is related to dose and plasma level. Addition of tepid water sponging increases maximum antipyresis of ASAP, but does not shorten time of onset of antipyresis. Ineffectiveness of intermittent antipyretic treatment in the prevention of febrile seizures is sometimes linked to failure to determine plasma levels, poor compliance, and difficulty in recognizing the onset of the febrile illness. Further controlled studies may be indicated.

Ibuprofen was significantly superior to acetaminophen in antipyretic efficacy, in a randomized, multiple dose, double-blind study comparing ibuprofen (5 mg/kg) and acetaminophen (10 mg/kg) in 70 outpatients (mean age, 2.1 years) at risk for febrile seizure recurrence. Antipyretics were administered every 6 hours for 1 to 3 days during fever, and rectal temperatures were recorded at 0, 2, 4, 6, 12, and 24 hours after the first dose. Ibuprofen reduced fever 0.5°C more than acetaminophen at 4 hours, and in a cross-over trial, the differences in temperature reduction were 0.66 and 0.36°C, in favor of ibuprofen. (Van Esch A et al. Arch Pediatr Adolesc Med 1995;149:632-637). An anticonvulsant effect of the antipyretic was not established.

Dr Sheila Wallace, in memoriam. Febrile seizures were a major interest of Dr Wallace, Consultant Paediatric Neurologist, University Hospital of Wales, Cardiff. Dr Wallace died on December 25, 2002. An obituary, written by Dr John BP Stephenson, is published in Brain Dev Aug 2003;25:299-300, and is available online July 2, 2003. Among other articles, Dr Wallace contributed two papers to the symposium on Febrile Seizures, edited by Nelson KB & Ellenberg JH, New York, Raven Press, 1981. These pertained to "Prevention of recurrent febrile seizures using continuous prophylaxis: sodium valproate compared with phenobarbital" and "Supportive family management."

GENETICS OF FEBRILE SEIZURES

The genetics of febrile seizures (FS) are reviewed by members of the Department of Pediatrics, Fukuoka University; Department of Neuropsychiatry, Hirosaki University, Japan; and National Institutes of Health, Research Triangle Park, NC, USA. Several genetic loci for FS have been mapped, but the exact molecular mechanism is unknown. Mutations have been found in genes encoding Na^+ channel subunits and the g2 subunit of gamma amino-butyric acid $(GABA)_A$ receptors. These channels are associated with