PEDIATRIC NEUROLOGY BRIEFS A MONTHLY JOURNAL REVIEW

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

101. 27. 110. 10	Vol	. 24.	No.	10
------------------	-----	-------	-----	----

October 2010

ATTENTION DEFICIT DISORDERS

CYTOCHROMEP450 2D6 AND ATOMOXETINE METABOLISM

The relation of cytochrome P450 2D6 (CYP2D6) activity to metabolism, response and adverse effects of atomoxetine was determined by CYP2D6 genotyping in 10 out of 100 children treated for attention deficit hyperactivity disorder at Amphia Hospital, Breda, The Netherlands, Eight of 10 patients genotyped showed compromised CYP2D6 activity, and 2 had normal activity. Enzyme activity is expressed as 4 phenotypes: ultrarapid (high), extensive (70-80% have normal activity), intermediate (10-40% have lower), and poor (5-10% have no activity). A semiguantitative gene dose based on allele activity is defined as 0 for poor metabolizer, 0.5, 1, and 1.5 intermediate, 2 extensive, and >2 ultrarapid metabolizer. Four of 8 patients with compromised CYP2D6 activity (gene doses of 0.5 and 1.0) stopped atomoxetine treatment because of initial adverse effects (gastrointestinal, sleeping, malaise, and mood disorders). In 4 other patients (CYP2D6 gene doses of 1.0 and 1.5) atomoxetine doses were reduced after genotyping, leading to better tolerability and efficacy. A patient with only compromised CYP2C19 activity (a minor pathway in atomoxetine metabolism) responded better after a change in dose time to morning instead of evening. Cost versus benefit ratio of prospective cytochrome P450 2D6 genotyping before atomoxetine treatment requires consideration. (ter Laak MA. Temmink AH, Koeken A, van 't Veer NE, van Hattum PRM, Cobbaert CM, Recognition of impaired atomoxetine metabolism because of low CYP2D6 activity. Pediatr Neurol September 2010;43:159-162). (Respond: Dr ter Laak, Department of Clinical Pharmacy, Amphia Hospital, Molengracht 21, 4818 CK Breda, The Netherlands. E-mail: mtlaak@tsz.nl).

COMMENT. Cytochrome P450 2D6 genotyping before starting atomoxetine

PEDIATRIC NEUROLOGY BRIEFS (ISSN 1043-3155) © 2010 covers selected articles from the world literature and is published monthly. Send subscription requests (\$68 US; \$72 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 Professor Emeritus, 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.

treatment may be of benefit in avoidance of overdose or ineffectiveness and premature withdrawal. Atomoxetine is a selective norepinephrine reuptake inhibitor, approved in 2002 for the treatment of ADHD. The recommended daily dose is 1.2 mg/kg, ranging from 0.5 mg/kg initial dose to a maximum of 1.8 mg/kg. Unlike the dosage of stimulant medication that is not based closely on body weight, the initial recommended dose of atomoxetine is commonly calculated by weight. The results of the Netherlands study might indicate the need to begin treatment with atomoxetine using the smallest test dose (10 mg daily), with gradual increments based more on early response or side effects than body weight. The cost to a patient of cytochrome P450 2D6 genotyping is quoted by one laboratory at >\$700; that of CYP450 C19 is slightly greater. The cost-benefit ratio of initial enzyme testing of cytochrome P450 2D6 versus close monitoring of response to carefully graded doses of atomoxetine would require further study. Failed treatment with recommended dose schedules of atomoxetine or early occurrence of side effects should alter clinicians to a probable underlying abnormal cytochrome enzyme activity.

SERVICE NEEDS OF YOUNG ADULTS WITH ADHD

The need for ongoing adult mental health services for young people with attention deficit hyperactivity disorder (ADHD) in the UK was determined by a follow-up study of 102 young people with ADHD who were on medication and treated at a pediatric neurodisability clinic in Sheffield. Over 50% patients were well controlled, 71% had at least one comorbid condition, 46 received intervention from child and adolescort mental health services, 17% had committed criminal offenses, and 37% were likely to need transition to adult mental health services. Management of ADHD by specialist nurses working with a medical practitioner or adult mental health professional was considered ideal care for young patients transitioning from pediatric to adult clinics. (Taylor N, Fauset A, Harpin V. Young adults with ADHD: an analysis of their service needs on transfer to adult services. Arch Dis Child July 2010;95:513-517). (Respond: Dr Val Harpin, Ryegate Children's Centre, Sheffield Children's Hospital Foundation NHS Trust, Tapton Crescent Road, Sheffield S10 5DD, South Yorkshire, UK. E-mail: val.harpin@sch.nhs.uk).

COMMENT. In the US, treatment of children with chronic neurologic disorders past adolescence and during college often poses problems. The young adult care of myelomeningoccle, cerebral palsy and muscular dystrophy is particularly difficult to arrange. ADHD is a lesser problem, but those patients with persisting symptoms as young adults need specialized attention and supervision during the transition period. The nurse practitioner working closely with the pediatrician, pediatric neurologist or child psychiatrist is an ideal person to supervise this transitional care.

TV/Video game exposure and attention deficits in children and young adults.

A large sample (1323) of middle childhood participants and a smaller sample (210) of late adolescent/early adult participants were assessed during a 13-month period for television and video game exposure. The association of screen media and attention problems was similar across media type (TV or video games) and age (middle childhood or late adolescent/early adult). (Swing EL et al. **Pediatrics** Aug 2010;126:214-221).