Dispensing Tops List of ADHD Medication Errors

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TORONTO — Outpatient medication errors in the treatment of pediatric attention-deficit/hyperactivity disorder are numerous, but few of them seem to result in patient harm, Dr. David Bundy said at the annual meeting of the Pediatric Academic Societies.

An analysis of a national error-reporting database identified 361 outpatient medication errors involving ADHD medications for children aged 3-17 years from 2003 to 2005 in the U.S. Pharmacopeia MEDMARX database, which contains information on more than 1.1 million adverse drug events reported voluntarily by hospitals and health care systems.

Four medications accounted for 98% of all reports: methylphenidate (157 or 43%), dextroamphetamine alone and combined with amphetamine (149 or 41%) bupropion (28 or 8%), and atomoxetine (22 or 6%).

Methylphenidate errors were more likely to involve prescribing errors compared with dextroamphetamine/amphetamine (Adderall; 36% vs. 15%), and less likely to involve dispensing problems (49% vs. 67%).

Because more dextroamphetamine/amphetamine errors occurred during the dispensing phase, those errors were significantly more likely to reach patients than were errors involving methylphenidate (85% vs. 74%), said Dr. Bundy of Johns Hopkins University, Baltimore. Dextroamphetamine/amphetamine errors were three times more likely than were methylphenidate errors to involve the wrong dosage form (22% vs. 8%).

Overall, 297 errors reached patients but did not cause harm, 10 errors reached the patient and required monitoring to confirm no harm and/or intervention to preclude harm, and 2 errors occurred that may have contributed to or resulted in temporary harm and required intervention. There were no deaths related to the errors.

ADHD Drugs May Not Outlast Other Therapies

Using medication to treat children with attention-deficit/hyperactivity disorder offers no long-term advantage over other treatment methods, according to a follow-up study.

Dr. Peter S. Jensen and his colleagues at Columbia University, New York, found that children with ADHD who were treated with medication (including stimulants, bupropion, and tricyclics) showed greater improvements in symptoms, compared with children who had been treated with behavior therapy after 14 months of treatment. But those on the medication algorithm lost that advantage after 3 years, based on data from the Multimodal Treatment Study of Children With ADHD (J. Am. Acad. Child Adolesc. Psychiatry 2007;46:989-1002).

The original study included 579 children aged 7-10 years who had been diagnosed with "ADHD combined type." The children were randomized into one of four treatment groups—intensive multicomponent behavior therapy, intensive medication management, the combination, and routine community care—and they were followed for 14 months.

Of those, 485 children, now aged 10-13 years, took part in a long-term follow-up study. All of the children showed some ADHD and oppositional defiant disorder symptom (ODD) improvement, compared with baseline after 14 months, although the differences were significantly greater in the children in the medication and combination groups after 14 months and 24 months.

But none of the randomized treatment groups showed significant differences on any of five measures of clinical and functional outcomes by 36 months' follow-up. The clinical and functional outcomes were parent reports and teacher reports of ADHD and ODD symptoms, reading achievement scores, social skills, and functional impairment.

Intensive medication management of ADHD in children may have a long-term impact only if the intensity of the medication use is maintained over time, the researchers wrote.

The study was supported in part by the National Institute of Mental Health.

—Heidi Splete

Dr. Bundy suggested that ADHD medications themselves may have properties predisposing them to certain types of errors. He described an ADHD "medication bingo" that includes an array of dosages and formulations, including Adderall XR (5, 10, 15, 20, 25, 30 mg); Adderall (5, 7.5, 10, 12.5, 15, 20, 30 mg); methylphenidate (Concerta) (18, 27, 36, 54 mg); and three formulations of methylphenidate (Ritalin), including Ritalin SR and Ritalin LA.

Although few errors involving ADHD medications appear to be harmful to patients' health, the impact on school performance and behavior may be important, said Dr. Bundy, who disclosed no related conflicts of interest. Moreover, pediatric ADHD outpatient medications are associated with 3.5 million ambulatory visits annually in children under 15 years of age—second only to asthma as a cause of ambulatory care visits for a chronic disease.

Few errors seem harmful to patients' health, but the impact on behavior and performance at school may be important.

DR. BUNDY

Dispensing errors are common, and there are no checks and balances afterward to identify errors, the investigators found. Efforts aimed at reducing ADHD medication errors must include not only physician-based systems, but also dispensing/pharmacy systems, Dr. Bundy said.

Dispensing errors accounted for more than half of the reported errors (218 or 60%), whereas nearly one-quarter (84 or 23%) occurred during prescribing, and more than 1 in 10 (45 or 12%) during administration. The most common type of error was improper dose or quantity (131 or 36%) followed by wrong dosage form (51 or 14%), prescribing error (43 or 12%), omission error (39 or 11%), and wrong patient (32 or 9%).

Limitations of the study included the lack of a denominator, which made an incidence calculation impossible; no verification of report accuracy or completeness; underreporting and reporting bias; a nonrepresentative sample; and a lack of information from patients.

"ADHD-related medication error incidence is significant … so the importance of judicious use of ADHD medications is magnified," Dr. Bundy said in an interview. ■

Antidepressant 'Poop Out' May Be Placebo Effect

SAN DIEGO — If a patient with depression comes into the office and says that his antidepressant has stopped working, the drug you gave him probably was never working at all, Dr. Mark Zimmerman said at the annual meeting of the American Psychiatric Association.

That patient probably had a placebo response, said Dr. Zimmerman, director of outpatient psychiatric services at Rhode Island Hospital, Providence.

Dr. Zimmerman said he was interested in why antidepressants seem to "poop out" when patients take them long term, and so he conducted a meta-analysis of continuation studies.

He identified four extension studies—the only type of continuation study that can be analyzed for its placebo effect–related relapse; in these studies, the patients were treated for their acute depression with a selective serotonin reuptake inhibitor for 6-8 weeks, followed by a continuation phase in which patients continued to take their drug for up to an additional year.

Dr. Zimmerman pooled the studies' data and used a method first described in 1993 to estimate the percentage of cases that can be attributed to a loss of placebo response (Am. J. Psychiatry 1993;150:562-5).

Using that formula, he estimated that 84% of the patients who relapsed during the continuation period were most probably patients whose response was a placebo response.

"The bottom line is that, overwhelmingly, relapse in studies occurs in people who are placebo responders," he said. "It is not due to receptor down-regulation or up-regulation."

Dr. Zimmerman also noted that continuation studies are not clinical practice, and that in clinical practice placebo response rates are probably higher than the 24%-30% rate described in trials because patients have higher expectations than those enrolled in studies.

"More of our patients are placebo responders than in clinical trials, and perhaps we shouldn't attribute as much of their gain to the particular molecule they are taking," he said.

—Timothy F. Kirn