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WHAT'S NEW

Physical and sexual abuse might raise the risk of type 2 diabetes, a study of almost 70,000 women suggests. **2**

Nearly one-quarter of U.S. high school students reported binge drinking in 2009. **4**



A Chilean miner might get more emotional help from a colleague with whom he was trapped than from any mental health professional who rides into town, Dr. Paul J. Fink writes. **12**



Dr. Michael F. Myers says awareness is central in efforts to avert physician suicide. **13**



An Army program helps soldiers redirect the adrenaline rushes some of them experience when they return home. **18**



Interdisciplinary teams can help nursing homes in their efforts to stop excessive use of psychoactive medications in residents. **30**

Some antiepilepsy drugs raise the risk of self-harming behavior. **40**

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Minority medical school enrollment climbed in 2009, and Hispanic men made the biggest inroads. **56**

Poor Adherence Boosts Antidepressant Dosing

BY DIANA MAHONEY

FROM THE AMERICAN PSYCHIATRIC ASSOCIATION INSTITUTE ON PSYCHIATRIC SERVICES

BOSTON – Nearly one-third of patients on antidepressant pharmacotherapy in a large-scale analysis did not take their original antidepressant dose as prescribed within the 6 months prior to dose escalation, a study has shown.

The findings suggest that the lack of adequate treatment response that drives dosage increases in many patients might be linked to suboptimal medication adherence rather than to dose insufficiency, Dr. David J. Muzina reported at the institute.

To evaluate patient nonadherence to chronic antidepressant therapy and a re-

sulting upward dosage titration of the same medication, Dr. Muzina of Medco Health Solutions Inc. and his colleagues identified 53,530 patients from Medco's administrative patient claims database who were on antidepressant medications at the same dosage level for at least 6 months, followed by a subsequent submission of claims for a higher dose.

Patients with only one claim for antidepressant medication in a 6-month period were excluded from the analysis, as were those taking multiple antidepressants, Dr. Muzina explained.

To measure adherence status – which was determined by the proportion of days the patient possessed a supply of the medication, or the medication possession ratio (MPR) – researchers required a minimum of two claims for the same

A survey of 53,530 patients found almost 30% got higher antidepressant doses despite failing to take original doses.

antidepressant drug. According to the National Committee for Quality Assurance's antidepressant performance measures, adherence was defined as an MPR of at least 80%, Dr. Muzina said.

With respect to patient demographics and prescription characteristics, the study cohort was predominantly female (72%), with a mean age of 51 years. More than two-thirds of the sample (68%) filled their antidepressant prescriptions at retail pharmacies, and 62% received generic medications, Dr. Muzina said. Most of the prescriptions were ordered by nonpsychiatrists, with only 15% ordered by psychiatrists; nearly half of the 49,524 patients for whom Chronic Disease Scores (CDS) were available had scores indicating a high degree of comorbidity, *See Antidepressant page 59*

Mental Health Homes Built for the Homeless

BY DIANA MAHONEY

FROM THE AMERICAN PSYCHIATRIC ASSOCIATION INSTITUTE ON PSYCHIATRIC SERVICES

BOSTON – There are no walls or even a roof. But a new type of home being built in Jacksonville, Fla., seeks to shelter some of the city's most vulnerable residents from the devastating effects of persistent mental illness. Through an academic-public sector collaboration between the University of Florida department of psychiatry and a comprehensive service facility called the Sulzbacher Center, a transdisciplinary team of outreach workers takes to the streets to lay the foundation for "mental health homes" for the city's large population of unsheltered homeless men and women.

Modeled after the primary care concept of a "medical home" in which multidisciplinary teams of specialists and care administrators provide comprehensive and continuous care of an individual through active communication and coordination of

See Mental Health page 36



Dr. Richard C. Christensen (center, left) spends 2 days a week with his team trying to bring the unsheltered homeless into the health care fold.

COURTESY JEANNE CIASULLO

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Address Adherence Issues

Antidepressant from page 1

he said. Of the full study cohort, “only 70.3% were adherent to their antidepressant medication in the 6 months prior to their dosage increase. Nearly 30% were nonadherent,” Dr. Muzina reported.

Among the nonadherent patients, “one in four was in possession of their prescribed medication during less than 3 months of the 6-month period,” he said.

mulation, 19.2% of patients who filled their prescriptions by mail were nonadherent, which was significantly lower than the 34.6% of those who used a retail pharmacy.

Those receiving generic-only drugs had a small but significantly higher nonadherence rate (30.2%) than the 28.9% rate that was observed among patients receiving brand-name drugs, according to Dr. Muzina.

Older age, male sex, and a higher CDS – perhaps because of the increased interaction with clinicians required by sicker patients – were also associated with significantly improved adherence relative to their respective corollaries, he said.

Although the study did not investigate the reasons for patient nonadherence, some possibilities include undesired or intolerable side effects, negative stigma, and forgetfulness, Dr. Muzina hypothesized.

The findings are limited by the study’s retrospective design and the use

of an administrative claims database, which doesn’t provide certain relevant clinical information, according to Dr. Muzina. However, he suggested that the results indicate that clinicians should investigate and address adherence issues in all patients on antidepressant medications prior to prescribing a dose increase “to enable patients with depression to fully benefit from their medications.”

Additionally, factors associated with adherence to antidepressant treatment should be investigated in future studies, he said. ■

VITALS

Major Finding: Treatment nonadherence is behind dose escalation in one-third of patients who receive antidepressant therapy.

Data Source: A large-scale analysis of patient nonadherence to chronic antidepressant therapy and subsequent prescribed dose escalation of the same medication using a national patient claims administrative database.

Disclosures: Medco Health Solutions Inc. provided funding for the study. Dr. Muzina became an employee of Medco Neuroscience Resource Center after the study began and received no compensation for his participation.

An analysis of medication adherence by study subgroup – including age, sex, comorbidity, pharmacy channel (mail vs. retail), formulation (brand vs. generic), and prescriber (psychiatrist vs. nonpsychiatrist) – showed significant differences for all but the type of clinician prescriber, Dr. Muzina said, noting that similarly high rates of nonadherence were observed among the psychiatrist (30.4%) and nonpsychiatrist (29.5%) groups.

Regarding pharmacy channel and for-

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INTUNIV™ (guanfacine) Extended-Release Tablets

Rx Only

BRIEF SUMMARY: Consult the Full Prescribing Information for complete product information.

INDICATIONS AND USAGE

INTUNIV™ is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). The efficacy of INTUNIV™ was studied for the treatment of ADHD in two controlled clinical trials (8 and 9 weeks in duration) in children and adolescents ages 6-17 who met DSM-IV® criteria for ADHD (see *Clinical Studies in Full Prescribing Information*). The effectiveness of INTUNIV™ for longer-term use (more than 9 weeks) has not been systematically evaluated in controlled trials.

Maintenance Treatment The effectiveness of INTUNIV™ for longer-term use (more than 9 weeks) has not been systematically evaluated in controlled trials. Therefore the physician electing to use INTUNIV™ for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

CONTRAINDICATIONS

Patients with a history of hypersensitivity to INTUNIV™, its inactive ingredients (see *Description in Full Prescribing Information*), or other products containing guanfacine (e.g. TENEX®) should not take INTUNIV™.

WARNINGS AND PRECAUTIONS

Hypotension, Bradycardia, and Syncope Treatment with INTUNIV™ can cause decreases in blood pressure and heart rate. In the pediatric, short-term (8-9 weeks), controlled trials, the maximum mean changes from baseline in systolic blood pressure, diastolic blood pressure, and pulse were -5 mm Hg, -3 mm Hg, and -6 bpm, respectively, for all dose groups combined (generally one week after reaching target doses of 1 mg/day, 2 mg/day, 3 mg/day or 4 mg/day). These changes were dose dependent. Decreases in blood pressure and heart rate were usually modest and asymptomatic; however, hypotension and bradycardia can occur. Hypotension was reported as an adverse event for 6% of the INTUNIV™ group and 4% of the placebo group. Orthostatic hypotension was reported for 1% of the INTUNIV™ group and none in the placebo group. In long-term, open label studies, (mean exposure of approximately 10 months), maximum decreases in systolic and diastolic blood pressure occurred in the first month of therapy. Decreases were less pronounced over time. Syncope occurred in 1% of pediatric subjects in the clinical program. The majority of these cases occurred in the long-term, open-label studies. Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Use INTUNIV™ with caution in patients with a history of hypotension, heart block, bradycardia, or cardiovascular disease, because it can decrease blood pressure and heart rate. Use caution in treating patients who have a history of syncope or may have a condition that predisposes them to syncope, such as hypotension, orthostatic hypotension, bradycardia, or dehydration. Use INTUNIV™ with caution in patients treated concomitantly with antihypertensives or other drugs that can reduce blood pressure or heart rate or increase the risk of syncope. Advise patients to avoid becoming dehydrated or overheated.

Sedation and Somnolence Somnolence and sedation were commonly reported adverse reactions in clinical studies (38% for INTUNIV™ vs. 12% for placebo) in children and adolescents with ADHD, especially during initial use (see *Adverse Reactions in Full Prescribing Information*). Before using INTUNIV™ with other centrally active depressants (such as phenothiazines, barbiturates, or benzodiazepines), consider the potential for additive sedative effects. Caution patients against operating heavy equipment or driving until they know how they respond to treatment with INTUNIV™. Advise patients to avoid use with alcohol.

Other Guanfacine-Containing Products Guanfacine, the active ingredient in INTUNIV™, is also approved as an antihypertensive. Do not use INTUNIV™ in patients concomitantly taking other guanfacine-containing products (e.g., Tenex).

ADVERSE REACTIONS

Clinical Trial Experience Two short-term, placebo-controlled, double-blind pivotal studies (Studies 1 and 2) were conducted in children and adolescents with ADHD with a dose range of 1 to 4 mg/day of INTUNIV™. The most commonly reported adverse reactions (occurring in ≥2% of patients) that were considered drug-related and reported in a greater percentage of patients taking INTUNIV™ compared to patients taking placebo were: somnolence, headache, fatigue, upper abdominal pain, nausea, lethargy, dizziness, irritability, hypotension/decreased blood pressure, decreased appetite, dry mouth, and constipation. Less common adverse reactions (<2%) reported in pivotal Studies 1 and 2 that occurred in more than one patient taking INTUNIV™ and were more common than in the placebo group are atrioventricular block, bradycardia, sinus arrhythmia, dyspepsia, asthenia, chest pain, increased alanine aminotransferase, increased blood pressure, increased weight, postural dizziness, increased urinary frequency, enuresis, asthma, orthostatic hypotension, and pallor. In addition, the following less common (<2%) psychiatric disorders occurred in more than one patient receiving INTUNIV™ and were more common than in the placebo group. The

INTUNIV™ (guanfacine) Extended-Release Tablets

relationship to INTUNIV™ could not be determined because these events may also occur as symptoms in pediatric patients with ADHD: agitation, anxiety, depression, emotional lability, nightmares or interrupted sleep. Twelve percent (12%) of patients receiving INTUNIV™ discontinued from the clinical studies due to adverse events, compared to 4% in the placebo group. The most common adverse reactions leading to discontinuation of INTUNIV™-treated patients from the studies were somnolence/sedation (6%) and fatigue (2%). Less common adverse reactions leading to discontinuation (occurring in approximately 1% of patients) included: hypotension/decreased blood pressure, headache, and dizziness. In the controlled long term studies (mean duration of approximately 10 months) with a dose range of 1 to 4 mg/day of INTUNIV™, the most common adverse reactions (≥5%) reported during open label treatment were somnolence, headache, fatigue, upper abdominal pain, hypotension/decreased blood pressure, vomiting, dizziness, nausea, weight increased, and irritability. The most frequent adverse reactions leading to discontinuation (≥2%) were somnolence (3%), syncopal events (2%), increased weight (2%), depression (2%), and fatigue (2%). Other adverse reactions leading to discontinuation in the long-term studies (occurring in approximately 1% of patients) included: hypotension/decreased blood pressure, sedation, headache, and lethargy. In long-term open label studies, serious adverse reactions occurring in more than one patient were syncope (2%) and convulsion (0.4%). Adverse reactions that occurred in <5% of patients but ≥2% in open-label, long-term studies that are considered possibly related to INTUNIV™ include: syncopal events, constipation, stomach discomfort, hypertension/increased blood pressure, decreased appetite, diarrhea, dry mouth, lethargy, and insomnia.

Effects on Height, Weight, and Body Mass Index (BMI) Patients taking INTUNIV™ demonstrated similar growth compared to normative data. Patients taking INTUNIV™ had a mean increase in weight of 1 kg (2 lbs) compared to those receiving placebo over a comparative treatment period. Patients receiving INTUNIV™ for at least 12 months in open-label studies gained an average of 8 kg (17 lbs) in weight and 8 cm (3 in) in height. The height, weight, and BMI percentile remained stable in patients at 12 months in the long-term studies compared to when they began receiving INTUNIV™.

Laboratory Tests In short and long-term studies, no clinically important effects were identified on any laboratory parameters.

Effects on Heart Rate and QT Interval The effect of two dose levels of immediate-release guanfacine (4 mg and 8 mg) on the QT interval was evaluated in a double-blind, randomized, placebo- and active-controlled, cross-over study in healthy adults. A dose-dependent decrease in heart rate was observed during the first 12 hours, at time of maximal concentrations. The mean change in heart rate was -13 bpm at 4 mg and -22 bpm at 8 mg. An apparent increase in mean QTc was observed for both doses. However, guanfacine does not appear to interfere with cardiac repolarization of the form associated with pro-arrhythmic drugs. This finding has no known clinical relevance.

USE IN SPECIFIC POPULATIONS

Pregnancy: *Pregnancy Category B.* There are no adequate and well-controlled studies of guanfacine in pregnant women. This drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether guanfacine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when INTUNIV™ is administered to a nursing woman.

Pediatric Use: The safety and efficacy of INTUNIV™ in pediatric patients less than 6 years of age have not been established.

Geriatric Use: The safety and efficacy of INTUNIV™ in geriatric patients have not been established.

DRUG ABUSE AND DEPENDENCE

INTUNIV™ is not a controlled substance and has no known potential for abuse or dependence.

OVERDOSAGE

Two cases of accidental overdose of INTUNIV™ were reported in clinical trials in pediatric ADHD patients. These reports included adverse reactions of sedation and bradycardia in one patient and somnolence and dizziness in the other patient. Consult with a Certified Poison Control Center for up to date guidance and advice.

Manufactured for Shire US Inc., Wayne, PA 19087.

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