

Screening Tool May Help Identify Alcohol Use

BY DAMIAN McNAMARA
Miami Bureau

ORLANDO — It is a good idea to routinely ask patients—particularly those with risk factors for dependence—about their alcohol use, George F. Koob, Ph.D., said at a psychopharmacology congress sponsored by the Neuroscience Education Institute.

However, patients are not always honest, copresenter Dr. Stephen M. Stahl pointed out. “Most of us try to screen patients for alcohol, but . . . I can’t tell you the number of times I’ve been bamboozled by patients.

“In clinical practice, there are a lot of people who are heavy drinkers who do not think of themselves as alcoholics. They will be completely insulted if you tell them,” said Dr. Stahl of the department of psychiatry, University of California, San Diego, and chairman of the institute.

He and Dr. Koob, professor and chairman of the committee on the neurobiology of addictive disorders at the Scripps Research Institute, La Jolla, Calif., recommended use of the Alcohol Use Disorders Identification Test (AUDIT). However,

84% of those attending the meeting indicated they have never used the AUDIT screening tool, according to an electronic poll.

According to Dr. Koob, two neurologic systems reinforce alcohol dependence—both dopamine and serotonin pathways—and make it more difficult for people to stop drinking, and advances in neurobiology are offering new insights into how the brain is altered by alcohol use, dependence, and withdrawal.

“The neurobiology has led us where there are spectacular new targets for treatment of alcoholism,” Dr. Koob said. Rewarding effects of alcohol may be mediated by dopaminergic and opioidergic systems.

Researchers have long proposed that the pleasure provided through the mesolimbic pathway explains why people initially drink alcohol or take drugs. Dopamine is released in the front end of the brain while opioids activate the ventral tegmental area and nucleus accumbens. “So it’s a combination of the opioids and dopamine effects that causes a pleasurable experience.”

Impulsive drinking, particularly in young males, is an activation of reward mecha-

nisms driven by initial pleasurable effects, Dr. Koob said. “As a person continues to drink, the reward system gets impaired but hyperarousal in brain is set up that only alcohol will suppress. So [drinking] becomes self-medicating,” he noted.

“Those people you knew in college who could drink everyone under the table ultimately end up with a problem,” Dr. Koob said. “That starts the neuroadaptive process, so they end up needing that [higher] amount of alcohol.”

The acute double action of alcohol is to enhance γ -aminobutyric acid (GABA) and decrease glutamate, Dr. Koob said. Both dopamine and serotonin pathways may mediate alcohol dependence. The frontal cortex, amygdala, and hippocampus are

the brain areas that might contribute to dependence, Dr. Koob added.

Neurobiologists have found that consumption of alcohol also may alter regulatory agents of stress, particularly increasing corticotropin releasing factor (CRF) activity and decreasing neuropeptide Y. “While you are bingeing on alcohol, you are releasing the good guys like dopamine peptides, but when you get into withdrawal, you are recruiting the bad guys—the GABA system and the CRF stress hormone,” Dr. Koob said.

“You have a double-whammy effect when you become dependent—you lose the good guys and gain the brain stress system—so you continue to self-medicate with your drug of choice.”

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Motivations of Opioid and Stimulant Abusers Differ

BY MARY ELLEN SCHNEIDER
New York Bureau

BOSTON — College students who abuse opioids do so for different reasons than students who abuse stimulants, according to research presented at the annual meeting of the American Public Health Association.

Opioid users were more likely to report that they used the drugs to relax or to get high, while stimulant users were more likely to say that they used the drugs to help improve performance at school or to increase alertness.

These differences could be helpful in crafting interventions, said Julie Brevard of Inflexion Inc., a health, science, and technology research firm that is based in Newton, Mass.

Ms. Brevard, along with principal investigator Sarah Lord, Ph.D., and colleagues at Inflexion, conducted an online survey of college students who admitted to ever using prescription opioids and stimulants recreationally.

The survey was advertised on an online social networking forum for college students and at the 27 colleges nationwide with the highest usage of the networking forum Web site.

The researchers received 689 responses, 522 of which passed data validity checks and were analyzed. The research was funded with a grant from the National Institutes of Health.

About 61% of the respondents reported that they had used both stimulants and opioids. Of the rest, 18% had used opioids only and 21% had used stimulants only. About 41% of respondents said they were regular stimulant users, which was defined as using the drug once a month or more. And 25% of respondents reported that they were regular opioid users.

Among opioid users, more than 70% said they used the prescription pain relievers to relax and nearly 68% said they took them to get high. A smaller percentage (27%) reported taking opioids to help with depression and anxiety or for chronic pain (19%).

Regular opioid users were more likely than infrequent users to cite depression or pain management as reasons for use. They also reported more symptoms of abuse and dependence and beliefs that prescription medications could give them a better high than other drugs, said Ms. Brevard.

Among stimulant users, nearly 78% reported that they took the drugs to help them perform better in school, and nearly 74% said they took them to help increase alertness. Nearly 24% reported they took stimulants to lose weight or prevent weight gain.

Regular stimulant users were more likely than were infrequent users to report that weight loss was a reason for use. And similar to opioid users, frequent stimulant users were also more likely than infrequent users to report symptoms of abuse and dependence and to have more positive views about prescription drug abuse.

Nearly half (49%) of respondents said they first used prescription drugs non-medically during the years they were in high school. “It seems like high school is a critical experimentation time,” said Ms. Brevard.

The college students who were surveyed said that they accessed the prescription drugs primarily through friends (84%). Parents, other family members, and the Internet were also avenues for access. About 7% of respondents reported that they had a valid prescription for all the medications they used.

disorder **Central & peripheral nervous system:** Dizziness, Parkinsonism, Akathisia, Dystonia **Psychiatric:** Somnolence, Anxiety, Confusion **Respiratory system:** Rhinitis, Pharyngitis, Coughing **Body as a whole - general:** Asthenia **Urinary system:** Urinary incontinence **Heart rate and rhythm:** Tachycardia **Metabolic and nutritional:** Weight increase **Skin and appendages:** Rash. **Dose Dependency of Adverse Events:** Data from two fixed-dose trials provided evidence of dose-relatedness for extrapyramidal symptoms associated with risperidone treatment. These symptoms include: sleepiness, increased duration of sleep, accommodation disturbances, orthostatic dizziness, palpitations, weight gain, erectile dysfunction, ejaculatory dysfunction, orgasmic dysfunction, asthenia/lassitude/increased fatigability, and increased pigmentation. **Vital Sign Changes:** RISPERDAL® is associated with orthostatic hypotension and tachycardia (see PRECAUTIONS). **Weight Changes:** A statistically significantly greater incidence of weight gain for RISPERDAL® (18%) compared to placebo (9%). **Laboratory Changes:** A between-group comparison for 6- to 8-week placebo-controlled trials revealed no statistically significant RISPERDAL®/placebo differences in the proportions of patients experiencing potentially important changes in routine serum chemistry, hematology, or urinalysis parameters. Similarly, there were no RISPERDAL®/placebo differences in the incidence of discontinuations for changes in serum chemistry, hematology, or urinalysis. However, RISPERDAL® administration was associated with increases in serum prolactin (see PRECAUTIONS). **ECG Changes:** Between-group comparisons for pooled placebo-controlled trials revealed no statistically significant differences between risperidone and placebo in mean changes from baseline in ECG parameters, including QT, QTc, and PR intervals, and heart rate. When all RISPERDAL® doses were pooled from randomized controlled trials in several indications, there was a mean increase in heart rate of 1 beat per minute compared to no change for placebo patients. In short-term schizophrenia trials, higher doses of risperidone (8-16 mg/day) were associated with a higher mean increase in heart rate compared to placebo (4-6 beats per minute). **Adverse Events and Other Safety Measures in Pediatric Patients With Autistic Disorder:** In the two 8-week, placebo-controlled trials in pediatric patients treated for irritability associated with autistic disorder (n=156), two patients (one treated with RISPERDAL® and one treated with placebo) discontinued treatment due to an adverse event. **Incidence of Treatment-Emergent Adverse Events in Two 8-Week, Placebo-Controlled Trials in Pediatric Patients With Autistic Disorder.** **Body System Preferred Term: Psychiatric:** Somnolence, Appetite increased, Confusion **Gastrointestinal:** Saliva increased, Constipation, Dry mouth **Body as a whole - general:** Fatigue **Central & peripheral nervous system:** Tremor, Dystonia, Dizziness, Automatism, Dyskinesia, Parkinsonism **Respiratory:** Upper respiratory tract infection **Metabolic and nutritional:** Weight increase **Heart rate and rhythm:** Tachycardia **Other Events Observed During the Premarketing Evaluation of RISPERDAL®:** During its premarketing assessment, multiple doses of RISPERDAL® were administered to 2607 adult patients with schizophrenia and 1923 pediatric patients in Phase 2 and 3 studies and the following reactions were reported: (Note: frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients. It is important to emphasize that, although the events reported occurred during treatment with RISPERDAL®, they were not necessarily caused by it). Serious adverse reactions experienced by the pediatric population were similar to those seen in the adult population (see WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS). **Psychiatric Disorders:** Frequent: increased dream activity*, diminished sexual desire*, nervousness. Infrequent: impaired concentration, depression, apathy, catatonic reaction, euphoria, increased libido, amnesia. Rare: emotional lability, nightmares, delirium, withdrawal syndrome, yawning. **Central and Peripheral Nervous System Disorders:** Frequent: increased sleep duration*. Infrequent: dysarthria, vertigo, stupor, paraesthesia, confusion. Rare: aphasia, cholinergic syndrome, hypoesthesia, tongue paralysis, leg cramps, torticollis, hypotonia, coma, migraine, hyperreflexia, choreoathetosis. **Gastrointestinal Disorders:** Frequent: anorexia, reduced salivation*. Infrequent: flatulence, diarrhea, increased appetite, stomatitis, melena, dysphagia, hemorrhoids, gastritis. Rare: fecal incontinence, eructation, gastroesophageal reflux, gastroenteritis, esophagitis, tongue discoloration, cholelithiasis, tongue edema, diverticulitis, gingivitis, discolored feces, GI hemorrhage, hematemesis. **Body as a Whole/General Disorders:** Frequent: fatigue. Infrequent: edema, rigors, malaise, influenza-like symptoms. Rare: pallor, enlarged abdomen, allergic reaction, ascites, sarcoidosis, flushing. **Respiratory System Disorders:** Infrequent: hyperventilation, bronchospasm, pneumonia, stridor. Rare: asthma, increased sputum, aspiration. **Skin and Appendage Disorders:** Frequent: increased pigmentation*, photosensitivity*. Infrequent: increased sweating, acne, decreased sweating, alopecia, hyperkeratosis, pruritus, skin exfoliation. Rare: bullous eruption, skin ulceration, aggravated psoriasis, furunculosis, verruca, dermatitis lichenoid, hypertrichosis, genital pruritus, urticaria. **Cardiovascular Disorders:** Infrequent: palpitation, hypertension, hypotension, AV block, myocardial infarction. Rare: ventricular tachycardia, angina pectoris, premature atrial contractions, T wave inversions, ventricular extrasystoles, ST depression, myocarditis. **Vision Disorders:** Infrequent: abnormal accommodation, xerophthalmia. Rare: diplopia, eye pain, blepharitis, photopsia, photophobia, abnormal lacrimation. **Metabolic and Nutritional Disorders:** Infrequent: hyponatremia, weight increase, creatine phosphokinase increase, thirst, weight decrease, diabetes mellitus. Rare: decreased serum iron, cachexia, dehydration, hypokalemia, hypoproteinemia, hyperphosphatemia, hypertriglyceridemia, hyperuricemia, hypoglycemia. **Urinary System Disorders:** Frequent: polyuria/polydipsia*. Infrequent: urinary incontinence, hematuria, dysuria. Rare: urinary retention, cystitis, renal insufficiency. **Musculo-Skeletal System Disorders:** Infrequent: myalgia. Rare: arthrosis, synostosis, bursitis, arthritis, skeletal pain. Reproductive Disorders, Female: Frequent: menorrhagia*, orgasmic dysfunction*, dry vagina*. Infrequent: nonpuerperal lactation, amenorrhea, female breast pain, leukorrhea, mastitis, dysmenorrhea, female perineal pain, intermenstrual bleeding, vaginal hemorrhage. **Liver and Biliary System Disorders:** Infrequent: increased SGOT, increased SGPT. Rare: hepatic failure, cholestatic hepatitis, cholecystitis, cholelithiasis, hepatitis, hepatocellular damage. Platelet, Bleeding, and Clotting Disorders: Infrequent: epistaxis, purpura. Rare: hemorrhage, superficial phlebitis, thrombophlebitis, thrombocytopenia. **Hearing and Vestibular Disorders:** Rare: tinnitus, hyperacusis, decreased hearing. **Red Blood Cell Disorders:** Infrequent: anemia, hypochromic anemia. Rare: normocytic anemia. **Reproductive Disorders, Male:** Frequent: erectile dysfunction*. Infrequent: ejaculation failure. **White Cell and Resistance Disorders:** Infrequent: granulocytopenia. Rare: leukocytosis, lymphadenopathy, leucopenia, Pelger-Huet anomaly. **Endocrine Disorders:** Rare: gynecomastia, male breast pain, antidiuretic hormone disorder. **Special Senses:** Rare: bitter taste.* Incidence based on elicited reports. **Postintroduction Reports:** Adverse events reported since market introduction which were temporally (but not necessarily causally) related to RISPERDAL® therapy include the following: anaphylactic reaction, angioedema, apnea, atrial fibrillation, cerebrovascular disorder, including cerebrovascular accident, diabetes mellitus aggravated, including diabetic ketoacidosis, hyperglycemia, intestinal obstruction, jaundice, mania, pancreatitis, Parkinson's disease aggravated, pituitary adenomas, pulmonary embolism, precocious puberty, and QT prolongation. There have been rare reports of sudden death and/or cardiopulmonary arrest in patients receiving RISPERDAL®. A causal relationship with RISPERDAL® has not been established. It is important to note that sudden and unexpected death may occur in psychotic patients whether they remain untreated or whether they are treated with other antipsychotic drugs.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class: RISPERDAL® (risperidone) is not a controlled substance.

For more information on symptoms and treatment of overdose, see full Prescribing Information.

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