

Guidelines Issued on Evaluating Kidney Donors

BY ROBERT FINN
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SAN FRANCISCO — A panel of 70 transplant professionals has published a consensus document on the psychosocial evaluation of living unrelated kidney donors, Dr. Francis L. Delmonico reported at the American Transplant Congress.

The guidelines are intended to help transplant centers exclude donors who are unsuitable for a variety of nonmedical

reasons, such as coercion, unrealistic expectations, and psychological disorders. “The objective was to assess the characteristics of a prospective unrelated donor that might either increase the risk or serve as a protective factor against a poor donor psychosocial outcome,” said Dr. Delmonico, professor of surgery at Harvard Medical School, Boston.

Describing the current situation as “an era of changing donor-recipient relationships,” Dr. Delmonico said that the guide-

lines will likely allow transplant centers to be “somewhat more secure in proceeding ahead in very careful assessment and within an ethical framework.”

The new guidelines are the result of a meeting convened in May 2006 by the United Network for Organ Sharing in collaboration with the American Society of Transplant Surgeons and the American Society of Transplantation. That panel recommended several revisions to earlier consensus statements on living donors

and offered a new list of required components for the psychosocial evaluation of living unrelated kidney donors. (See box.)

The new document notes that biologically unrelated donors constitute 35% of the living kidney donors in the United States. Among living donors, the percentage without a biologic or close emotional relationship to the recipient rose from 6.5% to 23% between 1996 and 2006 (Am. J. Transplant. 2007;7:1047-54).

Some of the factors that would tend to increase the risks of living unrelated kidney donation are significant psychiatric symptoms or disorders; substance abuse or dependence; a lack of health insurance; a limited capacity to understand risks; motives reflecting a desire for recognition; a subordinate relationship to the patient, such as employee or employer; or an expectation of secondary gain.

Several other factors would tend to decrease the risk, including financial resources that could cover unexpected costs, realistic expectations about the donation experience, little or no ambivalence, a history of medical altruism, an absence of recent significant life stressors, and support from family for the donation.

In its changes to earlier consensus statements, the panel noted that novel forms of donor solicitation, such as Internet sites, point to an increased need to ascertain that the prospective donor was not pressured and does not expect financial gain.

This meeting was cosponsored by the American Society of Transplant Surgeons and the American Society of Transplantation.

LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION

(3% and <1%); Anorgasmia* (2% and <1%); *Events reported by at least 2% of patients treated with Lexapro for respiratory tract infection, back pain, pharyngitis, inflicted injury, anxiety. †Primarily ejaculatory delay. ‡Denominator used was for males only (N=225 Lexapro; N=188 placebo). †Denominator used was for females only (N=490 Lexapro; N=404 placebo). Generalized Anxiety Disorder Table 3 enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see TABLE 3). TABLE 3: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder* Lexapro (N=429) and Placebo (N=427): Autonomic Nervous System Disorders: Dry Mouth (9% and 5%); Sweating Increased (4% and 1%); Central & Peripheral Nervous System Disorders: Headache (24% and 17%); Paresthesia (2% and 1%); Gastrointestinal Disorders: Nausea (18% and 8%); Diarrhea (8% and 6%); Constipation (5% and 4%); Indigestion (3% and 2%); Vomiting (3% and 1%); Abdominal Pain (2% and 1%); Fatulence (2% and 1%); Toothache (2% and 0%). General: Fatigue (8% and 2%); Influenza-like symptoms (5% and 4%); Musculoskeletal: Neck/Shoulder Pain (3% and 1%). Psychiatric Disorders: Somnolence (13% and 7%); Insomnia (12% and 6%); Libido Decreased (7% and 2%); Dreaming Abnormal (3% and 2%); Appetite Decreased (3% and 1%); Lethargy (3% and 1%); Yawning (2% and 1%). Urogenital: Ejaculation Disorder[†] (14% and 2%); Anorgasmia[‡] (6% and <1%); Menstrual Disorder (2% and 1%). *Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo B Lexapro: inflicted injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. †Primarily ejaculatory delay. ‡Denominator used was for males only (N=182 Lexapro; N=195 placebo). †Denominator used was for females only (N=247 Lexapro; N=232 placebo). Dose Dependency of Adverse Events The potential dose dependency of common adverse events (defined as an incidence rate of 15% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). Table 4 shows common adverse events that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group. TABLE 4: Incidence of Common Adverse Events* in Patients with Major Depressive Disorder Receiving Placebo (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=125): Insomnia (4%, 7%, 14%); Diarrhea (5%, 6%, 14%); Dry Mouth (3%, 4%, 9%); Somnolence (1%, 4%, 9%); Dizziness (2%, 4%, 7%); Sweating Increased (<1%, 3%, 8%); Constipation (1%, 3%, 6%); Fatigue (2%, 2%, 6%); Indigestion (1%, 2%, 6%). *Adverse events with an incidence rate of at least 5% in either of the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. Male and Female Sexual Dysfunction with SSRIs Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence. Table 5 shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials (In Males Only: Lexapro (N=407) and Placebo (N=303); Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (8% and 2%); Impotence (2% and <1%). (In Females Only: Lexapro (N=727) and Placebo (N=536)); Libido Decreased (3% and 1%); Anorgasmia (3% and <1%). There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priligam has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. Vital Sign Changes Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. Weight Changes Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. Laboratory Changes Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. ECG Changes Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.7 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. Other Events Observed During the Premarketing Evaluation of Lexapro Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the ADVERSE REACTIONS section, reported by the 1428 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in Tables 2 & 3, those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; infrequent adverse events are those occurring in less than 1/100 patients but at least 1/1,000 patients; cardiovascular - frequent: palpitation, hypertension, infrequent: bradycardia, tachycardia, ECG abnormal, flushing, varicose vein, Central and Peripheral Nervous System Disorders - frequent: light-headed feeling, migraine, infrequent: tremor, vertigo, restless legs, shaking, twitching, disequilibrium, tic, carpal tunnel syndrome, muscle contractions involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased, Gastrointestinal Disorders - frequent: heartburn, abdominal cramp, gastroenteritis, infrequent: gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult, General - frequent: allergy, pain in limb, fever, hot flushes, chest pain, infrequent: edema of extremities, chills, tightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall, Hemiac and Lymphatic Disorders - frequent: bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical, Metabolic and Nutritional Disorders - frequent: increased weight, infrequent: decreased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia, Musculoskeletal System Disorders - frequent: arthralgia, myalgia, infrequent: jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness, Psychiatric Disorders - frequent: appetite increased, lethargy, irritability, concentration impaired, infrequent: jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruxism, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency, Reproductive Disorders/Female - frequent: menstrual cramps, menstrual disorder, infrequent: menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses. *% based on female subjects only; N= 905 Respiratory System Disorders - frequent: bronchitis, sinus congestion, coughing, nasal congestion, sinus headache, infrequent: asthma, breath shortness, laryngitis, pneumonia, tracheitis. Skin and Appendages Disorders - frequent: rash, infrequent: pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, lipoma, furunculosis, dry lips, skin nodule. Special Senses - frequent: vision blurred, tinnitus, infrequent: taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste. Urinary System Disorders - frequent: urinary frequency, urinary tract infection, infrequent: urinary urgency, kidney stone, dysuria, blood in urine. Events Reported Subsequent to the Marketing of Escitalopram - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during post marketing experience and were not observed during the premarketing evaluation of escitalopram: abnormal gait, acute renal failure, aggression, akathisia, allergic reaction, anger, angioedema, atrial fibrillation, choreoathetosis, delirium, delusion, diplopia, dysarthria, dyskinesia, dystonia, echymosis, erythema multiforme, extrapyramidal disorders, fulminant hepatitis, hepatic failure, hypospadias, hypoglycemia, hypokalemia, INR increased, gastrointestinal hemorrhage, glaucoma, grand mal seizures (or convulsions), hemolytic anemia, hepatic necrosis, hepatitis, hypotension, leucopenia, myocardial infarction, myoclonus, neuroleptic malignant syndrome, nightmare, nystagmus, orthostatic hypotension, pancreatitis, paranoia, photosensitivity reaction, priapism, prolidnemia, prothrombin decreased, pulmonary embolism, QT prolongation, rhabdomyolysis, seizures, serotonin syndrome, SIADH, spontaneous abortion, Stevens Johnson Syndrome, tardive dyskinesia, thrombocytopenia, thrombosis, torsade de pointes, toxic epidermal necrolysis, ventricular arrhythmia, ventricular tachycardia and visual hallucinations.

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Assessing Unrelated Prospective Donors

The following are the required components of psychosocial evaluations for living unrelated kidney donors, as agreed to by a panel convened by the United Network for Organ Sharing, the American Society of Transplant Surgeons, and the American Society of Transplantation:

► **History and current status.** Assess factors such as the prospective donor's educational level, employment, legal offense history, and citizenship.

► **Capacity.** Ensure that the prospective donor's cognitive status and capacity to comprehend information are not compromised.

► **Psychological status.** Determine whether the prospective donor has ever had any psychiatric disorders.

► **Relationship with the transplant candidate.** How close is the relationship, and would the transplant impose

expectations or perceived obligations?

► **Motivation.** Determine the voluntariness of the proposed donation. Is it consistent with past behaviors and values? Is it free of coercion, inducements, ambivalence, impulsivity, and ulterior motives?

► **Donor knowledge, understanding, and preparation.** Does the prospective donor understand potential short- and long-term risks, including recuperation time and financial ramifications?

► **Social support.** Evaluate familial, social, and employer support networks available to the prospective donor.

► **Financial suitability.** Determine whether the prospective donor is financially stable and has resources available to cover expected and unexpected donation-related expenses.

Source: Am. J. Transplant. 2007;7:1047-54.

Does OSA Raise Gestational Diabetes Risk?

BY ROBERT FINN
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SAN FRANCISCO — Pregnant women who have obstructive sleep apnea have a 2.3-fold increased risk of gestational diabetes and a 4.2-fold increased risk of pregnancy-induced hypertension, compared with women without the sleep disorder, according to a poster presentation at the International Conference of the American Thoracic Society.

Previous research has suggested that obstructive sleep apnea (OSA) may induce systemic hypertension and diabetes mellitus in the general population, but the connection was much less clear in pregnant women, investigator Dr. Michael S. Nolleto of the Robert Wood Johnson Medical School, Princeton, N.J., said in a press briefing.

“A lot of times for patients who are pregnant and for ob.gyns., sleep-disordered breathing is not on the radar screen,” he said. When a woman who's pregnant goes to see her obstetrician, the physician asks a zillion things but almost never inquires about risk factors for sleep apnea.

Dr. Nolleto suggested that physicians dealing with women with gestational diabetes or pregnancy-induced hypertension (PIH) should inquire about sleep-disordered breathing, especially because OSA is

so simple to treat with continuous positive airway pressure (CPAP).

“It may be a condition that you need treatment for just for the time you're carrying your baby,” he said. “Once you deliver, the sleep apnea may resolve.”

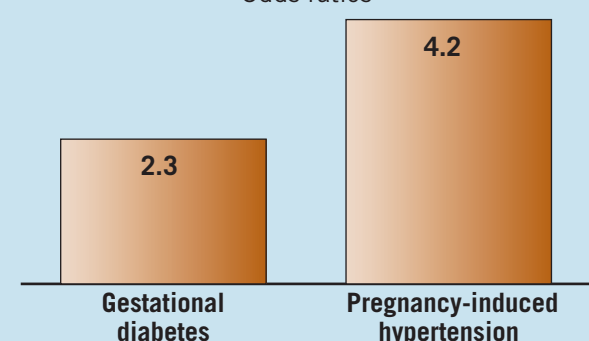
Dr. Nolleto acknowledged, however, that his study contains no direct evidence that treating sleep apnea will improve PIH or gestational diabetes. The study relied on data from the 2003 National Inpatient Sample, sponsored by the Agency for

Healthcare Research and Quality. This large database includes all inpatient records from a sample of about 20% of U.S. community short-stay hospitals and provides weights to calculate national estimates.

Using this database, the investigators calculated that there were 3,979,840 deliveries in the United States in 2003, of which 167,227 were complicated by gestational diabetes and 300,902 were complicated by PIH. The overall rate of sleep apnea for these women was

Obstructive Sleep Apnea Linked With Gestational Diabetes and PIH

Odds ratios



Note: Based on data from the National Inpatient Sample used to calculate the 3,979,840 deliveries in the United States in 2003.

Source: Dr. Nolleto