New Turner Guidelines: Adult Care Falling Short

The international group consensus emphasizes early diagnosis, estrogen treatment, and CV evaluation.

BY CHRISTINE KILGORE
Contributing Writer

Updated guidelines on evaluating and treating girls and women with Turner syndrome advise against the practice of delaying puberty to increase height and emphasize the importance of early diagnosis, estrogen treatment, and more comprehensive cardiovascular evaluation—including the use of diagnostic MRI—than is typically done today.

The guidelines detail how children should be evaluated and cared for and clearly state that care for adults is falling short.

"The care of adults with TS has received less attention than [has] the treatment of children, and many seem to be falling through the cracks with inadequate cardiovascular evaluation and estrogen treatment," say the new guidelines from the international, multidisciplinary Turner Syndrome Consensus Study Group, published in the Journal of Clinical Endocrinology & Metabolism.

On the other hand, while medical care must be improved and while many questions about care "remain unanswered," the experts "realize now that we have a lot more well-functioning people with TS," Dr. Carolyn A. Bondy said in an interview.

Dr. Bondy, chief of the developmental endocrinology branch at the National Institute of Child Health and Human Development in Bethesda, Md., chaired the consensus conference and guideline-writing committee for the consensus group, which met last summer to update recommendations issued in 2001.

The guidelines mainly represent "consensus judgments" rather than evidence-based conclusions, the committee noted in its document.

The clinical spectrum of TS is "much broader and often less severe than that described in many textbooks"—a finding that seems at odds with a "high elective abortion rate for incidentally diagnosed 45,X and 45,X/mosaic fetuses," the guidelines say. This means that the content of prenatal counseling "needs updating" with the input of TS patient and parent groups, the document says.

That's especially true now that the American College of Obstetricians and Gynecologists is recommending that all women, regardless of their age, be offered screening for Down syndrome.

Parents who receive a Turner syndrome diagnosis from such screening (TS can be an incidental finding) must be given information about the broad phenotypic spectrum of the syndrome and the high quality of life for many patients, Dr. Brody said.

Recent reports of an often-normal quality of life for those receiving comprehensive medical care should encourage—not mitigate—the efforts of physicians to diagnose TS as early as possible and better appreciate its many consequences, she said.

The diagnosis should be considered in any female with unexplained growth failure or pubertal delay or any constellation of the syndrome's characteristic physical features, the guidelines say.

"Regrettably, late diagnosis of TS, even in adults, is still a problem. No matter what the age of the patient, a full workup with assessment of congenital malformations should be performed, including all screening tests recommended for younger patients," the document says.

Adults with TS should then be regularly screened for hypertension, diabetes, dyslipidemia, aortic enlargement, hearing loss, osteoporosis, and thyroid and celiac diseases (J. Clin. Endocrinol. Metab. 2007;92:10-25).

The guidelines offer age-specific suggestions for ovarian hormone replacement and say that "ideally, natural estradiol and progesterone, rather than analogs, should be delivered by transdermal or transmembranous routes so as to mimic age-appropriate physiological patterns as closely as possible."

Regimens can vary to meet individuals' tolerance and preference, however, and "the most important consideration is that women actually take ovarian hormone replacement," the authors say.

Without it, the risk of significant osteoporosis is high. "These women can have severe osteoporosis at 25," said Dr. Bondy. "I have a 30-year-old patient who has lost 2 inches of height and has a hump."

Estrogen therapy often is required to induce pubertal development (30% or more will undergo some spontaneous pubertal development), but experts used to recommend delaying estrogen therapy until age 15 to optimize height potential.

Today, Dr. Bondy said, the consensus is that such delay undervalues the psychosocial importance of age-appropriate puberty.

Recent evidence also suggests that low-dose estrogen does not inhibit growth hormone–enhanced increases in stature. "There's a new focus on natural, sensitive, and timely puberty induction," she commented.

Recent studies have also suggested a broader spectrum of cardiovascular abnormalities than were previously recognized, and the consensus group agreed to bring "the heart to the forefront," Dr. Bondy said. "There's a new emphasis [in the guidelines] on the fact that everyone needs cardiovascular screening—from the newborn to the woman who's 20 and just found out she's infertile [and has TS] to the woman who's 40 and just got the [TS] diagnosis."

And while echocardiography usually is adequate for screening infants and young girls, MRI also must be performed in older girls and adults.

Reports of fatal aortic dissection during pregnancy and the postpartum period have raised concern about the safety of pregnancy in TS, and "preconception assessment must include cardiology evaluation with MRI of the aorta," the experts say. ■

Intermittent Dosing Succeeds in Premenstrual Dysphoric Disorder

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Women with premenstrual dysphoric disorder usually respond rapidly to the first treatment cycle of an antidepressant, allowing intermittent dosing that follows the menstrual cycle, Dr. Andrea J. Singer said at a meeting on women's health sponsored by OB.GYN. NEWS.

Three selective serotonin reuptake inhibitors (SSRIs) are approved for the treatment of premenstrual dysphoric disorder (PMDD)—fluoxetine, sertraline, and paroxetine. "You don't necessarily have to have people on these long term to see a benefit," said Dr. Singer, director of women's primary care at Georgetown University Medical Center, Washington.

Dr. Singer is on the speakers' bureau of Pfizer Inc., which makes sertraline.

PMDD causes severe premenstrual symptoms that result in significant impairment of normal function, usually during the last 6-7 days of the menstrual cycle. American women with PMDD experience the symptoms on average for 8 years during their reproductive lives—from 576 to 672 days, approximately. "That's a lot of days to feel lousy or be incapacitated," Dr. Singer said.

Because the disorder is intermittent and treatment with an SSRI brings rapid onset of improvement, intermittent therapy is sufficient, which lowers medication costs and limits side effects, compared with treatment of overt depression. In addition, low doses typically are effective for PMDD.

A diagnosis of PMDD requires the exclusion of underlying overt depression and the presence of at least five symptoms, including at least one of four core symptoms—anger or irritability; depressed mood; moodiness; and anxiety/edginess/nervousness.

Other symptoms include fatigue or lethargy, decreased interest in usual activities, insomnia or hypersomnia, difficulty concentrating, food cravings or appetite changes, feeling overwhelmed or out of control, and physical symptoms such as headache, breast tenderness, bloating, and joint or muscle pain.

For women on oral contraceptives with PMDD, using a pill containing the novel progestin drospirenone and ethinylestradiol improved symptoms of PMDD in several studies. Other studies suggest that shortening the hormone-free interval during oral contraceptive regimens from the standard 7 days to 3-4 days can improve some PMDD symptoms, Dr. Singer said. ■

Ibandronate May Have Fewer Gastrointestinal Side Effects

BY JOHN R. BELL
Associate Editor

NASHVILLE, TENN. — Postmenopausal women with a history of gastrointestinal side effects on bisphosphonate therapy had a decline in GI symptoms after 6 months of either oral or intravenous ibandronate, although the decline was more pronounced with the intravenous drug, according to interim results presented at the annual meeting of the North American Menopause Society.

Dr. Mark Martens of the University of Oklahoma, Tulsa, reported 6-month data from the ongoing 12-month PRIOR study, which is assessing the tolerability of ibandronate (Boniva) in women with a history of daily or weekly bisphosphonate treatment for osteoporosis or osteopenia.

This trial is not randomized; the patients initially requested either 150-mg ibandronate orally once a month or quarterly intravenous 3-mg ibandronate, and they have the option of switching to the other arm if they experience side effects but may do so only once. The study initially enrolled 546 patients. Patients are assessed every 3 months.

Among 146 patients initially in the oral group, 11 (7.5%) switched to intravenous treatment, and 15 (3.8%) of 396 patients in the intravenous group chose to switch to the oral arm, Dr. Martens said.

Serious adverse events were reported by 4% of all patients—4% of the oral group and 3% of those on the intravenous treatment.

Dr. Martens reported that the total change from baseline in GI tolerance scores was 130 at month 1 for the oral group and 377 at month 1 for the intravenous group.

The primary diagnosis was osteoporosis for 85 patients in the oral group (58%) and 281 patients in the intravenous group (71%). Osteopenia was the primary diagnosis for 61 patients (42%) in the oral group and 115 patients (29%) in the intravenous group.

Dr. Martens disclosed that he has received financial support from GlaxoSmithKline, Procter and Gamble, Merck & Co., and Eli Lilly. ■