GnRH Agonist May Curb Ovarian Failure in Lupus

BY TIMOTHY F. KIRN
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SNOWMASS, COLO. — A gonadotropin-releasing hormone agonist can prevent ovarian failure in lupus patients on cyclophosphamide, according to a small, case-control study conducted at the University of Michigan.

Evidence suggests that by the time a patient with lupus has taken a total 30 g of cyclophosphamide (equivalent to about a year of treatment at 100 mg a day) the rate of ovarian failure is about 70%, W. Joseph McCune, M.D., said at a symposium sponsored by the American College of Rheumatology.

The regimen can also result in cervical dysplasia, which is why patients started on cyclophosphamide should have a Pap smear early in the course of their treatment, advised Dr. McCune, a lupus expert and the codirector of the nephrology/rheumatology vasculitis clinic at the University of Michigan, Ann Arbor.

In their prospective study, Dr. McCune and his colleagues enrolled 40 patients with lupus nephritis or severe systemic lupus erythematosus (SLE), whose average age was 23 years. Their regimen was sequential, with monthly intravenous cyclophosphamide for 6 months followed by a switch to azathioprine and then mycophenolate mofetil. If the disease did not respond after 6 months of cyclophosphamide, patients were treated with 4 more months of cyclophosphamide.

Among the 20 patients treated with leuprolide acetate in depot suspension (Lupron, 3.75 mg a month), only 1 developed ovarian failure at the end of 3 years, compared with 6 of 20 matched women who did not receive GnRH.

Treatment-group patients received their first monthly injection of depot leuprolide acetate after receiving their first dose of cyclophosphamide, and the hormone agonist therapy was readministered after each course of cyclophosphamide—including when the patients had a flare after initial treatment and had to go back on the alkylating agent.

Patients who developed menopausal symptoms from the GnRH agonist were given an estrogen patch, together with depot medroxyprogesterone acetate (Depo Provera) to prevent a pregnancy.

The average cumulative dose of cyclophosphamide received by the patients and controls during the study was 12.9 g.

"These patients were relatively young, their cumulative dose was relatively low, and yet they still appeared to benefit from" leuprolide treatment, Dr. McCune said. "A randomized controlled trial obviously would be more convincing, and we are going to try to do that. But, this study suggests that this approach benefits patients, particularly if they are going to have relapses and if they are young."

Dr. McCune noted that his study did not address those patients who are on oral cyclophosphamide, but he predicted that leuprolide treatment would be of greater merit in those patients because they generally are exposed to higher cumulative doses.

Dr. McCune added that the increased risk of cervical dysplasia associated with cyclophosphamide use has been documented at his own institution. In that report, 61 patients with SLE were given cervical smears at baseline and then followed annually or as practice indicated for 7 years (J. Rheumatol. 2004;31:1763-7).

At enrollment, patients were excluded from the study if they had an abnormal smear or a history of cervical dysplasia. The study also did not enroll any patients on daily oral cyclophosphamide. However, use of monthly intravenous cyclophosphamide was permitted.

At 3 years, there were no cases of biopsy-proven cervical intraepithelial neoplasia in those who had taken only prednisone (23 patients) or prednisone and azathioprine (four patients). But there were two cases among eight patients treated with intravenous cyclophosphamide alone, and four cases among the 26 patients treated with intravenous cyclophosphamide together with azathioprine and/or prednisone.

In 3-7 years of follow-up, fewer cases of dysplasia occurred. Three of the 45 patients who remained in the study developed cervical intraepithelial neoplasia, and none of these cases occurred among patients who had received prednisone alone.

Overall, most patients with abnormal smears had resolution of their cervical dysplasia, but three patients required surgery and one continued to have persistently abnormal smears throughout the 7-year follow-up period. ■

Efficacy Most Important To Parents for STI Vaccines

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Parents of adolescents appear to accept the idea of vaccinating their teens against sexually transmitted infections, expressing the most concern about the efficacy of the vaccine and the severity of the infection it could prevent, rather than the mode of transmission, Gregory D. Zimet, Ph.D., and his colleagues have reported.

Some surveys have suggested that pediatricians and other adolescent health providers might be reluctant to recommend STI vaccines, perhaps because of concerns about how parents might react.

"The high acceptability ratings reported by most parents in this study suggest that most parents would not react negatively to the suggestion," said Dr. Zimet of Indiana University, Indianapolis (Arch. Pediatr. Adolesc. Med. 2005;159:132-7).

The researchers surveyed 278 parents of adolescents aged 12-17 years. The mean age of parents was 41 years.

The mean age of children was 14 years, and 69% were female.

The survey presented nine different vaccine scenarios, each of which uniquely defined four variables: mode of transmission (STI or non-STI), severity of infection (curable, chronic and incurable, usually fatal); vaccine efficacy (50%, 70%, or 90%); and availability of behavioral methods of prevention (such as condoms or hand washing).

For each scenario, parents were asked, "If this vaccine were available today and you had the time, would you let your child get vaccinated?" Parents rated vaccine acceptability on a scale of 0-100, with 100 being "I would definitely let my child get this vaccine."

The parents were recruited from urban, Midwestern adolescent medicine clinics and private practices. More than half (56%) were white, and about 40% were African American. Less than 2% were Hispanic.

The least acceptable scenario, with a mean score of about 75, was a vaccine with 50% efficacy against a non-STI that could be prevented by hand washing.

The most acceptable scenario, with a mean score of 88.6, was a vaccine with 90% efficacy that protected against a usually fatal non-STI that could not be prevented by hand washing.

The mean score for the six STI scenarios was slightly, but not significantly, higher than the mean score for the three non-STI scenarios. The lowest-scoring STI vaccine scenario was a vaccine that was 50% effective against a curable STI that could not be prevented with condoms (75.7). The highest-scoring STI scenario was a vaccine that was 70% effective in preventing a usually fatal STI that could be prevented by the use of condoms (84.4).

For the majority of parents, sexual transmissibility had the least influence on acceptability ratings. Vaccine efficacy was the most influential factor in the ratings, followed by severity of infection and availability of behavioral protection. However, 31 parents (11%) indicated a relatively strong preference for an STI vaccine, and 16 parents (6%) indicated a relatively strong opposition to it.

About a quarter (27%) of the parents gave ratings of 100 to every vaccine. High accepters were more likely to be in the urban clinics and to have only a high school diploma. Acceptability was not related to the child's age, suggesting that parents might not make these decisions based on the proximity of their child's sexual activity. ■

Urinary Cytology Not Useful as Screen for Bladder Invasion

BY MARY ANN MOON
Contributing Writer

WASHINGTON — Urinary cytology was found to be "of limited use" in detecting whether pelvic cancer has invaded the bladder, Kelly L. Molpus, M.D., reported at the annual meeting of the Central Association of Obstetricians and Gynecologists.

He and his associates hypothesized that a pelvic tumor that has invaded the bladder might shed malignant cells that could be detected by microscopic examination of the urine, in much the same way that peritoneal "washes" are examined for the microscopic spread of ovarian or other cancers.

In a retrospective study using databases at two medical centers, the researchers reviewed the findings on urine samples collected from 93 women with pelvic cancer (mean age 48 years) who were treated between 1999 and 2004. The samples were collected when the women underwent cystoscopy for staging of their pelvic cancer.

Urinary cytology gave no extra information on the extent of disease in those with known stage I or II pelvic cancer and was 'of limited diagnostic value.'

Most of the women had primary cervical cancer. Six had locally extensive endometrial cancer; three each had vulvar, vaginal, or recurrent cervical cancer; one had ovarian cancer; and one had a primary rectal cancer that also involved the vagina, said Dr. Molpus, the McClure L. Smith Professor of Gynecologic Oncology at the University of Nebraska, Omaha.

Two-thirds of the samples were classified as normal on urinary cytology. The other one-third showed some abnormality, but these turned out to reflect benign changes such as inflammation or subclinical cystitis in most cases.

Urinary cytology detected malignant cells in only four women (4.3%), all of whom had extensive, locally advanced tumors. It failed to detect bladder invasion in three. In contrast, biopsy confirmed cancerous invasion of the bladder in all seven subjects (7.5%).

Thus, urinary cytology showed only a 57% sensitivity as a screen for detecting bladder invasion. It yielded "no additional information on the extent of disease in any patient with known stage I or II pelvic cancer," so it was deemed to be "of limited diagnostic value," Dr. Molpus said.

However, given its 100% specificity and 100% positive predictive value in this study, urinary cytology may be useful in specific situations, such as when bladder biopsy results are inconclusive or biopsy samples are inadequate or unavailable, he said. ■