Oral Steroid Use Tied To Bladder Cancer

BY BRUCE JANCIN

DENVER — Prolonged oral glucocorticoid use may be associated with an increased risk of bladder cancer, findings from a population-based case-control study suggest.

The working hypothesis for the observed link is that the immunosuppression induced by prolonged use of oral glucocorticoids results in diminished immunosurveillance against growing tumors, Dr. Karl Dietrich explained at the annual meeting of the American Association for Cancer Research.

He reported on 786 patients with bladder cancer and 1,083 controls who underwent structured personal interviews regarding their history of medication use as well as the prevalence of standard risk factors for bladder cancer. Oral glucocorticoids had been used for 1 month or more by 61 cancer patients and 51 controls.

After adjusting for age, gender, and smoking, current prolonged users of oral glucocorticoids had a 2.2-fold greater risk of bladder cancer than individuals who had not taken the medication for at least 1 month, said Dr. Dietrich of Dartmouth University, Hanover, N.H.

The risk of bladder cancer was greatest in individuals who used oral glucocorticoids for a total of 5 years or more. They had an adjusted 3.4-fold increased risk of the malignancy, compared with nonusers.

Prednisone accounted for close to 90% of all oral glucocorticoid use in the study. Dose information was provide by 63 subjects. Those who took at least 50 mg/day had a 4.1-fold increased risk of bladder cancer; however, patients who took less than 49 mg/day didn't have a significantly greater rate of bladder cancer than nonusers.

Dr. Dietrich noted in an interview that the bladder cancer study is a sequel to earlier groundbreaking work led by Margaret R. Karagas, Ph.D., also of Dartmouth. Her similar population-based case-control study demonstrated that use of glucocorticoids for 1 month or longer was associated with an adjusted 2.3-fold increased risk of cutaneous squamous cell carcinoma and a 1.5-fold increased risk of basal cell carcinoma (Br. J. Cancer 2001;85:683-6).

Dr. Karagas was subsequently a coinvestigator in a confirmatory Danish population-based cohort study which concluded that patients with 15 or more filled prescriptions for oral glucocorticoids had a 2.5-fold increased risk of squamous cell carcinoma and a 1.5-fold increased risk of basal cell carcinoma (J. Natl. Cancer Inst. 2004;96:709-11).

The bladder cancer study results suggest that the same glucocorticoid-induced reduced immunosurveillance that allows growth and development of skin cancers also confers an increased risk of internal malignancies, Dr. Dietrich said.

The study was partly funded by the National Cancer Institute and National Institute of Environmental Health Sciences. ■

NSAIDs May Lower Risk of Bladder Ca in Nonsmokers

DENVER — Use of nonaspirin NSAIDs more than twice per week was associated with a 45% reduction in the risk of developing bladder cancer in a pooled analysis of three prospective cohort studies totaling more than half a million subjects.

The strongest inverse association was seen with daily use, which conferred a 50% reduction in bladder cancer risk among nonsmokers after adjustment for sex, smoking status, body mass index, race, and aspirin use, Sarah Daugherty, Ph.D., reported at the annual meeting of the American Association for Cancer Research.

The use of aspirin proved to be unrelated to bladder cancer risk in this pooled analysis, added Dr. Daugherty of the National Cancer Institute.

The three prospective cohort studies incorporated in this analysis were the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, the NIH-AARP Diet and Health Study, and the U.S. Radiologic Technologist Health Study.

Together the three cohorts totaled 508,807 adults, of whom 2,553 developed bladder cancer during a median of 7 years of follow-up.

—Bruce Jancin

MINDFUL PRACTICE

'As Needed' SSRI for Premature Ejaculation

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

A 63-year-old retired mechanic with a history of diabetes mellitus and hypertension presents to you for a new medical issue. One year ago you treated him for tobacco dependence with 6 months of varenicline, and he has remained abstinent from tobacco. Three months after discontinuing varenicline, he presented with his wife for lifelong issues with depression, which became more manifest after he quit smoking. You diagnosed him with depression and started him on bupropion SR, and his mood subsequently improved. He has now presented alone for issues related to premature ejaculation "for as long as he can remember," which has become a significant issue in his marriage. He reports little voluntary control over his ejaculation and says that he is developing significant "performance anxiety." He says that he achieves intromission about 20% of the time. He denies issues with libido or erectile dysfunction. He is currently on lisinopril, metformin, bupropion, aspirin, and simvastatin. He is reluctant to take more medications and is wondering if there is something that he could take "as needed." You are aware that selective serotonin reuptake inhibitors (SSRIs) have some efficacy for this but wonder if he can take them as needed.

The Question

In patients with premature ejaculation, are SSRIs taken as needed more helpful for prolonging ejaculatory latency than placebo?

The Search

You log on to PubMed (www.pubmed.gov) and enter search terms "premature ejaculation" AND "antidepressants" and limit the search to randomized, controlled trials. You find a relevant study. (See box at right.)

Our Critique

In this crossover study, subjects had a reasonable washout period of 3 weeks before they crossed over to the other treatment arm. As suggested by the authors, the improvement in ejaculatory intervals within the first 2 weeks of paroxetine treatment suggest that this effect is mediated by a direct blocking of central serotonergic reuptake and not through alleviation of depressive symptoms, which typically takes several weeks. The dose given (20 mg) is the starting dose for depression and is only taken as needed, which makes this an attractive clinical intervention with proven benefit and a low likelihood of significant side effects. Your patient would have been excluded from the current study because he is on an antidepressant.

Clinical Decision

You continue the bupropion SR and prescribe paroxetine 20 mg by mouth as needed to be taken 3-4 hours before sexual intercourse.

DR. EBBERT *and* DR. TANGALOS *are with the Mayo Clinic in Rochester, Minn. They have no conflict of interest to report. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at imnews@elsevier.com.*

C.G. McMahon and K. Touma

Treatment of premature ejaculation with paroxetine hydrochloride as needed: Two single-blind, placebo-controlled crossover studies. J. Urol. 1999;161:1826-30.

► **Design:** Two single-blind, crossover studies were included in this report. The first study prescribed paroxetine ad lib, and the second prescribed paroxetine ad lib after a 3-week course of daily paroxetine. The first study is most relevant to our patient who wishes to take a medication only "as needed."

► **Subjects:** Eligible subjects had to be male, heterosexual, in a stable relationship, and have normal sexual potency. Potential subjects were excluded if they had a sexual disorder, erectile dysfunction, reduced sexual desire, inhibited male orgasm, alcohol or substance abuse, use of psychotropic or antidepressant medications, or a chronic depressive, psychiatric, or physical illness.

► **Intervention:** Subjects were randomized to 20 mg paroxetine (group A) or placebo (group B) as needed 3-4 hours before planned intercourse for 4 weeks. Crossover was conducted after a 3-week drug-free washout period. Subjects crossed over for an additional 4 weeks of treatment.

► **Outcomes:** The primary outcome was coital frequency and ejaculatory latency times. Pretreatment ejaculatory latency time was measured during a 3-week baseline period during which time patients were asked to have sexual intercourse 3 times per week. Pretreatment coital frequency was the mean number of attempts during the previous 3 months. Subjects were given a diary to record the frequency of coitus, quality of erection and orgasm, and measurement of ejaculatory latency time using a stopwatch.

► **Results:** A total of 26 men with mean age of 39.5 years (range 19-55), mean pretreatment ejaculatory latency time of 0.3 minutes, and mean pretreatment coital frequency of 0.5 times/were randomized into two groups. For group A, both parameters increased during initial paroxetine treatment (3.2 minutes and 3.2 times/week 4) and decreased during subsequent placebo treatment (0.45 minutes and 0.9 times/week at week 11). For group B, both parameters increased slightly during initial placebo treatment (0.6 minutes and 1.3 times/week at week 4) but increased dramatically during subsequent paroxetine treatment (3.5 minutes and 3.1 times/week at week 11). Ejaculatory latency time for groups A and B was statistically superior with the drug, compared with placebo. Intravaginal ejaculation was achieved by one-third of patients who had never achieved it after 2 weeks of treatment. Intravaginal ejaculation was not achieved with placebo.