Weekly Regimen Not Optimal for Cisplatin

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BY DOUG BRUNK
San Diego Bureau

Palm Springs, Calif. — Women with cervical cancer who received weekly cisplatin treatment had significantly worse progression-free survival rates and significantly worse toxicity than did those who received cisplatin 5 days in a row every 21 days, according to results of a long-term, single-site, retrospective study.

The finding is important, because about 5 years ago the weekly regimen became the standard of care, due primarily to the ease of weekly dosing and the lower cost of outpatient administration, Dr. Mark Einstein said in an interview at the annual meeting of the Society of Gynecologic Oncologists.

"In the past we used to do an inpatient infusional dosing of cisplatin concomitant with radiation therapy for the treatment of locally advanced cervical cancer," he explained. "In 2001 there was a switch over to outpatient weekly regimens, but there was never really a trial to show that the [outcomes] are the same between the two patient regimens."

He and his associates studied 77 consecutive patients with stages IB2-IV cervical cancer who were treated with cisplatin concomitant with external mean radiotherapy and two 9-Gy high-dose-rate brachytherapy insertions at the Montefiore Medical Center of the Albert Einstein College of Medicine, Bronx, N.Y., between 1995 and 2004. The 50 women in the 5-day treatment group received cisplatin 20 mg/m^2 for 5 days every 21 days with concomitant radiotherapy. The 27 women in the weekly treatment group received 40 mg/m^2 weekly with concomitant radiotherapy.

Nearly half of the women in the 5-day treatment group (48%) had stage III or IV disease, compared with 26% of women in the weekly treatment group. The rest of the women had stage IB2 or II disease. The median follow-up was 42 months.

Dr. Einstein, a gynecologic oncologist with the Albert Einstein College of Medicine, reported that there were no significant differences between the two treatment groups in terms of age, race, histology, body mass index, anemia, and total radiotherapy doses.

Overall, 3-year progression-free survival was 81% for the 5-day treatment group, compared with 66% for the weekly treatment group, a difference that was statistically significant.

After the researchers adjusted for cancer stage, patient age, and completion of treatment, women in the weekly treatment group were 3.5 times more likely to fail treatment than were their counterparts in the 5-day treatment group. Similarly, women in the weekly treatment group were 2.7 times more likely to die from cervical cancer than were those in the 5-day treatment group.

Dr. Einstein also reported that women with late-stage disease who received weekly treatment were 3.43 times more likely to develop acute toxicity—primarily in the GI tract—compared with their counterparts in the 5-day treatment group. "That's probably [because the 5-day group] got a lot more fluids when the patients were in the hospital, while they were getting their chemotherapy," he speculated. "But that difference is hard to glean out."

Dr. Einstein emphasized that a multicenter, randomized, controlled trial is needed to confirm the findings. He and his associates are working on such a trial design and may add a third treatment arm of women who receive sustained low-dose cisplatin throughout their radiation therapy. "The idea [is] that with the 5-day infusion, they're getting a relatively sustained dose once every 3 weeks," he said. "Maybe it's that sustained dose that's improving the survival benefit." ■

Prophylaxis Cuts DVT Rate in Surgical Oncology Patients

BY JANE SALODOF MacNEIL
Southwest Bureau

San Diego — Pharmacologic prophylaxis can sharply reduce the risk of deep venous thrombosis when cancer patients undergo surgery, Dr. Michael J. Leonardi said at a symposium sponsored by the Society of Surgical Oncology.

The deep venous thrombosis (DVT) rate falls from 35% without prophylaxis to 12% when surgical oncology patients are given heparin, according to Dr. Leonardi of the University of California, Los Angeles. A combination of mechanical prophylaxis with heparin further reduces the DVT rate to just 5%.

"Cancer patients need some form of prophylaxis," Dr. Leonardi said in an interview after his review of data from dozens of randomized, controlled trials. "If bleeding risk is not a concern," he added, "pharmacological prophylaxis is better than mechanical prophylaxis, and combination therapy has been shown to be even more effective."

'If bleeding risk is not a concern, pharmacological prophylaxis is better than mechanical.'

DR. LEONARDI

Dr. Leonardi and his colleagues in the UCLA surgery department searched the Medline database for English-language trials and found 55 randomized controlled trials published from 1966 to 2005 on DVT prophylaxis in general surgery. Among these, 26 trials reported outcomes for 7,639 cancer patients, Dr. Leonardi said.

Colorectal and major abdominal surgical procedures accounted for 39% and 38% of cases, respectively. Upper gastrointestinal and small bowel operations were the next most common at 11%, followed by gynecologic surgery at 3%. Biliary, pancreatic, urologic, and noncardiac thoracic cancers each accounted for just 1% of the surgical procedures in Dr. Leonardi's presentation.

After a review of the wide variety of patients and surgeons in these trials, he said the best prophylaxis for individual cancers is still not known. For example, not even one randomized controlled trial was found that evaluated DVT prophylaxis in breast cancer patients. The incidence of DVT in breast cancer "is probably not as high as in some other cancers, but because breast cancer is so common a lot of DVTs are associated with it," he said.

Among the findings from the analysis, Dr. Leonardi reported that:

▶ DVT rates vary with the detection method used. Venography was the most sensitive method, and ultrasound the least sensitive.

▶ Higher heparin doses are more effective than lower doses. DVT rates were 8% for higher doses and 14% for lower doses of the forms of heparin in 17 trials with a total of 4,005 patients.

▶ Low-molecular-weight heparin and low-weight unfractionated heparin are equally effective. Both cut DVT rates to 8% at high doses in the 17 trials just cited. At low doses, the rate was 14% for low-molecular-weight heparin and 13% for low-weight unfractionated heparin.

▶ Heparin reduces the rate of proximal DVTs. The rate went from 41% to 13% in nine trials reporting on 284 patients with DVTs. Location was unaffected by the use of low-molecular-weight heparin vs. low-weight unfractionated heparin.

▶ Major complications occur in only 1% of cases with pharmacologic prophylaxis. Based on seven trials, minor complications occurred in 10% of patients and major complications in 1%, he reported. There was no difference between low-molecular-weight heparin and low-weight unfractionated heparin. In four trials, 3% of patients discontinued prophylaxis. ■

Routine Care Fails to Aid Ovarian Cancer Detection in Older Women

BY DOUG BRUNK
San Diego Bureau

Palm Springs, Calif. — Routine medical care and comprehensive health insurance coverage seem to improve the early detection of epithelial ovarian cancer in women aged 59 and younger, but not in those aged 60 and older, Dr. Sherry H. Weitzen reported in a poster session at the annual meeting of the Society of Gynecologic Oncologists.

"It surprised me that there was very little effect of access to care for older women in terms of being diagnosed at an earlier stage," Dr. Weitzen, an epidemiologist in the obstetrics and gynecology department at Brown University, Providence, R.I., said in an interview.

"I was disappointed because … it seems like older women are doomed to being diagnosed later. That's what the literature says anyway, and there seems to be no kind of help for them [even] if they are vigilant about their health care."

Dr. Weitzen and her associates reviewed the medical charts of 832 women diagnosed with epithelial ovarian cancer at Women and Infants Hospital in Providence between 1991 and 2004.

They used International Federation of Gynecology and Obstetrics (FIGO) standards to determine tumor stage during or after surgery, and defined health insurance as private/Medicare and Medicaid/uninsured/self-pay/none documented.

Of the 832 women, most (540) were diagnosed with late-stage disease, 82% were insured by Medicare or private insurance plans, and 66% reported having a "usual" care provider.

Of the 292 women diagnosed with early-stage disease, 71% reported having routine medical care, compared with 63% of their counterparts who were diagnosed with late-stage disease. In addition, 85% of women with early-stage disease had Medicare or private insurance, compared with 80% of women diagnosed with late-stage disease.

After adjusting for age at diagnosis, the researchers found that women who had routine medical care plus Medicare and/or private insurance were 1.74 times more likely to have ovarian cancer diagnosed at an early stage, compared with those who had no routine care and no other insurance plans.

"For women less than 60 years of age, the combined effect of having both routine care and better health insurance had two times the odds of earlier diagnosis, compared to women with no routine care and other health insurance," the researchers wrote in their poster.

Dr. Weitzen said the study underscores the importance of early detection, noting that physicians "should encourage their patients to come in regularly." ■

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