FDA Advises Against Anesthetic Joint Infusions

BY ELIZABETH MECHCATIE

Cases of chondrolysis diagnosed a median of 8.5 months after administration of a continuous intra-articular infusion of a local anesthetic for postsurgical pain with an infusion pump have prompted the Food and Drug Administration to issue a statement recommending against this practice.

"Because the reported cases involved significant injury to otherwise healthy young adults, the FDA wants to advise health care professionals that elastomeric infusion devices or any other infusion pump are not cleared by [the agency] to deliver intra-articular infusions of local anesthetics and should not be used for this purpose," according to the statement, which lists bupivacaine, chlorprocaine, lidocaine, mepivacaine, procaine, and ropivacaine as the marketed local anesthetics.

The statement also pointed out that local anesthetics are approved as injections "for the production of local or regional anesthesia or analgesia" and are not approved for continuous intra-articular postoperative infusions. "It is important to note that single intra-articular injections of local anesthetics in orthopedic procedures have been used for many years" without any reports of chondrolysis, the statement added.

The 35 reports of chondrolysis—the necrosis and destruction of cartilage—reviewed by the FDA were reported between 2006 and 2008 in people aged 16-58 years (median 25 years), mostly after shoulder surgery; 6 were in people aged 16-18. They were given continuous infusions of a local anesthetic over 48-72 hours, administered directly into the intra-articular space with an elastomeric infusion pump, with and without epinephrine.

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Of the 35 cases, 34 (97%) involved shoulder surgeries; the remaining case was in the knee. Almost half (46%) of the infusions involved the glenohumeral (glenoid) space. Most of the cases (32 or 91%) involved bupivacaine.

Symptoms of chondrolysis—joint pain, stiffness, and loss of motion—were reported as early as the second month after the infusion. In more than half of the cases, additional surgery, such as arthroscopy or joint replacement, was needed, according to the FDA. The cases were not associated with any single brand of infusion device.

Although the cause of the 35 cases is not known, "the infused local anesthetic drugs, the device materials, and/or other sources may have resulted in the development of chondrolysis," the statement said. There have also been recent reports of chondrolysis in the literature of people who have had bupivacaine infusions, as well as preclinical studies that found that exposure of chondrocytes to bupivacaine, lidocaine, and ropivacaine resulted in chondrolysis. ■

Pancreatectomy Complication Rate Not Higher With Diabetes

BY DAMIAN McNAMARA

CHICAGO — Patients with diabetes mellitus who undergo resection for pancreatic cancer do not have significantly increased risk for delayed gastric emptying, symptomatic fistulae formation, or extended length of hospital stay, compared with nondiabetic patients, data from a retrospective study suggest.

"We are all concerned that diabetics will have more gastric emptying issues, and we might be more likely to put a J [jejunostomy] tube into that patient. Our data suggest rates [of delayed emptying] are not significantly higher," said Dr. David A. Kooby of the division of surgical oncology, Emory University, Atlanta.

Dr. Kooby was a coauthor of research presented by Dr. Carrie K. Chu at the annual clinical congress of the American College of Surgeons.

To compare 60-day complication rates, they and their associates reviewed the records of 251 patients with pancreatic ductal adenocarcinoma who underwent resection in 2000-2008. Of this group, 116 patients (46%) had preoperative diabetes.

The patients with diabetes were more likely to have at least one comorbidity than were those without diabetes, Dr. Chu said.

The type of pancreatectomy did not differ significantly between groups, nor did hospital length of stay (13-14 days). Most patients underwent pancreaticoduodenectomy. Just 1% of nondiabetic patients had total pancreatectomy, while none of the diabetes patients did. The remainder underwent left pancreatectomy.

There were no dramatic differences in complications by organ system, except for renal dysfunction. A total of 23% of 116 patients with diabetes versus 13% of 135 nondiabetic patients experienced renal dysfunction, "but it was mostly a mild elevation of creatinine," said Dr. Chu, a surgical resident at Emory.

The 30-day mortality rates were 2.2% in the diabetes mellitus group and 1.7% in the nondiabetic patients, a difference that was not statistically significant, Dr. Chu said.

"The key point is that there was no major difference between diabetics and nondiabetics," Dr. Kooby said. ■

Unfractionated Heparin Best Deal for VTE Prophylaxis

BY NEIL OSTERWEIL

PHOENIX — Low-dose unfractionated heparin for thromboprophylaxis following abdominopelvic cancer surgery gives the most protection for the lowest overall cost, a cost analysis showed.

With good patient compliance, low-dose unfractionated heparin after discharge was a better bargain than even daily aspirin at preventing venous thromboembolism (VTE), Dr. Ciaran Bradley reported at a symposium sponsored by the Society of Surgical Oncology.

"Low-dose unfractionated heparin in fact saves money over the currently commonplace practice of doing nothing," Dr. Bradley said. "It would be cost effective even if compliance with medication were low," he noted. "Only if the cost of low-molecular-weight heparin were less than $100 would it start to compete for dominance in the model, and currently, it's seven times more expensive than that."

Aspirin also appears to be an attractive alternative in this clinical situation because of its low cost, oral administration, and absence of heparin-induced thrombocytopenia.

"Even though aspirin has been relatively discounted as a primary agent for thromboprophylaxis for inpatients in the perioperative setting, it may have some utility after the discharge period, and further clinical studies using aspirin for this very scenario may be warranted," said Dr. Bradley of the Medical College of Wisconsin, Milwaukee.

Patients who undergo abdominopelvic cancer resection are at high risk for VTE, with a postdischarge rate up to 25% reported in one study (BMJ 1988;297:28). Up to 4 weeks of VTE prophylaxis is recommended in guidelines published by the American College of Chest Physicians, National Comprehensive Cancer Network, and American Society of Clinical Oncology, he noted.

"However, we postulate that these guidelines are rarely followed, likely because of concerns over the costs of the agents as a result of bleeding complications and heparin-induced thrombocytopenia, as well as concern that patients may not be compliant with medications because those currently used are injectable formulations," he said.

Dr. Bradley and his colleagues created a model using a reference case of a patient more than 40 years old who has undergone an open or laparoscopic procedure for abdominopelvic malignancy under general anesthesia and lasting at least 45 minutes. The hypothetical patient received in-hospital chemical prophylaxis for VTE, and was discharged on the seventh postoperative day.

The authors compared the relative costs of four postdischarge thromboprophylaxis strategies: 40 mg of low-molecular-weight heparin given subcutaneously once daily, 5,000 U of low-dose unfractionated heparin given subcutaneously three times daily, 325 mg of aspirin given orally daily, and no prophylaxis. The model assumed a constant risk of VTE and bleeding complications over the 3 weeks after discharge.

The model also assumed that the patient would not always be compliant with dosing. For example, the model assumes that daily compliance with injectable low-molecular-weight heparin would be 79% with once-daily dosing, and that compliance would drop to 65% with injectable low-dose unfractionated heparin dosed three times daily.

Using Medicare and Red Book 2006 data, the authors determined that the cost of VTE would be $4,715, which includes hospitalization plus 6 months of subsequent warfarin therapy and monitoring. Heparin-induced thrombocytopenia would cost $5,184, which includes 5 days of treatment with the thrombin inhibitor lepirudin followed by warfarin for 6 months. Bleeding complications, primarily minor bleeds not requiring treatment but some requiring transfusion, would cost $388.

The cost to patients would be $623 for low-molecular-weight heparin, $72 for low-dose unfractionated heparin, and $2 for aspirin.

But when the researchers factored in the VTE rates associated with each medication in the baseline analysis, they found that low-dose unfractionated heparin was the low-cost leader. The differences would translate into annual population savings relative to no prophylaxis of $50.1 million for low-dose unfractionated heparin and $28.8 million for aspirin, compared with excess costs of $81.3 million for low-molecular-weight heparin.

"This is a great paper," Dr. Edward A. Levine commented in a postpresentation discussion. "This is something we all wrestle with, since we all work with oncology patients who have more than one risk factor for DVT or VTE," he said. However, "there are a number of papers that I've seen showing that aspirin doesn't do anything in terms of preventing thromboembolism at all," noted Dr. Levine, who is chief of surgical oncology at Wake Forest University Baptist Medical Center in Winston-Salem, N.C.

Dr. Bradley agreed that in the inpatient setting, aspirin does not appear to protect against immediate VTEs. "However, some studies have looked at aspirin after the point of discharge, and they do show a benefit, particularly in patients who have an increased VTE risk," he said.

Dr. Bradley said that he has no relevant financial disclosures. ■