Notas de la FDA

Rev. Mex. Anest
1998;21:146-147

Health Advisory for Certain Anticoagulant Drugs (Low Molecular Weight Heparins and Heparinoids).

The FDA is alerting doctors about a serious safety problem associated with the use of certain anticoagulant drugs used in patients undergoing certain types of surgery to prevent complications from blood clots that can form in the deep log veins.

The drugs — low molecular weight heparins and a heparinoid marketed as Lovenox, Fragmin, Normiflo and Orgaran — when used concurrently with spinal or epidural anesthesia, or spinal puncture may cause bleeding or hematomas (collection of blood) within the spinal column. When bleeding occurs in the spinal column, increased pressure on the spinal cord may result in permanent paralysis if not detected and treated immediately.

Because this may be a preventable problem, FDA is advising doctors to carefully monitor patients receiving low molecular weight heparins or heparinoids for possible spinal or epidural bleeding.

The risk for bleeding or hematomas is increased by use of catheters placed in the spinal canal to administer pain medication or by the use of other drugs that can affect blood clotting such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk of adverse effects also appears to be increased by traumatic or repeated spinal or epidural punctures.

FDA's alert was prompted by more than 30 reports, received as of November 1997, of patient who developed bleeding within the spinal column, some of which resulted in prolonged or permanent paralysis. These reports were associated with Lovenox used in conjunction with spinal or epidural anesthesia or spinal puncture.

To provide additional information on the safe use of these drugs, FDA has requested that the manufacturers add a boxed warning to the labeling discussing the risk of spinal or epidural hematomas and the importance of monitoring patients for signs or symptoms of neurologic injury.

Health care professionals should report any serious adverse events, including cases of epidural or spinal hematomas, occurring with the use of low molecular weight heparin, heparinoids, or other anticoagulants to the FDA's MEDWATCH program at 1-800-FDA-1088, fax 1-800-FDA-0178; or to the respective pharmaceutical manufacturers:

Fragmin® (dalteparin sodium injection); Pharmacia & Upjohn: 1-800-253-8600, ext. 38244.

Lovenox® (enoxaparin sodium) Injection; Rhone-Poulenc Rorer Pharmaceuticals Inc., 1-800-340-7502.

Normiflo® (ardeparin sodium) Injection; Wyeth Laboratories Inc.; 1-800-934-5556.

Orgaran (danaparoid sodium) Injection; Organon Inc.; 1-800-631-1253.

The public health advisory is being sent to general and orthopedic surgeons, anesthesiologists, pain management specialists, nurses, hematologists and other physician groups.

U.S. Department of Health and Human Services
Public Health Service
Food and Drug Administration
Rockville, MD 20857
15 December 1997

Reports of epidural or spinal hematomas with the concurrent use of low molecular weight heparin and spinal/epidural anesthesia or spinal puncture.

Dear Health Care Professional:

The Food and Drug Administration (FDA) would like to call to your attention recent post marketing reports of patients who have developed epidural or spinal hematomas with the concurrent use of low molecular weight heparin and spinal/epidural anesthesia or spinal puncture. Many of the hematomas caused neurologic injury, including long-term or permanent paralysis. Because these events were reported voluntarily from a population of unknown size, estimates of frequency cannot be made. However, given the potential seriousness of this complication, we believe that patients and health care professionals should be notified of this information.

The postmarketing reports received to date involved patients who were treated the Lovenox® (enoxaparin sodium) Injection. However, the adverse event would be expected to occur if drugs with similar pharmacological activity were used in the same manner. Therefore, the FDA has asked all manufacturers of low molecular weight heparins and heparinoids to revise their package inserts to provide further information for the safe and effective use of these drugs. Specifically, the manufacturers have been asked to include additional safety information and recommendations in a boxed warning in their package inserts.

Rev. Mex. Anest 1998;21:146-147

Summary of Reports

As of November 1997, there have been more than 30 spontaneous safety reports describing patients who have developed epidural or spinal hematomas with concurrent use of enoxaparin sodium and spinal/epidural anesthesia or spinal puncture. Many of the epidural or spinal hematomas caused neurologic injury, including long-term or permanent paralysis.

Approximately 75 percent of the patients were elderly women undergoing orthopedic surgery.

At this time, the FDA believes practitioners should be aware of the following points if using these products:

When neuraxial anesthesia (epidural/spinal anesthesia) or spinal puncture is employed, patients anticoagulated or scheduled to be anticoagulated with low molecular weight heparins or heparinoids for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis.

The risk of these events is increased by the use of indwelling epidural catheters for administration of analgesia or by the concomitant use of drugs affecting hemostasis such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, or other anticoagulants. The risk also appears to be increased by traumatic or repeated epidural or spinal puncture.

Patients should be frequently monitored for signs and symptoms of neurological impairment. If neurologic compromise is noted, urgent treatment is necessary.

Practitioners should consider fully the potential benefit versus risk before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis.

The FDA will continue to monitor closely post marketing reports for additional events. We encourage all health care professionals to report any serious adverse events, including cases of epidural or spinal hematomas, occurring with the use of low molecular weight heparins, heparinoids, or other anticoagulants to the FDA's MEDWATCH program at 1-800-FDA-1088, fax 1-800-FDA-0178; or to the respective pharmaceutical manufacturers: Fragmin® (dalteparin sodium injection); Pharmacia & Upjohn: 1-800-253-8600, ext. 38244. Lovenox® (enoxaparin sodium) Injection; Rhone-Poulenc Rorer Pharmaceuticals Inc., 1-800-340-7502. Normiflo® (ardeparin sodium) Injection; Wyeth Laboratories Inc.; 1-800-934-5556. Orgaran (danaparoid sodium) Injection; Organon Inc.; 1-800-631-1253.

Sincerely yours,

Murray M. Lumpkin, M.D.
Deputy Center Director (Review Management) Center for Drug Evaluation and Research
Food and Drug Administration U.S. Department of Health and Human Services Public Health Service 5600 Fishers Lane
Rockville, Maryland 20857