

FDA warned against drug used on troops in Iraq

Military says it saves lives on battlefield

By Robert Little
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BAGHDAD, Iraq — U.S. military doctors have injected more than 1,000 wounded troops with a potent and largely experimental blood-coagulating drug despite evidence linking it to deadly blood clots.

The drug, Recombinant Activated Factor VII, is approved in the United States for treating rare forms of hemophilia affecting about 2,700 Americans.

In a warning last December, the Food and Drug Administration said that giving it to patients with normal blood could cause strokes and heart attacks. Its researchers published a study in January blaming 43 deaths on clots that developed after injections of Factor VII.

The Army medical command considers Factor VII to be a medical breakthrough in the Iraq war, giving frontline physicians a powerful new means of controlling bleeding that can be treated otherwise only with surgery and transfusions.

They have posted guidelines at military field hospitals encouraging its liberal use in all casualties with severe bleeding.

"When it works, it's amazing," said Col. John Holcomb, an Army trauma surgeon and the service's top adviser on combat medical care. "It's one of the most useful new tools we have."

But doctors and researchers at civilian hospitals, including Johns Hopkins and Massachusetts General Hospital, have rejected the drug, which costs \$6,000 a dose, as a standard treatment for trauma patients. Other hospitals say they are cautious about administering it because of clots found in their patients, including some that

have caused deaths.

Doctors at military hospitals in Germany and the United States have reported unusual and sometimes fatal blood clots in soldiers evacuated from Iraq, including unexplained strokes, heart attacks and pulmonary embolisms, or blood clots in the lungs. Some have begun to suspect Factor VII.

Doctors at Walter Reed Army Medical Center in Washington said they tried to determine last year whether a high incidence of clots was related to Factor VII use in Iraq, but they discovered that the Army was not collecting sufficient information about the drug to draw any conclusions.

Doctors at Landstuhl Regional Medical Center in Germany said they plan to track complications among war casualties who got Factor VII after concluding that a heart attack in a patient last August likely was caused by an injection of the drug in Iraq.

Civilian trauma and blood specialists think the military is taking an unwarranted risk with wounded soldiers because the drug has never been subjected to a large-scale clinical trial to verify that it is safe for patients without hemophilia.

"It's a completely irresponsible and inappropriate use of a very, very dangerous drug," said Dr. Jawed Fareed, director of the hemostasis and thrombosis research program at Loyola University in Chicago.

Army trauma specialists say that using Factor VII is worth the risk, considering reports from military doctors in Iraq describing its success at controlling severe bleeding.

But some civilian doctors who have worked with the drug say its clotting capabilities are so profound that they have to assume it is responsible for deaths among the military casualties who have received it.

"Of course some of them are dying from it," said Dr. Louis Aledort, a professor of hematology at Mount Sinai School of Medicine in New York. "If you give people this kind of dangerous coagulating product, some of them are going to have (blood clots)."

Yet he and other civilian specialists were less troubled by the dangers, which they said might be justified given the injuries in Iraq, than by the lack of scientific evidence that war casualties are getting any benefit for taking the risk.

"If you don't have that," Aledort said, "then you're just experimenting on people with a dangerous drug."

Officials at Novo Nordisk, the manufacturer, say evidence of complications doesn't mean that Factor VII is too dangerous to use, only that the side effects need to be weighed against its potential to help.

"It's really not a question of an absolute safety level, but rather a ratio of benefit to risk that has to be established," said Dr. Michael Shalmi, vice president of biopharmaceuticals for Novo Nordisk.

Military officials are unapologetic about moving aggressively toward a new treatment for the types of deadly bleeding they see frequently in Iraq.

Wounded troops requiring transfusions of 10 or more units of blood have a 25 percent to 50 percent chance of dying from injuries, they say. Anything that stops severe bleeding is worth exploring, they say, even if it carries risk.

"We're making decisions, in the middle of a war, with the best information we have available to us," said Holcomb, commander of the Army's Institute of Surgical Research.

"We're not waiting" for more clinical research, he said. "We'd still be talking about these things 10 years from now."