Pharmaceutical study: Less hemorrhaging after stroke, but not fewer deaths

June 11 2008

An international study published in May 2008 in the *New England Journal of Medicine* has shown that the coagulation factor VIIa can limit the extent of a cerebral hemorrhage. However, in the long term it does not prevent death or severe impairment.

Further studies must clarify whether the new treatment with the genetically engineered substance is suitable for a special group of patients who – as the study suggests – could profit from therapy in spite of this. These are patients with a limited hemorrhage size (delta 60ml), with limited amounts of blood in the cerebrospinal fluid space (delta 5ml), who are not over an age 70 years and who will be treated within 2.5 hours or less.

Some 841 patients in 73 centers in 20 countries took part in the study. Member of the steering committee, study coordinator for Europe, and co-author of the published article is Professor Dr. Thorsten Steiner, Senior Physician at the Department of Neurology, University of Heidelberg Hospital (Medical Director: Professor Dr. Werner Hacke).

Cerebral hemorrhages account for 15 percent of all strokes. They are often fatal; some 80 percent of the surviving patients are severely disabled. Especially problematic is further increase of the hematoma, which occurs in one third of patients in the first four hours. Thus far there is no way of treating.

An earlier study proved reduction of outcome and mortality

Three years ago, a phase-2 study with recombinant coagulation factor VIIa with the trade name NovoSeven, which is not yet approved for clinical use, showed that the compound could lower the death rate after a hemorrhage and limit impairment. This study was also published in the *New England Journal*.

The new study compares the effectiveness of factor VIIa in two dosages (20 and 80 micrograms) with a placebo. The extent of the hemorrhage – visible on a CT scan – was noticeably larger (26%) in the placebo group than in the patients treated with 80 micrograms (11%) and 20 micrograms (18%). But there was still no difference in the number of patients who died after a stroke or were severely disabled by it. However, patients who were treated with the higher dosage of factor VIIa suffered more frequently from thromboses and embolisms.

Fewer high-risk patients in the placebo group / New study on a certain patient group?

"A decisive reason for the negative result is the fact that there were more high-risk patients in the patient groups treated with factor VIIa than in the placebo group," stated Professor Steiner. These patients more frequently had intraventricular hemorrhages (bleeding in the spaces of the brain containing cerebral spinal fluid) and high blood pressure. "Intraventricular bleeding increases the mortality by a factor of 4 to 5 and high blood pressure increases the risk of a secondary hemorrhage," said Professor Steiner. The age of the patients and timing of treatment were also factors.

"We have also determined that after a cerebral hemorrhage reaches a

certain size, clinical improvement is very unlikely, irrespective of treatment," continued Professor Steiner. It is possible that the medication is effective mainly in patients whose hemorrhages have not yet exceeded a certain size, who have no or only a limited amount of blood in the ventricle, and do not exceed a certain age. This should be examined in another study.

"We would welcome a decision of the manufacturer of this medication decide to conduct a study on this special group of patients," said Professor Steiner. To what extent high blood pressure increases the risk of secondary hemorrhaging in the acute phase of a hemorrhagic stroke is currently being examined in another study.

Source: University Hospital Heidelberg