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A safety study of the use of Vivostat[®] patient-derived fibrin sealant containing tranexamic acid in neurosurgery.

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Fibrin sealants are widely used in neurosurgery for sealing of the dural closure fibrin sealant clots may be stabilized against fibrinolysis by the addition of agents (such as tranexamic acid) that inhibit the binding of plasminogen to fibrin or agents which inhibit plasmin activity (such as aprotinin). Aprotinin is of bovine origin and may cause immunological reactions, and fatal anaphylactic reactions have been reported.

Tranexamic acid is an effective alternative to aprotinin in fibrin sealants. Tranexamic acid has a long history of safe use when used systemically. However, if applied at high concentration when applied topically in fibrin sealants it has been associated with neurotoxicity.

Aim: To study the safety of Vivostat[®]-derived sealant containing tranexamic acid when used in neurosurgery to prevent CSF leakage.

Based on a study of the effect of concentration of tranexamic acid in an animal model, we found the safety margin for the clinical application of Vivostat[®] fibrin sealant prepared with 100 mg TA (containing approximately 0.5 mg/ml) **sufficient** to proceed with clinical studies in humans

Methods: Fifty adult patients (ages 23 to 72 years, 17 male and 33 female) undergoing neurosurgical procedures in the skull base at the Rigshospitalet, Copenhagen, and in whom fibrin glue were planned to be used, were enrolled. During surgery, 120 ml of donated patient blood was processed to produce a fibrin sealant in the Vivostat[®] System. Tranexamic acid (100mg) was added to the Vivostat[®] Preparation Unit (together with the citrate anticoagulant) prior to collection of the blood. Previous studies have identified that this results in a residual concentration of about 0.5mg/ml tranexamic acid in the fibrin sealant.

At the end of surgery the Vivostat[®] fibrin glue was used to seal the dural closure. The surgeon was permitted to use the fibrin sealant in whatever manner and quantity he wished to provide an effective seal. In all other aspect the patients were treated according to normal procedures. No special instructions were given to avoid contact with the brain surface.

Observations were carried out to identify any adverse effect that could be ascribed to the use of Vivostat[®] fibrin glue up to the time of the patient leaving hospital.

Results: Thirty-nine of the fifty patients had a translabyrinthine approach for an acoustic neuroma. Six patients were operated for non-acoustic neuroma diseases in the posterior fossa. One patient had a transspenoidal approach for a pituitary tumor and four patients were operated for anterior fossa tumor. Between 0.7 ml and 4.7 ml fibrin sealant was used.

There were no adverse effects that could be related to the use of fibrin sealant.

Conclusion: We found no safety issues with the use of Vivostat[®]-derived fibrin sealant prepared from autologous blood using tranexamic acid to prevent fibrinolysis.

The Vivostat[®] fibrin sealant can be used in neurosurgical procedures without any safety problems.