

HEMOFILTRATION-INDUCED NEUROPROTECTION FOLLOWING ISCHEMIC STROKE

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INTRODUCTION.

Ischemic stroke is accompanied by a three to four hundred percent increase in the brain's extracellular fluid and cerebrospinal fluid glutamate concentration, which diffuses and damages surrounding neurons. In preclinical models of permanent middle cerebral artery occlusion, neurological outcomes correlate closely with blood or plasma glutamate levels. Previous attempts to reduce glutamate-induced excitotoxicity after stroke have included inhibition of glutamate receptors and administration of pyruvate and oxaloacetate (which help natural enzymes metabolize glutamate into α -ketoglutarate). These strategies, including competitive (Selfotel, NBQX, YM872) and non-competitive (GV150526, dextrorphan, aptiganel and eliprodil) glutamate receptor antagonists improved *preclinical* stroke outcomes but were without favorable outcomes or had significant unfavorable side-effects in human trials. We propose to decrease glutamate levels via an alternative mechanism, which should improve survival and neurological outcomes, without drug-induced side effects and complications. Glutamate, glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT) concentrations are decreased during standard 4-hour long hemofiltration in chronic renal failure patients (Zlotnik et al 2012).

MATERIALS AND METHODS.

Plasma and CSF glutamate levels were measured at the beginning of the treatment, and 8 and 23 hours later. Disability was assessed by the modified Rankin test at 14 days or at the discharge if sooner.

Inclusion criteria: patients 18 to 75 years old, any gender; patients with verified diagnosis of acute ischemic stroke by CT or MRI and moderate to severe disability (NIHSS 7-20 points, GCS – less than 12 points and more than 4 points). Can start hemofiltration within 4 hours, signed written informed consent.

RESULTS.

The results are summarized in Table 1. The average time from the onset of stroke symptoms until starting hemofiltration was 154 minutes. The average frequency of hemofiltration was 2 procedures. Even though the sample size is small ($n = 20$), these results indicate a promising trend in the response to hemofiltration: hemofiltration is associated with reduced ICU stays and time on mechanical ventilation (MV). The between group NIHSS score differences were not statistically significant however it is possible that a difference can be detected with a larger sample size.

Table 1. The response of stroke patients to hemofiltration treatment.

Treatment	Duration of ICU treatment (days)	Duration of MV (days)	Average NIHSS score at intake and discharge
HF	25.6 \pm 4.0*	23 \pm 4.5*	25.4 \pm 2.1- intake 9.9 \pm 1.8- discharge
Control	28.5 \pm 3.7	26 \pm 4.6	25.4 \pm 3.0- intake 10.7 \pm 1.5- discharge

CONCLUSION.

The average time from the onset of stroke symptoms until starting hemofiltration was 154 minutes. On average each patient underwent two HF procedures. In a small patient cohort, hemofiltration was not associated with significant adverse events differently from the control group and was associated with a small but significant decrease in both ICU stays and days on the ventilator.