

Fibrinolytic therapy

Although fibrinolytic therapy is an upcoming treatment for [Intracerebral hemorrhage](#) (ICH), standard [guidelines](#) are lacking, and some clinical issues persist.

Masomi-Bornwassser et al. used a devised clot model of ICH to systematically analyse the effects of irrigation and cerebrospinal fluid (CSF) on fibrinolysis.

In vitro [clots](#) of human blood (25 ml) were generated and a catheter irrigation system was applied to deliver fluid/treatment. Clots were weighed before and after treatment and compared to [Recombinant human tissue plasminogen activator rtPA](#) treatment alone. First various drainage periods (15, 30 and 60 min; n = 3 each) and irrigation rates (0, 15, 90 and 180 ml/h; n = 3-5 each) were tested, followed by rtPA administration (1 mg, 15 min incubation) at each irrigation rate. Potential fibrinolytic effect of CSF was examined by incubation with 5 ml healthy vs. haemorrhagic CSF (n = 3 each). To assess a washout effect treatment with saline (0.9%), rtPA (1 mg) and high-rate irrigation (180 ml/h) were compared with measuring plasminogen level before and after. Furthermore, clots were treated with a combination of [plasminogen](#) (150% serum concentration) and rtPA (1 mg).

Results: Relative clot end weights after 60 min irrigation system treatments were $66.3 \pm 3.8\%$ (0 ml/h), $46.3 \pm 9.5\%$ (15 ml/h), $46.5 \pm 7.1\%$ (90 ml/h) and $53.3 \pm 4.1\%$ (180 ml/h). At a lower irrigation rate (15 ml/h), relative end weights were lowest ($49.5 \pm 4.6\%$) after 60 min (15 min: $62 \pm 4.3\%$, $p = 0.016$; 30 min: $62.90 \pm 1.88\%$, $p = 0.012$). The combination of rtPA and irrigation produced following relative end weights: 0 ml/h, $35 \pm 3.2\%$; 15 ml/h, $32.1 \pm 5.7\%$; 90 ml/h, $36.7 \pm 6.3\%$ and 180 ml/h, $41.9 \pm 7.5\%$. No irrigation (0 ml/h) versus rtPA alone showed a significant difference ($p < 0.0001$) in higher clot weight reduction by rtPA. Similar rtPA+15 ml/h irrigation achieved a significant higher weight reduction compared to 15 ml/h irrigation alone ($p = 0.0124$). No differences were evident at 90 and 180 ml/h irrigation rates with and without rtPA. Healthy ($55.1 \pm 5\%$) or haemorrhagic ($65.2 \pm 6.2\%$) CSF showed no fibrinolytic activity. Plasminogen levels in clots declined dramatically ($> 80\%$ initially to $< 10\%$) after 1 mg single rtPA dosing and high-rate (180 ml/h) irrigation. The fibrinolytic benefit of adding plasminogen to rtPA was marginal.

In this in vitro clot model, irrigation combined with rtPA (vs. rtPA alone) conferred no added lytic benefit. Likewise, exposure to haemorrhagic CSF did not increase clot lysis ¹⁾.

¹⁾

Masomi-Bornwassser J, Freguia F, Müller-Werkmeister H, Kempfski O, Giese A, Keric N. Effect of irrigation on fibrinolytic rtPA therapy in a clot model of Intracerebral hemorrhage: a systematic in vitro study. *Acta Neurochir (Wien)*. 2018 Jun;160(6):1159-1165. doi: 10.1007/s00701-018-3517-9. Epub 2018 Mar 21. Erratum in: *Acta Neurochir (Wien)*. 2020 Oct 29;; PMID: 29564653.

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