Intensive blood pressure lowering reduces hematoma growth after intracerebral hemorrhage in rats

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Background

Blood pressure is often elevated in acute phase after intracerebral hemorrhage (ICH) and linked with a poor outcome. Recent studies showed safety of intensive blood pressure lowering in the first hours after onset and a strong trend towards a better outcome.^{1,2} The aims of the present study were to evaluate the influence of intensive blood pressure lowering in the acute phase after ICH on hematoma growth after and the pathophysiological background.

Methods

In total, 84 spontaneously hypertensive rats (SHR, 10 weeks) were used. For blood pressure lowering we established oral administration of nifedipine to achieve systolic blood pressure of approximately 130 mmHg vs. 185 mmHg for controls. For ICH induction collagenase was injected stereotactically. We assessed functional outcome (modified Neurological Severity Score, mNSS) and hematoma growth 24h after ICH.³ Histopathological analysis and post-mortem MRI was used for further hematoma analysis and evaluation of edema formation and inflammatory response.

Photometric hemoglobin assay showed a significant reduction for hematoma growth 24h after ICH by collagenase-injection ($p = 0.0234$, $n=9$). Scatter dot plot with means (nifedipine 88.6µl, control 146.3µl), 24h after ICH.

Neurological deficit was significantly improved after ICH by collagenase-injection with consecutive intensive blood pressure lowering. Scatter dot plot with medians (nifedipine 7 vs. control 13, $p = 0.0107$), 24h after ICH. mNSS = modified Neurological Severity Score.

Histopathological analysis showed no significant differences for edema formation, blood-brain barrier disruption and inflammatory processes between both groups 72h after ICH induction (blinded histopathological scoring, $n=5$ per group). Representative stainings (HE, IgG) are shown.

Explorative ICH and edema volumetry by post-mortem MRI (T2). No essential differences between both groups could be seen in fixed rat heads 24 or 72h after collagenase-injection. Additional histopathological analysis afterwards (HE staining) confirmed the imaging results. Here, MRI (T2) shows fixed rat head 24h after ICH by collagenase-injection and consecutive blood pressure lowering with a calculated hematoma volume of 90µl.

A) **Dosis finding** (systolic blood pressure after oral administration of nifedipine (tail-cuff-method). Means are given. B) **Intraoperative blood pressure monitoring** under inhalation anesthesia with isoflurane (means, $n=5$). C) **Systolic blood pressure during the first 72h** (nifedipine 15mg/kg body weight per nasogastric tube (means).

Results

Hematoma growth was significantly reduced 24h after ICH by blood-pressure lowering (88.6µl vs. 146.3µl, $n=9$, $p = 0.023$). Neurological deficit, assessed by mNSS, was also significantly improved (7 vs. 13 points, $n=9$, $p = 0.011$). Histopathological analysis showed no significant differences for edema formation, blood-brain barrier disruption and inflammatory processes between both groups 72h after ICH induction (blinded histopathological scoring), confirmed by explorative MRI analysis.

Conclusion

Our experimental data suggest that intensive blood pressure lowering in the acute phase after ICH reduces hematoma growth and improves neurological deficit.

References

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