Standardized induction of subarachnoid hemorrhage in mice by intracranial pressure monitoring.

Abstract:
Subarachnoid hemorrhage (SAH) is the subtype of stroke with the most unfavorable outcome but the least well investigated molecular pathophysiology. Among others, not sufficiently well standardized in vivo models suitable for the use with transgenic animals may be responsible for this situation. Therefore the aim of the current study was to detect suitable intra-operative parameters for the controlled and standardized induction of SAH in mice and to characterize the long-term functional and histopathological outcome of mice subjected to this procedure. Experimental study in mice using the intraluminal Circle of Willis perforation (CWp) model of SAH. SAH induced a sharp increase of intracranial pressure (ICP) from 5.1 +/- 1.2 to 78.5 +/- 9.3 mm Hg (mean +/- SD; p<0.05), a concomitant drop of cerebral blood flow (rCBF) by 81 +/- 4% (p<0.05), and a significant Cushing reflex response (p<0.05). rCBF measurements alone could not reliably detect SAH. SAH resulted in significant brain edema formation (brain water content increase at 72 h: 2.9 +/- 0.9%; p<0.05), loss of hippocampal neurons (CA1: -56%, CA2: -55%; CA3: -72%; 7 days; p<0.05), severe neurological dysfunction over 7 days, and a mortality of 30%. Our results indicate that CWp in mice can be standardized by intra-operative ICP monitoring. CWp leads to prolonged intracranial hypertension, selective neuronal cell death in the hippocampus, and severe
neurological dysfunction. CWp in mice with ICP monitoring may therefore become a valuable tool for future investigations of the molecular pathophysiology of SAH.