Murine Model of Subarachnoid Hemorrhage

Aneurysms are difficult to model in animals and therefore animal models of SAH are either performed by injection of blood into the subarachnoid space/cerebral ventricles or by endovascular perforation of a subarachnoid vessel.

At least three rodents murine models studying early injury following subarachnoid hemorrhage are available. Two of these create SAH by injecting autologous blood directly into the cisterna magna (single injection model) or into the prechiasmatic cistern (prechiasmatic SAH) [1) 2)].

The third model creates SAH by perforating the intracranial bifurcation of intracranial artery (endovascular perforation; EVP model) [3)].

Results indicate that Circle of Willis perforation (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 [4)].

Lin et al. characterized a mouse model of experimental SAH, which produces consistent constriction of large cerebral arteries. Adult mice received injections of autologous blood into the cisterna magna, and the diameters of large intracranial vessels were measured 1 h to 7 days post-SAH. A diffuse blood clot was evident in both the anterior and posterior circulations after SAH. Vascular wall thickening, lumenal narrowing and corrugation of the internal elastic lamina were observed. Both acute (6-12 h) and delayed (1-3 days) phases of vasoconstriction occurred after SAH. Overall mortality was only 3%. A reproducible, low mortality model of SAH-induced cerebral vasospasm in mice is described. This mouse model should facilitate the delineation of cellular and molecular mechanisms of SAH-induced pathologies because of the widespread availability of various technologies for this species (e.g. genetically-altered animals and gene expression arrays). This model also represents a replicable and inexpensive approach for screening therapeutic candidates [5)].

Altay et al. reported a reproducible and technically feasible method to induce SAH, and subsequently CVs, in mice. They tested this model in multiple strains of mice that are commonly used for genetic manipulation.

SAH was induced in C57BL/6NCr, FVB, 129S1, BalbC and SJL mice, weighing 28-32 g, by an intracisternal vessel transection technique. Animals were perfused with India ink at 24h postprocedure and vessel diameters were quantified. Brain slices were obtained for hematoxylin-eosin staining (H&E) to look for vascular changes consistent with CVs.

There was no mortality during or after the procedure. Four of the five mouse strains showed significant CVs at 24 h postprocedure characterized by decreased vessel diameter of the middle cerebral artery close to the Circle of Willis. Histologically, the vessel wall displayed significant corrugation and thickening, consistent with CVs.

A novel mouse model to induce SAH is described and tested in several mouse strains. Four of the five strains used in this study developed CVs after the induction of SAH. The procedure is brief,

straightforward, reproducible with low mortality, and applicable to commonly used background strains for genetically engineered mice [6].

Endovascular perforation murine model

Endovascular perforation murine model of Subarachnoid Hemorrhage.

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