1- Simplified experimental cerebral aneurysm model in rats: Comprehensive evaluation of induced aneurysms and arterial changes in the circle of Willis

Establishing a simple and comprehensive experimental model is one of the most important issues in the study of cerebral aneurysms. Previous models in the rat required two stage surgeries and observations were limited to a few branching sites. The present study aimed to introduce a simplified model in rats and to provide a comprehensive evaluation of induced arterial changes in the circle of Willis. Sprague-Dawley rats underwent ligation of the right common carotid artery, and posterior and inferior (group 2, n=9) or only posterior (group 3, n=12) branches of the bilateral renal arteries, and bilateral oophorectomy. Dahl salt-sensitive rats underwent only carotid ligation and bilateral oophorectomy (group 5, n=11). All surgical procedures were completed in one procedure instead of two in the original method. Salt loading was started after the surgery. Five rats of each strain without treatment served as controls (groups 1 and 4, respectively). Three months later, vascular corrosion casts of the cerebral arteries were examined by scanning electron microscopy. Experimental rats in groups 2, 3, and 5 developed 43 aneurysmal lesions at branching sites. Forty-eight arterial changes including dilatation, tortuosity, and fusiform or lateral wall aneurysms were observed at non-branching sites. Group 3 appeared to be superior to the other groups for experimental studies. The frequency and degree of the induced lesions were comparable with previous studies even after the surgical simplification. The present model may be more practical for the study of experimental cerebral aneurysms.

2- Fasudil, a Rho-kinase inhibitor, attenuates induction and progression of cerebral aneurysms: Experimental study in rats using vascular corrosion casts

Fasudil (a Rho-kinase inhibitor) has been shown to attenuate abdominal aortic aneurysm development, but any preventive effect against development of cerebral aneurysms is unclear. The effect of fasudil on the development of cerebral aneurysms was investigated in 55 female Sprague-Dawley rats divided into 4 groups: Group 1 (n = 10) was the control group without treatment. Groups 2–4 (n = 15 each) were subjected to cerebral aneurysm induction procedures plus 1% NaCl in the drinking water. Groups 3 and 4 were also treated with 0.5 or 1.0mg/mL of fasudil in the drinking water, respectively. Vascular corrosion casts of the cerebral arteries were prepared and examined using a scanning electron microscope after 2 months. No significant differences were observed in the degree of induced hypertension between Groups 2, 3 and 4. No aneurysms were found in Group 1. Examination of the left anterior cerebral–olfactory artery junction, which is the most susceptible site for aneurysm development, found significantly fewer aneurysmal lesions in Groups 3 (60%) and 4 (53%) compared to Group 2 (100%) (P < 0.02). This study suggests that fasudil attenuated induction of cerebral aneurysms in the rat model.

3- Effect of olmesartan and pravastatin on experimental cerebral aneurysms in rats
The major initiation process of intracranial aneurysms is thought to involve endothelial dysfunction due to hemodynamic stress. Angiotensin II type 1 receptor blockers and statins improve vascular endothelium function. The effects of olmesartan and pravastatin were investigated on the development of experimental aneurysms in rats. Eighty-three rats underwent aneurysm induction. Seven groups of 10–14 rats were treated with low or high dose olmesartan, low or high dose pravastatin, low doses of olmesartan and pravastatin, hydralazine, or no drug (control) for 12 weeks, when rats were sacrificed for vascular corrosion casting and scanning electron microscopy. Aneurysmal changes at the anterior cerebral–olfactory artery bifurcation were divided into stages 0 (no abnormality) to III (saccular aneurysm). Systolic arterial blood pressure was elevated over 170 mm Hg in the control, low dose pravastatin, and high dose pravastatin groups, but not in the other groups. The control group demonstrated aneurysmal changes in 100% and stage III in 50% of rats. Aneurysmal changes were observed in most rats in the other groups, but the incidence of stage III was 10% or less. The staging pattern showed significant differences between the groups (P=0.028). Pravastatin reduced both stages III and II+III and olmesartan ameliorated stage III, implying that these may prevent aneurysmal formation through acting on different steps.