Testing Dopamine for Treatment of Cerebral Vasospasm After Subarachnoid Hemorrhage Using an *In Vitro* Model.

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Introduction: Cerebral vasospasm (CV) is a significant cause of mortality (11,000 per year in the US) and morbidity in patients surviving a subarachnoid hemorrhage (SAH). Onset of CV occurs 3-10 days after the SAH, and this affords a valuable therapeutic window. There are currently no effective therapies for this debilitating pathology. The aim of our study was to determine the possible efficacy of dopamine therapy *in vitro* in preventing or reversing smooth muscle contraction during CV after SAH. We hypothesized that stimulation of the nitric oxide synthase (NOS) pathway *via* dopaminergic receptor activation may be an effective way to prevent or reverse cerebral vasospasm after subarachnoid hemorrhage. **Methods:** Sections of porcine internal carotid arteries (0.5 mm in length) were placed in a water-jacketed organ bath (physiological saline solution, pH 7.4 @ 37°C) and isometric force measured. KCl-induced contraction was set as 100% contraction (Fmax) and the contractile response of the arteries under various conditions was compared to Fmax. *In vitro* vasospasm was induced using cerebrospinal fluid from patients who suffered CV after SAH (CSF_V). Arteries were treated with dopamine (10μm) both before and after addition of CSF_V. Selected dopamine antagonists (L-SPD vs. D_1 receptors, haloperidol vs. D_2, U99194A vs. D_3) were used to determine through which receptor dopamine was having its effects on the CV *in vitro*. Immunohistochemical staining for both inducible and endothelial NOS (iNOS and eNOS) of these arterial rings was performed. **Results:** Both pretreatment and postreatment with dopamine reduced the vasoconstriction caused by CSF_V significantly (70% ± 9%, 36% ± 5% of F_{max}, respectively). Blockade of D_2 receptors with haloperidol abolished this effect, whereas the D_1 and D_3 antagonists did not. Immunohistochemical staining suggests that the mechanism of dopamine's action here includes induction of iNOS in the smooth muscle layers of the arteries. **Conclusions and Significance:** Our data suggests that the effects elicited by dopamine against vasospasm were mediated by D_2 receptors. This statistically significant, *in vitro* data may be used to develop clinical therapies of dopamine D_2 receptor agonists for use as a treatment for CV after SAH. This could add an important weapon to the armory of the neurosurgeon, for a pathology where current therapies are inconsistent and moderately effectual at best.