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Vascular

Reversal of cerebral vasospasm by sphenopalatine ganglion stimulation in a dog model of subarachnoid hemorrhage☆

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Abstract

Background: Sphenopalatine ganglion stimulation dilates the ipsilateral arteries of the normal dog anterior circle of Willis. This experiment tested whether similar stimulation would reverse cerebral vasospasm.

Methods: Six dogs underwent baseline angiography followed by creation of subarachnoid hemorrhage (SAH) by injection of autologous blood into the cisterna magna. Two days later, subarachnoid blood injection was repeated. Seven days later, angiography was repeated and the left sphenopalatine ganglion was exposed microsurgically. Angiography was repeated 15 minutes after exposure of the ganglion. The ganglion was then stimulated electrically 3 times and angiography repeated during, and 15 and 30 minutes after stimulation. The protocol was repeated again. Adequacy of stimulation was confirmed by the presence of immediate ipsilateral nasal mucus production.

Results: Subarachnoid hemorrhage was associated with significant vasospasm of both middle cerebral arteries (11% ± 4% and 18% ± 7%, $P < .05$, paired t tests). Exposure of the ganglion and sham stimulation produced no substantial changes in arterial diameters compared with the diameter before stimulation and after ganglion exposure (n = 2-6 per measurement, paired t tests). Ganglion stimulation produced significant dilatation of the ipsilateral extracranial and intracranial internal carotid, middle cerebral, and anterior cerebral arteries compared with the contralateral arteries (13% ± 6% to 32% ± 14%, $P < .05$, paired t tests).

Conclusions: The mild to moderate vasospasm that results from SAH in dogs was reversed by sphenopalatine ganglion stimulation. Since this method carries a potential for human application, additional studies are warranted to determine the effects on more severe vasospasm.

Keywords: Cerebral arteries; Models, Animal; Sphenopalatine ganglion; Subarachnoid hemorrhage; Vasospasm

1. Introduction

Cerebral vasospasm is a common complication of aneurysmal subarachnoid hemorrhage (SAH), occurring radiographically in nearly 70% of patients and clinically in 30% to 40% during the first 2 weeks after the hemorrhage. Among the approximately 3500 patients with aneurysmal SAH entered into randomized, controlled trials of tirilazad, 30% developed symptomatic neurological deterioration that was attributed to vasospasm [6,8-10]. Sixteen percent of deaths were due to vasospasm. This high impact on outcome has motivated the development of many therapeutic regimens over the years in an attempt to prevent or reverse

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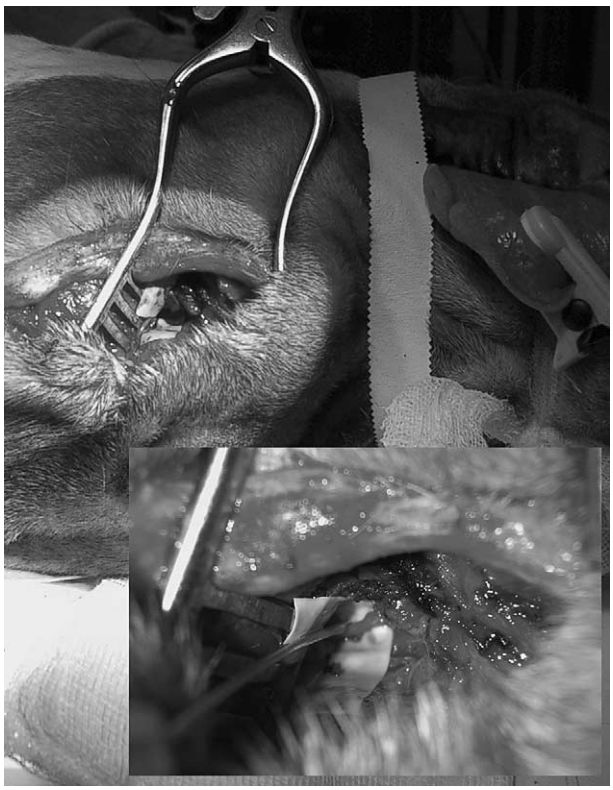

Fig. 1. Photograph of surgical exposure of the left sphenopalatine ganglion. The view is of the left side of the head of a dog that is positioned supine. The inset shows the ganglion separated from the underlying tissues by a strip of latex. A bipolar electrode consisting of 2 hook-shaped wires can be seen around the ganglion.

the vasospasm and thereby prevent ischemic cerebral damage. These include nimodipine, hemodynamic therapy, and interventional neuroradiological procedures such as intra-arterial papaverine infusion and balloon angioplasty [17]. To date, no remarkable success has been achieved with any of these approaches.

The sphenopalatine ganglion is the source of parasympathetic innervation to most of the anterior part of the cerebral vasculature [2]. Stimulation of this ganglion induces vasodilation of the ipsilateral, intradural arteries of the anterior circle of Willis in normal rats [12], cats [5], dogs [14], and monkeys [16]. The extracranial arteries dilate as well. The purpose of this study was to determine whether this vasodilation would also be effective on vasospastic cerebral arteries.

Table 1
Percent change in angiographic arterial diameters, day 0 to day 7

Artery	Right (%)	Left (%)
Extracranial ICA	−1 ± 7	−1 ± 8
Intracranial ICA	0 ± 10	−3 ± 14
MCA	−11 ± 4*	−18 ± 7*
ACA	−8 ± 13	−16 ± 10

Values are means ± SEM. n = 6 per measurement.
* $P < .05$, paired t test.

2. Methods

2.1. Angiography, creation of subarachnoid hemorrhage, and protocol

Female mongrel dogs (n = 6) weighing 15 to 20 kg were sedated by intravenous injection of sodium pentothal (15 mg/kg) and then intubated and ventilated on oxygen and 1% to 2% isoflurane. They underwent baseline cerebral angiography by catheterization of a vertebral artery to visualize the basilar artery and posterior circulation and by catheterization of one or both internal carotid arteries (ICAs) to visualize the anterior circulation (day 0). Dogs were then turned prone, the cisterna magna was punctured percutaneously with a spinal needle, and 0.3 mL/kg cerebrospinal fluid was allowed to drain spontaneously. Fresh, autologous, arterial, nonheparinized blood (0.5 mL/kg) was injected into the cisterna magna. The cisternal injection was repeated 2 days later. Seven days later (day 7), dogs were placed under general anesthesia and angiography of the

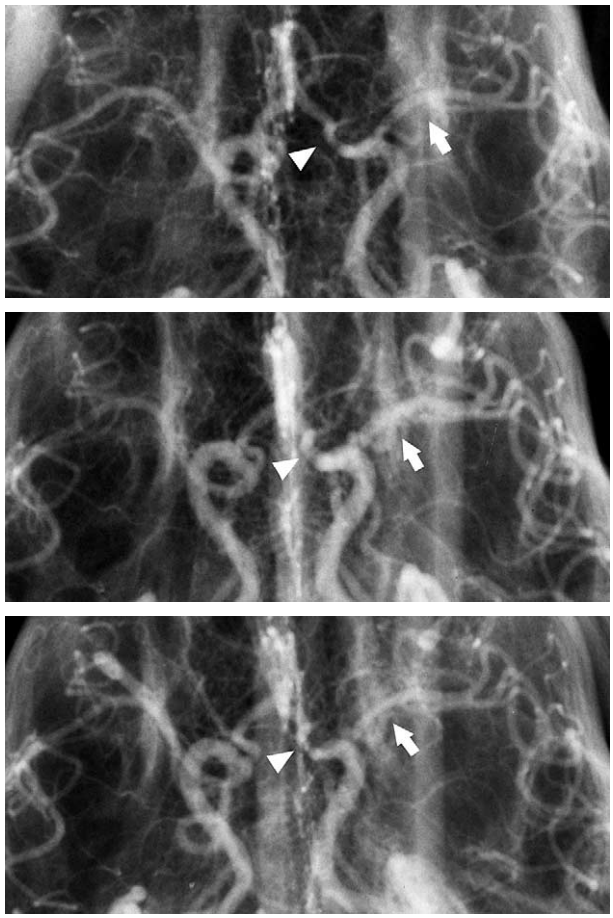

Fig. 2. Photographs of representative anteroposterior cerebral angiograms of a dog taken before stimulation and before exposure of the sphenopalatine ganglion (top), during the second series of stimulations (middle), and 70 minutes after the beginning of stimulation (30 minutes after cessation of the last stimulation, bottom). Arrows show the left MCA, which dilates during stimulation and then returns to a vasospastic diameter after stimulation. Similar changes are observed in the anterior cerebral artery (arrowheads).