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EFFECTS OF CERVICAL SYMPATHECTOMY ON VASOSPASM INDUCED BY MENINGEAL HAEMORRHAGE IN RABBITS

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ABSTRACT - This study investigates the role of cervical sympathectomy in the prevention of acute vasospasm induced by meningeal haemorrhage in rabbits. Sixteen adult English Norfolk rabbits were divided into 2 experimental groups: bilateral cervical sympathectomy of the superior sympathetic ganglion (SSSG, n=8), and bilateral SSSG and sympathectomy of the inferior sympathetic ganglion (SISG, n=8). Other 24 animals were used as controls. Basilar artery diameter was evaluated by angiography. SSSG protected the animals against developing cerebral vasospasm; SSSG associated with SISG did not increase this effect.

KEY WORDS: subarachnoid haemorrhage, vasospasm, cervical sympathectomy .

Efeitos da simpatectomia cervical sobre o vasoespasmo induzido por hemorragia meníngea em coelhos

RESUMO - Este estudo investiga o papel da simpatectomia cervical na prevenção do vasoespasmo agudo induzido por hemorragia meníngea em coelhos. Para tanto, foram utilizados 16 coelhos adultos da raça Norfolk inglesa, divididos em 2 grupos experimentais: simpatectomia cervical bilateral do gânglio simpático cervical superior (SSSG, n=8) e SSSG associada a simpatectomia cervical bilateral do gânglio simpático cervical inferior (SISG, n=8). Outros 24 animais foram usados como controles. Os diâmetros das artérias basilares foram avaliados por medições após angiografias. SSSG protegeu os animais contra o vasoespasmo; SSSG associada a SISG não aumentou este efeito.

PALAVRAS-CHAVE: hemorragia subaracnóidea, vasoespasmo, simpatectomia.

The association between menigeal haemorrhage after aneurism rupture and localized constriction of cerebral blood vessels was described in man by Robertson, in 1949[1], although the first clear angiographic description of vasospasm under these conditions was made by Ecker and Riemenschneider in 1951[2]. Purkinje in 1836 and Remak in 1841, (quoted by White et al.[3]) discovered nerve fibres with the arteries of the Willis polygon. Penfield, in 1932, (quoted by White et al.[3]), showed sensitive afferent and efferent motor nerves in the adventitia and in the space between the adventitia and the muscle layer of all cerebral large and small arteries, and vein walls[3].

Innervation of the human carotid vessels is supplied by the sympathetic system, originating mainly from the superior cervical ganglion, but also from the inferior[4]. Different methods have demonstrated profuse adrenergic innervation of the cerebral blood vessels[5-10] and regulation of blood flow by the sympathetic system[11,12]. Functional[13] and morphological[14] alterations have been reported in cerebral arteries after cervical sympathectomy, but vasospasm pathogenesis after subarachnoid haemorrhage remain controversial.

The objective of this study is to investigate the effects of cervical sympathectomy on the development of vasospasm after subarachnoid haemorrhage induced in rabbits.

METHOD

Male and female 1,000 to 2,000 g adult English Norfolk rabbits were used; they were randomly distributed into 5 experimental groups:

Group G1 – Sympathectomy controls (n=8), submitted

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to bilateral surgical manipulation of the superior cervical ganglion without ablation; after 6 weeks meningeal haemorrhage was simulated with suboccipital intrathecal 0.9% saline 0.15 mL/kg injection into the magna cistern.

Group G2 – Simulated sympathectomy with meningeal haemorrhage controls (n=8), submitted to bilateral surgical manipulation of the superior cervical ganglion, without ablation; after 6 weeks they were submitted to meningeal haemorrhage by suboccipital intrathecal injection of 0.15 mL/kg autologous blood into the magna cistern.

Group G3 – Sympathectomy and meningeal haemorrhage (n=8), submitted to bilateral gangliectomy of the superior cervical sympathetic ganglion; after 6 weeks they were submitted to meningeal haemorrhage by suboccipitally intrathecal injection of 0.15 mL/kg autologous blood into the magna cistern.

Group G4 – Simulated superior and inferior gangliectomy, and meningeal haemorrhage controls (n=8), submitted to bilateral surgical manipulation of the superior and inferior cervical ganglion, without ablation; after 6 weeks they were submitted to meningeal haemorrhage by suboccipital intrathecal injection of 0.15 mL/kg autologous blood into the magna cistern.

Group G5 – Superior and inferior sympathectomy and meningeal haemorrhage (n=8), submitted to bilateral surgical gangliectomy of the superior and inferior cervical ganglion; after 6 weeks they were submitted to meningeal haemorrhage by suboccipital intrathecal injection of 0.15 mL/kg autologous blood into the magna cistern.

Histological examination – All gangliectomy specimens were sent to the Pathology Department, fixed in formol, included in paraffin, and colored by hematoxilin-eosin, for histological confirmation of ganglionar tissue.

This study was performed in 2 phases; preparation of experimental groups, and analysis of angiographies.

Phase 1: Surgical access to the cervical sympathetic ganglion, for manipulation or ablation, during general anaesthesia with 30 mg/kg tionembutal, administered endovenously in the ear dorsal vein, in spontaneous respiration with open mask adjusted to the muzzle with 2% O_2.

Phase 2: (6 weeks later) inhalatory anaesthesic was used to prevent cardiovascular disturbances and intracranial pressure variations. Induction: 1.5% isofluorane and 0.5% O_2 for 2 minutes; maintenance: 0.5% isofluorane and 0.5% O_2, with anaesthetic apparatus with mask adjusted to the animal muzzle.

Autologous blood was obtained from the femoral artery. After subarachnoid haemorrhage or simulation, animals were maintained in 30° Trendelenburg position to ensure full diffusion across the basilar artery.

Angiographies were obtained by injecting 0.2 mL/kg Hexabrix 280 - Guerbet into the carotid artery via a catheter inserted after local anaesthesia with 0.5 mL xylocaine. Comparison between groups was by Analysis of Variance[15] with F and p-value determination. For $p<0.05$ cases, group means were compared by the Tukey test using a minimum significant difference of 5%.

Table 1. Basilar artery diameter (mm) for all groups, means with SD.

Groups	Mean	Standard deviation
G1	1.06	0.06
G2	0.69	0.12
G3	0.91	0.09
G4	0.89	0.05
G5	0.94	0.10

Statistical analysis: $F=16.69$; $p<0.001$; G1>(G3=G4=G5)>G2.

RESULTS

Histological examinations of surgical specimens confirmed ganglion tissues in all cases.

Table 1 shows mean basilar arterydiameters for all groups. There were significant statistical differences between groups.

G1 animals, with simulated bilateral gangliectomy and simulated meningeal haemorrhage, presented normal basilar artery diameter without demonstrable vasospasm.

G2 animals, with simulated gangliectomy and meningeal haemorrhage, presented the smallest basilar artery diameter, the highest vasospasm in all 5 groups.

There was no significant difference between G3, 4, and 5 animals in basilar artery diameter, but they were significantly larger than G2, and smaller than G1 (Table 1). Thus, animals with superior cervical ganglion sympathectomy presented similar basilar artery diameter to animals with superior and inferior gangliectomy; vasospasms were minimal in these groups.

DISCUSSION

In this experiment, simulation of meningeal haemorrhage with suboccipital intrathecal saline injection into the magna cistern did not produce vasospasm (G1). Animals with induced subarachnoid haemorrhage presented vasospasm (G2). Similar results have been reported[14,16-22].

Bilateral extirpation of the sympathetic ganglion 6 weeks before subarachnoid haemorrhage (G3 and 5) prevented the development of acute vasospasm, demonstrating that the sympathetic system plays an important role in its pathogenesis. A similar effect was observed for animals with manipulation of the

sympathetic ganglion and meningeal haemorrhage (G4); this is difficult to explain. Perhaps under the simulation conditions in G4, careful and delicate surgical manipulation of the sympathetic ganglion caused unintentional lesions in the sympathetic fibres. In a study performed in our laboratory, sympathectomy just before subarachnoid haemorrhage did not produce a protector effect for vasospasm development[23].

In rabbits, the basilar artery is the largest in the cerebral base, and its constriction is a normal response to stimulation of the sympathetic terminals.

The chronic bilateral cervical superior sympathectomy could provoke norepinephrine depletion in the small granular vesicles of the sympathetic terminals, impairing adrenergic transmission; this would then eliminate the constrictor sympathetic effect[13]. Our study is in agreement with published data where pharmacological or anatomical exclusion of the sympathetic activity prevented vasospasm[24].

In conclusion, in this experimental model of subarachnoid haemorrhage in rabbits, and under the conditions that procedures were performed: 1) bilateral gangliectomy of the superior sympathetic ganglion performed 6 weeks before meningeal haemorrhage prevented development of acute vasospasm; 2) additional gangliectomy of the inferior sympathetic ganglion did not increase this effect.

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