



Intra- and Post-operational Changes in Pupils Induced by Local Application of Cisternal Papaverine During Cerebral Aneurysm Operations

Serebral Anevrizma Ameliyatları Sırasında Lokal Sisternal Papaverin Uygulaması ile İndüklenen İntra ve Postoperatif Gözbebeği Değişiklikleri

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ABSTRACT

AIM: To investigate the effect of locally administered intracisternal papaverine on the pupils during cerebral aneurysm clipping.

MATERIAL and METHODS: Four patients that received cerebral aneurysm clipping were included in the study. Papaverine (3%, 60 mg) was dropped into the internal carotid artery cistern to relieve vascular spasm and act on the oculomotor nerve intentionally at the same time. The size, shape and reflection of light of the bilateral pupils were monitored at different times after application of papaverine and every 30 min after surgery continuously for 4 hours.

RESULTS: Prior to the application of papaverine, the bilateral pupils in 4 patients were the same in size and shape. Two to 5 minutes after the application of papaverine, the ipsilateral pupils of the surgical site were dilated in all four patients and the contralateral pupil showed dilation in 1 patient, and recovered to a normal size at 2–5 hours after the application of papaverine. Papaverine reduced light reflection of the ipsilateral pupil of the surgery site; Papaverine changed the ipsilateral pupil of the surgery site to an irregular elliptical shape, which lasted for different times. Four patients regained consciousness normally without demonstration of nerve damage.

CONCLUSION: Our results confirmed previous reports that local application of papaverine in the carotid artery pool during artery aneurysm surgery resulted in dilation of the ipsilateral pupil of the surgery site. In addition, our results indicated that the pupil changes induced by papaverine occurred within several minutes after the application of papaverine.

KEYWORDS: Papaverine, Pupil, Aneurysm, Oculomotor nerve

ÖZ

AMAÇ: Serebral anevrizma kliplleme sırasında lokal olarak uygulanan intrasisternal papaverinin gözbebeği üzerindeki etkisini araştırmak.

YÖNTEM ve GEREÇLER: Serebral anevrizma kliplleme yapılan dört hasta çalışmaya alındı. Damar spazmını gidermek için internal karotid arter sisternine Papaverin (%3, 60 mg) damlatıldı ve okülomotor sinir üzerine olan etkisine bakıldı. İki gözbebeğinin büyüklüğü, şekli ve ışık yansımaları papaverin uygulanmasından sonra farklı zamanlarda ve ameliyat sonrası sürekli olarak 4 saat boyunca her 30 dakikada bir izlendi.

BULGULAR: Papaverin uygulanmadan önce 4 hastada gözbebekleri boyut ve şekil olarak aynıydı. Papaverin uygulamasından 2 ila 5 dakika sonra, cerrahi bölge tarafındaki gözbebeği 4 hastada genişlerken kontralateral gözbebeği 1 hastada genişledi ve papaverin uygulanmasından 2-5 saat sonra normal boyutuna döndü. Papaverin cerrahi bölge tarafındaki gözbebeğinin ışık yansımalarını azalttı ve yine bu gözbebeğinin şeklini çeşitli süreler devam edecek şekilde düzensiz eliptik şekle dönüştürdü. Dört hastanın da bilinci herhangi bir sinir hasarı görülmeden yerine geldi.

SONUÇ: Sonuçlarımız arter anevrizma cerrahisi sırasında karotid arter havuzuna lokal papaverin uygulamasının cerrahi bölgeyle ipsilateral göz bebeği genişlemesi ile sonuçlandığına dair önceki raporları doğruladı. Buna ek olarak, sonuçlarımız papaverin ile indüklenen gözbebeği değişikliklerinin papaverin uygulanmasından sonra birkaç dakika içinde meydana geldiğini göstermiştir.

ANAHTAR SÖZCÜKLER: Papaverin, Gözbebeği, Anevrizma, Okülomotor sinir

INTRODUCTION

Ipsilateral pupil dilation induced by local application of papaverine in the carotid artery pool during artery aneurysm surgery was first reported by Pritz (7). Subsequently, there have been similar reports (1,6), and it has been hypothesized that this change in pupils induced by papaverine was due to the transient anesthesia of the oculomotor nerve. We also noticed this phenomenon clinically. However, all of

these phenomena were observed after surgery, and there is no related report about intra-surgery changes in pupils. There is no direct evidence confirming the correlation of papaverine with pupil changes. We speculated that pupil changes induced by papaverine should appear at an early stage after local application of papaverine in the artery cistern while the observation of pupil changes after surgery should be the extension of pupil changes during surgery. There are

no reports on when pupil changes occur or descriptions of the characteristics of pupil changes induced by papaverine. In the present study, we observed dynamic changes of the pupils induced by local application of papaverine in the carotid artery cistern of 4 patients receiving craniotomy for cerebral aneurysm clipping and confirmed, for the first time, that papaverine resulted in size and shape changes of the ipsilateral pupil at an early stage of application of papaverine. Here, we report our observations.

MATERIAL and METHODS

Clinical data: Four patients were admitted to our department in 2012, including 2 males and 2 females that were 38–65 years old. Cerebral artery aneurysm was confirmed with digital subtraction angiography (DSA) and computerized tomographic angiography (CTA) after admission, including 2 posterior communicating aneurysms, 1 anterior communicating aneurysm and 1 middle cerebral artery aneurysm. All four aneurysms were non-complex aneurysms. The 4 patients were admitted to hospital owing to sudden severe headache induced by spontaneous subarachnoid hemorrhage. Prior to surgery, 2 patients were unconscious and 2 patients were somnolent. Physical examination before surgery indicated the bilateral pupils had the same size and shape with sensitive light reflections. There were no signs of paralysis in the oculomotor nerve or ptosis. Artery clipping with craniotomy was performed at 3–7 days after admission.

Surgery: A transpterional approach was applied to dissect the Sylvian fissures and internal carotid artery pool during surgery. All surgeries were performed smoothly without rupture of the aneurysm. During surgery, the segment of the ipsilateral oculomotor nerve in the carotid artery cistern was intentional avoidance of damage to the oculomotor nerve was carried out with sharp separation to avoid stretching, without electric coagulation to avoid heat transduction. Spasms of the internal carotid and branches were observed after clipping of the aneurysm. Papaverine solution (3%, 60 mg) was dropped onto the internal carotid artery and its branches in the carotid cistern, resulting in immersing of the internal carotid in papaverine solution for 10 min. Then the solution was rinsed with saline, and the dura matter was sutured. Prior to suturing, brain pressure was normal and brain pulsation was good. The dura matter was closely sutured with peripheral suspension. The bone flap was relocated and fixed with a skull lock. A drainage tube was put under the skin flap. During surgery, the size, shape and reflection of light of the bilateral pupils were monitored before and after application of papaverine and at different time after application of papaverine by the assistant under the premise of no pollution of the surgical area. Pupils were monitored every 30 min after surgery continuously for 4 hours.

RESULTS

Pupil size: Prior to the application of papaverine and post aneurysm clipping, bilateral pupils in 4 patients were the same in size and shape, but had a smaller size under anesthesia and there was disappearance of light reflection. In

4 patients, dilation in the ipsilateral pupil of the surgical site was observed at 2–5 minutes after application of papaverine. In 1 patient, dilation in the contralateral pupils was also observed after application of papaverine. Dilated pupils in 4 patients recovered to a normal size at 2–5 hours after the application of papaverine.

Pupil shape: All 4 patients showed changes in ipsilateral pupils to oval or irregular shapes at 2–5 min after the application of papaverine, which was simultaneous with changes in pupil size but lasted for different amounts of times, with the fastest case lasting for a few minutes to recovery to a circle and the slowest case of lasting 10 hours.

Light reflection: The light reflection of the contralateral light of the surgical site reflection gradually recovered following fading of the anesthetic effect. In 2 patients, the ipsilateral pupil of the surgical site showed more delayed light reflection than the contralateral pupil, and 2 patients showed disappearance of light reflections in the ipsilateral pupil. All patients recovered sensitive light reflections at 2–5 hours after local application of papaverine.

Eyelids: There was no ptosis observed until the patients recovered consciousness and eye-opening response to stimulation.

Consciousness: The recovery process of patients was normal, and there was no demonstration of disorder in the nervous system. Re-examination of cranial computed tomography (CT) scanning showed normal postsurgical changes.

DISCUSSION

Local application of papaverine in the internal carotid cistern during cerebral aneurysm surgery is commonly used to relieve vascular spasms (3,5). There have been several reports on pupil changes induced by local application of papaverine. However, there has been no direct evidence supporting the correlation between pupil changes and papaverine.

Prior to the application of papaverine, bilateral pupils in 4 patients were the same in size and shape and the ipsilateral pupil was dilated at 2–5 minutes after local application of papaverine in the carotid cistern. At this stage, there was no bleeding or high intracranial pressure, excluding other possible factors that could result in pupil changes. Our observation also verified previous reports that local application of papaverine in the internal carotid pool resulted in dilation of the ipsilateral pupil through the effect on the oculomotor nerve. In addition, the results also confirmed our hypothesis that the pupil changes occur during the early stage of application of papaverine.

There were individual differences in pupil changes after local application of papaverine in the cistern, such as the occurrence time of pupil dilation, the dilation extent and shape change. We noticed that the effect of papaverine on pupils occurred at 2–5 min after application and recovery to normal at 2–5 h after application. The light reflection in the ipsilateral pupil was obviously weaker than the contralateral

pupil. In addition, we also noticed that the change in pupil shape in all four patients. The pupil change induced by papaverine usually occurs in the ipsilateral pupil; however, in the present study we observed a shape change in the contralateral pupil in one patient, which we did not notice previously. Bala reported 1 case with changes in both pupils and considered it as a result of the effect of papaverine on the bilateral oculomotor nerves due to the flow of papaverine into the contralateral carotid pool (1). Pritz reported 1 case with dilation of the contralateral pupil induced by papaverine and considered it a result of the effect of papaverine on the contralateral oculomotor nerve due to the gravity-induced flow of papaverine to the contralateral carotid pool (8).

By summarizing our observation and the related literature, the pupil changes induced by local application of papaverine have the following features: 1) Local application of papaverine in the internal carotid pool produces dilation in the ipsilateral pupil within several minutes after the application of papaverine. 2) The pupil changes are transient and last for 2–5 hours. 3) The pupil changes usually occur in the ipsilateral and occasionally in the contralateral pupil. Owing to the small sample size in the present study, more observation of the pupil changes during intra- and post-surgery is required to understand the features of the changes and regulation of pupil changes induced by papaverine.

Based on the literature, there has been no reasonable explanation for the mechanism of pupil change induced by local application of papaverine. Bala et al. considered that papaverine has a mild effect of local anesthesia (1). The oculomotor nerve passes between the posterior cerebral artery and superior cerebellar artery as it exits the brainstem and enters the cavernous sinus parallel with the posterior communicating artery. The parasympathetic fibers of the oculomotor nerve in this segment control the sphincter papillae located in the dorsa-medial superficial layer of the oculomotor nerve, which are exposed to the carotid pool, mostly being subjected to papaverine. The local mild anesthetic effect of papaverine on these superficial fibers blocks the conduction of nerves, resulting in transient paralysis of the oculomotor nerve, which is the cause of pupil dilation and disappearance of the light reflection. Our observation is also consistent with this explanation.

The dilation of the ipsilateral pupil after cerebral aneurysm surgery should be given attention. For patients administrated papaverine, all possibilities of papaverine should be considered, but the malignant factor such as intracranial hypertension and cerebral hernia induced by recurrent bleeding after surgery should be excluded first. Based on our observation, the change in pupils induced by papaverine should occur at an early stage of papaverine application. It is not suggested to regularly observe pupil changes during surgery while monitoring of pupil changes should be performed immediately after surgery. Pupil changes induced by papaverine should be noticed immediately after surgery, displaying as a transient dilation of the ipsilateral pupil. Patients regain conscious-

ness smoothly. Regarding cerebral hernia due to bleeding, pupil changes usually occur at a certain time after surgery but rarely occur immediately after surgery. The pupil dilation usually develops progressively and infers the contralateral pupil. The patient usually cannot regain consciousness or falls into coma again after regaining consciousness. In these situations, emergent cranial computerized tomography (CT) scanning should be performed to clarify the intracranial condition for resurgery with necessity. Damage of the oculomotor nerve during surgery also can produce post-surgical changes in ipsilateral pupils. The pupil changes induced by damage to the oculomotor nerve vary according to the damage extent. The pupil size and shape can change, for a duration ranging from days to months. Damage to the oculomotor nerve is usually accompanied by ptosis while pupil changes induced by papaverine are not accompanied by ptosis, which may be related to the fiber distribution of the oculomotor nerve; i.e., papaverine blocks the conduction of superficial dorsal fibers controlling the pupils while the deeper fibers controlling the eye muscles are not affected. Complete damage of the oculomotor nerve will display as an obviously permanent dilation of the ipsilateral pupil and ptosis.

Chittiboina proposed that dilution of 3% papaverine with saline to 0.3% could achieve satisfactory effects in relieving vascular spasms without transient paralysis of the oculomotor nerve (2). Dalbasti also considered that 0.3% papaverine could achieve a better spasmolytic effect and reduce side effects (4). However, the real effect of a low concentration of papaverine remains to be further verified in the clinic.

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