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Forhad Hossain Chowdhury & Md. Raziul Haque

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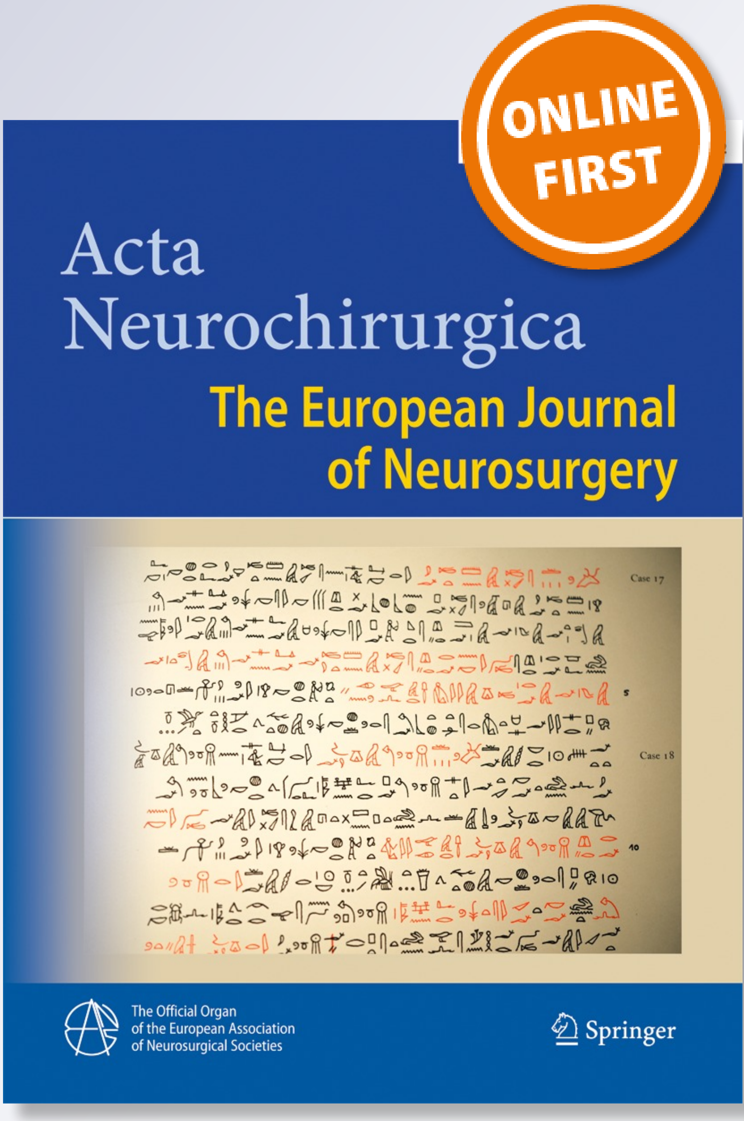

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LETTER TO THE EDITOR - BRAIN TUMORS

Severe hypotension, cardiac arrest, and death after intracisternal instillation of papaverine during anterior communicating artery aneurysm clipping. A case report

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Dear Editor,
Cerebral vasospasm is still a serious complication in subarachnoid hemorrhage (SAH) from aneurysm rupture [3, 7]. Prophylaxis with nimodipine and treatment with "triple-H" therapy [1, 7] have improved the outcome in many patients, but not in all. Balloon angioplasty and intra-arterial papaverine are alternatives for refractory vasospasm [4, 7]. All have complications, however [5]. The application of intracisternal vasodilators such as papaverine has become a common practice after craniotomy for aneurysmal SAH [6, 7], but the severe complications associated with such use have not adequately been reported. Here, we describe a case of anterior communicating artery aneurysm where the patient underwent microsurgical clipping of the aneurysm followed by instillation of papaverine at the surgical site that caused fatal bradycardia, hypotension, and cardiac arrest.

Case report: A 47-year-old woman was admitted with typical clinical features of SAH (H&H grade I). A CT scan of the brain showed SAH in basal cisterns and in the area of anterior communicating artery complex. Digital subtraction angiography and CT angiogram of the brain confirmed the presence of anterior communicating artery aneurysm with asymptomatic mild vasospasm of both anterior cerebral and middle cerebral arteries. The patient was on oral nimodipine. During elective operation, routine monitors were connected. The heart rate and noninvasive blood pressure (BP) of the patient were 92 beats/min and 120/80 mmHg, respectively, and the ECG showed normal tracings in lead II. After i.v. access was secured, anesthesia was induced with thiopentone 300 mg and fentanyl 125 μg. Tracheal intubation was facilitated with suxamethonium 90 mg. Anesthesia was maintained with halothane in a mixture of O_2 and N_2O in addition to intermittent doses of vecuronium (0.1 mg/kg) and fentanyl. Monitoring parameters included were ECG, pulse oximetry, end-tidal capnography, arterial BP, central venous pressure, and urine output. Left pterional craniotomy was done and aneurysm was clipped satisfactorily without temporary clip placement. No local skin infiltration or i.v. of mannitol was used. The patient was hemodynamically stable throughout the operation. After complete hemostasis, the surgical field was irrigated with normal saline. Before the closure, 2 ml of 3 % papaverine diluted to 25 ml with normal saline at room temperature (36 °C) was instilled topically at the surgically exposed areas. After 20 to 30 s, a sudden decrease of heart rate from 90 to 25 beats/min and a reduction in BP from 120/80 to 35/20 mmHg followed. After another 15–20 s, BP became un-recordable and the patient's heart stopped beating. Immediate external cardiac massage and intravenous + intracardiac injection adrenaline were given but the heart did not restart, even after 10 min. Then in a desperate situation, a nonscheduled emergency left anterior thoracotomy was done and internal cardiac massage was given. Even with this effort, the patient expired on the table.

Papaverine, a potent vasodilator, acts by direct smooth muscle relaxation of arteries and arterioles. Complications associated with intra-arterial papaverine are mydriasis, confusion, seizure, reversible brainstem depression, increased intracranial pressure, hypotension, tachycardia, and thrombocytopenia [7]. Complications such as mydriasis, facial nerve palsy, malignant hyperthermia, hypotension, bradycardia/tachycardia, cardiac arrest, and death were reported after topical use of papaverine at the surgical site [2, 6–9].

Patients with vasospasm are more prone to hemodynamic instability during aneurysm anesthesia. However here, hemodynamic changes took place immediately after instillation of papaverine solution. This association suggests the possible role

F. H. Chowdhury (✉) · M. R. Haque
Department of Neurosurgery, Dhaka Medical College Hospital,
32 Bokshi Bazar,
Dhaka, Bangladesh
e-mail: forhadchowdhury74@yahoo.com

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of papaverine in the causation of hemodynamic disturbances and cardiac arrest, though the exact cause is not clear. Incidences of hemodynamic changes have been reported after instillation of hot or cold saline instillation in the operative field [10] but here the papaverine solution was used at room temperature. As the injection of papaverine did not contain any solvent with potential neurotoxic effect, we believe the drug itself is responsible for these complications. The possible mechanism of such complications might be due to inhibition of sympathetic area and stimulation of parasympathetic hypothalamus or inhibition of brainstem. Baltaci et al. [2] first reported such a fatal case. We occasionally use intracisternal papaverine. So far we used papaverine in 14 cases without any complication. We think, application of papaverine on brain surface (especially on basal brain surface) may cause an idiosyncratic-type of effect on hemodynamics & heart and this type of effect might kill our patient. Should we re-think on the safe use of papaverine on brain surface?

Conflicts of interest None.

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