Treatment of aneurysmal hemiplegia with dopamine and mannitol

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Three patients with severe postoperative hemiplegia and one with hemiplegia following a subarachnoid hemorrhage are presented. None had hematomas. All were treated with dopamine-induced hypertension, mannitol, and large quantities of intravascular fluids. All showed a remarkable degree of clinical improvement, presumably secondary to an increase in cerebral blood flow.

KEY WORDS □9 postoperative hemiplegia □9 mannitol □9 dopamine □9 hypertension, therapeutic □9 subarachnoid hemorrhage

Hemiplegia is well recognized as a complication of both subarachnoid hemorrhage (SAH) and of the surgical treatment of intracranial aneurysms. This report concerns four patients, of whom hemiplegia followed surgery in three and was associated with the initial spontaneous hemorrhage in one. All four were treated with a combination of dopamine hydrochloride and mannitol and large volumes of intravascular fluid. The three patients with postoperative incidence were the most seriously affected of eight patients (in a consecutive series of 139 operated aneurysms) who developed this complication. Three of the four patients reported made a complete recovery. One has a residual monoparesis but has quite useful gross strength in her hand and walks normally.

Summary of Cases

All three patients with postoperative hemiplegia awoke from anesthesia neurologically intact and subsequently deteriorated in the first 24 hours. The unoperated patient was chosen for this unusual hypertensive treatment because the alternative seemed to be a catastrophic aphasia and hemiplegia. Hematoma was excluded by computerized tomography (CT). Angiography was not undertaken during the acute hemiplegic incident lest it should add any risk of further neurological damage. Although angiography might have added some interesting radiographic data on the degree or extent of vasoconstriction, we did not believe that it could contribute to the main issue, which was therapy.

The dosages of the drugs used varied from patient to patient depending on the clinical response. Dopamine was given at a rate of 9 to 46 μg/kg/min to maintain a systolic blood pressure of 160 to 200 mm Hg. The desired blood pressure varied because a patient might improve at 180 mm Hg but deteriorate if the systolic blood pressure was lowered to 160 mm Hg. This critical pressure had to be discovered. Mannitol was titrated against intracranial pressure (ICP), which was checked by repeated lumbar punctures or continuous intraventricular pressure monitoring; ICP was kept below 300 mm H2O. However, mannitol was given at a minimum of 2.4 gm/kg/24 hours, even if ICP was normal, because of
evidence to be presented later that mannitol will increase cerebral blood flow independent of a reduction in ICP.

In addition to the intravenous dopamine, which was given in a solution of 5% dextrose in water, and the mannitol, each patient received additional intravenous fluid to maintain a cerebral venous pressure (CVP) of 8 to 15 cm H₂O. This additional fluid usually consisted of 0.2 normal saline with 5% dextrose in water, but the percentage of saline was adjusted should any electrolyte abnormalities occur. In general, more fluid was required in those patients who received higher doses of mannitol because of increased urinary fluid losses.

Case Reports

Case 1

This 49-year-old man was admitted because of the sudden onset of a severe headache. He was temporarily dazed and confused, but on reaching the hospital he was alert and fully oriented. The initial neurological examination was normal. A lumbar puncture revealed evenly blood-stained cerebrospinal fluid (CSF) and an opening pressure of 450 mm H₂O. Angiography revealed a left posterior communicating aneurysm, which was clipped at craniotomy 5 weeks after the original hemorrhage (the operation had been delayed because of persistently elevated ICP).

Twenty hours after surgery he was noted to have partial weakness of his right side, and this progressed over the next 2 hours, leaving him completely hemiplegic and aphasic. His blood pressure at the time was 140/70 mm Hg. An infusion of dopamine at 9.0 μg/kg/min raised his blood pressure to 170/80 mm Hg, and simultaneously a continuous infusion of mannitol (3.5 gm/kg/24 hours) was given. He was given up to 10 liters of intravenous fluid per day to expand his intravascular volume and to replace urinary fluid losses; CVP was maintained between 10 and 15 cm H₂O.

Within 1 hour of initiation of the above regimen the patient had some return of tone in his right arm. Within 2 days he moved his right extremities spontaneously and could say a few words. His dependence on the induced hypertension was dramatically illustrated on three separate occasions. At 2½ and 7 days his dopamine infusion was inadvertently slowed as a result of problems with the intravenous lines. During these times his blood pressure dropped to 90 mm Hg systolic and he again became hemiplegic and aphasic. After restoration of the blood pressure to 180 to 200 mm Hg systolic, on each occasion his neurological function recovered within several hours to where it had been before each period of deterioration.

By 12 days his strength had completely returned to normal, and his speech had recovered to the point that he could say a few words clearly but was moderately aphasic. Over the next 36 hours the dopamine and mannitol infusions were gradually stopped. His speech (he speaks two languages fluently) and strength are completely normal 1 year after surgery, and he has returned to work as an international construction foreman.

Case 2

This 43-year-old woman complained of headaches and neck stiffness of 2 months duration. She was alert, and the only neurological finding was a right third nerve palsy. Angiography demonstrated a right posterior communicating aneurysm, which was clipped 2 weeks after hemorrhage.

After clipping of the aneurysm, the patient was confused but not paretic at first. At 21 hours after surgery, she had a left hemiplegia and became more confused; her blood pressure was 110/70 mm Hg at this time. She was given 1½ gm/kg of mannitol as an intravenous bolus, followed by a further infusion of 4 to 6 gm/kg/24 hours. After the bolus there was some return of muscle tone within 1 hour. A dopamine infusion was given at 25 μg/kg/min to maintain blood pressure at 160/100 mm Hg. Within 7 hours she had a return of hand grasp and spontaneous movement of the left arm. She also received 8 liters of fluid/24 hours intravenously, including three units of whole blood, to maintain a CVP of 10 to 15 cm H₂O. At the end of 24 hours of treatment her strength had returned to normal, and medications were gradually stopped over the ensuing 24-hour period. After 10 days her mentation had returned to normal.

Case 3

This 40-year-old woman complained of the sudden onset of headaches. On initial examination she had neck stiffness and a right third nerve palsy, but otherwise was clinically normal. The headache was severe and pulsatile and lasted for 4 weeks. A lumbar puncture was performed, and the CSF was bloody (opening pressure of 45 cm H₂O). The patient was treated with intravenous dopamine and mannitol and the symptoms rapidly resolved. The patient was discharged after 5 weeks of hospitalization, and follow-up examination 6 months later showed no evidence of recurrent symptoms.

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Dopamine and mannitol for aneurysmal hemiplegia

intact. A lumbar puncture revealed evenly blood-stained CSF with an opening pressure of 340 mm H2O, and an angiogram showed a right posterior communicating aneurysm. The operation was delayed until the opening pressure was below 200 mm H2O. At 4 weeks posthemorrhage the aneurysm was clipped, but intraoperatively, the aneurysm bled twice before clipping was achieved. In the initial postoperative period, she was alert and had no neurological deficits except for the third nerve palsy.

Twelve hours postoperatively she had the sudden onset of a complete left hemiplegia without an alteration in her consciousness level. Her blood pressure was 140/90 mm Hg at the time. A lumbar puncture revealed an opening pressure of 140 mm H2O. A mannitol infusion was started at a rate of 6.7 gm/kg/24 hours. Simultaneously, a dopamine infusion was started, and a rate of 46 ug/kg/min was required to maintain a blood pressure of 180/100 mm Hg. Also, intravenous fluids were given at a rate of 7 liters/24 hours.

Within 1 hour the patient moved the left extremities spontaneously. Over the next 24 hours her strength deteriorated to movement in response to pain only. It was noted that she had a reduction of hourly diuresis and that the serum creatinine was rising while the serum sodium was falling. It was decided that she was overhydrated with failing renal function, possibly secondary to one or a combination of her medications. Therefore, she was treated with fluid restriction, and over the next 3 days dopamine and mannitol were slowly reduced and her serum creatinine and electrolytes returned to normal.

The patient's neurological function was lethargic with an appropriate response to pain on the right and minimal response on the left. Lumbar punctures revealed opening pressures of 250 to 300 mm H2O, consistent with brain swelling, but she responded well to supportive management. At 1 month after surgery, she had minimal movement of the left fingers. At 3 months she walked with a cane and could grasp objects with her left hand. At 1 year she walked normally and had a strong grip with the left hand but still had difficulty with fine movements of the left fingers.

Case 4

This 37-year-old man was admitted complaining of severe headaches of 7 days duration. Physical examination revealed a blood pressure of 220/120 mm Hg but no other findings. He was started on methyl-dopa 500 mg/6 hours, and his blood pressure was reduced to 140/90 mm Hg. Nine days after the onset of the headaches, he suddenly developed a right hemiparesis and global dysphasia. A lumbar puncture demonstrated an opening pressure of 550 mm H2O and xanthochromic CSF. An intravenous infusion of mannitol was then started at a rate of 3.6 gm/kg/24 hours. A CT scan of the brain showed no hematoma, and angiography disclosed a left middle cerebral artery aneurysm. He did not improve after 24 hours of mannitol, and actually deteriorated so that he was completely aphasic and hemiplegic. A catheter was placed in the right lateral ventricle to monitor ICP continuously and to assure its adequate reduction. After 4 hours of intermittent drainage of CSF along with continuation of the mannitol infusion to maintain an ICP of 25 mm Hg or less, he still showed no signs of improvement. He remained alert but was completely aphasic and hemiplegic. Therefore, despite the fact the aneurysm was not clipped, an infusion of dopamine was started at 25 ug/kg/min to raise his blood pressure from 140/90 mm Hg to a range of 180/80 to 200/100 mm Hg. Also, he was given approximately 5 liters of intravenous fluids/day to maintain a CVP of 8 to 10 cm H2O.

Before the dopamine was started, the ICP was 25 mm Hg, and the compliance was normal; that is, there was no rise in ICP after 1 cc of saline was instilled through the ventricular catheter. Within minutes after the dopamine was started, the ICP remained at 25 mm Hg; however, testing of compliance showed a rise of 6 mm Hg in ICP in response to a 1-cc increase in ventricular volume. The mannitol infusion was then increased from 2.4 to 3.6 gm/kg/24 hours, and 17 hours later when the intracranial compliance was retested, it had returned to normal; the intracranial pulse pressure appeared to be reduced within 1 hour of the increase in the mannitol dosage.

Within 15 hours of the initiation of dopamine there was an increase in muscle tone, and the patient could speak in monosyllables. He continued to improve, and over the next few days he could hold his right arm against gravity and could count aloud. The dopamine was maintained at a dose sufficient
to keep his blood pressure near 180 mm Hg systolic for 3 days. At this time his hands and feet were cyanotic but improved as the dopamine dosage was slowly reduced over the following 6 days. Several weeks later he walked with a minimal paresis and had a moderate dysphasia.

Discussion

All of these patients were presumed to be suffering from ischemic complications of cerebral vasospasm. The three patients with postoperative hemiplegia met the criteria of vasospasm in that they awoke from anesthesia intact and deteriorated within the first 24 postoperative hours.

Treatment of the cerebral ischemia consisted of various maneuvers directed toward increasing cerebral blood flow. The cerebral blood flow is equal to the cerebral perfusion pressure divided by the cerebrovascular resistance; the cerebral perfusion pressure is equal to the difference between the mean arterial blood pressure and the ICP. Therefore, cerebral blood flow could be increased by increasing the mean arterial blood pressure and the ICP. Therefore, cerebral blood flow could be increased by increasing the mean arterial blood pressure, decreasing the ICP, or decreasing the cerebral vascular resistance.

Dopamine was employed to increase cerebral blood flow by raising the mean arterial blood pressure. In low doses (less than 5 µg/kg/min), dopamine produces peripheral dilatation secondary to beta-adrenergic stimulation; however, in high doses (greater than 10 µg/kg/min), it produces peripheral constriction secondary to alpha-adrenergic stimulation, and an increase in mean arterial blood pressure results. Blood flow was expected to follow blood pressure because recent intracranial aneurysm surgery or SAH would probably act against autoregulation.

Whether dopamine augments or reduces cerebral blood flow by some mechanism other than increasing mean arterial blood pressure in normal cerebral vessels is unknown. It has been reported to produce vasospasm when injected into the cisterna magna of dogs. Allen and Gross demonstrated contraction of in vitro canine basilar arteries to intraluminally placed dopamine; however, the contraction was weaker than that of any of the other alpha-adrenergic agents tested. Furthermore, Wurtman and Zervas have suggested that dopamine may play a role in the pathophysiology of stroke.

There is evidence, however, that dopamine, per se, does not contribute to cerebral vasospasm. Battista, et al., using an experimental vasospasm model, prevented vasospasm in cats that had been pretreated with a dopamine-beta-hydroxylase inhibitor. This enzyme stimulates the conversion of dopamine to norepinephrine. Therefore, any vasospasm produced by intracisternal dopamine may result from its conversion to norepinephrine. Intravenous dopamine is quickly metabolized as evidenced by its very brief duration of effect, and, therefore, any conversion to norepinephrine is negligible. Von Essen measured cerebral blood flow in dogs before and after dopamine and found a decrease in flow with low doses and an increase with high doses.

Mannitol may be helpful in improving cerebral blood flow for several reasons. It reliably reduces ICP and improves intracranial compliance within minutes of administration. Moreover, these actions would counteract the tendency of the dopamine-induced hypertension to worsen intracranial compliance and possibly lead to elevated ICP, as illustrated by Case 4. Also, there may be improvement in cerebral blood flow which is not mediated through a reduction in ICP. Johnston and Harper have shown that in baboons with a normal ICP, an infusion of mannitol will lead to an increase in cerebral blood flow without significantly altering ICP, and we have confirmed this finding in the brain-injured rhesus monkey. The increased flow may result from either a reduction in cerebral vascular resistance or some alteration in the physical properties of the blood. It should be noted that hypertonic solutions in general have this property of increasing vascular flow. The high levels of fluid administration are necessary to maintain a high blood volume and prevent its depletion by the mannitol. The hypertensive properties of dopamine are present only when the CVP is high and a merely "normal" volume of fluid administration would, in the presence of continuous mannitol administration, result in a very low CVP.

Of our patients with postoperative hemiplegia, Cases 1 and 2 had excellent results. Both patients were eventually neurologically normal. One patient (Case 3) is still...
improving 1 year after her operation. We believe that Case 1 is the most significant because on three separate occasions clinical deterioration occurred promptly with reduction of therapy and was followed by improvement after an increase in medication (dopamine). Thus, there is good evidence that the patients improved due to the treatment.

The unoperated patient (Case 4) was treated as a desperation maneuver and because therapeutic hypotension was presumably a factor in initiating this complication. Since the aneurysm had not been clipped, it was still prone to rebleed. We were aware that raising the mean arterial blood pressure or reducing the ICP would increase the tendency of the aneurysm to burst. However, it seemed certain that the patient would be doomed to aphasia and a right hemiplegia if nothing were done. We have not in other unoperated instances of hemiplegia had the success that others have enjoyed with a non-hypertensive regimen, such as isoproterenol and lidocaine. Therefore, we treated Case 4 with mannitol and intravascular fluid expansion, and eventually dopamine, and achieved a good outcome. This case also demonstrates that the dopamine dosage occasionally has to be reduced to avoid the known complication of peripheral gangrene.

Hypertensive therapy for postoperative cerebral vasospasm has been advocated with norepinephrine and expansion of the intravascular volume. It was shown to be effective in the majority of patients who received it, but it may have accelerated the brain swelling that eventually killed one of those patients. Similarly, our two patients who had evidence of brain swelling (Cases 3 and 4) might have had worse outcomes if hypertensive treatment alone had been used. It would seem, therefore, that the addition of mannitol to a regimen of hypertension and intravascular volume expansion would be beneficial. Not only would it counteract brain swelling, but mannitol, per se, may add to the improvement in cerebral blood flow.

References

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