Anesthesiology
V 35, No 4, Oct 1971

Clinical Workshop

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Pulmonary Edema Complicating Intrathecal Hypertonic Saline Injection for Intractable Pain

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The injection of large volumes of hypertonic, hypothermic saline solution into the subarachnoid space for relief of pain was first advocated by Hitchcock in 1967.[1] Unlike many other approaches to the treatment of pain, this technique rarely disturbs normal sensory or motor function. At this time the mechanism of action of the injected saline solution is not clear. Possibilities include osmotic dehydration from the hypertonic solution or a direct effect of cold on small-diameter pain fibers. Variations of the original technique have included the use of either cold or hypertonic solutions alone.

Most reported series concern patients with the intractable pain of terminal cancer. The incidence of successful results and duration of pain relief have been variable. Some patients have had dramatic relief of pain, whereas others show minimal if any change. Although the technique is used less frequently for nonmalignant conditions, Collins has reported good results in the treatment of causalgia and postherpetic neuralgia.[2]

The complications of this procedure have been relatively minor and of short duration. Various tachyarrhythmias and ectopic beats have been seen with electrocardiographic monitoring. Other common side-effects include fasciculations of face, arm and leg muscles, tachypnea, vertigo, and vomiting. One case in which transient hemiplegia followed the block has been reported.[3] The following case illustrates another serious complication of this procedure.

REPORT OF A CASE

A 47-year-old woman was admitted to the hospital in April 1970 with a three-week history of diarrhea and rectal pain. Laparotomy disclosed an adenocarcinoma of the sigmoid colon with local extension to perirectal fat and multiple lymph node involvement. Anterior sigmoid resection was performed. Postoperatively the patient received external radiation with ^{60}Co over an eight-week period. During this time she began to complain of pain in the sacral and rectal areas. At first this was relieved by Percodan. However, because of increasing severity of pain, the patient was readmitted for trial of possible pain relief procedures. Chordotomy and posterior rhizotomy were considered unfeasible because of the midline location of the pain. A subarachnoid alcohol block was tried, with good (75 per cent) pain relief. The patient had slight weakness of the legs and some difficulty voiding following this block. However, she was able to walk and also able to control urination. A month later the pain in the rectal area recurred. Because of the motor and sensory changes which had followed the subarachnoid alcohol block, it was elected to do a block with hypertonic saline solution.

Following premedication with 15 mg morphine sulfate, the patient was lightly anesthetized with intravenous methohexital while in a sitting position. Forty ml of spinal fluid were slowly removed through a 19-gauge needle at the L3–L4 level. Forty ml of 5 per cent saline solution at nearly 0 C were injected through the same needle over a three-minute period. Before the injection was completed, the patient began to hyperventilate up to rates of 40 to 50/min, and heart rate increased from 86 to 136 beats/min. Blood pressure rose from 130/80 torr to 210/120 torr. These changes reverted toward normal over the following hour except for a persistent tachycardia of

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110–120 beats/min. It was also observed that the patient had a wet and rumbling, but nonproductive, cough, and appeared cyanotic. Analysis of arterial blood gases showed *p*H 7.46, P_{CO_2} 24 torr, P_{O_2} 34 torr. Oxygen was given by nasopharyngeal catheter and skin color improved. However, over the next four hours the patient became increasingly short of breath and diaphoretic, and began coughing up moderate amounts of pink, frothy sputum. Chest x-ray revealed bilateral fluffy infiltrates. At that time, it was suspected that the cause of the pulmonary edema was some previously overlooked metastatic or infectious pulmonary process. Blood and sputum cultures were taken and supportive treatment given with oxygen and elevation of the head of the bed. Only in retrospect was it recognized that treatment should have been more vigorous. A total of 1,000 ml of 5 per cent dextrose in Ringer's lactate solution had been given intravenously during the day of the block.

The following morning the patient was greatly improved. She was smiling, complained of only minimal pain, and was eager to have breakfast. Auscultation disclosed a few moist rales at both lung bases. The patient still appeared cyanotic when breathing room air, and analysis of blood gases showed *p*H 7.49, P_{CO_2} 28 torr, P_{O_2} 44 torr. The patient showed slow improvement over the next 24 hours, with episodes of tachypnea and tachycardia on exertion. Forty-eight hours after the block, she was asymptomatic. Blood gases during breathing of room air were *p*H 7.48, P_{CO_2} 28 torr, P_{O_2} 78 torr. Chest x-ray was completely normal. In view of the rapid and complete resolution of the pulmonary problems, and in the absence of an apparent underlying cause of pulmonary edema, another etiology was sought.

Discussion

There are numerous case reports of pulmonary edema following isolated closed head injuries without trauma to any other portion of the body. Various pathophysiologic explanations have been proposed, but recent work has done much to illuminate the sequence of events. The Cushing phenomenon, first described in 1901,[4] serves as a basis for explanation. Cushing showed that any increase in intracranial pressure is followed by an increase in systemic blood pressure such that the diastolic pressure attained will exceed intracranial pressure by several torr. The exact stimulus and the site of action for this response in man are unknown, but it is obviously a protective response to ensure cerebral perfusion.

Simmons[5] has reported experimental work in chimpanzees in which intracranial pressure was raised in graded elevations by injections of saline solution into balloons previously placed in the epidural space. The consequent increases in systolic arterial pressure were accompanied by normal central venous pressures but elevated pulmonary arterial and venous pressures. At the same time, central blood volume increased by as much as 45 per cent. Similar experiments in dogs have shown that arteriovenous shunting occurs in the splanchnic and somatic beds following acute elevation of intracranial pressure.[6] Blood is mobilized centrally from the peripheral circulation, and passive overload of the pulmonary bed may occur.

Luisada[7] describes three elements essential to the development of what he terms "neurogenic pulmonary edema": 1) following the acute elevation of intracranial pressure there is intense peripheral vasoconstriction, leading to systolic overload of the left ventricle; 2) diastolic overload of the left ventricle occurs following mobilization of blood from the periphery to the pulmonary bed; 3) the inordinate rise in left ventricular diastolic pressure is followed by increases in left atrial and pulmonary capillary pressures.

Hammermeister and Reichenbach[8] have suggested a more direct pathophysiologic explanation for pulmonary edema associated with intracranial disease. This does not involve blood volume shifts to the pulmonary bed, but rather emphasizes the direct myocardial damage that results from massive sympathetic discharge. They have reported a case in which pulmonary edema occurred in a patient soon after rupture of an intracranial aneurysm. Postmortem examination revealed little or no coronary disease, yet there was spotty focal necrosis of myocardial cells. Other authors have also reported direct damage to myocardial cells from exogenous vasopressors.[9]

That the pulmonary edema in the present case was associated with the hypertonicity of the injected solution is very likely. A 5 per cent saline solution will increase its volume about five times as it reaches equilibrium with body fluids. A volume of 40 ml of 5 per cent solution injected into the subarachnoid space has the potential for expanding to 200 ml as it draws water by the osmotic gradient which it produces. The final total volume of cere-

brospinal fluid would then approximate twice normal, or 300 ml, if there were no transfer of isotonic fluid out of the subarachnoid space. A volume increase of this magnitude within the bony confines of the skull and spine could lead to a marked increase in intracranial pressure and set the stage for pulmonary edema, as indicated in the experimental work cited above.

Anesthesiologists should be aware that pulmonary edema can occur following intrathecal blocks with hypertonic saline solution as well as in neurosurgical patients with head injuries. Conversations with other anesthesiologists reveal that the "wet lung" syndrome following blocks with hypertonic saline solution has been observed in other hospitals. Blood pressure must be monitored closely and enriched oxygen mixtures given. Should pulmonary edema become manifest, a potent intravenous diuretic such as furosemide is indicated. Treatment of hypertension must be tempered with an awareness that the hypertensive response may not be entirely detrimental and, in fact, it may even be beneficial when it ensures cerebral perfusion in a patient in whom the Cushing reflex is operative.

REFERENCES

1. Hitchcock E: Hypothermic subarachnoid irrigation for intractable pain. Lancet 1:1133–1135, 1967
2. Collins JR, Juras EP, Van Houten RJ, *et al.*: Intrathecal cold saline solution: A new approach to pain (evaluation). Anesth Analg 48:813–823, 1969
3. O'Higgens JW, Padfield A, Clapp H: Possible complications of hypothermic saline subarachnoid injection. Lancet 1:567, 1970
4. Cushing H: Concerning a definite regulatory mechanism of the vasomotor center which controls blood pressure during cerebral compression. Bull Hopkins Hosp 12:290–292, 1901
5. Simmons RL, Ducker TB, Anderson RW: Pathogenesis of pulmonary edema following head trauma. J Trauma 8:800–809, 1968
6. Berman IR: Changes in pulmonary, somatic and splanchnic perfusion with increased intracranial pressure. Surg Gynec Obstet 128: 8–14, 1969
7. Luisada AA: Mechanism of neurogenic pulmonary edema. Amer J Cardiol 20:66–68, 1967
8. Hammermeister KE, Reichenbach DD: QRS changes, pulmonary edema, and myocardial necrosis associated with subarachnoid hemorrhage. Amer Heart J 78:94–100, 1969
9. Szakacs JE, Mehlman B: Pathologic changes induced by l-norepinephrine. Amer J Cardiol 5:619–627, 1960

Hypoxia, Hyperdynamic Circulation, and the Hazards of General Anesthesia in Patients with Hepatic Cirrhosis

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The association of arterial hypoxemia with hepatic cirrhosis has been known for almost a century.[1] More recently, it has been determined that at least some patients with cirrhosis show evidence of a hyperdynamic state of the systemic circulation, with increased cardiac output, decreased total peripheral resistance, a bounding pulse and, often, widened pulse pressure.[2, 3] The hypoxemia and the circulatory changes probably have a common etiology, namely, shunting in the systemic and pulmonary beds.

Below we describe the cases of two patients with Laennec's cirrhosis. The preoperative status of the first patient did not raise our index of suspicion sufficiently, yet his course

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Received from the University of Pennsylvania School of Medicine, Department of Anesthesia, Philadelphia, Pennsylvania 19104. Supported in part by USPHS Research Grant 5-P01-GM-15430-04 and USPHS Training Grant 5-T01-GM-00215-13.