Naloxone infusion combined with cerebrospinal fluid monitoring and drainage during thoracic aorta exploration: A case report

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A 95-kg, 34-year-old male presented for exploration of the thoracic aorta to resect an apparent sarcoma. A significant complication for this surgery is that of paraplegia and/or paraparesis. Continuous monitoring of cerebrospinal fluid pressure and drainage to maintain the pressure at 10 mmHg or less has been advocated to preserve nominal spinal cord perfusion pressure. However, this intervention alone has not demonstrated any greater efficacy in the prevention of paraplegia or paraparesis than no such intervention at all.

Naloxone, the narcotic antagonist, has been studied extensively in relation to human paralysis and endogenous opioid actions. More recently, investigators have proposed combining a naloxone infusion with cerebrospinal fluid monitoring and drainage to attempt to prevent the occurrence of paraplegia and/or paraparesis in patients undergoing thoracic or thoracoabdominal aortic surgery. These interventions would seem at least theoretically appropriate to maximize spinal cord perfusion pressure and preserve spinal cord function. However, the extent of investigations is currently limited and the results somewhat controversial.

Key words: Cerebrospinal fluid pressure, naloxone infusion, paraparesis, paraplegia, spinal cord perfusion pressure.

Introduction

Adams and Van Geertruyden, in 1956, presented the first analysis of the risk of paraplegia and/or paraparesis for patients undergoing surgery on the thoracic or thoracoabdominal aorta. The occurrence of this complication is not consistent; reports from various studies show an incidence rate of 5% to 30%. Moreover, many patients recover from anesthesia neurologically intact, then develop some type of neurologic deficit hours to days after the complication of surgery. Thus far, this complication remains unpredictable.

Numerous treatments have been put forth intended to reduce, if not prevent, paraplegia or paraparesis after thoracic or thoracoabdominal aortic surgery. They include intrathecal papaverine, mannitol, calcium-channel blockers, atriofenoral bypass, hypothermia, and reattachment of intercostal and lumbar arteries. This is a case report of a patient on whom cerebrospinal fluid pressure monitoring and drainage was combined with an infusion of naloxone while undergoing exploration of the descending aorta, localized thromboembolectomy, and primary closure.

Case report

A 34-year-old, 95 kg, ASA physical status II, white male presented for exploration of the descending aorta. The patient had a history of moderate alcohol use in the past and a 15 pack-year history of smoking cigarettes, which he had stopped 2 years previously. Approximately 4 weeks prior to hospitalization, he had experienced a seizure of unknown origin suspected to have resulted from alcohol use.
The patient was admitted one week prior to this surgery for sudden onset of pain and numbness in both lower extremities. He came to the operating room at that time for emergent bilateral embolectomies and returned that same night for a repeat right popliteal embolectomy. During efforts to determine the origin of the clots that resulted in the previous surgeries, computed tomographic scan identified a possible sarcoma of the descending aorta. The patient was scheduled for exploration of the descending aorta and resection of the aortic tumor.

Preinduction lines included a right arterial pressure line, a balloon flotation pulmonary artery catheter, and bilateral 14-gauge peripheral intravenous lines. An 80-cm lumbar catheter was inserted into the subarachnoid space through a 14-gauge Tuohy needle and sutured in place. The catheter was connected to a 500-mL, 0.9% saline, nonpressurized bag to flush and a Becker® CSF-External Drainage and Monitoring System. Cerebrospinal fluid pressure (CSFP) was monitored with a Baxter® pressure transducer interfaced with a Hewlett-Packard® Merlin monitor. The initial CSFP was recorded at 15 mmHg. A naloxone infusion was started at 1 μg/kg/hr.

The patient was preoxygenated and anesthesia induced with midazolam 5 mg, sodium thioptental 500 mg, and fentanyl 750 μg. Intubation was facilitated with vecuronium 10 mg. A 39-French, left-sided, double lumen endobronchial tube was inserted via direct laryngoscopy; proper placement of the tube was confirmed with a fiberoptic endoscope and the tube taped securely in place. Cerebrospinal fluid pressure increased to 19 mmHg with intubation. Cerebrospinal fluid (CSF) was drained periodically to maintain a spinal fluid pressure increased to 19 mmHg with intubation. Cerebrospinal fluid (CSF) was drained periodically to maintain a spinal fluid pressure (CSFP) of 10 mmHg or less. A total of approximately 200 mL of CSF was removed during the case.

After induction and intubation, methylprednisolone 2.5 g was given intravenously. When the chest cavity was opened, the patient was placed on one-lung ventilation. Mannitol 25 g was given intravenously after the thoracic aorta had been dissected free. The aorta was “test-occluded” for 2 minutes and 5 seconds. The patient's systolic blood pressure increased to 170-180 mmHg with cross-clamping. When the cross-clamp was removed, his oxygen saturation dropped from 97% to 88% but quickly returned to the previous level. Amrinone 100 mg was given intravenously.

Amrinone, in combination with sodium thiopental, is used to reduce hypertension proximal to the cross-clamp and eliminate the need for nitroprusside. Amrinone is used because of its combined positive inotropic effects and direct vascular smooth muscle relaxation as well as the absence of the thiocyanate metabolite from nitroprusside. In addition, the combined use of amrinone and sodium thiopental avoids “nitroprusside steal” which would further exacerbate spinal cord ischemia.

The administration of amrinone was followed by a second “test-occlusion,” which lasted 53 seconds. The patient was given 7,000 units of heparin sodium per the surgeon's order. Four minutes later, the aorta was cross-clamped approximately 5-6 cm distal to the subclavian artery. The systolic blood pressure again rose to 170-180 mmHg. Additional fentanyl and sodium thiopental were given throughout the period of aortic cross-clamping. Cerebrospinal fluid was drained periodically to maintain a CSFP of 10 mmHg or less. The patient was given 7,000 units of heparin sodium per the surgeon's order. Four minutes later, the aorta was cross-clamped approximately 5-6 cm distal to the subclavian artery. The systolic blood pressure again rose to 170-180 mmHg. Additional fentanyl and sodium thiopental were given throughout the period of aortic cross-clamping. Cerebrospinal fluid was drained periodically to maintain a CSFP of 10 mmHg or less. A total of approximately 200 mL of CSF was removed during the case.

The aorta was unclamped after 16 minutes and 58 seconds. At that time the patient's oxygen saturation dropped from 100% to 60% but returned to 100% within one and one-half minutes. The heparin was reversed with protamine sulfate. The total aortic occlusion time was 20 minutes and 56 seconds. A chest tube was inserted, the patient returned to normal two-lung ventilation, and the wound was closed. At the end of surgery, the endobronchial tube was replaced with an endotracheal tube. The patient was given midazolam 10 mg, fentanyl 250 μg, and vecuronium 10 mg, to facilitate postoperative mechanical ventilation. He was then transferred to the postanesthesia care unit with assisted ventilation at 100% oxygen.

Anesthetic management

In addition to administering a safe and effective general anesthetic, all interventions for this procedure were directed toward minimizing the spinal cord ischemia during aortic cross-clamping. The lumbar drain was placed prior to anesthesia,
and the naloxone infusion was started at the recom-
mended 1 μg/kg/hr. We followed the recommen-
dations of Acher et al and Hollier et al. After
induction, methylprednisolone 2.5 grams was
given intravenously to provide cellular and lys-
somal membrane stabilization. Sodium thiope-
ntal was given periodically throughout the case for
two reasons: first, large doses were used because of
the central nervous system (CNS) protection ef-
effects of decreasing CNS metabolic rate, relaxa-
tion of the CNS vascular smooth muscle, and reduction
of CNS pressure. The total amount of sodium
thiopental given to this patient was 3,000 mg or
31.5 mg/kg. Second, thiopental was used in con-
junction with amrinone 1.05 mg/kg to help reduce
the systolic blood pressure proximal to the cross-
clamp. These two agents, in combination, allow
one to avoid using nitroprusside for blood pres-
sure control, thus avoiding the “steal” effect en-
countered with nitroprusside.

Cerebrospinal fluid pressure was monitored
continuously and recorded every 15 minutes. Cere-
brospinal fluid drainage was done whenever the
CSFP was consistently greater than 10 mmHg. No
more than 50 mL was withdrawn at any single
instance. The total amount of CSF withdrawn was
approximately 200 mL.

The patient’s postoperative course was un-
eventful. The lumbar drain was removed on the
first postoperative day. The naloxone infusion was
discontinued on the third postoperative day, and
the patient denied any neurological deficit. He did
not report a spinal headache at any time and was
discharged home 8 days after surgery.

Pathophysiology
Paraplegia or paraparesis is a significant risk
for the patient undergoing thoracic or thoracoab-
dominal surgery. There are, as yet, no clear indi-
cators with which one can predict preoperatively
the occurrence of either. In addition, from various
reports, some patients may recover from anesthe-
sia neurologically intact only to develop a delayed-
onset paraplegia 12 hours to 5 days postopera-
tively. The incidence of paraplegia is related to
the severity of the ischemic insult to the spinal
cord.

The spinal cord is supplied by three longitu-
dinal arteries: the anterior spinal artery and two
posterior spinal arteries. The anterior spinal ar-
tery originates from the vertebral artery. The pos-
terior spinal arteries can originate from either the
vertebral or the posterior, inferior cerebellar ar-
teries. These three main arteries supplying the spinal
cord receive additional flow from the intercostal and
lumbar branches of the branches of the de-
scending aorta, of which the most significant con-
tribution comes from the great radicular artery or
artery of Adamkiewicz.

Spinal cord perfusion is analogous to cerebral
perfusion, in that spinal cord perfusion pressure
equals the difference between the mean spinal ar-
tery pressure and either the local venous pressure
or the cerebrospinal fluid pressure, whichever is
greater:

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\text{Spinal cord perfusion pressure} = \text{mean arterial pressure}_{\text{spinal}} - \text{[venous pressure}_{\text{local}} \text{or CSFP]}
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This perfusion gradient decreases drastically
when the thoracic aorta is cross-clamped for two
reasons: first, with cross-clamping the significant
collateral flow from the intercostal and lumbar ar-
teries is effectively stopped. Second, cross-clamp-
ing of the aorta results in a greatly increased cere-
bral blood volume. The resultant increased mean
arterial pressure (MAP) exceeds the autoregula-
tory capacity of the CNS resulting in increased
CSF production, therefore, increased CSFP.

There is controversy as to the efficacy of CSF
drainage on the prevention of paraplegia or para-
paresis resulting from aortic cross-clamping. As a
theoretical concept, one would anticipate CSF
drainage to be beneficial in that when the CSFP is
lowered, the gradient between MAP and CSFP
would increase and result in greater spinal cord
perfusion pressure. In fact, Acher et al, Crawford
et al, Hollier et al, and Murray et al have all re-
ported that CSF drainage, alone, provides no
greater degree of spinal cord protection during
thoracic or thoracoabdominal aortic cross-clamp-
ing than no CSF drainage. However, these
investigators all point to the fact that the relation-
ship between spinal cord ischemia and the occur-
rence of paraplegia or paraparesis is a multifac-
torial problem.

One factor which has been investigated is the
role of opioids in relation to spinal cord ischemia
and/or injury, and more specifically, the effect the
endogenous opioids (i.e., enkephalins, endorphins,
dynorphins, etc.) might have on spinal cord isch-
emia and/or injury. Normally, the endogenous
opioids are relatively dormant during homeo-
stats. The introduction of a stressor (e.g., disease,
pain, or injury) activates the endogenous opioids
which then act at their receptor sites and produce
drastic changes in “behavioral, autonomic or im-
mune function.” Exactly how opioids affect neu-
rologic function has not been delineated yet. It has
been demonstrated that opioids “reduce cerebral
blood flow, increase vascular resistance, depress the
firing rate of single neurons by hyperpolarizing
cell membranes, and depress CNS acetylcholine

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turnover." Similarly, morphine is known to reduce cerebral oxygen consumption and potentiate stroke-induced paralysis in humans. In short, opioids, whether endogenous or exogenous, are inhibitory agents.

As mentioned above, pain is one stressor that activates the endogenous opioid systems. Numerous studies have linked endogenous opioids to deleterious and negative effects on spinal cord blood flow. Naloxone is a pure opioid antagonist which has no agonist activity. It is a competitive antagonist at the mu, delta, kappa, and epsilon receptor sites. Naloxone has been shown to improve spinal cord blood flow, inhibit proteolysis, stabilize lysosomal membranes, and reverse deregancements in calcium flux across cell membranes, among other functions. Naloxone has shown particular effectiveness in improving spinal cord hemodynamics in spinal cord injury and stroke victims, although the precise mechanisms are unclear. An analogous situation occurs with aortic cross-clamping. Holaday and Malcolm report "that opioid antagonists significantly improve hemodynamic, metabolic, and neurologic function as well as survival in many models of circulatory shock, trauma and CNS ischemia."

Archer et al, in two studies published in 1990 and 1994, reported an increased effectiveness in preventing and treating neurological deficits after thoracic and thoracoabdominal aortic surgery, when they combined the use of CSF drainage with a naloxone infusion at 1 μg/kg/hr. This combination would theoretically, at least, be more effective for several reasons: first, because the elevated levels of endogenous opioids are higher within the CSF, draining the CSF would remove some of the opioids on a continuing basis. Second, as stated earlier, draining the CSF would tend to improve the spinal cord perfusion pressure by increasing, somewhat, the gradient between MAP and CSFP or local venous pressure. Finally, naloxone is a stereospecific opioid antagonist. The low dose infused, as recommended, is not sufficient to reverse analgesia from exogenous opioids that are administered but does seem to reverse the negative effects of the endogenous opioids on the spinal cord. Archer et al recommend using a naloxone infusion at 1 μg/kg/hr, initiated prior to induction and continued throughout surgery and anesthesia. They also recommend the infusion be continued for 48 hours postoperatively. Hollier et al point out that for CSF drainage to be helpful, relatively large volumes of CSF may have to be removed, of which a total of 500 mL of CSF drainage should not be unexpected. Hollier also recommends continuation of the CSF monitoring and drainage postoperatively to help prevent delayed-onset paraplegia.

**Summary**

Paraplegia and paraparesis are significant risks for anyone undergoing surgery on the thoracic or thoracoabdominal aorta. The occurrence of this complication remains unpredictable. It is a great challenge to the anesthetist to provide interventions which will help to minimize the extent and depth of the ischemic event. In this report, several interventions have been outlined. Although not widely accepted, all of them are intended to minimize the ischemia while helping to maximize spinal cord perfusion.

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