

Acute pancreatitis associated with scoliosis surgery: Could opioids be a determinant factor in its development?

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ABSTRACT

Various medical complications can occur after spinal surgery in the pediatric population. Current surgical techniques have allowed a greater degree of scoliosis correction, but at the same time, unusual complications have been described that seem to be associated and have a multifactorial etiology. We present a case series of three pediatric patients who underwent scoliosis correction surgery with continuous use of full-dose opioids, and during hospitalization and post-operative surveillance developed acute pancreatitis. The association between prolonged exposure to high-dose opioids and the onset of pancreatitis in the context of major surgery suggests a potential relationship that warrants further study.

Key words: Acute pancreatitis, Opioids, Scoliosis, Spine

Idiopathic scoliosis is the most common form of spinal deformity in young patients. Usually, it presents after 10 years of age until skeletal maturity is achieved. Other less frequent forms of scoliosis are neuromuscular, syndromic, or congenital [1]. There are reports in the literature about pancreatitis as a complication of scoliosis correction surgery, supported by pathophysiological theories such as hemodynamic imbalance associated with intraoperative instability, as well as, changes in visceral vascular architecture leading directly to tissue distress due to vascular elongation from curve correction [2-4]. Several studies have examined the development of pancreatitis in the context of surgery and have proposed various factors as potential triggers [1,3-5]. However, one of the most recent studies proposes the prolonged use of high-dose opioids during the post-operative period as a pathophysiological hypothesis [6].


CASE SERIES

Three patients 9, 15, and 16 years of age were taken to scoliosis correction surgery, two of them with a diagnosis of neuromuscular scoliosis, secondary to Duchenne muscular

dystrophy (DMD) and cerebral palsy, and one with congenital scoliosis due to hemivertebra. The details of the three patients are shown in Table 1. On average, 15 vertebral segments were instrumented. Two of the patients required two surgical stages for final correction, with only one patient needing just one stage. The average surgical time was 6.06 h, with a mean blood loss of 1766 ml in the final correction. All three patients required intraoperative blood product transfusions because of their hemodynamic status.

Regarding the diagnosis of pancreatitis, the main symptom in all patients was abdominal pain, perhaps initially mistaken for post-operative constipation secondary to opioid use for analgesic management. However, increased pain intensity and pancreatic enzyme elevations led to the suspicion of pancreatitis, with an average of 5 days until the diagnosis was made.

In terms of analgesic management, the majority of patients taken to surgery for scoliosis correction were managed with parenteral opioids in the immediate post-operative period. For our patients, the total use of opioids during their hospital stay was 26 days with continuous use and even maximum dose adjustments given the presence of abdominal pain. The main opioids used were morphine, tramadol, and hydromorphone.

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Table 1: Cases of pancreatitis following scoliosis correction surgery

Variables	Patient 1	Patient 2	Patient 3
Sex	Female	Female	Male
Age	9	15	16
Scoliosis type	Neuromuscular	Congenital	Neuromuscular
Related Diagnosis	Cerebral palsy due to neonatal hypoxia	Hemivertebra+ butterfly vertebra	Duchenne's disease
Surgical stages	2	2	2
Surgical time	Stage 1: 5.10 Stage 2: 6.40	Stage 1: 5.25 Stage 2: 7.05	Stage 1: 6.5
Instrumentation levels	T2-S2	T6-L4	T3-S2
Blood loss	Stage 1: 1200 cc Stage 2: 1800 cc	Stage 1: 950 cc Stage 2: 600 cc	Stage 1: 2900 cc
Transfusion	Yes	Yes	yes
Pre-operative Cobb angle	T2-T7 41° T8-L5 102°	T9-L1 70° L1-L5 57°	T7-L3 80°
Post-operative Cobb angle	T2-T7 12° T8-L5 36°	T9-L1 4° L1-L5 12°	T7-L3 25°
Total number of days on opioids	15	25	38
Days on opioids until abdominal pain	10	13	28
Days on opioids until pancreatitis diagnosis	13	15	37

Case 1

A 9-year-old female developed progressive and disproportionate pain associated with progressive pancreatic enzyme elevations and was managed conservatively with parenteral nutrition and hydration, with no ensuing complications.

Case 2

A 15-year-old female with a congenital scoliosis diagnosis developed abdominal pain 3 days after the final scoliosis correction. The pain was associated with abdominal distension and progressive pancreatic enzyme elevations. Imaging revealed gallbladder adenomyomatosis and the pancreatitis diagnosis was made more than 10 days after the procedure. Initially, the patient was managed with hydration and parenteral nutrition until significant clinical improvement. Finally, she was taken to elective cholecystectomy with no complications and was discharged 5 days after the surgery.

Case 3

A 16-year-old male with a history of DMD as an underlying condition was readmitted during the late post-operative period due to a surgical site infection. After that, the patient had a torpid course with the requirement of a prolonged stay in the intensive care unit (ICU) secondary to a refractory septic shock and ventilation compromise. During his stay in the ICU, the patient presented with abdominal pain and progressive distention. Initially, imaging revealed intraperitoneal fluid and dilation of intestinal loops, so the patient was managed conservatively. In the context of a critically ill patient with no significant improvement, pancreatitis was diagnosed because of the persistence of

abdominal pain associated with pancreatic enzyme elevation and a large peripancreatic collection found in an abdominal CT which required urgent drainage.

DISCUSSION

Acute pancreatitis is a severe condition with varying clinical manifestations directly associated with its severity. According to the Atlanta criteria [5], two out of three of the following characteristics are required to make the diagnosis: abdominal pain with clinical signs (nausea or vomiting) suggestive of pancreatitis; serum lipase level at least 3 times higher than the upper limit of normal; and characteristic findings of acute pancreatitis on transabdominal ultrasound or on computed tomography. Amylase elevation is also taken into account in many settings (3 times higher than the upper limit of normal) [2], although lipase measurement is more specific [3].

The presence of pancreatitis has been documented as a common post-operative complication in the setting of gastrointestinal and cardiovascular surgery. However, the study of this condition as a post-operative complication of spinal orthopedic surgery has gained momentum. There is no clear pathophysiology in the perioperative context although several theories have been proposed, such as mechanical causes in the setting of abdominal surgery, the effects of some medications, metabolic and electrolyte disorders, regional and systemic hypoperfusion, embolism of arteries supplying the pancreas, and pancreatic ischemia [3,4]. In pediatric patients, its presence has been related to trauma (13–33%), the use of diuretics and immunomodulators such as azathioprine, infections, and idiopathic etiology (20–25%) [3].

In scoliosis correction surgery, pancreatitis has been described as a post-operative complication without a clear etiology. The potential causes proposed are bleeding, anesthesia-related

hypoperfusion, tumor necrosis factor alfa peak during the procedure, and prone position as a cause of compression of the large vessels and the pancreatic parenchyma². On the other hand, other studies have shown that factors such as the length of the procedure, curve correction percentage, the surgical technique, and the length of the fusion would not be factors leading to the development of pancreatitis [3,4,6].

The symptoms of pancreatitis usually manifest between the second and 4th post-operative days [3], and include nausea, vomiting, and mainly abdominal pain. Post-operative clinical manifestations are often mistaken for symptoms inherent to the post-operative period such as pain and ileus, which are not uncommon due to the site and nature of the procedure. Moreover, nausea is usually associated with the use of analgesics and opioids [3]. Furthermore, pancreatic enzyme elevations cannot be attributed solely to pancreatitis because they can occur due to multiple reasons and persist from the 4th–6th post-operative day, and even up to 9 days [2].

High-dose opioids are frequently used for long periods of time for the management of post-operative pain after scoliosis correction, with emerging literature showing the relationship between the development of pancreatitis and the use of opioids and their derivatives [7-9]. It has been proposed that the increased amplitude and frequency of mu receptor-mediated phasic contractions of the sphincter of Oddi favor the development of this condition [7]. Kim *et al.* showed that codeine-induced pancreatitis probably exists as a result of the sphincter of Oddi dysfunction [8]. In their study, using manometry analysis, Wu *et al.* found that morphine can increase sphincter of Oddi and common bile duct baseline pressures, as well as the frequency and amplitude of phasic contractions which trigger an excitatory effect on the sphincter, potentially predisposing to dysfunction due to functional obstruction and compromising diastolic filling of the sphincter segment [9]. In turn, tramadol, another analgesic commonly used in the postoperative period, could reduce the baseline pressure of the sphincter and the amplitude of the phasic contractions, showing an inhibitory effect on the sphincter of Oddi⁹, also potentially causing pancreatitis.

Based on the above, we believe that a causal relation exists between high-dose opioids and prolonged opioid-based regimens and the potential development of acute pancreatitis after scoliosis correction surgery. This risk appears to be higher in patients with neuromuscular scoliosis. Additional studies of better quality are needed to improve the knowledge of the safe and rational use of opioids among health-care staff.

CONCLUSION

Acute pancreatitis, although infrequent, has been described in patients taken to scoliosis correction, attributed to vascular causes. However, documented effects of opioids on the sphincter of Oddi beg reconsideration of the etiology of pancreatitis in patients taken to scoliosis correction surgery and the implementation of different options in post-operative analgesic management. The relationship between prolonged exposure to high-dose opioids and the development of pancreatitis in the context of major surgery suggests a potential causal relation that needs to be studied to rationalize the use of post-operative analgesia with a view to prevent these types of complications.

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