ORIGINAL ARTICLE

Association of acute pancreatitis or high level of serum pancreatic enzymes in patients with acute spinal cord injury: a prospective study

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Background: Spinal cord injuries has increased together with urban violence and show a high rates of incidence. Besides the onus to patient and society, it can also cause other serious complications to victims. Acute pancreatitis has an important impact on this disease and has been underdiagnosed in several patients.

Objectives: The aim of this study was investigate the association of acute pancreatitis in acute spinal cord injuries. The secondary aim was to propose an investigation protocol to early diagnose and prevent it.

Methods: A prospective observational study was conducted in 78 patients who presented acute spinal cord injury (SCI) at our emergency department, confirmed by clinical and imaging examination, in according to the American Spinal Injury Association (ASIA) Classification. Exclusion criteria were chronic or associate diseases in spinal cord, pancreatic direct trauma, alcoholism and chronic pancreatic disease.

Results: The association of acute pancreatitis in patients with SCI was 11.53%. The occurrence of pancreatitis or high levels of serum pancreatic enzymes in patients with ASIA A was 41.7% and only 4.17% in patients with ASIA E. In all, 55.2% of patients who presented pancreatitis or high levels of serum pancreatic enzymes had cervical level of SCI and 34.5% had thoracic level. Adynamic ileus was observed in 68.96% of this group.

Conclusion: We concluded that, in acute spinal cord injuries, the occurrence of acute pancreatitis or high serum levels of pancreatic enzymes are more frequent in patients with ASIA A Classification, cervical/thoracic level of spinal injury and adynamic ileus.

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INTRODUCTION

Based on the available epidemiological data from 2010, the number of new cases/year of spinal cord trauma (SCT) is estimated in 8950. Currently, there are 250 000 patients with spinal cord injury (SCI) in our country. In our University accounts for 1950 new cases/year and 55 000 patients with SCI.¹ The incidence in male and female population is 9:1 in the age group of 10–30 years.

SCT is an acute SCI that causes several complications. Many of them are progressive, such as pain, spasticity, pressure ulcer, urinary retention, urinary tract infection, vascular and cardiorespiratory alterations, major depression and severe gastrointestinal alterations.^{2,3} Spinal cord trauma (SCT) also represents a significant socioeconomic setback to patients and their families, as many of them do not have financial and/or sociocultural conditions to support that situation. Patients with SCT present a high number of years of potential life lost.

The main causes of SCT are gunshot injury, falls injury (from paving slabs at low buildings), traffic accidents, diving accidents (into shallow water) and accidents at sports, recreational and leisure activities.¹

Pancreatitis can be defined as an inflammatory process in the pancreas, with intraparenchymal corrosion caused by the pancreatic juice. It may cause partial or total organ destruction, with necrosis and infection, and it may reach other adjacent or distant organs. It is

a clinical syndrome characterized by recurring or persistent abdominal pain, associated with an increase in serum pancreatic enzymes. Pancreatitis is most of the times a benignant disease and, in most cases, the organ recovers its normal structure and functions. In all, 10–30% of patients may develop systemic inflammatory response syndrome, having a fulminant development with massive pancreatic necrosis and multiple organ failure.⁴

Gastrointestinal complications can be noticed in patients with SCT, and the incidence range from 6.2% to 11%, according to few papers on the subject in the international literature. Authors report an incidence of up to 20.9%.^{4,5} Gastrointestinal complications are: 'paralytic' or adynamic ileus, gastric dilatation or gastroparesis, gastrointestinal ulcer, upper digestive tract hemorrhage, and acute pancreatitis.^{5,6} These are severe complications that substantially increase the morbidity rate of SCT. Usually, there are other problems associated with it that may worsen SCT, such as decubitus ulcer and the infections resulting from it, muscular hypotrophy, urological dysfunction and sexual dysfunction, among others.^{5–7}

Ultrasonography and, preferably, computed tomography (CT) may be used to confirm diagnosis and enable the evaluation of the organ, helping to find out the etiology of the disease and leading to the right diagnosis in 80–95% of the cases.⁸ CT with contrast is considered a 'gold standard' for patients with pancreatitis who need that decision is

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taken without delay.⁹ However, CT is contraindicated in patients admitted to intensive care unit and mainly in those patients with SCI who should not be moved.

SCI may be followed by severe gastrointestinal complications or may cause them. The incidence of pancreatitis is roughly 3–4.7%.¹⁰ Relatively low incidence (1%) of acute pancreatitis is seen in adult patients, as a postoperative complication, after surgical correction for lumbar spine trauma. Mortality due to acute pancreatitis is about 30%, and in case it evolves to acute necrotizing pancreatitis, mortality rate may reach 80%.⁷

The occurrence of acute pancreatitis in SCT is related to the direct trauma to pancreas and/or to the structures interconnected to it or by altering the autonomic function in spinal cord, which causes stimulation on the sphincter of Oddi (SO).¹⁰ Therefore physiopathological mechanism includes a SO dysfunction. Recent neuroanatomic studies demonstrate a neurohormonal circuit between intestinal mucosa and pancreas. The existing distension or the increase of the duodenal motor activity during the initial phase of SCT stimulates and constricts the SO ganglia, through neurohormonal impulses.¹¹ Another mechanism that stimulates pancreatic exocrine function is related to the action of parasympathetic fibers originating in the brain, when the proximal thoracic and cervical spines are intact in SCT, and there is an injury from T₄ to T₁₂, which blocks the stimulus in the sympathetic innervation (parasympathetic–sympathetic dysfunction).¹²

Even though the retrospective study conducted by Nobel *et al.*¹³ demonstrates an average incidence of 3% of acute pancreatitis in cases of SCI, it is known that the disease is underdiagnosed (12–42%) even in non-paraplegic patients studied by Wilson and Imrie in 1988.¹⁴ Therefore, there are few statistical data about it, and there is no protocol for early diagnosis and first care, which would improve patient condition.¹⁰

The primary aim of this study was investigate the association of acute pancreatitis or high levels of serum pancreatic enzymes in patients with acute SCI.

METHODS

The present study followed the guidelines of the Declaration of Helsinki. We recruited a sample of 78 participant from the patient pool of the Vertebral Column Unit of the University. After explaining the study, as recommended by the Research Ethics Committee, written consent was obtained from each participant.

Patients were identified according to age, gender, referred race, medical history, prevailing mechanism of trauma, associated fractures, Classification of injury according to American Spinal Injury Association (ASIA) scale, medication use, personal history of systemic diseases, infectious and inflammatory diseases and medications used during hospital admission contained in the patient's medical chart.

Seventy-eight patients with diagnosis of acute SCI were admitted to the Vertebral Column Unit of our University during the period between April 2005 and April 2006, according to the following inclusion and exclusion criteria. All patients were treated according to the guidelines of the Spinal Cord Trauma Group.

Inclusion criteria

1. Patients with acute SCI (first 4 weeks after trauma) with diagnosis confirmed by clinical examination and image analysis with CT and/or magnetic resonance imaging, with partial, complete deficit or without deficit, according to the ASIA Classification.
2. Patients who did not have direct trauma to the pancreas, referred to or confirmed by image analysis with multi-detector CT and/or ultrasonography, when required.

Exclusion criteria

Patients who did not have serum measurements in predetermined periods, if refused to sign the informed consent, cases of direct trauma to the pancreas and the presence of acute or chronic pancreatitis due to other causes, such as: choledocholithiasis, and alcoholism with clinical and subsidiary signs of pancreatic injury.

Diagnosis of acute pancreatitis

The diagnosis of acute pancreatitis was based only on laboratory methods with serum amylase and lipase tests and with radiographic examinations (CT or magnetic resonance imaging), as clinical parameters could be absent or attenuated because of either the neurological deficit or the symptoms caused directly by the SCI.

International standards for confirmation of acute pancreatitis were maintained: threefold or more increase in the higher value of normal serum levels of amylase ($<100 \text{ U l}^{-1}$) and/or lipase enzymes ($13\text{--}60 \text{ U l}^{-1}$) according to critical values (limits of normality) currently used for analyses of blood samples at the Laboratory of the University.

All patients with serum levels of amylase $>300 \text{ U l}^{-1}$ and/or serum levels of lipase $>180 \text{ U l}^{-1}$ were diagnosed as having acute pancreatitis.^{10,15}

Classification of patients according to the level of serum enzymes

Patients were classified according to the levels of serum pancreatic enzymes as follows:

1. Not altered: Patients who did not develop acute pancreatitis during hospitalization.
2. Altered: Patients with serum pancreatic enzymes concentrations above the upper normal limit but not as high as the threshold levels for confirmation of acute pancreatitis.
3. Acute pancreatitis: Patients who developed acute pancreatitis during hospitalization.

Adynamic ileus

Adynamic ileus is characterized by the presence of sudden abdominal distension with mild or moderate pain and air–fluid noises through the intestinal lumen that are not noticed in physical examination. Plain abdominal radiography shows distension, usually restricted to the small gut, with mild-to-moderate edema of the intestinal wall and diffuse distribution of gases.

Statistical analysis

Frequency occurrence of each attribute (quality) were categorized into contingency tables: ASIA Classification (Table 1), level of SCI (Table 2), occurrence of adynamic ileus (Table 3), and associated trauma (Table 4) according to the patient's levels of serum pancreatic enzymes: not altered, altered, and acute pancreatitis.

Comparisons of frequencies of classes between different groups were tested by the Fisher's exact test typically used for associations in contingency tables (Tables 1–4); with $P\text{-value} < 0.05$ being considered statistically significant.

Table 1 Distribution of the patient's ASIA Classification according to serum pancreatic enzyme level and acute pancreatitis

	SPEL normal	SPEL altered	Pancreatitis	
<i>ASIA Classification</i>				
A	6	7	5	18
B–C–D	20	12	4	36
E	23	1	0	24
Total	49	20	9	78

Abbreviations: ASIA, American Spinal Injury Association; SPEL, serum pancreatic enzyme level. Fisher's exact test = 0.015.

Table 2 Distribution of the patient's level of spinal cord injury according to serum pancreatic enzyme level and acute pancreatitis

	SPEL normal	SPEL altered	Pancreatitis	
<i>Spinal cord level</i>				
Cervical	22	10	6	38
Thoracic	12	7	3	22
Lumbar	15	3	0	18
Total	49	20	9	78

Abbreviation: SPEL, serum pancreatic enzyme level.
Fisher's exact test = 0.003.

Table 3 Distribution of the presence of adynamic ileum according to serum pancreatic enzyme level and acute pancreatitis

<i>Adynamic ileum</i>	SPEL normal	SPEL altered	Pancreatitis	
No	48	9	0	57
Yes	1	11	9	21
Total	49	20	9	78

Abbreviation: SPEL, serum pancreatic enzyme level.
Fisher's exact test < 0.0001.

Sample analysis

The target population was males and females with acute SCI. We obtained the sample at convenience.

The mean age of total sample was 37.6 years, instead of 34.0 years in a group of patients who presented with acute pancreatitis.

The gender distribution was 65 M:13 F; it was tested by the Kolmogorov-Smirnov, which showed not a normal distribution of the sample.

RESULTS

The association of acute pancreatitis in patients with SCI was 11.53% in our series. The occurrence of pancreatitis or high levels of serum pancreatic enzymes in patients with total or partial neurological deficit was 96.55% (41.7% ASIA A and 55.17% ASIA B-C-D); only one patient without neurological deficit (ASIA E) showed altered SPEL (serum pancreatic enzyme level) (Table 1).

In all, 55.2% of patients who presented pancreatitis or high levels of serum pancreatic enzymes had cervical level of SCI, 34.5% had thoracic level of SCI and only 10.3% had lumbar level of SCI (Table 2).

Adynamic ileus was observed in 68.96% of patients who presented pancreatitis or high levels of serum pancreatic enzymes (Table 3).

There was no difference between the presence or absence of associated fractures in the determination of pancreatitis or high levels of serum pancreatic enzymes (Table 4).

DISCUSSION

The importance of the present study lies on the continuous and fast increase of SCI cases, mainly in the urban centers, as warned by Barros Filho.^{1,16}

Mann *et al.*¹⁷ in 1994, considering a scale of non-paraplegic patients, demonstrate an incidence of 12–42% of undiagnosed acute pancreatitis and refer to the lack of information and studies on acute pancreatitis after SCT; in our series, we have observed 11.53%.

The elevation of pancreatic enzymes occurs in up to 15.4% cases of SCT according to Nobel *et al.*,¹³ and in our series, we have observed the same in 37.17%.

According to Wilson and Imrie,¹⁴ acute pancreatitis is undiagnosed in up to 33% patients, and they have demonstrated

Table 4 Distribution of the associated fracture according to serum pancreatic enzyme level and acute pancreatitis

	SPEL normal	SPEL altered	Pancreatitis	
<i>Associated fractures</i>				
No	30	8	5	43
Yes	19	12	4	25
Total	49	20	9	78

Abbreviation: SPEL, serum pancreatic enzyme level.
Fisher's exact test = 1.0.

that 66% of the patients are diagnosed with acute pancreatitis only during the autopsy, mostly because of the atypical clinical picture or the omission in requesting tests to measure serum pancreatic enzymes levels. The group with SCI and loss of sensorial and motor functions, signs and symptoms were absent, we agree with it and we recommend an investigation protocol with serum pancreatic enzymes each 7 days since trauma until 4 weeks follow-up. These are some of the important reasons to support and propose assistance protocol with the usual laboratory research of pancreatic enzymes in patients with SCT.^{6,12,18}

In the retrospective studies conducted by Carey *et al.*¹⁹ and Nobel *et al.*,¹³ they emphasize that SCI may cause loss or decrease of splanchnic sensibility, and the signs and symptoms of abdominal complications after the SCT may be absent or atypical.

Patients with SCI above T₁₂ present loss of abdominal sensation, and in patients with SCI below T₁₂ the abdominal sensation may be partially preserved. 89.7% of our sample with pancreatitis or high levels of serum pancreatic enzymes presented SCI level cervical or thoracic.¹⁸

Another important aspect we support and propose is the required test for lipase along with amylase. Rattner *et al.*²⁰ and Mitchell *et al.*⁸ demonstrate that the measurement of serum amylase levels may be reported as normal (false negative) in 10–30% cases of pancreatitis, in patients with alcoholism and hyperglycemia. Rattner *et al.*²⁰ and Mitchell *et al.*⁸ explain that, as it is known, lipase is originated only in the pancreas and, thus, it represents a specific indicator, especially when the elevation levels are three times higher than the upper limits of normality recommended to confirm diagnosis; these data agrees with our protocol of laboratory research.²⁰

Acosta-Rua *et al.*²¹ point a higher incidence of hemorrhagic gastrointestinal complication, such as upper digestive hemorrhage (22%), mainly in the complete cervical spine injury cases. However, they do not determine the cause or motive of it. They also state that the occurrence of acute pancreatitis appears not to be related to the SCI, according to the National Spinal Cord Injury Statistics.⁷

Gore *et al.*⁷ suggest that the onset of pancreatitis may be connected to the mechanism of SCI caused by the alteration in the function of sympathetic descending pathway and the maintenance of the parasympathetic activity on the intestine and SO, causing the stimulation of that sphincter and of the pancreatic secretion, the distension of intestinal smooth muscle and inducing the adynamic or prolonged ileus (5–8%). That is a plausible triggering mechanism for acute pancreatitis. The association of adynamic ileus and acute pancreatitis was also observed in patients with an incidence of 11.3%.⁷

Only in the first year of the twenty-first century, researchers such as Kennedy *et al.*,²² Chang *et al.*¹⁸ and Nobel *et al.*¹³ conducted neuroanatomic studies to determine the physiopathology of acute pancreatitis in SCI.^{11,12,18,23}

Mawe and Kennedy²⁴ developed an experimental model in guinea pigs and proved the existence of bidirectional interaction and neuronal answer between the duodenal mucosa and the SO, by measuring fast and slow excitatory postsynaptic potential of nicotinic receptors and alpha 2-adrenoceptors inhibitor.¹¹

One of the physiopathology mechanisms, established by neuroanatomic studies,²⁵ includes the periduodenal ganglia and perisphincter of Oddi, which receive parasympathetic stimulus with spasms of the smooth muscle of the SO, and confirm the hypotheses of the sympathetic-parasympathetic system imbalance, due to the sympathetic system deficit and to the parasympathetic system prevalence, which has a extramedullary circulatory pathway as a result of SCT.

CONCLUSION

The incidence of acute pancreatitis in patients with SCI was 11.53%. Acute pancreatitis was most frequent in patients with SCI ASIA A. Acute pancreatitis was most frequent in patients with adynamic ileus. The period of major incidence of acute pancreatitis in SCI occurred within the first and forth week after trauma.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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