Original Article

Gallstones in spinal cord injury (SCI): a late medical complication?

KP Rotter^{*,1} and CG Larraín¹

¹Hospital del Trabajador de Santiago, Asociación Chilena de Seguridad, Chile

Study design: Prospective controlled study.

Objectives: To assess the prevalence of cholelithiasis among chronic spinal cord injured (SCI) male patients of the ACHS (Asociación Chilena de Seguridad). To evaluate statistically the prevalence of cholelithiasis among SCI patients compared to a control group and to the general male Chilean population. To assess the correlation between cholelithiasis in chronic SCI patients and usual risk factors such as age, obesity and diabetes mellitus. To assess the association of cholelithiasis in chronic SCI patients and the duration of the spinal cord injury.

Setting: Rehabilitation Service at the Hospital del Trabajador, in Santiago, Chile.

Methods: One hundred SCI patients followed up at the Hospital del Trabajador on a regular basis were included in the study; one group consisted of 76 subjects rated ASIA A or B and the other group consisted of 24 subjects rated ASIA C and D. They were all male, older than 20 years old (average age: 41.9 and 42.6 respectively), and suffered from a spinal cord injury greater than one year of evolution. The control group (CG) consisted of 100 male volunteers, without both SCI and history of biliary disease, aged 40.3 years old in average. All three groups underwent ultrasonographic imaging evaluation of the gallbladder and the biliary tract between 1998 and 2000.

Results: The prevalence of cholelithiasis among the groups was the following: 25% in the SCI patients ASIA A and B (19/76), 25% in the SCI patients ASIA C and D (6/24) and 9% (1/100) in the CG. The statistical analysis showed a value of $P=0.0037$, thus establishing a significant association between cholelithiasis and SCI, both complete and incomplete. The difference was not statistically significant when correlating the presence of cholelithiasis with the neurological level of the injury – above and below T10 (24.1 and 25%, respectively) – with the duration of the SCI, with age, obesity and diabetes mellitus.

Conclusions: SCI represents a major risk factor for the development of cholelithiasis, and it should be considered a late, secondary complication of a spinal cord injury.

Sponsorship: The present work is sponsored by the Fundación Científica y Tecnológica of the ACHS, grant No 2899.

Spinal Cord (2003) 41, 105–108. doi:10.1038/sj.sc.3101408

Keywords: spinal cord injury; cholelithiasis; gallstones; risk factors

Introduction

Life expectancy of SCI patients is currently high (30–40 years) and shows a trend to further increase. Several late complications involving various organ systems have been observed and described in chronic SCI patients, among which are gastrointestinal complications, with cholelithiasis being notable due to its prevalence. North American studies^{1,2,3,4,5} have reported a significantly higher prevalence of cholelithiasis

among such patients and thus have suggested that the spinal cord injury is a risk factor for developing cholelithiasis. Patients with gallstones are at risk of developing several medical complications, which in spinal cord injured patients, in view of their neurological condition, are likely to be of late and difficult diagnosis.

Inasmuch as Chile is considered to have a high prevalence of cholelithiasis among the general population,^{6,7,8} the aim of the study we conducted was to verify if the high prevalence of cholelithiasis observed among SCI patients in the USA would be observed in

*Correspondence: KP Rotter, Servicio de Rehabilitación, Hospital del Trabajador, Ramón Carnicer 201 Providencia, Santiago, Chile

our population as well. The reasons for the high prevalence of cholelithiasis in Chile remain unknown, and at present, ethnic and racial factors appear to be the most relevant.⁹ Additionally, there is also a greater prevalence of cancer of the biliary tract among the Chilean population.^{10,11}

Methods

Spinal cord injury ASIA = International Standards for Neurological and Functional Classification of Spinal Cord Injury patients from the American Spinal Injury Association.¹² ASIA Impairment Scale: ASIA A: motor and sensory functions complete with no movement or sensation below the lesion; ASIA B: incomplete sensory function but no motor function preserved through S4-5; ASIA C: motor and sensory functions incomplete with strength grade 3 or less for most of the muscles below the lesion; ASIA D: motor and sensory functions incomplete with strength 3/5 or greater for most muscles; ASIA E: normal motor and sensory functions: ASIA A–D patients who were followed up at the Rehabilitation Service of the Hospital del Trabajador of Santiago were included in the study. These patients came from all the regions of the country and they met the requirements of being male, older than 20 years old, without a history of biliary condition prior to SCI, and with more than one year of evolution since the injury.

The Study Group consisted of 100 SCI patients, divided into 76 SCI ASIA A or B and 24 ASIA C and D.

The Control Group comprised 100 male volunteers without SCI, without history of biliary disease, and aged 20 years and older. Such subjects were patients with hand lesions attending our physical therapy unit.

Table 1 Characteristics of the study groups

SCI	ASIA A, B, C & D	Control	P value
<i>n</i>	100	100	
Average age (range)	44.2 (24–72)	40.3 (20–69)	0.036
Years with SCI: average (range)	8.3 (1–24)	–	–
Obesity (%)	11.8	11.1	0.637
D. mellitus (%)	4.0	1.0	0.369

Table 2 Characteristics of The Spinal Cord Injury Group

SCI	ASIA A & B	ASIA C & D
<i>n</i>	76	24
Average age (range)	42.6 (24–72)	48 (32–52)
Years with SCI: average (range)	6.5 (1–20)	9.3 (3–24)
Obesity (%)	11.8	0
D. mellitus (%)	3.9	4.1

Tables 1 and 2 show the characteristics of the study groups. Such characteristics included data concerning age, years of evolution of the SCI, presence of obesity – measured as body mass index (BMI) – and presence of diabetes mellitus. The distribution, according to the neurological level of the SCI ASIA A or B, was the following: 16 cervical, 31 dorsal T1–T10 and 29 below T10.

Diabetes Mellitus was considered as present when glycemia were >120 mg %. Obesity was diagnosed when BMI was above 29.

The totality of patients in both groups, SCI and control, were evaluated with ultrasound imaging studies of the gallbladder and the biliary tract during 1998, 1999 and 2000.

Statistical analysis

The χ^2 test was used to obtain a raw comparison of the frequencies of cholelithiasis between the groups. The model of logistic regression was used for the comparison when adjusting to risk factors. The association was considered statistically significant at the 0.05 level.

Results

The prevalence of cholelithiasis was 25% in the SCI ASIA A or B group, also 25% in the SCI ASIA C and D group, and 9% in the control group. The statistical analysis revealed a significant association between chronic SCI and the presence of cholelithiasis, both when the groups with SCI were considered separately ($P=0.011$), and when they were considered as a whole group (Odds Ratio = OR = 3.37, $P=0.0037$).

When comparing the results of our study with those from other studies conducted on the Chilean population – which describe a prevalence of cholelithiasis among males aged 40 years old in average of 13% – a significantly higher prevalence of this disease can be observed among SCI patients ($P<0.001$).

When evaluating the frequency of cholelithiasis according to the neurologic level of the injury in ASIA A or B patients, no significant association can be observed (Table 3). No correlation can be seen either between the length of the evolution of the spinal cord lesion and the presence of cholelithiasis in none of the two groups (Table 4). The usual risk factors, such as age, obesity and diabetes mellitus have no impact on the association between chronic SCI and the presence of cholelithiasis (adjusted OR = 3.27 vs raw OR = 3.37).

Table 3 Neurological level of SCI: ASIA A and B and cholelithiasis

Level	Cholelithiasis present <i>n</i>	%	Cholelithiasis absent <i>n</i>	%
C4–T10	12	25.5	35	74.5
T1–L5	7	24.1	22	75.9

Table 4 Duration (years) of SCI: ASIA A and B, ASIA C and D and cholelithiasis

	With cholelithiasis			Without cholelithiasis		
	n	Average	SD*	n	Average	SD*
ASIA A or B	19	8.8	4.1	57	6.9	4.5
ASIA C or D	6	5.7	4.4	18	10.4	5.6
Total	25	8.0	4.3	75	7.7	5.0

*SD = standard deviation

Discussion

A prevalence of cholelithiasis of 25% detected in our study among chronic SCI male patients, surpasses extensively the prevalence among the general male population of our country, reported by Miquel⁹ and which is of 13.1% for Hispanics and of 12.6% for Mapuches. In view of this, we cannot assume that the prevalence we found among our SCI patients is due to the higher prevalence of cholelithiasis reported for the general Chilean population.

Such significant association has already been described in the last 10 years in several international studies (USA) carried out both *in vivo* and in autopsies,^{1,2,3,4,5} and the figures reported are around 30%, somewhat higher than the results of our study. Nevertheless, the average age of the SCI patients of the North American studies is somewhat higher than the age of our patients (42 *versus* older than, 50 for ASIA A and B lesions).

Our study agrees with other foreign studies in that the duration of the SCI does not correlate with the higher prevalence of cholelithiasis.^{2,3,4}

The work of Moonka,⁴ the most complete and with the greater casuistry of all the studies published at present, is in agreement with our results inasmuch as this higher prevalence of cholelithiasis among SCI patients does not involve known risk factors such as age and obesity (measured as body mass index = kg/m²). But BMI of SCI patients are likely to be relatively inaccurate, due to the severe osteopenia and great loss of muscular mass with severe atrophy of the affected limbs. There are no simple clinical methods to measure accurately the proportion of adipose tissue mass in such patients, and therefore the latter might be underestimated. Further studies in this field are required to determine with accuracy the correlation with obesity as a risk factor.

Tandon⁵ describes the development of sludged bile as a frequent condition during the first stages after a spinal cord injury, when usually a significant and rapid weight loss occurs. Such factors are considered potential risk factors for the genesis of gallstones.¹³

As part of our study, we have the results of the ultrasounds performed within the first year of evolution of the SCI on 30 male subjects. We only found sludged bile in one case, after 5 months of the SCI, in a patient who had previously required parenteral feeding. The patient was followed up once

a year and did not show evidence either of sludged bile or of gallstones, and continues in the same condition at present. Another case presented, at an early stage after the SCI, with a subacute non-lithiasic cholecystitis, and also had a history of parenteral feeding during the acute stage of the SCI. In view of those findings, we don't consider the initial and rapid weight loss as a major factor in the ethiopathogenesis of cholelithiasis among SCI patients.

Our work did not show a correlation between the severity of the spinal lesion and the frequency of cholelithiasis. In our cases the prevalence is similar in ASIA A and B and in ASIA C and D groups, as opposed to Moonka's work in which an increased prevalence of cholelithiasis among complete spinal cord lesions *versus* incomplete ones was observed.

Both our work and Moonka's⁴ fail to reveal a significant correlation between cholelithiasis and the level of the lesion. This is opposed to the work of Apstein,³ where a greater and significant prevalence among lesions affecting levels above T10 is described and which relates it to a dysfunction of the spinal sympathetic system.

There are several reports of scintigraphic evaluations carried out 10 years ago^{14,15} with a small number of cases, describing a slowness of the gallbladder voiding among SCI patients. More recent studies using ultrasound imaging of the gallbladder voiding and contractility in SCI patients,¹⁶ have found voiding time and residual volume values within the normal range. Smaller volume at rest and smaller ejection fraction are described especially in SCI affecting levels above T10. We find unlikely the fact that such subtle changes could play an ethiopathogenic role, since it is clear that the major effect on the contractility of the gallbladder is exerted by the vagus and cholecystocinin, the functions of which are completely preserved in chronic SCI patients, and thus account for the normal contractility.

Finally, it is worth noting that SCI patients are carriers of a neurogenic bowel, with slow intestinal transit, and quite usual severe constipation, which require a specific management.¹⁷

The work of Thomas,¹⁸ conducted on subjects without SCI, reveals a significant correlation between slow colonic transit and increased plasma levels of deoxicholic acid. The presence of a greater proportion of this acid has been found in many patients with cholelithiasis, who also suffer from a slow colonic transit.

The ethiology of cholelithiasis among SCI patients might well respond to an alteration of the intestinal cycle of biliary salts, resulting from a slow intestinal transit, which is characteristic of such patients. The slow intestinal transit might explain the greater prevalence of cholelithiasis found within incomplete spinal cord lesions. The hypothesis relating deoxicholic acid levels to the development of cholelithiasis is not widely accepted.¹⁹ Further studies on SCI patients to clarify the role of the deoxicholic acid in the

pathogenesis of gallstones could result in great benefits.

Conclusions

When compared to the general male population, the prevalence of cholelithiasis among chronic SCI male patients is significantly greater. And this is observed independently of age, duration of the evolution of the SCI, neurologic level of the lesion, and the presence of obesity, measured as BMI.

Taking into account the totality of the findings observed in the present study, and those previously published in the foreign literature, we are in the position of establishing that cholelithiasis in SCI male patients is a late medical complication.

Therefore, it is advisable to include among the annual follow up examinations of these patients in Chile, an ultrasound evaluation of the gallbladder and the biliary tract, which has the advantage of being non-invasive and of relatively low cost.

Acknowledgements

Thanks to Mrs Valeria Rojas and Pilar Alcaíno our secretaries.

References

- Meshkinpour H, Vaziri N, Gordon S. Gastrointestinal pathology in patients with chronic renal failure associated with spinal cord injury. *Am J Gastroenterol* 1982; **77**: 562–564.
- Apstein MD, Dalecki-Chipperfield K. Spinal cord injury is a risk factor for gallstone disease. *Gastroenterology* 1987; **92**: 966–968.
- Apstein MD, George B, Tchakarova B. Spinal cord injury is a risk factor for cholesterol gallstone disease. *Gastroenterology* 1991; **100**: A715.
- Moonka R *et al.* The prevalence and natural history of gallstones in spinal cord injury. *J Am Coll Surg* 1999; **189**: 274–281.
- Tandon RK, Garg PK, Jain RK. Increased incidence of biliary sludge in high spinal cord injury. *Gastroenterology* 1995; **108**: A438.
- Medina E *et al.* Epidemiología de las colecistopatías en Chile. *Rev Méd Chile* 1972; **100**: 1376–1381.
- Medina E, Pascual JP, Medina R. Frecuencia de la litiasis biliar en Chile. *Rev Méd Chile* 1983; **111**: 668–675.
- Covarrubias C, Del Pino G, Ferreiro O, Nervi F. Epidemiología e historia natural de la litiasis biliar. Implicancias para el manejo clínico de la enfermedad. *Rev Méd Chile* 1992; **120**: 432–438.
- Miquel JF *et al.* Genetic epidemiology of cholesterol cholelithiasis among Chilean hispanics, amerindians, and maoris. *Gastroenterology* 1998; **115**: 937–946.
- Maynard Jr FM *et al.* International standards for neurological and functional classification of spinal cord injury patients. *Spinal Cord* 1997; **35**: 266–274.
- Chianale J, Del Pino G, Nervi F. Increasing gallbladder cancer mortality rates during the last decade in Chile, a high risk area. *Int J Cancer* 1990; **46**: 1131–1133.
- Zapata R. Epidemiología del cáncer vesicular. *Gastroenterol Latinoam* 1998; **9**: 84–90.
- Yang H *et al.* Risk factors for gallstone formation during rapid loss of weight. *Dig Dis Sci* 1992; **37**: 912–918.
- Nino-Murcia M *et al.* Gallbladder contractility in patients with spinal cord injuries: A sonographic investigation. *AJR* 1990; **3**: 521–524.
- Milne N *et al.* Biliary kinetics in spinal cord injury. *J Nucl Med* 1987; **28**: P688.
- Ketover SR *et al.* Gallstones in chronic spinal cord injury: is impaired gallbladder emptying a risk factor? *Arch Phys Med Rehabil* 1996; **77**: 1136–1138.
- Correa GI, Rotter KP. Clinical evaluation and management of neurogenic bowel after spinal cord injury. *Spinal Cord* 2000; **38**: 301–308.
- Thomas LA *et al.* Mechanism for the transit-induced increase in colonic deoxycholic acid formation in cholesterol cholelithiasis. *Gastroenterology* 2000; **119**: 806–815.
- Gustafsson U, Sahlin S, Einarsson C. Biliary lipid composition with cholesterol and pigment gallstones and gallstone-free subjects: deoxycholic acid does not contribute to formation of cholesterol gallstones. *Eur J Clin Invest* 2000; **30**: 1099–1106.