

Irritable bowel syndrome following laparoscopic cholecystectomy. A prospective cohort study

Síndrome de intestino irritable posterior a colecistectomía laparoscópica. Estudio de cohorte prospectivo

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Palabras clave:

Colecistectomía, laparoscopia, diarrea, síndrome de intestino irritable.

ABSTRACT

Introduction: Laparoscopic cholecystectomy is one of the most frequently performed digestive surgical procedures in the world. Irritable bowel syndrome has been reported to occur more frequently in patients submitted to cholecystectomy, especially the diarrhea-predominant subtype. **Objectives:** To evaluate the presence of irritable bowel syndrome before and after laparoscopic cholecystectomy. **Material and methods:** A prospective cohort study, with control group. Irritable bowel syndrome was defined according to ROMA IV criteria, and was followed up at one, three, six, and 12 months postoperatively in search of symptomatology. The statistical analysis was performed with Fisher's exact one-way test. **Results:** Out of 166 patients, six presented an irritable bowel syndrome beyond six months postoperatively. In the control group there was two new cases at the end of follow-up. There were eight cases of post-cholecystectomy syndrome. **Conclusions:** It was not possible to establish a relationship different from chance between patients who underwent laparoscopic cholecystectomy and the presence of irritable bowel syndrome in any of its variants.

RESUMEN

Introducción: La colecistectomía laparoscópica es uno de los procedimientos quirúrgicos digestivos que se realiza con más frecuencia en el mundo. Se ha descrito que el síndrome de intestino irritable se presenta con mayor frecuencia en pacientes sometidos a colecistectomía, sobre todo el subtipo con predominio de diarrea. **Objetivos:** Evaluar la presencia de síndrome de intestino irritable antes y después de una colecistectomía laparoscópica. **Material y métodos:** Estudio de cohorte prospectivo, con grupo de control. Se definió síndrome de intestino irritable de acuerdo con los criterios de ROMA IV, y se dio seguimiento al mes, tres, seis y 12 meses postoperatorios en busca de sintomatología. El análisis estadístico se realizó con prueba exacta de Fisher unidireccional. **Resultados:** De 166 pacientes, seis presentaron síndrome de intestino irritable más allá de los seis meses postoperatorios; en el grupo de control hubo dos casos nuevos al término del seguimiento. Se presentaron ocho casos de síndrome post-colecistectomía. **Conclusiones:** No se puede establecer una relación diferente al azar entre pacientes intervenidos de colecistectomía laparoscópica y la presencia de síndrome de intestino irritable en cualquiera de sus variantes.

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Abbreviations:

BLD = bladder lithiasis disease
LC = laparoscopic cholecystectomy
IBS = irritable bowel syndrome
IBS-D = irritable bowel syndrome-subtype diarrhea
IBS-C = irritable bowel syndrome-constipation subtype
IBS-M = irritable bowel syndrome-mixed subtype
PCS = post-cholecystectomy syndrome

INTRODUCTION

Bladder lithiasis disease (BLD) is highly prevalent in the western population.¹ Laparoscopic cholecystectomy (LC) is one of the most performed digestive surgical procedures worldwide; in the United States it

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exceeds 750,000 procedures per year.² Irritable bowel syndrome (IBS) is a common functional digestive disorder in general practice and in gastroenterology characterized by abdominal discomfort and pain and abnormal bowel habits, among other nonspecific symptoms.³ Ryle noted that multiple abdominal surgical procedures are notably more common in patients with this syndrome, such as hysterectomy, appendectomy and cholecystectomy.⁴ The multicenter collaborative study by Corazziari et al (MICOL) concluded that patients with IBS are more prone to cholecystectomy than the general population.⁵ A retrospective study by the Amieva-Balmori team,⁶ evaluated the presence of IBS and its subtypes according to the ROME IV criteria in a group of patients with a history of cholecystectomy, finding that irritable bowel syndrome subtype diarrhea (IBS-D) occurred more frequently in patients submitted to cholecystectomy patients. There are abdominal pain/discomfort⁷ in a non-negligible number of patients after cholecystectomy, and diarrhea stands out; however, there are no prospective studies that demonstrate this association, which is why we conducted the present prospective cohort study.

MATERIAL AND METHODS

This was a comparative, prospective, dynamic cohort, controlled study conducted at the Hospital Regional de Monterrey of the *Instituto para la Salud y Seguridad Social de los Trabajadores del Estado* (ISSSTE) in patients surgically intervened during 2017 and followed up during 2018. The study was approved by the ethics and research committee of hospital (folio

042, October 2016). According to probability sampling (10% difference in proportions, 5% adjusted for losses), 171 study subjects were included. Patients were not informed about the follow-up objective and were not given postoperative dietary recommendations different from those usually given for a healthy diet, with the aim of decreasing the Hawthorne effect. Patients with GBD diagnosis scheduled for CL and not having gastrointestinal alarm data suggesting other more serious disorders were randomly included (through a simple table of numbers). Patients with diagnosis of digestive malignancies, liver cirrhosis, upper or lower GI bleeding, chronic renal failure, uncontrolled diabetes, or psychiatric conditions that prevented a reliable direct questioning were excluded. Cases with IBS prior to surgery were also excluded from the analysis if they had been converted to open surgery and had presented any of the previously described situations during the intraoperative, immediate postoperative, and follow-up periods. The follow-up in search of IBS according to ROMA IV criteria (*Table 1*) was performed at one, three, six and 12 postoperative months. The investigator who performed the initial assessment was different from the surgeon, as well as the investigator of the subsequent follow-up. At the same time, an age- and sex-matched control group was included, randomly obtained from the general medical practice of two of the investigators, who were followed up in person and by telephone during the same periods of time, in search of symptoms compatible with IBS according to ROMA IV. This was done for both groups in these periods.⁸ Data were collected in an electronic data sheet,

Table 1: ROME IV diagnostic criteria.

Signs			
Abdominal pain,* at least one day a week (3-months minimum)	Related to defecation	Associated with a change in the frequency of stool	Associated with a change in the shape of the stool (Bristol scale)
* The presence of abdominal pain in addition to one or more of the signs shown is a necessary condition for diagnosis. Modified from: Sebastián-Domingo JJ. ⁸			

Table 2: Initial distribution of the groups to be followed, homogeneously distributed by age, sex, and prevalence of irritable bowel syndrome. N = 336.

	Patients scheduled for laparoscopic cholecystectomy N = 168	Control patients N = 168	Homogeneity (p-value)
Age (average) years	46.4	45.2 ± 10.0	p ≤ 0.01
Sex			
Female	105	105	p ≤ 0.01
Male	63	63	
IBS (initial)			
IBS-D	2	1	p ≤ 0.01
IBS-C	0	0	
IBS-M	0	1	
Remaining healthy patients	166	166	

IBS = irritable bowel syndrome, IBS-D = irritable bowel syndrome subtype diarrhea, IBS-C = irritable bowel syndrome subtype constipation, IBS-M = irritable bowel syndrome subtype mixed.

from the patient's clinical history that included all the questionnaires both preoperatively and at follow-up. The data obtained were tabulated to calculate the relative risk, absolute increase in risk, and one-way Fisher's exact test, taking as significant a p -value < 0.05.

RESULTS

Of a total of 171 patients with GBD sent to surgery during the study period, two were eliminated due to loss to follow-up, and one more due to the finding of gallbladder cancer, and for the statistical analysis, two with IBS prior two surgery were also eliminated (total losses: five cases, 2.92%). Of the total number of patients (166) who underwent surgery, 91.57% (152) were elective; 8.43% (14) were admitted through the emergency department for early LC for acute cholecystitis. The mean surgical time was 92 ± 51 minutes and there were no cases of open-surgery conversion (Table 2). At initial assessment, two cases of diarrhea subtype IBS were found in the group of cases that were to undergo LC; six more cases of diarrhea subtype IBS occurred during follow-up in the surgically operated group, with persistent symptoms even

12 months postoperatively (specifically IBS-D) (Table 3). It should be noted that eight patients presented symptoms (including diarrhea) from the first postoperative days compatible with post-cholecystectomy syndrome (PCS), which subsided within the first four postoperative weeks, and were different from those who presented IBS. In the control group, two cases were initially found, one diarrhea subtype and one mixed subtype; and during the follow-up period, two new cases were found, equally distributed. The statistical analysis showed a relative risk of 3.00 (0.61-14.54), the absolute risk increase (ARI) was 2.41 for IBS-D, with a p -value = 0.0875 (not statistically significant). Considering patients who presented with diarrhea, within the spectrum of symptoms of PCS, compared to the open population, their relative risk (RR) was 4 (0.86-18.55), the absolute risk increase was 4.05, with a p -value = 0.032 (statistically significant), with 28.5 as the number needed for harm (NNH). Although the RR seems to be high, it was not statistically significant, and that association seems to be given by chance (other variables). For post-cholecystectomy syndrome, the RR was four times higher; and the NNH leads us to conclude

that up to one in 28 patients undergoing LC may develop this syndrome, which will be transient, and a limited number of patients will develop chronic diarrhea apparently without a direct and complete relationship to the lack of gallbladder. There are other variables that should be studied.

DISCUSSION

The evidence^{5,6} derived from retrospective studies suggests that patients who develop IBS, mainly the diarrhea subtype (IBS-D), have a history of cholecystectomy,⁹ with no difference between conventional or laparoscopic. In the classic surgical literature,^{10,11} has mentioned the existence of diarrhea derived from the surgical procedure itself as a possible complication, even chronic, and hence the recommendations of restricting fatty foods in the diet after the surgical procedure, information that has passed from generation to generation in surgical teaching, although

without substantial evidence. We consider that there is no solid evidence to support this practice, as demonstrated in this work. An epidemiological study reported a higher frequency of IBS in patients who underwent hysterectomy and cholecystectomy;¹² and another study performed at the Mayo Clinic concludes that patients with cholecystectomy have a 2.2 higher risk of developing and irritable bowel syndrome.¹³ Manríquez and collaborators, in a study of 100 patients (non-probabilistic sample), found that 15% presented postoperative diarrhea and 8% had chronic diarrhea, and in the rest of their population it subsided within the first 28 days.¹⁴ We obtained similar data in our group, but with a probabilistic sample. The theory that supports the current conclusions is the result of some experiments in which the retention of some radiolabeled bile acids was evaluated in patients with IBS, which correlate with the severity of symptoms, especially in the mixed alternating and diarrhea-predominant varieties.¹⁵ Post-

Table 3: New cases of irritable bowel syndrome presented at follow-up. N = 166.

	Months			
	1	3	6	12
Patients undergoing laparoscopic cholecystectomy				
Postcholecystectomy syndrome	8*	0	0	0
IBS-D	0	6	6	6 [‡]
IBS-C	0	0	0	0
IBS-M	0	0	0	0
	Remaining healthy = 160			Total = 6
Control patients				
IBS-D	0	0	1	1 [‡]
IBS-C	0	0	0	0
IBS-M	0	1	1	1 [‡]
Total	Remaining healthy = 164			Total = 2

* For post cholecystectomy syndrome, a separate analysis is performed; cases of this syndrome presented rapidly and were self-limited also quickly.

‡ The patients who presented irritable bowel syndrome were different from those who presented post cholecystectomy syndrome. Patients with a previous diagnosis of irritable bowel syndrome were not included in the analysis. For descriptive purposes, they continued with the same symptoms after laparoscopic cholecystectomy.

IBS = irritable bowel syndrome, IBS-D = irritable bowel syndrome subtype diarrhea, IBS-C = irritable bowel syndrome subtype constipation, IBS-M = irritable bowel syndrome subtype mixed.

cholecystectomy syndrome has also been described,⁷ which should be differentiated from IBS-D by morning predilection of symptoms, intolerance to fatty foods, nausea, vomiting, aerophagia, aero-coly and, in some cases, fecal urgency¹⁶ that is clearly relieved by evacuation. The physiopathology of this syndrome was excellently described by Jaramillo and Otero.¹⁷ They stated that malabsorption of bile acids or their contribution increases the concentrations of these bile acids in the colon, which modifies the displacement of water and electrolytes, causing osmotic diarrhea, which could be due to a poorly diagnosed chronic cause, especially in patients with cholecystectomy cases¹⁸ and its possible treatment with bile acid sequestrants.¹⁹ However, the evidence from clinical studies not specifically designed has failed to demonstrate causality,^{6,7,20,21} therefore, there must be other variables besides bile acids in the pathophysiology of chronic diarrhea. Reviews on IBS continue to place a history of cholecystectomy in a statistically significant association with IBS according to ROMA criteria.²²⁻²⁴

CONCLUSIONS

Our team concluded that there is no a randomly different association between laparoscopic cholecystectomy and the development of symptoms of abdominal pain and chronic intermittent diarrhea compatible with the diagnosis of IBS-D.

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Ethical considerations and responsibility:

The procedures in humans must comply with the principles established in the Declaration of Helsinki of the World Medical Association (WMA) and with the provisions of the General Health Law Title Five and Regulations of the General Health Law on Research for Health, and NOM-

012SSA3-2012, which establishes the criteria for the execution of research projects for health in human beings, as well as with the rules of the Research Ethics Committee of the institution where they are carried out. In case of having a registration number, please provide it.

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