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Cholelithiasis Prophylaxis after Bariatric Procedures using Ursodeoxycholic Acid (UDCA)

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Abstract

Aims: An unfortunate metabolic complication of rapid weight loss after bariatric procedure is cholelithiasis. Serious complications from gall stones may occur.

A preventive therapy for gall stone formation is recommended. Prophylactic cholecystectomy remains controversial. An alternative for prophylaxis using Ursodeoxycholic Acid (UDCA) has been suggested.

This study determines the efficacy of non-surgical preventive option in cholelithiasis prophylaxis using Ursodeoxycholic Acid given in a daily dose of 500 mg for six months after bariatric procedure.

Methods: Patients with (LSG) laparoscopic sleeve gastrectomy and laparoscopic mingastric Bypass (LMGB) were enrolled in this study. This prospective study evaluated the effect of 250 mg of (UDCA) given twice daily, starting 15 days after surgery in group I versus control group II not given UDCA, and continuing for 6 months or until cholelithisis occur. Transabdominal ultrasound was done 2, 4 and 6 months after surgery or until gall stone develop. The result was found to be positive and due to this many patients received the correct method of dose.

Results: From June 2016 to April 2017, one hundred morbidly obese patients with BMI ≥ 40 Kg/m^2 with intact acalculous gall bladder were submitted to LSG and LMGB. The study showed that age, sex, initial body weight, BMI and EWL% and type of bariatric procedure have no role in increasing the risk of cholelithisis. There was a significant reduction in incidence of cholelithisis in patients taking UDCA in a dose of 250 mg twice daily after the procedure (6%) in comparison to 40% in the control group.

Conclusion: A daily dose of 500 mg Ursodeoxycholic Acid (UDCA) for 6 months is effective in cholelithiasis prophylaxis following gastric bariatric procedures.

Keywords: Bariatric surgery; Gall stone; Ursodeoxycholic Acid, Body mass index

Introduction

Obesity and rapid weight loss such as is usually experienced after bariatric surgery are major risk factors for cholelithiasis and biliary sludge formation [1].

The risk is 10%-25% in persons losing weight through very low calorie dieting (VLCD) and 35%-38% in morbid obese patients after bariatric procedures. The risk is maximal during the period of rapid weight loss and decreases when weight stabilizes around 2 years [2].

However, there is a high incidence of cholelithiasis in this group of patients, only a minority will develop symptomatic disease and 10%-15% will require cholecystectomy for complaints related to gall stone disease. Serious complications from gall stones such as cholecystitis, cholangitis, pancreatitis and cholecystoenteric fistula may occur [3,4]. Thus it is necessary to employ medical or surgical preventive methods for gall stone formation in this high risk group. Some centers recommend routine synchronous cholecystectomy during bariatric surgery. However this practice remains controversial because not all patients develop gall stones after bariatric surgery and prophylactic cholecystectomy during bariatric surgery can be a difficult procedure with a high incidence of complications and increase time of operation [5,6].

An attractive alternative to prophylactic cholecystectomy is the use of preventive medication such as Ursodeoxycholic Acid (UDCA) to prevent gall stone formation after bariatric surgery.

UDCA safely prevent gall stone formation in obese persons losing excessive and rapid weight during strict very low calorie dieting (VLCD) or after bariatric procedures. It inhibit biliary cholesterol crystallization [7].

The short term duration of use in compliant patients and safety of the drug makes it an effective non-surgical option in preventing gall stone formation during rapid weight loss after bariatric procedure [8].

Aim of the Study

This randomized controlled prospective study was designed to investigate and determine the efficacy and safety of non-surgical options as Ursodeoxycholic Acid (UDCA) in prevention of gall stone formation after bariatric surgery.

Patients and Methods

From June 2016 to April 2017 one hundred morbidly obese patients (BMI ≥ 40 Kg/m^2) with intact acalculous gall bladders were submitted to bariatric procedure (LS and MGB) in Cairo, Beni-Suef and Fayoum University hospitals. Informed consent was obtained from all patients.

Patients refusing to participate and patients with previous cholecystectomy or diagnosed gall stones preoperatively were excluded.

The patients were divided into two groups:

Group I: Included 50 morbid obese patients (BMI 40 Kg/m^2) submitted to LSG and MGB with postoperative prophylactic dose of UDCA given 15 Days after surgery and continuing for 6 months or until gall stone development.

Group II: Included 50 morbid obese patients (BMI 40 Kg/m^2) submitted to LSG and MGB without postoperative prophylaxis using UDCA.

All patients were subjected to history taking, full clinical evaluation as well as laboratory investigations. All patients had normal preoperative abdominal ultrasound as regard gall stones.

In the postoperative period, all patients were given 3rd generation cephalosporines, anticoagulants, opioids, proton pump inhibitors and antiemetics. All patients started early oral fluids after 6 hours if tolerated. The drain was removed before discharge.

The patients continued on a liquid diet only for two weeks, then advanced to semi-solid diet for another two weeks and then mashed food for two weeks then followed by regular diet.

Antihypertensive and oral hypoglycemic drugs and insulin were continued and adjusted by primary care physician. Patients also receive follow up nutritional counseling for a protein-enriched diet and multivitamins, oral iron and calcium supplements.

Group I patients were given Ursodeoxycholic Acid (UDCA) 250 mg caps twice daily for 6 months starting 15 days postoperative, while Group II patients were discharged without prescription of UDCA.

All patients in both groups were subjected to regular follow up by using clinical data and ultrasonography for early defection of cholelithiasis.

Abdominal ultrasound was obtained for all patients in both groups 2, 4 and 6 months following surgery or until gall stone formation with development of symptoms as nausea, vomiting and abdominal pain.

Data were statistically described in terms of mean ± standard deviation (± SD), median and range or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using student t test for independent samples. For comparing categorical data, Chi-square (× 2) test was performed. Exact test was used instead when the expected frequency is less than 5. P value less than 0.05 was considered statistically significant.

Results

One hundred morbidly obese patients with BMI ≥ 40 Kg/m^2 or BMI ≥ 35 Kg/m^2 with associated comorbidities were submitted to bariatric procedure (82 patients LSG and 18 MGB).

The study included 23 males and 77 females. The age of the patients ranged from 17 to 50 years with a mean age 30.63. The BMI was variable and ranged from 33 to 69 Kg/m^2 with a mean of 46.3.

The patients were divided into two groups:

Group I: Includes 50 morbidly obese patients, who received UDCA orally postoperative in a dose of 250 mg twice daily starting on the 15th day after surgery.

Group II: Includes 50 morbidly obese patients without receiving Ursodeoxycholic Acid (UDCA) postoperative. All procedures were performed laparoscopically with no mortalities and morbidities.

Results were collected regarding Age, Sex, BMI, Initial body weight, percentage of excess weight loss and type of bariatric procedure done. The efficiency of the drug (UDCA) in preventing cholelithiasis in group has been monitored during the first 6 months after the bariatric procedure, by regular transabdominal ultrasound at (2, 4, 6 months) or by development of symptomatic cholelithiasis.

Results in our study showed that age, sex and BMI have no role in increasing risk of development of cholelithiasis and the risk isn't specified to certain age group, as in age group (15-25 years) (25-45) and (45-64) incidence was 20.8% (5/24) 23% (17/74) and 50% (1/2) respectively.

Also sex is insignificant in increasing risk of development of cholelithiasis, as in females in evidence was 25.3% (19/77) while in males was 16% (4/23).

Results showed that initial body weight and BMI have no significant role in increasing risk as in patients with BMI <40, between 40-50 and >50 Kg/m^2 ,the incidences were 75% (3/4), 18.4% (14/76) and 30% (6/20) respectively.

In addition, percentage of excess weight loss (EWL%) has no effect on increasing incidence of gall stone development as patients with EWL <50%, from 50%-60% and >60% after 6 months showed incidence of 34.8% (7/16), 19.2% (5/26) and 19% (11/58) respectively.

In comparison between the types of bariatric procedures the incidence was near equal between La paroscopic sleeve gastrectomy (LSG) 22% (18/82) and mini gastric Bypass (MGB) 27.8% (5/18)

The use of ursodioxy cholic acid (UDCA) after bariatric procedure showed significant role in prophylaxis of gall stone development, incidence is 6% (3/50) in patients receiving (UDCA) in comparison to incidence 40% (20/50) in those not receiving UDCA after bariatric procedure (significant P value).

Finally, presentation of patients developing cholelithiasis after bariatric procedure included nausea and vomiting the most common presentation 56.5% (13/23) and those presenting with pain 34.8% (8/23) while those asymptomatic patients discovered by routine ultrasound were 8.7% (2/23). Therefore early postoperative nausea and

vomiting may be a symptom of early development of biliary mud or stones (P value significant).

Discussion

The prevalence of cholelithiasis in developed countries ranges between 6% and 16% in adults especially women during their reproductive years and increases to 30% in morbidly obese women [2].

Both Dieting and weight reduction surgeries are associated with an increasing risk of cholelithiasis.

Rapid and considerable weight loss generates an 18-fold increase in cholelithiasis, whereas less rapid weight loss appears relatively safe. The risk of cholelithiasis increases if weight loss is more than 24% and most form in the first 6 months after bariatric surgery with symptomatic onset after a mean period of 10.2 months [9].

Litho genesis is modified following weight reduction surgeries. It is postulated that during rapid weight loss, cholesterol is mobilized from fatty tissues enhancing cholesterol crystallization resulting in cholesterol I hypersaturation of bile.

Others found that decreased secretion of biliary acids due to caloric restriction and increased gall bladder secretion of mucin and calcium enhances crystallization [10].

Some studies have shown impaired gall bladder motility (stasis) secondary to decreased cholecystokinin secretion related to hypocaloric diet or obesity related resistance to cholecystokinin, to gastroduodenal exclusion or due to intraoperative injury to hepatic branches of the vagus nerves [11].

Pure restrictive procedures such lap sleeve Gastrectomy (LSG) and lap Gastric Banding (LGB) should result in less risk of cholelithiasis because food continues to follow the normal gastrointestinal transit, maintaining the enteric endocrine reflex intact .However ,the mechanism of cholelithiasis after SG remains unclear [12].

The incidence for both asymptomatic and symptomatic cholelithiasis seemed to be higher after malabsorptive procedures such as RYGB and Mini By pass [13].

In series using regular ultrasound screening after gastric bypass, the rate of asymptomatic gall stone ranged from 30% to 52.8% within 6 to 12 months after the operation with 7% to of 16% of patients experienced symptomatic gall stones [14].

Li et al. reported that LSG and RYGB had comparable incidences of symptomatic and complicated cholelithiasis [15]. The guidelines for Perioperative Nutritional, Metabolic and Nonsurgical Support of the Bariatric surgery patient now recommend an ultrasound examination within the first six months as a routine examination after bariatric surgery for detection of gall stones [16].

Efforts have been made to prevent cholelithiasis after bariatric procedures. Concomittant cholecystectomy had been proposed, but the added morbidities as well as prolongation of the operation time and hospital stay have rendered this option controversial. Raziel et al. found that concomittant prophylactic cholecystectomy with bariatric procedures should be applied only in the presence of symptomatic gall stones [17].

Worni et al. advocated the use of UDCA as a prophylactic measure against postoperative cholelithiasis. UDCA acts by inhibiting cholesterol secretion in bile, thereby preventing the supersaturation of bile and cholesterol stone formation [18].

Sugerman et al. and Miller et al. reported that daily oral administration of UDCA for 6 months was associated with a decreased rate of cholelithiasis after LSG [19,20]. In a study comprising 406 patients, and was the largest series to assess the prophylactic role of UDCA after LSG. It is found that the overall incidence of post LSG cholelithiasis ranges from 2% to 5% in group that did not receive UDCA therapy, which is close to the incidene of symptomatic gall stones after LSG (3.8%) reported by Li et al. [21].

This disparity is probably due to the different baseline patient characteristics between the studies and variable rates of EWL among patients in the first 3 months postoperatively.

At 1 Year after LSG, none of the patients who received prophylactic UDCA therapy developed cholelithiasis, while 5% of patients who did not receive UDCA therapy developed CL. Almost all patients who developed gall stones in this study were females in their third decade of life with a BMI over 50 Kg/m^2 [20].

In another study, the incidence of gall stone formation was 47.9% and the incidence of symptomatic gall stones was 22.9%. None of the weight loss parameters during the early and late postoperative period were significantly different between the patients who developed gall stones and those who did not [12].

Another meta-analysis of randomized controlled trials reported that the use of UDCA reduced the incidence of gall stones formation from 27.7% in placebo group to 8.8% in the treatment group [22]. These findings imply strongly the important role of UDCA in prevention of cholelithiasis.

Our study showed that using UDCA has significant role in prophylaxis of CL. Patients receiving UDCA developed CL by incidence of 6% and patients not receiving UDCA developed CL by incidence of 40%. In addition, Age, Sex, initial body weight, BMI and percentage of EWL and type of bariatric procedure have no significant role in increasing the risk of CL. Also Chang et al. reported that these factors are not predictive factors in postoperative cholelithiasis [3].

However, despite the encouraging results of UDCA, It has not yet been widely applied as a routine prophylactic measure against CL after bariatric surgery. This is likely due to the lack of distinct criteria that define the proper indications for UDCA based on measurable risk factors and to the adverse effects of UDCA including, nausea, vomiting and diarrhea, that affect patient compliance [22].

Conclusion

A daily dose of 500 mg Ursodeoxycholic Acid (UDCA) for 6 months is effective in cholelithiasis prophylaxis following gastric bariatric procedures.

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