

## The Role of Ursodeoxycholic Acid After Bariatric Surgery

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### ABSTRACT:

**Background:** currently obesity and overweight are two of the major public health problems worldwide, which haunts the health of more and more young people around the world, as this problem advances so does medicine, treatments and surgical procedures, such is the case of bariatric surgeries, which can have a great positive impact on the lives of patients who undergo these procedures, however, there are also post-surgical complications, such as acute cholestatic syndromes, which are becoming more and more frequent, so finding and describing a treatment to avoid these complications could be a fundamental piece in the management of these patients.

**Methods:** We conducted a purely observational and descriptive study by collecting data and information through a national and international literature review, where we selected control cases and meta-analysis which are detailed and described during this review.

**Results:** During the last years the popularity of the use of ursodeoxycholic acid has grown, since it has been mentioned its use out of indications as a prophylactic treatment after bariatric surgery, this alternative may sound favorable for the treating physician and for the patient, since it is safe and avoids complications according to different studies.

**Conclusions:** Multiple studies, including all those reviewed during this research show a highly positive benefit of the use of ursodeoxycholic acid, it is noteworthy that during this research, the only study that does not mention a positive effect of the use of ursodeoxycholic acid is the study of Muriel Coupaye et al. which mentions that no difference was found between the groups treated and not treated with ursodeoxycholic acid with 500mg/day.

**KEYWORDS:** Ursodeoxycholic Acid, bariatric surgery, cholestatic syndromes, gallbladder stones, cholecystectomy.

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### INTRODUCTION

Nowadays obesity and overweight are one of the major public health problems worldwide, WHO estimated that in the year 2022 16% of adults aged 18 years and older, were obese globally and that the prevalence of obesity worldwide increased by more than 100% between 1990 to 2022 <sup>1</sup>. In addition to this, obesity causes an increased risk of type 2 diabetes, heart disease, bone disease as well as increases the risk of certain types of cancer due to the pro-inflammatory state of obesity <sup>1</sup>.

Bariatric surgery has had a significant increase in recent years, due to the need for effective and efficient long-term treatment for both obesity and associated comorbidities, however not everything is sweet within these surgical procedures, since bariatric surgeries (Roux-en-Y gastric bypass, gastric sleeve and adjustable gastric banding) are a risk factor for the development of bile duct stones due to the oversaturation of bile by rapid weight loss and mobilization of cholesterol <sup>3</sup>.

Risk factors for acute biliary pathology have been clearly identified where female sex, age, overweight and obesity, as well as rapid weight loss <sup>4</sup>. Several studies show that a decrease between 4 and 10 kg in two years is related to an increase of up to 44% risk for developing cholelithiasis, compared to a decrease of less than 4 kg; the decrease of more than 10 kg in a short period of time the risk increases by 94% for developing biliary cholelithiasis <sup>5</sup>.

Several studies report that cholelithiasis increases after bariatric surgery, up to 5.5 times more likely to undergo cholecystectomy compared to people without bariatric surgery, this risk mainly increases within the first 12 months after surgery, as well as in patients who already had biliary pathologies in an asymptomatic way increase the chances of becoming acute and needing a cholecystectomy <sup>6</sup>. Due to this there are some therapeutic measures that can be used to avoid acute cholelithiasis after bariatric surgery, such is the case of a prophylactic intraoperative cholecystectomy, however this procedure has some contraindications such as: heart failure, unstable coronary artery disease, terminal lung disease, active cancer, liver cirrhosis, pulmonary hypertension, drug dependence, uncontrolled alcoholism, Crohn's disease, severe impairment of intellectual capacity, current or expected pregnancy in the next 1 to

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2 years<sup>7</sup>. Another measure used conservatively is the use of ursodeoxycholic acid, multiple authors and studies report that management using this drug is safe as it significantly prevents gallstone formation following bariatric procedures<sup>3,8</sup>.

The proper management of gallstones and gallbladder

disease in these patients is controversial and not yet fully clarified as several therapeutic modalities can be used, including intraoperative cholecystectomy, regardless of the presence or not of gallstones (symptomatic/asymptomatic), simultaneous cholecystectomy in patients with gallstones with previous symptomatology, and management with prophylactic administration of ursodeoxycholic acid<sup>5</sup>.

### METHODOLOGY

An observational and descriptive study was conducted by collecting data and information through national and international literature review from 2005 to 2024, in different platforms: Google Scholar, Pubmed, SciELO, Elsevier, Frontiers in Neurology. Multiple articles were selected: case reports and meta-analysis through search terms: “ursodeoxycholic acid and bariatric surgery” “bariatric surgery and cholelithiasis”.

### OBJECTIVE

To identify and describe the role of ursodeoxycholic acid as a prophylaxis therapy in patients undergoing bariatric surgery who have a high probability of acute cholelithiasis secondary to such surgery.

### RESULTS

Author	Year	Total sample	Excluded	Control group	Patients without ursodexocholic acid treatment	Patients with ursodexocholic acid	Ursodexocholic acid dosage	Decrease of cholestatic syndromes	Surgical procedure
Andrea Della Penna <i>et al</i> <sup>34</sup>	2019	838	135	0	642	61	500 mg/day	Only 2 female patients became symptomatic without requiring cholecystectomy.	593 Sleeve gastrectomy (SGx) and 245 Roux-en-Y Gastric Bypass (RYGB)
Muriel Coupaye <i>et al</i> <sup>23</sup>	2019	223	34	189	46	143	500 mg/day	It was confirmed that 500 mg/day of ursodeoxycholic acid for 6 months is very effective in preventing gallstone formation at 1 year but also at 3 years after bariatric surgery.	Roux-en-Y Gastric Bypass (RYGB)
Manley C. Uy <i>et al</i> <sup>36</sup>	2018	521	0	521	199	322	300 - 1,200 mg/day	A significant difference in the relative risks of gallstone formation was found in favor of ursodeoxycholic acid.	Roux-en-Y Gastric Bypass (RYGB)
Lindsay B. Adams <i>et al</i> <sup>37</sup>	2015	75	0	75	38	37	300mg/day for 6 months	We found a significant difference in the number of patients reporting gallstones or biliary sludge to compliance with ursodeoxycholic acid prescription after the first 6 months.	Roux-en-Y Gastric Bypass (RYGB)
Muriel Coupaye <i>et al</i> <sup>38</sup>	2016	466	126	340	34	306	500mg/day for 6 months	No difference was found between the groups treated and untreated with ursodeoxycholic acid at 500mg/day.	Roux-en-Y Gastric Bypass (RYGB) and Sleeve gastrectomy (SG)

**Figure 1:** description and detail of articles reviewed and analyzed

Ursodeoxycholic acid is a drug currently indicated for dissolution of cholesterol gallstones, specifically; radiolucent and functionally healthy gallbladder stones, as well as in treatment of primary biliary cirrhosis. It has shown its ability to desaturate lithogenic bile with subsequent lysis of cholesterol stones<sup>33</sup>.

During the last few years the popularity of ursodeoxycholic acid has grown, since its off-label use has been mentioned as a prophylactic treatment after bariatric surgery, this alternative may sound favorable for the treating physician and for the patient, since it is safe and avoids complications according to different authors in studies and analysis in patients.

In a 2019 study Andrea Della Penna et al. evaluated 838 patients post bariatric surgery, which 61 patients were administered 500 mg/day of ursodeoxycholic acid, only 2 female patients had cholestatic syndromes without requiring surgical management<sup>34</sup>. In 2019 Muriel Coupaye et al. followed 223 post bariatric surgery patients, of which 143 patients were administered ursodeoxycholic acid 500mg/day post-surgical procedure for 6 months, confirming the efficacy of ursodeoxycholic acid<sup>35</sup>. Manley C. Uy et al. during 2018, analyzed a sample of 521 postoperative patients, 322 patients were treated with 300-1200 mg ursodeoxycholic acid per day, significant differences in gallstone formation were demonstrated in favor of ursodeoxycholic acid<sup>36</sup>. In 2015 Lindsay B. Adams et al. evaluated a total sample of 75 postoperative patients, of which 37 patients were administered 300mg/day of ursodeoxycholic

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acid, significant differences were found in favor of compliance with the drug prescription<sup>37</sup>. Muriel Coupaye et al. during 2016, studied a total of 466 patients of which 306 patients were treated with ursodeoxycholic acid and 34 without treatment, this study mentions that there is no significant difference before the use of Ursodeoxycholic Acid (**Figure 1**)<sup>38</sup>.

### DISCUSSION

There is clinical evidence on the high incidence of cholelithiasis following bariatric surgery including: Roux-en-Y gastric bypass, gastric sleeve and adjustable gastric banding<sup>10</sup>; being of utmost importance the diagnosis and prevention of calculi in the preoperative assessment, however in the previous studies the efficacy and evidence of the use of ursodeoxycholic acid in the prevention of complications following a surgical procedure compared to patients who were not administered with ursodeoxycholic acid<sup>16</sup>. The studies collected demonstrated a high prevalence of patients with cholestatic syndromes following bariatric surgery in those who were not given prophylactic and post-surgical treatment with ursodeoxycholic acid. The incidence of cholelithiasis after the surgical procedure undoubtedly decreases with the use of ursodeoxycholic acid, however there is variability of values in the literature depending on the design of the study.

### CONCLUSION

After bariatric surgery, accelerated weight loss contributes to the development of gallstones, other influencing factors are: presence of asymptomatic cholelithiasis and absence of cholecystectomy prior to the surgical procedure; ursodeoxycholic acid is a secondary bile acid that inhibits the secretion and saturation of cholesterol in the bile, administered as a drug it helps to be less prone to gallstone formation and its complications.

We can conclude that different studies and authors demonstrate the efficacy and safety of the administration of 250-500 mg daily of ursodeoxycholic acid for 6 months for the prevention of cholelithiasis after bariatric surgery. All the studies show a benefit/positive effect of the use of ursodeoxycholic acid, during this research, the only study that does not mention a positive effect of the use of ursodeoxycholic acid is the study by Muriel Coupaye et al. which mentions that no difference was found between the groups treated and not treated with ursodeoxycholic acid with 500mg/day, so we conclude that the sample to which ursodeoxycholic acid was not administered was very small, 34 patients: a statistically non-significant sample compared to the sample that was administered the drug to 306 patients.

### CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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