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Original Article

Effectiveness of ursodeoxycholic acid for the treatment of gall bladder stones and sludge in pregnant women

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Abstract

Aim: The objective of this study is to evaluate the effectiveness of ursodeoxycholic acid (UDCA) for the treatment of symptomatic pregnant women with gall bladder stones and/or sludge.

Materials and Methods: Gynecology and obstetrics clinic patients who were symptomatic with gallbladder stones and/or microlithiasis were included in the study. Group 1 consisted of cases with conservative treatment and group 2 consisted of cases with UDCA treatment. After treatment, the groups were compared for symptomatic and radiological relief and hospitalization.

Results: For group 2, the mean treatment time with UDCA was 7.6 weeks. After treatment, a full cure was achieved in 28% of cases and symptomatic relief was achieved in 36% of cases. In group one; there was response to treatment in only 12% of cases. In the UDCA group, none of the patients needed hospitalization; however, in the conservative treatment group, five cases needed hospitalization.

Conclusion: UDCA is effective for the treatment of symptomatic gall bladder disease in pregnancy. It both relieves symptoms and decreases the need for hospitalization.

Keywords: Gall bladder; gallstone; pregnancy; sludge; ursodeoxycholic acid

INTRODUCTION

Gall bladder cholesterol stones are more common in women. Pregnancy is a known risk factor for gall bladder stones and sludge. There is a positive relationship between gallbladder stones and the number of pregnancies. A decrease in bladder motility due to increased levels of progesterone and changes in lipid metabolism play important roles in the formation of stones (1-3). Gall bladder stones and sludge can cause complications, such as cholecystitis, cholangitis and pancreatitis. Gall bladder disorders in pregnancy may require hospitalization and invasive treatment modalities, such as cholecystectomy or endoscopic retrograde cholangiopancreatography (ERCP). Moreover, complications due to stones may cause mortality and morbidity, both for the mother and fetus (4,5). In most cases, gall bladder disorders relieve after delivery. Therefore, conservative methods are suggested for such complications during pregnancy, (1).

Ursodeoxycholic acid (UDCA) has been used for the treatment of gall bladder stones since 1972. UDCA decreases stone formation and relieves symptoms by improving bladder muscle contraction and decreasing cholesterol levels in bile (6,7).

The effects of UDCA on cholesterol stones are well known. However, there are no studies showing the effect on bile stones/sludge in pregnancy. The objective of this study is to evaluate the effect of UDCA for the treatment of symptomatic gall bladder stones and/or sludge during pregnancy.

MATERIALS and METHODS

Study Design

This study, cross-sectional and single-center, was conducted from 1 Jan 2016 to 31 Dec 2019 in the general surgery and Gynecology and obstetrics clinics in accordance with the Declaration of Helsinki of the World

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Medical Association after being approved by the Medical University Ethics Review Committee . Informed consents ware obtained from all patients.

Pregnant patients who presented to the gynecology and obstetrics clinic and general surgery clinic with the complaint of symptomatic gallstones and who had gallstones and sludge in ultrasonography were included in the study. For clinically symptomatic gallstones, colic right upper quadrant pain (biliary colic) was based. Also, those patients who had nausea and vomiting were evaluated further. All patients underwent ultrasonography to confirm the presence of stones and or sludge in the gallbladder. As a result, patients who clinically described biliary colic and whose ultrasonography was compatible with stone and sludge were included in the study. Patients with a history of gallstones and those who had previously received medical treatment for gallstones, those with stones larger than one cm in ultrasonography, those who did not accept medical treatment, and those with gestational week <12 or> 32 were excluded from the study. In addition, patients who gave up treatment during the study left the study.

Study Groups

Patients were divided into the two groups as follows: group 1; conservative treatment group and group 2; UDCA treatment group. Patients in the group 1 were given analgesic and spasmolytic agents, along with oral or intravenous fluid therapy. Patients in the group 2 were administrated orally 10 mg/kg/day UDCA, divided into two doses. Treatment of patients whose clinical complaints eased or disappeared and gallstone or sludge disappeared on ultrasonography was stopped. Treatment was continued for a maximum of two months, and patients who could not respond to two months of treatment were considered to be resistant to treatment and directed to surgery.

Ultrasonography and Improvement Subgroups

According to the USG findings, patients were divided into 5 subgroups; total bile sludge, bile sludge >50%, bile sludge <50%, only microlithiasis, and sludge+microlithiasis.

According to radiological and clinical improvements, patients were divided into 5 subgroups; total radiologic and symptomatic relief, only symptomatic relief, symptomatic relief with partial radiologic relief, and no relief.

Follow-up

Both a gynecologist and a general surgeon followed the all patients. At the time of gallbladder complications such as, cholangitis, acute cholecystitis, choledocholithiasis, and pancreatitis patients were hospitalized. After delivery, the patients were controlled for a follow up visit at three and six months.

Statistical analysis

Data were analyzed using SPSS (Statistical Package for Social Science) for Windows 15.0 package program. Data normality was tested by one-sample Kolmogorov-Smirnov test. . Continuous variables were given as mean± standard deviation, and were compared with One-Way ANOVA or Kruskal Wallis variance analysis. When p value was significant, Mann-Whitney U multi variance analysis was used to detect the group creating the difference. Non-continuous variables were given as median (min-max), and were compared using Chi-Square test. A p value < 0.05 was considered statistically significant.

RESULTS

Demographic features of patients are summarized in Table 1. The mean age of the patients was 27.9±7 years, and their mean gestational age was 19.2±6.7 weeks. The groups were similar in terms of age, gestational week, parity and body mass index (BMI). In the group 2, no patients needed hospitalization due to biliary complications during pregnancy. However, in the group 1, five cases (1-3 times) required hospitalization (p=0.045).

Table 1. Age, gestational age, parity and body mass index of the patients

	Group 1	Group 2	p
Age	28.9±6.7	26.9±7.4	0.865
Gestational age	18.8±7.3	19.6±6.2	0.712
Multiparity	19	13	0.102
Nulliparity	6	12	0.320
BMI	27.4±5.6	24.8±3.7	0.452
Hospitalization	5	0	0.045

BMI: body mass index

Ultrasonographic findings of the patients and patient's complaints are given in Table 2 and 3. The groups were similar regarding patient complaints and the amount and density of stones and sludge in the gall bladder.

Table 2. Ultrasonographic findings of the patients

Sludge-Stone	Group 1	Group 2	p
Total gall bladder stone	3	5	0.152
<50% gall bladder sludge	5	2	0.346
>50% gall bladder sludge	1	2	0.404
Microlithiasis	15	10	0.389
Sludge and stone	2	6	0.212

Table 3. Patient's complaints

Complaint	Group 1	Group 2	p
Nausea vomiting	15	7	0.102
Pain	6	5	0.895
Itching	1	3	0.223
Weight loss and decreased oral intake	4	6	0.202
Other	2	3	0.456

Relief rates after the treatment are given in Table 4. Mean time of patients in the group 2 received UDCA

treatment was 7.6±1 weeks. After treatment, 28% of the patients (n=7) achieved total relief (p=0.130), 36% (n=9) had only symptomatic relief (p=0.010), and 32% (n=8) had symptomatic relief with partial radiological relief (p=0.004). There was only one treatment resistant case. In the group 1, there was relief of symptoms in only 12% (n=3) of patients.

Table 4. Relief rates after the treatment (symptomatic and ultrasonographic)

Treatment result	Group 1	Group 2	p
No change	22	1	<0.001
Full relief	2	7	0.130
Only symptomatic relief	1	9	0.010
Symptomatic and partial radiological relief	0	8	0.004

In nine patients who experienced total relief (2 cases in group 1 and 7 cases in the group 2), there were no symptoms and no pathological findings on USG at six months follow up. Eight of those cases had sludge in the gall bladder.

Laparoscopic cholecystectomy was necessary for six symptomatic cases with cesarean-section and six cases in the first six months after the delivery. No patients needed surgery during pregnancy.

DISCUSSION

UDCA treatment is effective for symptomatic relief and decreases the need for hospitalization in patients with symptomatic gall bladder stones during pregnancy. Moreover, cases with full relief had no biliary pathology at the six months follow up after pregnancy.

Excluding obstetric problems, biliary disorders are the second most common reason for abdominal pain during pregnancy. Biliary stone or sludge formation are observed in 12% of all pregnancies. However, during pregnancy or during the first year after delivery, cholecystectomy is necessary for only 1-3% of cases (1,3,8,9). In symptomatic cases, conservative treatment causes frequent hospitalizations. For these patients, cholecystectomy may be need during the pregnancy or during the early period after delivery due to clinical symptoms and biliary complications. Moreover, cholecystectomy is less common during pregnancy (7.5-17%), although nearly 75-80% of the cases require surgery during the first three months after delivery. In our study, this ratio was 24%.

In symptomatic cases, invasive methods, such as surgery or ERCP are suggested (10,11). ERCP and laparoscopic cholecystectomy are not reported to increase maternal and fetal mortality. However, according to some reports, laparoscopic cholecystectomy during pregnancy increases cost, hospital stay and morbidity (11,12).

UDCA has been used for a long time in the treatment of gallstones. The effectiveness of UDCA for treating cholesterol stones is between 30-80%, and 50% of the cases do not have recurrences during the long-term follow up (13-15). After the dissemination of laparoscopic cholecystectomy with low morbidity and mortality rates, the use of medical treatment modalities became less common. Recently, UDCA use is recommended for avoiding gall bladder stone formation during the rapid weight loss period after bariatric surgery (16-18). Moreover, UDCA is effective for the prevention of stent obstruction for non-extractable biliary duct stones (19). UDCA improves gall bladder contraction and function by decreasing oxidative stress (6,19). However, according to several authors, UDCA does not improve symptoms in cases with cholesterol stones and these authors suggest early laparoscopic cholecystectomy (20).

The pregnancy status of UDCA is class B, and therefore it can be used during pregnancy after the first trimester. Pregnancy induced intrahepatic cholestasis is a temporary situation that occurs during the second and third trimester, causing itching and an increase in liver enzymes and bilirubin levels. It is associated with increased fetal mortality and morbidity. UDCA is effective in 90% of cases with intrahepatic cholestasis. In pregnancy induced cholestasis, UDCA use is safe for both the mother and fetus (21-23).

The primary limitations of this study include the small treatment group and a shorter period of UDCA administration than is generally suggested. Moreover, the groups are heterogeneous because both sludge and microlithiasis cases are included in the study.

CONCLUSION

In conclusion, UDCA is effective for the symptomatic relief of and decreased need for hospitalization due to gall bladder stones/sludge. Furthermore, it is useful for both the treatment and prevention of complications due to pregnancy-induced gall bladder sludge. For this reason, we believe that UDCA can be used safely both in reducing symptoms and preventing complications in the second trimester, especially when findings related to gallstones occur. However, we think that comprehensive studies should be conducted to determine the maximum dose that can be used, whether it is safe to use it in other trimesters of pregnancy and the necessity of surgery following the end of pregnancy.

Conflict of interest : The authors declare that they have no competing interest.

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