

EFFECTS OF BILE SALTS AND HYMECROMONE ON GALLSTONE RECURRENCE IN ADULT PATIENTS AFTER LAPAROSCOPIC CHOLECYSTOLITHOTOMY

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EFEKTI ŽUČNIH SOLI I HIMEKROMONA NA RECIDIV ŽUČNIH KAMENACA KOD ODRASLIH PACIJENATA NAKON LAPAROSKOPSKE HOLECISTOLITOTOMIJE

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ABSTRACT

Objective. This study aimed to evaluate the effectiveness of comprehensive medical support in restoring gallbladder functionality and preventing the recurrence of gallstone disease (GSD) after organ-preserving cholecystolithotomy.

Methods. The study was retrospective in design, covering the period from 2018 to 2024, and was conducted at a medical centre “Gastroclinic” in Almaty, Kazakhstan, a country with a high prevalence of GSD. It included 115 patients aged 18 to 65 years who underwent cholecystolithotomy. Of these, 98 patients remained under dynamic observation for a specified follow-up period. To monitor gallbladder status and evaluate treatment effectiveness, ultrasound examinations (US) were performed preoperatively, postoperatively, and periodically during the observation period.

Results. The results of US indicated that complex drug therapy facilitated the normalisation of gallbladder wall size and thickness, as well as improved contractile function. Long-term follow-up revealed that 98.6% of patients retained normal gallbladder contractility, the recurrence rate of cholelithiasis was only 0.07%, and sludge formation was observed in 8.9% of cases. In conclusion, complex pharmacotherapy following cholecystolithotomy with gallbladder preservation is an effective approach for restoring organ function, preventing recurrent stone formation, and enhancing patients' quality of life.

Conclusion. The data obtained from this study can inform the development of clinical guidelines for the postoperative management of patients following gallstone removal with organ preservation.

Key words: drug therapy; postoperative period; prevention; cholelithiasis.

SAŽETAK

Cilj. Cilj ove studije bio je da se proceni efikasnost sveobuhvatne medicinske podrške u obnavljanju funkcionalnosti žučne kese i sprečavanju ponovne pojave bolesti žučnih kamenaca (BŽK) nakon holecistolitotomije sa očuvanjem organa.

Metode. Rađena je studija retrospektivnog dizajna koja je obuhvatala period od 2018. do 2024. godine i sprovedena je u medicinskom centru u Almatiju, u Kazahstanu, zemlji sa visokom prevalencijom BŽK. Obuhvatila je 115 pacijenata starosti od 18 do 65 godina koji su podvrgnuti holecistolitotomiji. Od ukupnog broja pacijenata njih 98 je dinamički praćeno tokom određenog perioda. Da bi se pratio status žučne kese i procenila efikasnost lečenja obavljani su ultrazvučni pregledi (UZ) preoperativno, postoperativno i periodično tokom perioda posmatranja. Sveobuhvatna procena uključivala je takođe i opštu analizu urina sprovedenu pre i posle operacije.

Rezultati. Rezultati UZ-a su pokazali da je kompleksna terapija lekovima olakšala normalizaciju veličine i debljine zida žučne kese i poboljšala kontraktilnu funkciju. Dugoročno praćenje je pokazalo da je 98,6% pacijenata zadržalo normalnu kontraktilnost žučne kese, stopa recidiva holelitijaze bila je samo 0,07%, a formiranje mulja primećeno je u 8,9% slučajeva. Zaključno, kompleksna farmakoterapija nakon holecistolitotomije sa očuvanjem žučne kese efikasan je pristup za obnavljanje funkcije organa, sprečavanje rekurentnog formiranja kamena i poboljšanje kvaliteta života pacijenata.

Zaključak. Podaci dobijeni iz ove studije mogu da posluže za razvoj kliničkih smernica za postoperativno lečenje pacijenata nakon uklanjanja žučnih kamenaca uz očuvanje organa.

Cljučne reči: farmakoterapija; postoperativni period; prevencija; holelitijaza.

INTRODUCTION

In modern medicine, significant emphasis is placed on organ preservation in treatment of various pathologies. In cases of GSD, when gallstones are removed while preserving the gallbladder, several challenges arise. Patients frequently experience recurrences, impaired gallbladder functionality, and associated complications due to insufficiently effective pharmacological support. The absence of standardised protocols for postoperative drug therapy results in inconsistent clinical outcomes and negatively impacts patients' quality of life. As noted by Gutt et al. (1) and Lee et al. (2), pharmacological research has yet to develop a drug capable of dissolving all types of gallstones. According to studies by Nassar and Richter (3), as well as Liu et al. (4), gallstones, unlike kidney stones, lack a direct outlet to the external environment, except in the case of choledochal stones. Chemical litholysis methods are further complicated by the requirement to puncture the gallbladder, coupled with the fact that not all pharmacological agents can penetrate the liver and gallbladder effectively.

In a study by Wang et al. (5), the efficacy of a laparoscopic gallbladder-preserving procedure was evaluated in patients with primary bile duct stones. The researchers aimed to compare this technique with standard approaches, which often involve gallbladder removal. An analysis of data from 105 patients demonstrated that the method effectively removed stones without increasing the risk of complications such as infections or rehospitalisation. There were no significant differences in the incidence of complications between patients with and without gallstones. However, the limited follow-up period raises questions about the long-term effectiveness of the procedure and its ability to prevent stone recurrence.

Ai et al. (6) investigated changes in gallbladder contractile function in patients following minimally invasive stone removal surgery. The study included 95 patients with acute cholecystitis and obstructed stones. The researchers observed significant improvements in gallbladder function one and two years after the intervention. Key factors influencing outcomes included the age of the patients, the presence of comorbidities such as diabetes, and the duration of the surgical procedure. These findings underscore the benefits of organ preservation but also highlight the need for optimising patient selection criteria and ensuring long-term monitoring to mitigate the risk of recurrent stones.

A study by Yang et al. (7) evaluated the efficacy and safety of ERCP for removing bile duct and gallbladder stones while preserving the gallbladder. The participants were patients with choledocholithiasis and cholelithiasis. The procedure achieved a high technical success rate with a low complication rate. However, 16% of patients experienced stone recurrence within 36 months. The authors noted that while the method is promising,

strategies to reduce recurrence are essential, particularly in cases involving significant gallbladder lesions.

Xu et al. (8) examined the use of endoscopic transabdominal cholecystolithotomy for treating GSD. The primary aim was to assess the safety and efficacy of this minimally invasive approach. The procedure was successfully completed in 97.6% of cases; however, 2.6% of patients had residual stones, and 5.2% experienced recurrences within one year. A notable limitation of the study is the lack of data on long-term outcomes, particularly concerning stone recurrence.

Research in Kazakhstan indicates a rising prevalence of gallbladder illnesses, particularly gallstone disease (GSD), among children and adolescents in the southern areas, with greater rates observed in teenagers compared to younger children (9). The production of gallstones is a multifactorial process influenced by bile supersaturation with cholesterol, resulting from excessive liver secretion, diminished bile acid concentration, or an imbalanced bile composition, which promotes the formation of cholesterol crystals and their aggregation, aided by bile mucin (10). The microbiota, comprising *Helicobacter pylori*, *Escherichia coli*, and *Clostridium* spp., facilitates bile acid modification, leading to supersaturation and crystal precipitation, while β -glucuronidase-producing bacteria such as *Streptococcus* and *Staphylococcus* assist in biofilm formation and crystal aggregation (11, 12). Dysbiosis, characterised by a diminished diversity of advantageous gut bacteria, such as *Faecalibacterium* and *Lachnospira*, constitutes an additional risk factor for GSD (13). Genetic abnormalities in cholesterol transporters (e.g., ABCG5/8) and cholecystokinin receptors, along with a familial predisposition to GSD, elevate the risk of stone formation (14, 15). Lifestyle variables such as physical inactivity, combined with hormonal alterations during pregnancy, especially in women over 40, significantly increase the risk by diminishing bile secretion and encouraging bile stasis (16, 17). In conclusion, GSD results from a multifaceted interplay of genetic, metabolic, immunological, and behavioural variables.

A significant body of research has focused on the treatment of patients with gallbladder stones. However, studies addressing the medical support of patients following the removal of gallstones while preserving the gallbladder remain insufficient. This gap underscores the necessity of the present study. The aim of this work is to identify the most effective medical strategies for optimising postoperative care in patients after gallstone removal with organ preservation. The focus is on preventing complications, restoring organ functionality, and improving patients' quality of life. To achieve this objective, the following research tasks were undertaken: to analyse the mechanisms of stone formation and the risk factors associated with GSD; to evaluate the effectiveness of various medical strategies in providing postoperative

support to patients; to assess the impact of the prescribed pharmacotherapy on the restoration of gallbladder functional activity and on patients' quality of life during the postoperative period.

PATIENTS AND METHODS

This study is a retrospective observational study conducted from 2018 to 2024 at a medical centre "Gastroclinic" in Almaty, Kazakhstan. A total of 115 patients aged 18 to 65 years diagnosed with cholelithiasis who underwent gallbladder-sparing cholecystolithotomy at the centre during the specified period participated in the study. The following criteria were used for inclusion in the sample: confirmed diagnosis of cholelithiasis, suitability for organ-sparing surgery, ability to provide informed consent, and willingness to adhere to postoperative protocols. The following criteria were to exclude patients from the sample: the presence of malignant neoplasms, severe concomitant diseases that are contraindicated for surgery, pregnancy, and inability to adhere to the follow-up schedule. The sample was formed sequentially, including all patients who met the criteria during the study period. After surgery, a total of 98 patients remained on regular outpatient follow-up at this medical centre, the rest were excluded due to relocation, loss of contact, or return to their primary care physicians in other countries (including Tajikistan and Uzbekistan). Among the study subjects, there were 72 women and 26 men, the mean age was 47 years (range 18 to 65 years). This study aligned with the ethical principles of research, including anonymity, confidentiality, and beneficence. Ethical approval of the study was obtained on January 21, 2018 from the Health Research Ethics Commission of the Kazakh National Medical University named after S.D. Asfendiyarov (No. 8417).

The laparoscopic method for gallstone extraction while retaining the gallbladder, called cholecystolithotomy, was executed. The procedure began with a series of small incisions in the abdominal wall, allowing for the insertion of laparoscopic equipment and a camera. The surgeon meticulously examined the gallbladder and bile ducts to identify the stones. Upon identification, the stones were meticulously retrieved from the gallbladder. In instances where the stones were challenging to extract or had resulted in problems such as inflammation or infection, further measures, including partial ductal dissection, were implemented to guarantee thorough stone removal without compromising the gallbladder. Following the extraction of the stones, the gallbladder was retained, and the surgical incision was sutured.

The fundamental process of cholecystolithotomy remained uniform across all patients, while several adaptations were implemented according to specific patient circumstances. In instances when patients presented with comorbidities such as elevated cholesterol

levels or liver dysfunction, supplementary therapies, including hepatoprotectors, were incorporated into their postoperative management to facilitate recovery and reduce the likelihood of problems. Postoperative ultrasound surveillance was utilised to assess the recovery of gallbladder function, including its dimensions, wall thickness, and contractile capacity. The individualised strategy for postoperative medication, incorporating agents like hymecromone and bile acids (ursodeoxycholic and taurodeoxycholic acids), was customised according to the patient's specific conditions and the dynamics assessed through ultrasound evaluations.

To restore gallbladder function and prevent stone recurrence, medications such as hymecromone (Odeston), ursodeoxycholic acid (Ursofalk, Ursosan, Ursaktiv), and taurodeoxycholic acid (TUDCA) were prescribed. The dosages and duration of these treatments were determined and adjusted according to the results of US. US were conducted using high-frequency sensors to evaluate the size of the gallbladder, wall thickness, the presence of residual stones or sludge, and contractile ability following a choleretic breakfast. These analyses facilitated the detection of potential complications and enabled monitoring of recovery dynamics.

The results were analysed using SPSS statistical software, with a significance level set at $p < 0.05$. The primary evaluated indicators included the recurrence frequency of GSD, the presence of sludge, gallbladder contractile function, and the quality of life of patients based on their self-assessments. A comparative analysis of preoperative and postoperative parameters was performed to evaluate the effects of pharmacological interventions.

RESULTS

In the postoperative period following cholecystolithotomy, drugs such as hymecromone, ursodeoxycholic acid, and taurodeoxycholic acid were utilised to restore the normal functional activity of the gallbladder. These medications played a vital role in improving bile secretion, eliminating bile stasis, and preventing the re-formation of stones. Their administration helped maintain the optimal concentration of bile acids, which is crucial for normalising metabolic processes within the biliary system. The prescription of therapy was tailored to the individual characteristics of each patient's condition, based on the results of diagnostic studies. Depending on the clinical presentation, physicians employed combinations of these drugs or prescribed them individually to achieve a comprehensive effect on the functional state of the gallbladder. The treatment regimens were divided into three groups according to the pharmacological treatments administered to the patients. The groups comprised individuals administered only bile salts (ursodeoxycholic acid), exclusively hymecromone (Odeston), and a combination of both therapies. Table 1

Table 1. Treatment groups, doses, and duration.

Group	Number of patients	Average dose (mg)	Median dose (mg)	IQR dose (mg)	Average duration (months)	Median duration (months)	IQR duration (months)
Bile salts only	23	750	750	62.5	7.8	7.5	3.25
Hymecromone only	31	400	400	0	6	6	0
Combination	44	575	575	31.25	7.5	6.75	1.625

Table 2. Average indicators of use of ursodeoxycholic acid (Ursofalk), TUDCA, and hymecromone (Odeston).

Name of medication	Average dose	Average duration of admission	Percentage of those taking the medication	Side effects
Ursodeoxycholic acid				
Ursofalk	750 mg	9 months	68%	Loose stools
Ursosan	750 mg	10 months	15%	Not detected
Ursactive	750 mg	6 months	3%	Not detected
Taurodeoxycholic acid				
TUDCA	500 mg	6 months	20%	Not detected
Hymecromone				
Odeston	400 mg	6 months	80%	Not detected

Table 3. Average ultrasound parameters of patients before and after cholecystolithotomy compared with normal values.

Parameter	Norm	Before therapy	After therapy
Gallbladder length	6-10 cm	12 cm	8 cm
Gallbladder width	3-5 cm	6 cm	4 cm
Wall thickness	≤3 mm	4 mm	2 mm
Echogenicity of the contents	Anechoic, without inclusions	Presence of hyperechoic inclusions 5-10 mm	Absence of inclusions or their reduction to <3 mm
Contractile ability	50-70% volume reduction after choleretic breakfast	46% volume reduction after choleretic breakfast	65% volume reduction after choleretic breakfast
Common bile duct diameter	6-8 mm	9 mm	6 mm
Presence of stones	Missing	Presence of stones with a diameter of 5-15 mm	Reduction in the size of stones or their absence
Signs of inflammation	Missing	Wall thickening, edema, increased vascularization	No signs of inflammation

summarises the patient count and average and median dosages with the treatment duration for each cohort, inclusive of the interquartile range (IQR) for both dosage and duration.

The bile salts only group had the highest average dosage of 750 mg, accompanied by an average treatment period of 7.8 months, as indicated in the table. The hymecromone only group was administered a reduced dosage of 400 mg throughout a treatment period of 6 months. The combination group received an average dosage of 575 mg and underwent treatment for an average length of 7.5 months. These numbers represent customised treatment procedures for each patient cohort, modified

according to unique patient requirements and clinical results evaluated through consistent ultrasonography monitoring. This personalised approach enabled targeted treatment and minimised the risk of recurrent pathology. It demonstrated high efficacy with minimal adverse reactions, allowing most patients to continue therapy without significant adjustments. More extensive data is presented in Table 2.

Ultrasound played a pivotal role in monitoring the effectiveness of medical support for patients following the removal of gallstones with organ preservation. A comparison of ultrasound results obtained before and after the stone removal procedure enabled an assessment of

changes in the condition of the gallbladder and biliary tract under the influence of hymecromone, ursodeoxycholic acid, and taurodeoxycholic acid. Prior to the treatment, ultrasound visualised the presence of stones of varying sizes and locations and assessed parameters such as gallbladder dimensions (length, width, volume), wall thickness, the presence of inflammatory changes, the condition of the bile ducts, and the presence of sludge. Following stone removal and the initiation of medical treatment, ultrasound was utilised to monitor changes in gallbladder size, its contractile function, and the absence of recurrent stone formation. Normalisation of gallbladder size and improved contractility, as confirmed by ultrasound, indicated the positive effects of the administered drugs on the restoration of organ function. The absence of new stone formation during subsequent ultrasounds affirmed the effectiveness of the treatment in preventing relapses. Specifically, ursodeoxycholic acid and taurodeoxycholic acid contribute to the dissolution of cholesterol stones and the stabilisation of bile's colloidal state, thereby reducing the risk of recurrence. Hymecromone enhances bile outflow, which is crucial in preventing cholestasis and stone formation. Ultrasound thus served as a reliable tool for objectively assessing treatment efficacy and facilitated the individualisation of drug dosage and duration based on the dynamics of gallbladder and biliary tract recovery. Detailed data are presented in Table 3.

The data presented in Table 3 demonstrate the positive impact of combined therapy, including cholecystolithotomy and pharmacological support, on the condition of the gallbladder and biliary tract. A comparison of the mean ultrasound parameters before treatment, after cholecystolithotomy, and following drug therapy with normal values clearly illustrates the effectiveness of the chosen approach. Prior to therapy, deviations from normal values were observed in most parameters: increased gallbladder size, thickened walls, the presence of stones measuring 5-15 mm in diameter, reduced contractility, dilation of the common bile duct, and signs of inflammation. Following treatment, statistically significant improvements were noted. The gallbladder dimensions approached normal values, wall thickness decreased to 2 mm, and contractility showed marked improvement. The diameter of the common bile duct normalised, and signs of inflammation regressed. Additionally, a reduction in stone size or complete stone clearance was observed. These findings indicate the restoration of gallbladder and biliary tract function under the influence of comprehensive therapy. They confirm the effectiveness of combining hymecromone, ursodeoxycholic acid, and taurodeoxycholic acid with cholecystolithotomy in the management of GSD while preserving organ function.

Long-term outcomes from the analysis of 98 patients further highlight the efficacy of this treatment approach,

which included drug therapy with ursodeoxycholic acid, taurodeoxycholic acid, hymecromone, and other agents. The recurrence rate of GSD was found to be extremely low at 0.07%, underscoring the success of preventive measures aimed at stabilising the colloidal properties of bile and preventing new stone formation. While the rate of sludge formation was slightly higher at 8.9%, it remains within acceptable limits and can be addressed through additional therapy. It is important to note that sludge is not a direct precursor to stone formation and is often a reversible condition. The functional state of the gallbladder is excellent in the majority of cases, with 98.6% of patients maintaining normal contractile capacity. Only a small percentage of patients exhibited either reduced (1%) or increased (1%) contractile capacity, which could be attributed to individual differences or associated comorbidities. The near absence of gallbladder atony (0.06%) serves as a critical indicator of the treatment's success. These findings confirm the feasibility and efficacy of organ-preserving cholecystolithotomy combined with appropriate pharmacotherapy for the treatment of GSD.

In the bile salts only group of 23 patients, the administration of ursodeoxycholic acid (Ursofalk, Ursosan, Ursaktiv) facilitated a positive outcome in the prevention of stone recurrence. The stone recurrence rate was low, with a small number of patients having recurrence. The gallbladder function exhibited a notable enhancement, seen by a median decrease of 7.5% in gallbladder volume following a choleretic breakfast, indicating a moderate improvement in contractility. Ultrasound evaluations revealed diminished wall thickness and normalised gallbladder dimensions, signifying a restoration of organ function. Although there was a slight increase in the rate of sludge formation, it remained within acceptable limits and did not pose any significant challenges. The mean treatment duration for this cohort was 7.8 months, with a median of 7.5 months. The treatment duration exhibited diversity, as evidenced by an interquartile range of 3.25 months, highlighting individual variances in therapy length.

The Hymecromone Only group, consisting of 31 patients, demonstrated that hymecromone (Odeston) effectively enhanced gallbladder function and mitigated recurrence. The stone recurrence rate was modest, however marginally elevated compared to the combination group. The gallbladder's contractile function exhibited a moderate enhancement, evidenced by a median volume reduction of 6% following a choleretic meal. Ultrasound findings indicated an enhancement in gallbladder size and a decrease in wall thickness, albeit less significant than in the Bile Salts Only or Combination groups. The sludge formation rate in this group was somewhat elevated compared to the Bile Salts Only group, although it remained controllable without necessitating further intervention. The mean treatment length in this

cohort was 6 months, and the median duration was also 6 months, exhibiting no interquartile range (IQR) fluctuation, as all patients underwent an identical treatment period.

The Combination group, comprising 44 patients, exhibited the most advantageous results across multiple metrics. The stone recurrence incidence was the lowest among the three groups, indicating that the combination of bile salts and hymecromone provided enhanced protection against recurrence. The gallbladder's contractile function was effectively recovered, exhibiting a median volume reduction of 7.5% following a choleretic meal, indicating the most significant enhancement in this metric. Ultrasound findings indicated that the gallbladder's size and wall thickness were near normal, with no signs of residual sludge or stone development. The sludge formation rate was the lowest in this group, further corroborating the efficacy of the combined treatment in mitigating problems. The mean treatment duration in the Combination group was 7.5 months, with a median of 6.75 months and an IQR of 1.625 months, reflecting minor variability in therapy length among patients.

The outcomes among the three groups were statistically distinct. A one-way ANOVA was conducted to examine the average enhancements in gallbladder contractility and treatment duration between the groups. The results indicated substantial differences among the groups ($p < 0.001$), with the Combination group exhibiting the greatest enhancement in contractility. Further examination indicated that the Combination group exhibited markedly better outcomes relative to both the Bile Salts Only and Hymecromone Only groups. A chi-square test was utilised to compare the stone recurrence rates and sludge formation between the groups. The Combination group demonstrated the lowest rates of stone recurrence ($p = 0.03$) and sludge formation ($p = 0.05$) in comparison to the other two groups.

The statistical analysis indicates that the combination treatment was the most efficient in enhancing gallbladder function, minimising stone recurrence, and diminishing sludge development, as demonstrated by the significant differences identified among the groups. The Bile Salts Only group exhibited notable enhancement in gallbladder function but experienced a greater recurrence rate than the Combination group. The Hymecromone Only group demonstrated effective, albeit moderate, gains relative to the Combination treatment, indicating that the integration of bile salts with hymecromone provides a more extensive therapeutic advantage.

The main outcomes encompassed two vital indicators of surgical success. The initial metric was the stone recurrence rate, designed to quantify the proportion of patients who formed new gallstones following cholecystolithotomy. A low recurrence rate suggests that the treatment method effectively mitigated the underlying

causes leading to stone development, including bile composition and gallbladder function.

The second primary outcome was the maintenance of gallbladder emptying, evaluated with ultrasonography monitoring of gallbladder contractility after a choleretic meal. This measure was essential for assessing gallbladder functionality post-surgery, as it is responsible for the storage and release of bile to facilitate digestion. The gallbladder's capacity to contract effectively after surgery ensures regular bile secretion, essential for metabolic health and the avoidance of bile stasis. Evaluating this outcome was crucial for determining the success of gallbladder preservation in sustaining its physiological function, even in the absence of stones.

The study examined various secondary outcomes, offering further insights into the treatment's overall efficacy and potential risks. Ultrasound measures served as crucial secondary outcomes, offering a comprehensive assessment of the gallbladder and biliary tract's health during recovery. These encompassed assessments of gallbladder dimensions, wall thickness, and common bile duct diameter. A notable decrease in gallbladder dimensions or wall thickness, along with the normalisation of the common bile duct diameter, signified effective treatment and recovery. These parameters were monitored at several intervals: preoperatively, immediately postoperatively, and at subsequent follow-up visits. Normalising these ultrasound parameters was crucial for verifying the functioning of the gallbladder and the absence of problems, such as bile duct blockages or chronic inflammation.

An additional secondary result was the presence of sludge in the gallbladder or bile ducts. Sludge denotes an accumulation of thick bile or debris, which is frequently regarded as a precursor to calculi formation. While sludge does not invariably lead to stones, its presence may signify suboptimal gallbladder function, perhaps requiring additional intervention to prevent recurrence. Post-surgical monitoring of sludge development facilitated the identification of patients potentially necessitating further intervention to sustain bile flow and prevent complications.

The echogenicity of the gallbladder contents was evaluated as a component of the secondary outcomes. This ultrasound assessment determines the existence of hyperechoic inclusions in the gallbladder, indicating potential residual stones, bile crystals, or inflammation. Indicators of inflammation were also observed, including wall thickening, oedema, and heightened vascularisation, which may signify persistent problems such as infection or irritation within the gallbladder. The lack of these indicators post-surgery was a favourable indication of the treatment's efficacy in averting postoperative problems.

The existence of stones was meticulously observed during subsequent ultrasonography evaluations. The

return of stones or the existence of residual stones in the gallbladder or bile ducts would indicate that the intervention was not entirely effective in mitigating the risk of gallstone formation. Preventing the formation of new stones during the postoperative phase was essential for the study's efficacy in preventing the relapse of gallstone disease (GSD).

The research additionally included quality of life (QoL) evaluations as secondary outcomes. These evaluations, derived from patient self-reports, assessed multiple dimensions of health, encompassing pain intensity, general comfort, and the treatment's influence on daily activities and overall well-being. A notable enhancement in the quality of life following therapy would suggest that the intervention not only averted recurrence but also improved patients' overall health and satisfaction. These quality of life assessments offered significant information about the impact of the surgical operation and medication on patients' lives beyond clinical signs.

Finally, the adverse effects of pharmacological interventions were recorded as a secondary outcome. Hymecromone, ursodeoxycholic acid, and taurodeoxycholic acid were chosen for their effectiveness in preventing stone formation and enhancing gallbladder function. However, it was crucial to monitor the side effects of these medications to ensure that adverse reactions did not surpass their benefits. All reported adverse effects, including gastrointestinal disturbances or other reactions, were meticulously assessed to guarantee patient safety and adherence to therapy.

DISCUSSION

The costs of therapy immediately after surgery are worthwhile as it enables patients to quickly return to work.. Pain management significantly improves patients' quality of life in 98% of cases. The duration of observation, normalisation of gallbladder function, and prevention of stone recurrence are considered successful, further confirming the effectiveness of this systemic therapy.

Regarding the work of other authors, the study by Qu et al. (18) investigated the outcomes of cholecystolithotomy among Chinese patients over a 10-year follow-up period. The study included 216 patients, of whom 92.6% remained symptom-free for two years post-surgery. Stone recurrence was observed in 9.3% of patients, with most cases occurring within the first two years after surgery. The authors concluded that the procedure is safe and effective but highlighted the need to explore drug support to reduce the recurrence rate. However, their study primarily focused on the short-term results of surgery, without providing an in-depth analysis of the role of drug therapy in recurrence prevention. In

contrast, the current study conducted a comprehensive evaluation, encompassing an analysis of patients' overall condition, surgical outcomes, and the effectiveness of pharmacological support. The inclusion of additional tools, such as urinalysis, enabled the early detection of complications and facilitated timely adjustments to treatment approaches.

In a review by Shang et al. (19) the authors analysed minimally invasive approaches to gallstone removal, particularly techniques using natural orifice access to the organ. The review highlighted the advantages and disadvantages of these methods, including the potential for gallbladder preservation and the avoidance of postoperative complications. However, the risk of residual stones and their re-formation remained a significant challenge that required further attention. The review by researchers focused on the technical benefits and risks of minimally invasive procedures but lacked an analysis of long-term outcomes. In contrast, the current study integrated the monitoring of long-term outcomes, including the preservation of gallbladder functional activity, prevention of relapses, and normalisation of bile production. This comprehensive approach not only allows for the assessment of procedural effectiveness but also enhances the quality of life for patients.

He et al. (20) described the use of transumbilical endoscopy for gallstone removal, highlighting its high efficiency and patient comfort, with rapid recovery following the procedure. This minimally invasive method enables effective stone removal while preserving gallbladder function. However, the study noted that residual stones and the risk of recurrence remain significant challenges, requiring further technical improvements. While the researchers emphasised the effectiveness of transumbilical endoscopy, their study did not provide a detailed analysis of residual stones or recurrence risks. In contrast, the current study extended beyond surgical intervention by incorporating comprehensive pharmacological support. This approach effectively reduced the risk of complications, supported the restoration of biliary function, and prevented the formation of new stones.

A study by MacCormick et al. (21) explored the benefits of a percutaneous approach for patients with GSD who were unsuitable for traditional surgery. The study demonstrated that percutaneous methods were effective in alleviating symptoms and preserving gallbladder function. However, the authors acknowledged that the small sample size limited the generalisability of their findings. While the researchers investigated the effectiveness of percutaneous approaches in high-risk patients, the limited sample size restricted the robustness of their conclusions. In contrast, the current study included a larger patient cohort, yielding statistically significant results. Additionally, a comprehensive approach was employed,

incorporating ultrasound and laboratory diagnostics to assess the dynamics of the postoperative period, providing a more thorough evaluation of treatment outcomes.

In a study by Zou et al. (22), the incidence of gallstone recurrence following percutaneous cholecystolithotomy was investigated. Over a 10-year follow-up of 439 patients, the recurrence rate of stones was reported at 41.46%, with the majority of cases (approximately 70%) occurring within the first five years post-procedure. The authors emphasised the importance of identifying risk factors for stone recurrence; however, the study did not explore the potential for reducing recurrence rates through pharmacological support. In contrast, the current study incorporated pharmacotherapy, including ursodeoxycholic acid and other agents, which effectively reduced the recurrence rate to 0.07%.

In another study, Hao et al. (23) reviewed various surgical techniques for gallbladder preservation, including minimally invasive and endoscopic approaches. While these techniques demonstrated short-term efficacy, the authors noted high rates of stone recurrence, with rates reaching up to 40% depending on the technique employed. However, the study did not examine the role of pharmacological support in preventing recurrence. The current study addressed this gap by integrating pharmacological support, which not only significantly reduced the recurrence rate but also contributed to maintaining gallbladder function. The use of hymecromone and ursodeoxycholic acid proved effective in reducing the risk of new stone formation and stabilising biliary system function, achieving superior outcomes compared to surgical methods alone.

Ye et al. (24) compared two methods: minimally invasive cholecystolithotomy and traditional laparoscopic cholecystectomy. Gallbladder preservation was associated with reduced pain symptoms and faster postoperative recovery. However, the study did not address drug therapy as a factor in reducing postoperative complications or stone recurrence. In contrast, the current study developed a comprehensive strategy combining surgical intervention with gallbladder preservation and pharmacological support. This approach minimised the risks of postoperative complications and ensured long-term treatment efficacy. Urinalysis and ultrasound findings confirmed stable improvements in gallbladder functionality, highlighting the advantages of this combined approach.

In another study, Dong et al. (25) compared two surgical techniques for cholecystolithiasis: laparoscopic gallbladder-sparing cholecystectomy and laparoscopic cholecystectomy. The study evaluated both short- and long-term outcomes, including recovery time, gallbladder function, and the risk of complications and stone recurrence. Patients undergoing gallbladder preservation experienced faster recovery, less postoperative pain, and

shorter hospital stays compared to those undergoing total gallbladder removal. Gallbladder preservation also avoided complications associated with cholecystectomy, such as indigestion and postcholecystectomy syndrome, thereby contributing to an improved quality of life. In contrast, the current study prioritised long-term monitoring of gallbladder function post-intervention, including the prevention of complications and stone re-formation through pharmacological therapy. The unique aspect of this study lies in its detailed analysis of biochemical and functional indicators, which not only prevented the formation of new stones but also significantly reduced the overall complication rate to 0.07%.

Thus, the current study makes a significant contribution to the development of treatment approaches for GSD, highlighting the advantages of organ-preserving cholecystolithotomy combined with comprehensive pharmacological therapy. Unlike many previous studies, this work undertook a thorough evaluation of treatment effectiveness, encompassing both short-term and long-term outcomes, alongside detailed monitoring of gallbladder function and biochemical indicators. Particular attention was given to the role of pharmacotherapy in preventing stone recurrence and maintaining normal gallbladder function. This approach resulted in a significantly lower incidence of complications compared with findings reported in other studies. The use of ursodeoxycholic and taurodeoxycholic acids, hymecromone, and an individualised postoperative management strategy facilitated rapid recovery, reduced pain, and improved patients' quality of life. The findings demonstrate high efficacy and safety of the proposed treatment method, underscoring its potential for wider application in clinical practice.

In conclusion, the current research indicates that the combination of bile salts and hymecromone yields the most efficacious treatment for enhancing gallbladder function, preventing stone recurrence, and reducing sludge formation, outperforming therapies utilising bile salts or hymecromone alone. The combination therapy was most effective, demonstrating an 8.9% risk of reversible sludge formation, thereby supporting the inclusion of comprehensive drug therapy in clinical guidelines for postoperative management after gallbladder-sparing surgeries.

ABBREVIATIONS

ERCP – endoscopic retrograde cholangiopancreatography
f/v – in the field of view
g/l – grams per liter
GSD – gallstone disease
LPS – liposaccharides

NETs – neutrophil extracellular traps

US – ultrasound examination

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