# Non-surgical treatments for gallstone disease

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**Abstract**. The steady increase in the incidence of cholelithiasis and its complications, called the slow epidemic of the XXI century, the high frequency of deaths is due to the severity of this disease, the complexity, multicomponent and multi-stage surgical treatment with high economic costs. The incidence of cholelithiasis in the Russian Federation is quite high, and there is a tendency to a progressive increase in the number of patients with cholelithiasis. VS Mayat et al. (1978) call cholelithiasis the second problem in gastroenterology (after peptic ulcer). However, it can be assumed that if the incidence of gallstone disease continues to increase at the same rate as at present, then cholelithiasis will soon become the number one problem.

## 1 Introduction

Gallstones (GSD) is a hepatobiliary system disorder characterized by the formation of stones in the biliary tract. Gallstone disease (GSD) is a hepatobiliary system disorder that consists of the formation of stones in the biliary tract. In the case of stones in the gallbladder, it is called "cholecystolithiasis", while in the common bile-duct, it is also described as "choledocholithiasis," and in the intrahepatic cholelithiasis.Aseptical demarcation type inflammation of the pancreas, as well as its instability is accompanied by autoaggression and necrobiosis of the organ. This leads to pancreas necrosis and the development of purulent complications. Aseptic inflammation of the pancreas of the demarcation type is associated with pancreas necrobiosis and enzyme autoaggression, leading to pancreas necrosis and the development of secondary purulent complications. As it is known, the etiology of this condition can be divided into three groups: The reason for this condition can be categorized into:

1. Mechanical Factors: This include conditions like fix choledocholithiasis, spasms, or injuries of the Oddi sphincter.

2. Among these factors are toxic-allergic factors: These include alcohol, diets that provoke pancreatic secretion and gallbladder contraction, food or drug allergies.

3. Neurohumoral Factors: This is in connection with hyperlipidemia and hormonal disorders (such as hyperlipidemia).

For example, the modern medicine offers several non-surgical treatment methods, including:

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1. The principle of extracorporeal cholecystolithotripsy: A technique to break down gallstones outside the body.

2. The following is the method of destruction of intracorporeal stone: Stones are disintegrated by laser, ultrasound or other energy source directly within the body.

3. Direct Contact Dissolution: This is a method of dissolving stones through specific agents delivered through drains and catheters.

4. Preparation of oral bile acids.

5. Mechanical instrumental fragmentation: The use of instruments to break down stone.

These methods of treatment have general drawbacks. It is worth noting that all of these conservative treatment methods have general drawbacks. They are often unsuccessful, can be costly, lead to serious complications, and importantly, they do not prevent disease recurrence. At times, a role of the gallbladder is overlooked in cholelithiasis. Langenbuch argued that the gallbladder should be removed, not only for stones but also as it plays an important role in its formation. It also applies to occasional attempts to return to cholecystotomy, a procedure for removing stones. This perspective is also applicable to the period of attempts to return to cholecystotomy, a procedure for removing stones. To be sure that conservative treatment methods are supplementary, they should be considered supplementary and used in exceptional circumstances, with an urgent need for further research in this direction.

## 2 Research Methodology

Extracorporeal lithotripsy. The emergence of high-tech units for extracorporeal lithotripsy based on electro-hydraulic, laser or chemical generators has attracted many followers from among practitioners. However, the first excitement and euphoria about the possibilities of treating gallstone disease with this method has passed. In the works of domestic and foreign researchers, the criteria for selecting patients whose gallstones can be subjected to lithotripsy are persistently substantiated, and the indications for it are narrowed. Only 5-7% of patients from the total number of those suffering from cholelithiasis are shown lithotripsy. The main requirements for the selection of patients: the presence of no more than 3 stones, the maximum size of the stone is not more than 30 mm, stones should not be calcified, a functioning gallbladder, a fairly wide bile duct, no sclerotic or inflammatory changes in the gallbladder.

The effectiveness of shock wave lithotripsy, which was used in combination with cheno- and ursodeoxycholic acids, is described. Successful fragmentation after the first session was achieved in 25% of patients, with repeated sessions in 48% [5]. The negative consequences of the use of lithotripsy include: the formation of a large number of fragments that can cause cholestatic complications and be the nuclei of recurrent stone formation; necrotic changes in the wall of the gallbladder, and possibly in neighboring organs. A prerequisite is the tolerance of bile acid preparations, which are used before and after crushing. Intracorporeal contact lithotripsy. This method of lithotripsy belongs to the group of invasive. It is based on the contact effect on the stone of pulsating ultrasonic or laser energy, for which a duodenoscope or drainage tubes are used, installed in the gallbladder or common bile duct. This is the method of choice when removing residual or recurrent gallstones, as well as when cholecystectomy is not possible. Direct contact chemical litholysis [6]. The experiment found that a 1% solution of ethylenediaminetetraacetate (EDTA) in combination with a 30% solution of dimethyl sulfoxide dissolves bilirubincalcium stones in 60% of cases at pH 9.4. With mixed gallstones, which include calcium bilirubinate (60%), cholesterol and its esters, fatty acids and calcium, a combined solvent of dimethyl sulfoxide and methyl tertbutyl ether is used in a ratio of 7:3. The use of monophasic multicomponent solvents made it possible to achieve

the dissolution of cholesterol stones in 90% of cases, bilirubin stones in 80%, calcium containing stones in 70%. To dissolve cholesterol stones, monoactonoin is successfully used by continuous infusion[7]. All these chemical solvents are brought directly to the stone using catheters and drains during endoscopic manipulations, by the method of percutaneous or transhepatic puncture of the gallbladder, or by postoperative drains.

## 3 Results and Discussions

Oral bile acid pharmacotherapy In the 1970s, the era of bile acid preparations began. In 1971 J.L.Tistle and in 1977 R.Danzinger and A.Hofman reported the use of chenodeoxycholic acid (CDCA) in 7 women with asymptomatic gallstones. In 1975, S.Nakojma reported on the use of ursodeoxycholic acid (UDCA). Recently, a large number of drugs containing cheno- and ursodeoxycholic acids have appeared on the pharmaceutical market [8]. These are chenofalk, henochol, ursofalk, lithofalk, ursodiol, urso-100 and others. CDCA - primary bile acid - normally makes up 20 - 30% of the total pool of bile acids. The mechanism of action of HDCA is based on inhibition of the synthesis of cholesterol and bile acids, a decrease in the activity of hydroxy-3-methylglutaryl-CoA reductase in the liver (an enzyme involved in the synthesis of cholesterol), a decrease in the absorption of cholesterol in the intestine, a change in the ratio of bile acids due to the prevalence of bile acids in the total pool. acids [9]. During the treatment of CDCA, quantitative and qualitative changes in bile are observed. The volume of secreted bile increases, the level of conjugated bile acids in it increases, the ratio of trioxycholic and dioxycholic bile acids decreases, the content of glycocholic acid increases compared to taurocholic acid, the concentration of phospholipids significantly increases. Indications for the use of CDCA drugs [10]: 1) multiple or single radiolucent (cholesterol) stones with normal contractile function of the gallbladder and a high risk of surgical treatment in elderly patients and severe comorbidities; 2) single cholesterol stones with a diameter of up to 20 mm; 3) multiple cholesterol stones, the volume of which is up to 50% of the gallbladder. With careful selection of patients, dissolution of stones can be achieved in 60-80% of cases, on average, 14-18 months. The dose of HDCA administered orally varies depending on the body weight of the patient and averages 750 mg per day [11]. It is usually taken 250 mg (1 capsule) in the morning and 500 mg at night. The duration of the course is individual - from several months to several years, averaging 6 - 18 months. Side effects include: diarrhea (in 50% of patients), which is eliminated by a temporary reduction in the dose of the drug; increased levels of transaminases (in 20% of those on treatment). The results of treatment, according to various authors, vary widely. Some note a decrease in the diameter of the stones in 28% of cases. Complete dissolution of stones is observed, according to various sources, from 13.5 to 61% of cases. The percentage of effective dissolution of the total number of patients taken for treatment fluctuates around [12]. Along with the widespread use of CDCA in clinical practice since 1974, ursodeoxycholic acid and preparations based on it have been used. Being the 7-b-CDCA isomer, it has some differences in the mechanism of action. Ursodeoxycholic acid (UDCA) promotes the formation of liquid crystals of lecithin-cholesterol-bile acids, which are located on the surface of gallstones, as if “packing” them at the same time. Dissolution occurs even in bile supersaturated with cholesterol. UDCA, unlike HDCA, does not suppress the synthesis of bile acids in humans, does not cause side effects such as diarrhea and increased levels of transaminases [13]. Its advantage is also a smaller, approximately 1/3, therapeutic dose (on average 500 mg per day) compared to HDCA. A combination of these drugs, lithofalk, has been widely used. In this combination, UDCA at a dose of 7 mg/kg is administered together with CDCA at a dose of 8.3 mg/kg, resulting in a significant decrease in bile lithogenicity, an increase in tolerability of treatment, and a decrease in its cost (approximately 25%) [14].

Contraindications to the use of drugs based on bile acids are well known and include the presence of radiopaque stones, stones more than 20 mm in diameter, obstructive jaundice, intrahepatic cholestasis, impaired liver function, disabled gallbladder, impaired renal function, inflammatory diseases, pregnancy.

## 4 Conclusions

Significant disadvantages in the treatment of bile acids are: long duration of treatment; the high cost of the drug and the complexity of control studies; side effects of drugs; frequent recurrence of stones after their dissolution; selective effect on cholesterol lithiasis. A number of authors note the possibility of eliminating the lithogenicity of bile and leveling biliary insufficiency and its clinical manifestations with bile acid preparations. Clinically, biliary insufficiency is manifested by a decrease in appetite, constipation, intolerance to fatty foods, a slight drop in body weight, fatigue, hypovitaminosis of the fat-soluble group. The appointment of bile acid preparations provides a significant increase in the total production of bile and cholic acid. By increasing the cholatocholesterol coefficient, there is a decrease in the concentration of cholesterol in bile, i.e. corrected biliary insufficiency.

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