Gallbladder Dysfunction

The gallbladder dysfunction is a disorder of the gallbladder contraction which reveals as biliary pain (1-15). The cause of the gallbladder hypomotility can be an increased basal cystic duct resistance or cystic duct spasm, the muscle hypertrophy, or the chronic gallbladder diseases.

Diagnostic criteria of the gallbladder dysfunction

1. Recurrent episodes of moderate or severe pain in the right hypochondrium or epigastrium which last for 20 minutes and more (pain is defined as moderate when it disrupts the patient's daily activities, and as severe when medical consultation or medication is necessary).
   In addition, a patient may also experience one or more of the following symptoms:
   a. Nausea and vomiting
   b. Irradiation of pain in the right scapular region or in the right shoulder
   c. Pain occurs after a meal
   d. Pain occurs at night
2. Impaired gallbladder emptying (the gallbladder ejection fraction is less than 40%).
3. Absence of structural (morphological) changes explaining these symptoms.

Causes of the gallbladder evacuation dysfunction

1. Pathology of the smooth muscle cells and epithelial cells in the gallbladder wall (high degree of COX-2 expression in the smooth muscle cells and epithelial cells of the gallbladder wall).
2. Contractile discoordination of the gallbladder and cystic duct (high degree of COX-2 expression in the smooth muscle cells of the gallbladder and cystic duct).
3. The cystic duct resistance increase (high degree of COX-2 expression in the smooth muscle cells of the cystic duct).

Mechanism of development of pathologic disorders

Decrease in the evacuation function of the gallbladder to less than 40% results in the decrease in the "active" and "passive" passage of the hepatic bile into the gallbladder and in the concentration of total bile acids in the gallbladder bile (fig. 11).

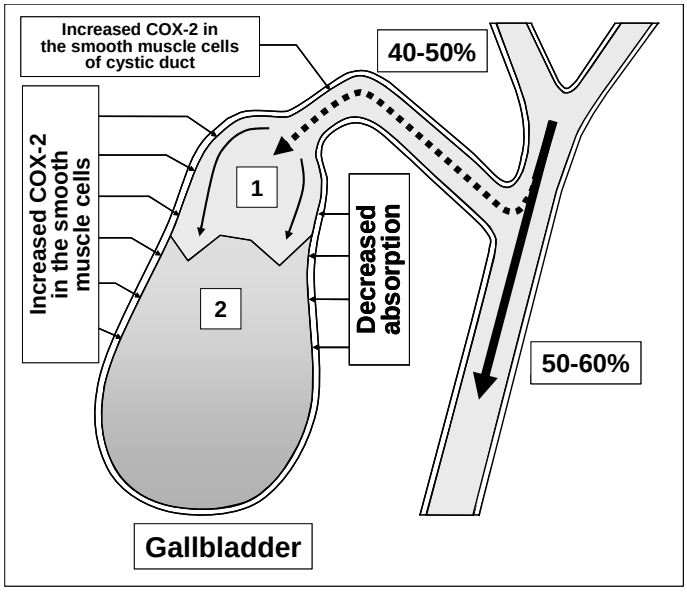

Fig. 11. "Active" and "passive" passage of hepatic bile into the gallbladder and into the duodenum in patients with gallbladder dysfunction.
1 = unconcentrated hepatic bile;
2 = low concentrated gallbladder bile.

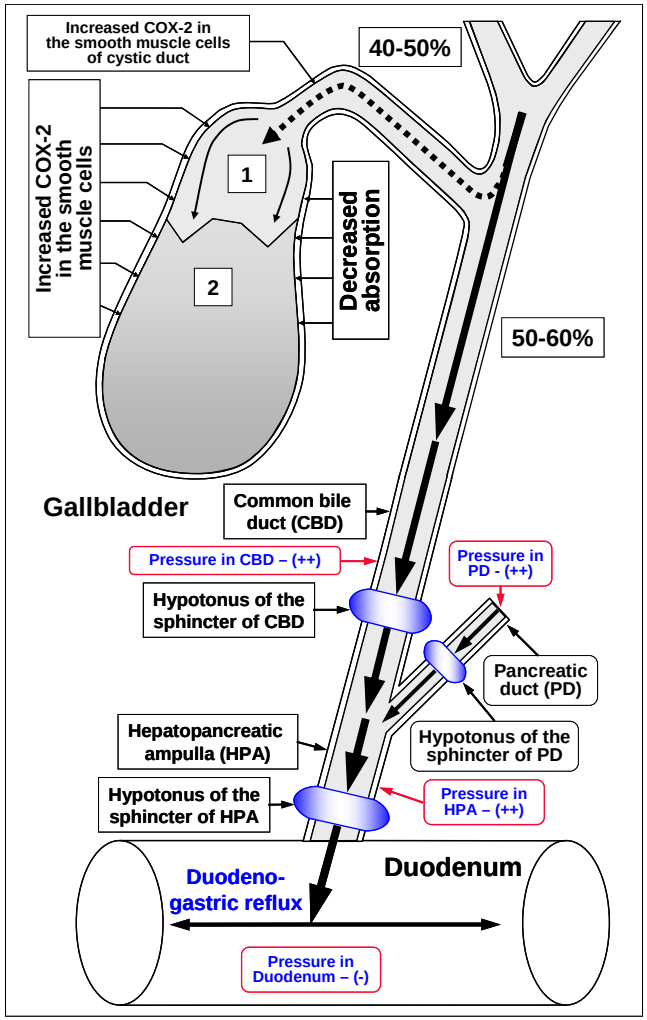

Fig. 11a. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with gallbladder dysfunction, sphincter of Oddi hypomotility and duodenogastric reflux** (chronic bile reflux gastritis). **1** = unconcentrated hepatic bile; **2** = low concentrated gallbladder bile (low con GB).

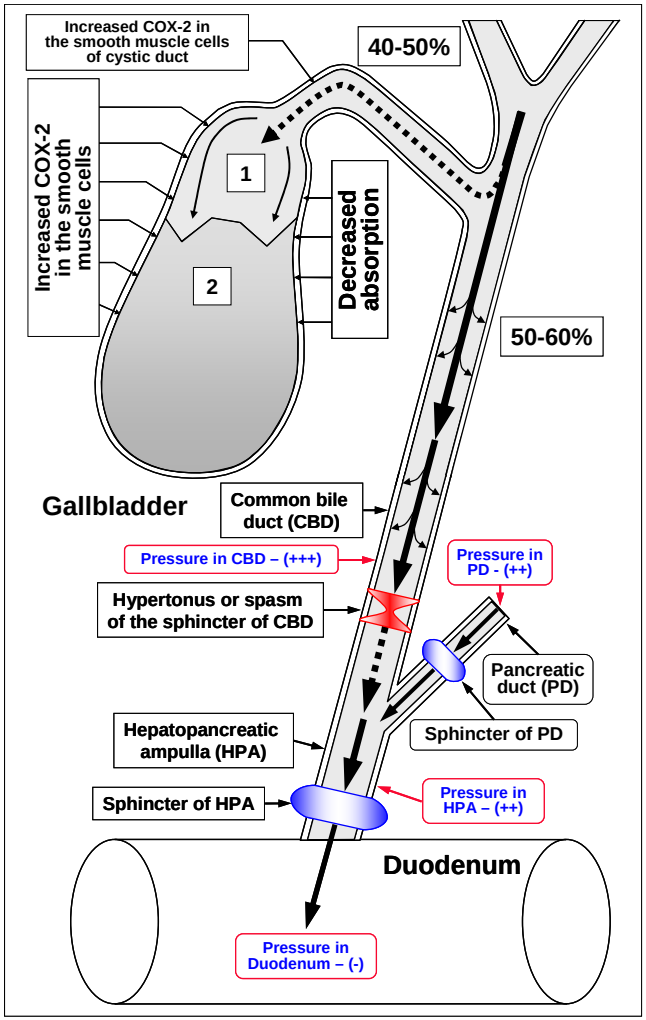

Fig. 11b. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with gallbladder dysfunction and biliary type III of sphincter of Oddi dysfunction. 1** = unconcentrated hepatic bile (uncon HB); **2** = low concentrated gallbladder bile (low con GB).

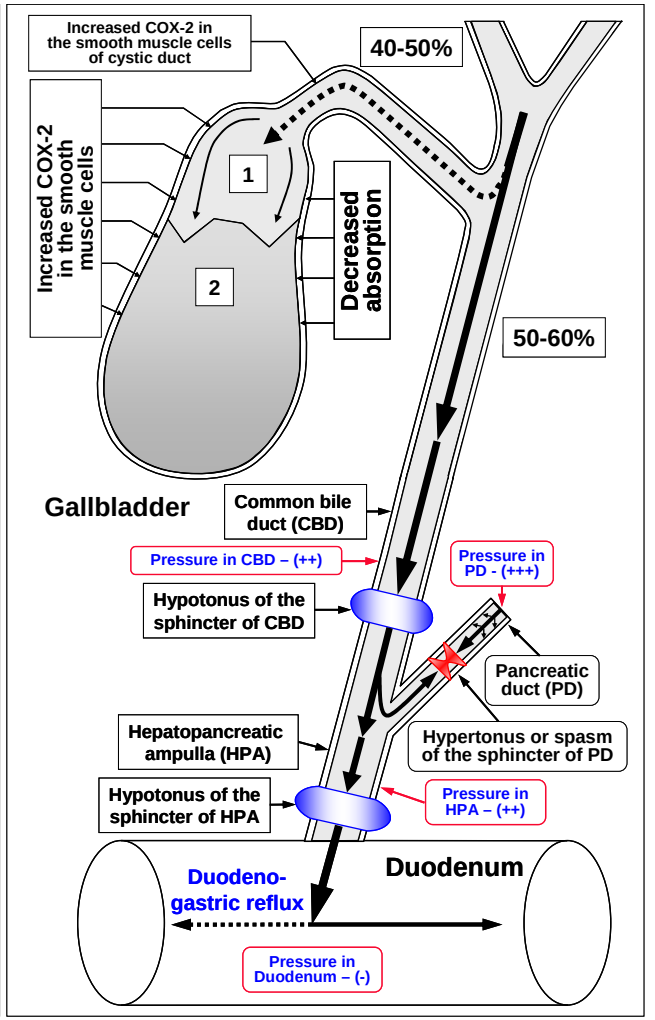

Fig. 11c. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with gallbladder dysfunction and pancreatic type III of sphincter of Oddi dysfunction** (chronic spastic aseptic pancreatitis). **1** = unconcentrated hepatic bile; **2** = low concentrated gallbladder bile (low con GB).

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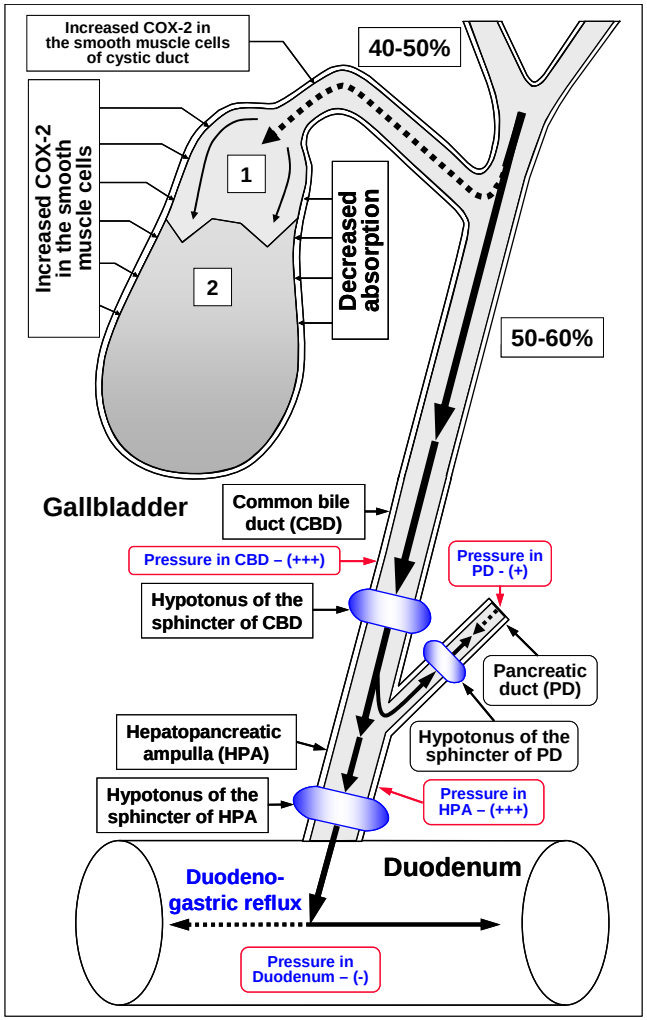

Fig. 11d. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with gallbladder dysfunction, sphincter of Oddi hypomotility and biliopancreatic reflux** (chronic biliary pancreatitis)**. 1** = unconcentrated hepatic bile; **2** = low concentrated gallbladder bile (low con GB)

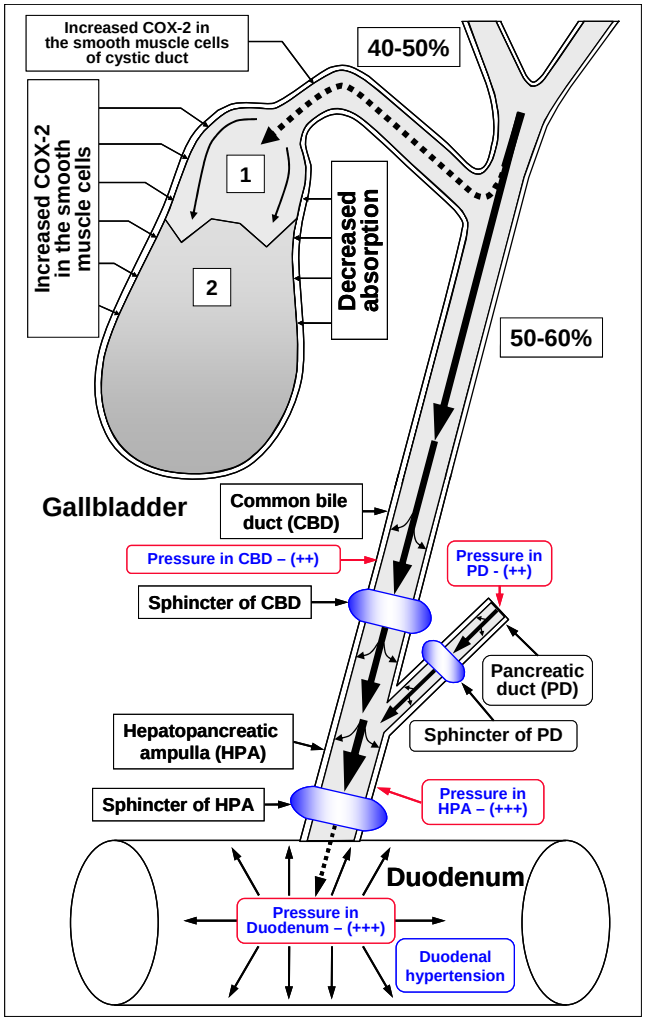

Fig. 11e. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with gallbladder dysfunction and small intestinal bacterial overgrowth syndrome** (duodenal hypertension – the increase of intraluminal pressure in the duodenum).
1 = uncon HB; **2** = low concentrated GB.

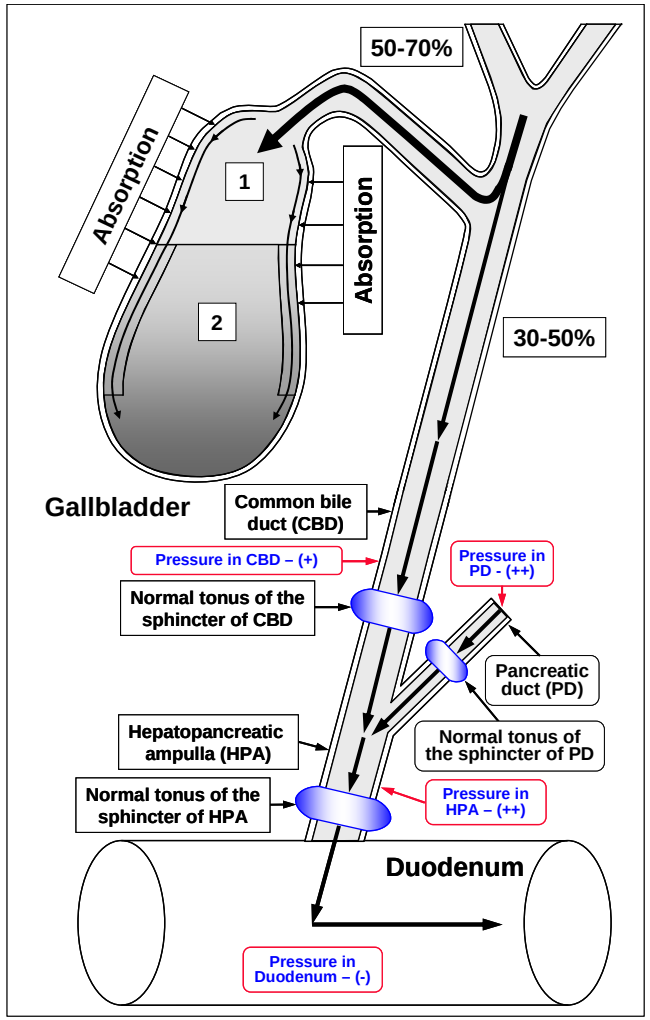

Fig. 11f. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with gallbladder dysfunction after treatment with celecoxib and UDCA** (normal motility of the sphincter of Oddi).
1 = unconcentrated hepatic bile;
2 = normal concentrated gallbladder bile.

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The decrease of the "active" and "passive" passage of the hepatic bile into the gallbladder results in the increase of the passage of the hepatic bile into duodenum and of the gallbladder-independent enterohepatic circulation of bile acids, biliary cholesterol and biliary bilirubin (fig. 12).

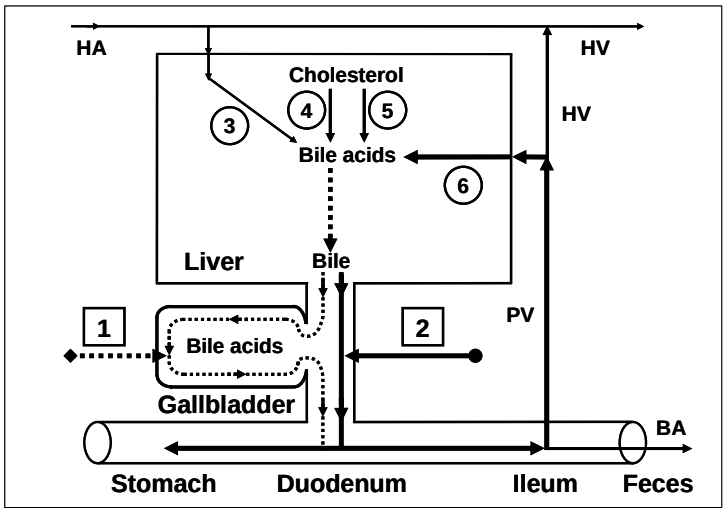

Fig. 12. Enterohepatic circulation of bile acids in patients with gallbladder dysfunction. **1** = gallbladder-dependent enterohepatic circulation of bile acids; **2** = gallbladder-independent enterohepatic circulation of bile acids; **3** = bile acids entering the liver through the hepatic artery; **4** = synthesis of cholic acid: cholesterol-7α-hydroxylase; **5** = synthesis of chenodeoxycholic acid: cholesterol-27-hydroxylase; **6** = bile acids entering the liver through the portal vein.
BA = bile acids;
HA = hepatic artery;
HV = hepatic vein;
PV = portal vein.

The increase of the gallbladder-independent enterohepatic circulation of bile acids causes increase in the concentration of bile acids in the hepatocytes and in the decrease of excretion function of the liver (i.e. formation of chronic "bland" intrahepatic cholestasis) (fig. 12).

The increase of the gallbladder-independent enterohepatic circulation of biliary cholesterol causes increase in the absorption of the biliary cholesterol in the small intestine, the biliary cholesterol entering the hepatocytes and the high secretion into hepatic bile (fig. 13). These two factors cause the formation of the "lithogenic" hepatic bile.

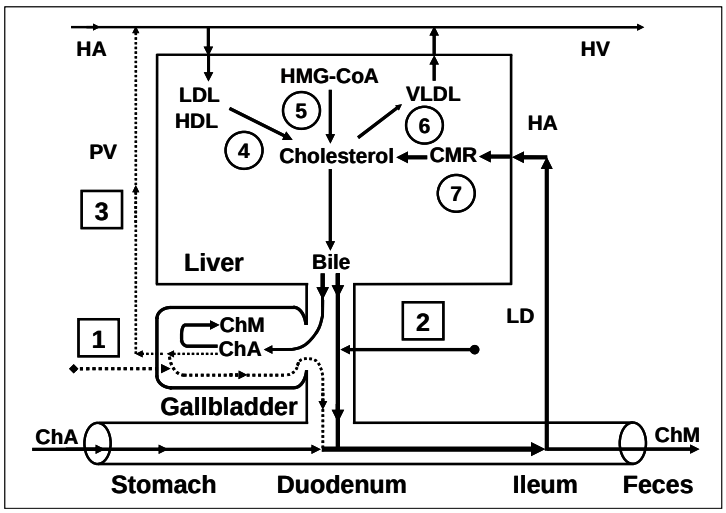

Fig. 13. Exchange of cholesterol in patients with gallbladder dysfunction.
1 = gallbladder-dependent output of biliary cholesterol; **2** = gallbladder-independent output of biliary cholesterol; **3** = gallbladder-hepatic circulation of biliary cholesterol; **4** = hydrolysis of cholesterol esters entered the hepatocytes with HDL and LDL; **5** = synthesis of cholesterol; **6** = synthesis of cholesterol esters for VLDL;
7 = hydrolysis of cholesterol esters entered the hepatocytes with CMR.
ChA = cholesterol anhydrous; **ChM** = cholesterol monohydrate; **HA** = hepatic artery; **HV** = hepatic vein; **PV** = portal vein; **LD** = lymphatic duct.

Decrease of the gallbladder-dependent output of biliary cholesterol and of the concentration of total bile acids in the gallbladder bile cause formation of the "lithogenic" gallbladder bile and precipitation of cholesterol monohydrate crystals in the gallbladder lumen on 10% of the patients with gallbladder dysfunction (fig. 14).

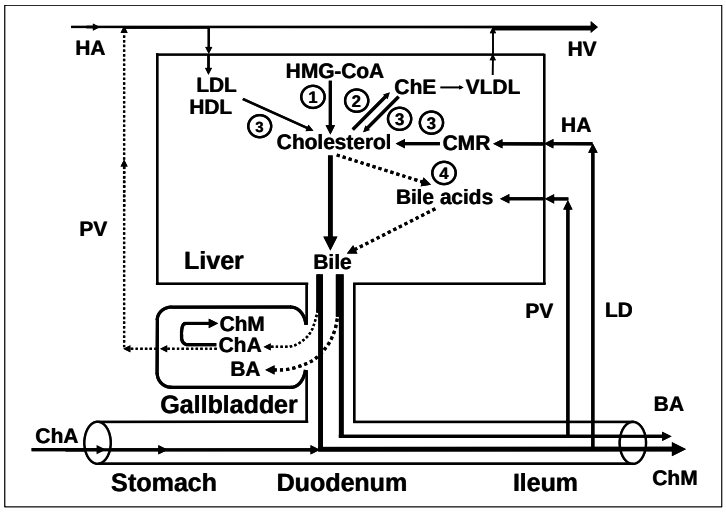

Fig. 14. Exchange of cholesterol and bile acids in patients with gallbladder dysfunction.
1 = synthesis of cholesterol;
2 = synthesis of cholesterol esters for VLDL;
3 = hydrolysis of cholesterol esters entered the hepatocytes with HDL and LDL, and hydrolysis of cholesterol esters entered the hepatocytes with CMR;
4 = synthesis of bile acids.
ChE = cholesterol esters; **ChA** = cholesterol anhydrous; **ChM** = cholesterol monohydrate; **BA** = bile acids; **HA** = hepatic artery; **HV** = hepatic vein; **PV** = portal vein; **LD** = lymphatic duct.

Precipitation of cholesterol monohydrate crystals on the epithelial cells of the gallbladder causes increase in COX-2 activity in the epithelial cells of the gallbladder mucosa and transformation of the gallbladder dysfunction into chronic acalculous cholecystitis without biliary sludge.

Pathogenetic treatment of patients with gallbladder dysfunction

Treatment of gallbladder dysfunction (gallbladder hypomotility with biliary pain) and for prophylactics of the chronic acalculous cholecystitis includes:

1. Celecoxib – 100 mg, 2 times a day after meal for 5-7 days, after which
2. Ursodeoxycholic acid – 750 mg, once a day in the evening for 2 month.

Celecoxib is a selective inhibitor of COX-2. Inhibiting COX-2 activity in the smooth muscle cells of the gallbladder wall and cystic duct results in the relief of the biliary pain within 3-5 days, restoration of the evacuation function of the gallbladder and the gallbladder-dependent output of biliary cholesterol, "active" and "passive" passage of the hepatic bile into the gallbladder, and decrease in the gallbladder-independent enterohepatic circulation of bile acids, biliary cholesterol and biliary bilirubin.

Ursodeoxycholic acid (UDCA) is a hydrophilic hepatoprotective bile acid. It helps in dissolving the cholesterol monohydrate crystals in the gallbladder, decrease in lithogenicity of the gallbladder and hepatic bile, disappearance of the chronic "bland" intrahepatic cholestasis (i.e. results in the restoration of the excretion function of the liver) (1-66).

Celecoxib is a selective inhibitor of COX-2. Inhibiting COX-2 activity in the smooth muscle cells of the biliary tract and the sphincter of Oddi it brings relief of the biliary pain within 3-5 days, restoration of the passage of the hepatic bile into the duodenum.

Celecoxib is a selective inhibitor of COX-2, inhibiting COX-2 activity in the epithelial cells of the biliary tract mucosa causes decrease in secretion of glycoprotein mucin into the biliary tract lumen, concentration of the glycoprotein biliary mucin in the hepatic bile and viscosity of hepatic bile, which prevents formation of biliary sludge and gallstones in the common hepatic duct and common bile duct. Low COX-2 activity in the epithelial cells and the smooth muscle cells of the biliary tract helps in lowering the risk of choledocholithiasis development.

Ursodeoxycholic acid (UDCA) is a hydrophilic hepatoprotective bile acid. It helps in dissolving the cholesterol monohydrate crystals in the biliary tract, decrease in lithogenicity of hepatic bile, disappearance of the chronic "bland" intrahepatic cholestasis (i.e. results in the restoration of the accumulation and excretion functions of liver), and in some patients helps in dissolving the biliary sludge in the biliary tract.

Ursodeoxycholic acid (UDCA) is a hydrophilic hepatoprotective bile acid, decreasing aggressive properties of bile, prevents development of chronic atrophic antral gastritis (duodenogastric reflux and bile reflux gastritis) and duodeno-gastroesophageal reflux (incompetence of Oddi's sphincter), chronic biliary pancreatitis (biliopancreatic reflux) or chronic spastic aseptic pancreatitis (pancreatic type III of sphincter of Oddi dysfunction).

Celecoxib and Ursodeoxycholic acid (UDCA), pathogenetically blocking main mechanisms of gallstone formation, help in prophylactics of gallstone formation in the biliary tract, and lower the risk of development of choledocholithiasis and chronic biliary pancreatitis (1-66).

Effectiveness is 95%.

Remission period is 18-24 months.

Attention!!! Information for patients:

Before using this scheme of treatment please check the contraindications (below) and side

effects of using pharmacological preparations of Celecoxib and Ursodeoxycholic acid (UDCA), and obtain your doctor's permission.

Contraindications for Celecoxib:

- allergic reactions (nettle-rash, bronchial spasm) to acetylsalicylic acid or other NSAIDs (in anamnesis);
- 3rd trimester of pregnancy;
- high sensitivity to sulphonamides;
- high sensitivity to any component of the preparation.

Contraindications for ursodeoxycholic acid (UDCA):

- high sensitivity to the preparation;
- acute inflammatory diseases of the gallbladder and the bile ducts;
- ulcerative colitis;
- Crone's disease.

This web page does not bear any legal responsibility for usage of the treatment schemes, given here, without consulting your doctor.

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