Current Concept of Etiology and Pathogenesis in Acute Obstructive Cholecystitis

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Abstract

403 older patients with acute calculous cholecystitis (catarrhal and destructive) with severe comorbid diseases and increased risk of surgery underwent minimally invasive laparoscopic cholecystolithostomy performed as a preliminary or definitive stage of surgical treatment. Based on observational methods stemming from this laproscopic technique, the role of mechanical obstruction (calculous cholecystitis) in the onset of an acute cholecystitis attack has been described in detail. Furthermore, two novel factors are identified: the inflammation of infundibular-cystic junction mucosa (inflammatory factor) and the increased viscocity of the bile (colloidal factor). The role of these in acute cholecystitis and on the development of intravesicular hypertension is described. All of the factors – mechanical, inflammatory, colloidal – form a vicious cycle in acute cholecystitis, their interdependency having a direct action on the progression of disease. The major role of laparoscopic bile decompression in solving the acute obstructive cholecystitis in high-risk patients has been emphasized.

Key-words: acute obstructive cholecystitis, impacted calculus, free calculus, calculous cholecystitis, inflammation of infundibular-cystic junction mucosa, increased bile viscosity, percutaneous cholecystostomy.

Современная концепция этиопатогенеза острого обструктивного холецистита

У 403 больных пожилого и старческого возраста с острым калькулезным холециститом и тяжелыми сопутствующими заболеваниями с высоким операционным риском была проведена щадящая лапароскопическая холецистолитостомия как предварительный или окончательный этап хирургического лечения. На основании современных методов исследования, исходящих из лапароскопической технологии, был изучен и детализирован механический фактор обструкции (вклиненные камни) желчного пузыря в развитии острого холецистита. Кроме того, было выявлено еще 2 новых дополнительных фактора: воспаление слизистой пузырно-шеечного сегмента (воспалительный фактор) и повышение вязкости желчи (коллоидный фактор), и их роль в патогенезе острого холецистита в развитии внутрипузырной гипертензии. Все факторы – механический, воспалительный и коллоидный создают порочный круг в возникновении и развитии острого холецистита, а их взаимозависимость имеет непосредственное значение в развитии болезни. Показана ведущая роль билиарной лапароскопической декомпрессии в разрешении острого обструктивного холецистита в группе больных повышенного риска.

Ключевые слова: острый обструктивный холецистит, вклиненный камень, свободно плавающий камень, повышенная вязкость желчи, лапароскопическая холецистолитостомия.

Introduction

For a long time acute cholecystitis was considered to be the result of an infectious process localized in the gallbladder, producing lesions of variable severity in its wall.

However, studies conducted in the last decades showed that the microbial factor was far from being the "primum movens" in the development of acute cholecystitis. According to data presented by many authors (4, 5, 6, 7) acute cholecystitis is initially an aseptic disease, the infection being secondary. At present, most of the authors consider biliary hypertension to be the dominant factor in the pathogenesis of acute cholecystitis. The mechanism triggering acute obstructive cholecystitis is the acute impaction of a gallstone in the cholecystic infundibulum or cystic duct; the real danger of a developing infection with subsequent cholecystic wall destruction is secondary.

At a pressure of 250-300 mmH2O, microcirculation impairments develop in the gallbladder wall, whereas at pressures of 700-800 mmH2O blood circulation disturbances in the cystic artery branches are present. It has been noted that patients with phlegmonous acute cholecystitis have an intravesicular pressure of 300 – 400 mm H2O, while those with gangrenous cholecystitis have increased pressures up to 1000 mm H2O (1, 4). It is certain that even with lower intravesicular pressures, the developement of microcirculation impairments contributes to the reduced resistance in the gallbladder wall tissues promoting infection penetration into deeper layers of the gallbladder wall and beyond.

Moreover, impaired blood circulation of the gallbladder affects the penetration of medications into both the gallbladder cavity and its wall.

Thus, conservative treatment fails to achieve good results. A sharp increase of intravesicular pressure, particularly in the elderly, may lead to thrombosis in the cystic artery branches, in which case conservative treatment will be ineffective (4, 8). Picovschi D L. (1980) states that gallbladder obstruction in most cases is the result of calculus impaction in the Hartmann pouch/gallbladder infundibulum, and less frequently in the cystic duct. The process can evolve in three directions:

Unblocking the cholecyst

Either spontaneously or with conservative treatment, the infundibular-cystic obstruction is cleared by calculus dislodgement. In this case the calculus dislodges distally into the gallbladder cavity. The gallbladder content is then drained through the cystic duct into the common bile duct and manifestations of intravesicular hypertension disappear, which in

turn decreases the inflammation. In these cases conservative treatment is efficient and the patient can choose to undergo an elective cholecystectomy at a future date.

Development of hydrops of the gallbladder

When infection is absent or its virulence is weak and elasticity and extension properties in the cholecyst wall are maintained, the acute attack can result in hydrops of the gallbladder (less then 5%) which is an indication for a scheduled surgery.

Destructive cholecystitis

If dislodging of the calculus does not occur, there is risk of secondary bacterial contamination in the obstructed gallbladder (fever, leukocytosis focal tenderness and guarding) - all these indicating the onset of destructive cholecystitis (phlegmonous, gangrenous) accompanied by a sharply increasing intravesicular pressure. In these cases the process goes out of control and requires emergent surgical intervention.

Zollinger R. et al. (1955) and Koroleov B A. et al. (1990) published data showing that initially the process of biliary occlusion results in increased water and bile acids reabsorption with increased bile pigment, calcium carbonate and cholesterol concentrations in the biliary ducts contributing to a rise in osmotic pressure. As a result, the walls of the obstructed biliary system become edematous, the gallbladder expandss and increases in size. If decompression or a surgical operation is not performed at that moment, suppuration and developing ischemia may lead to gangrene and perforation.

The founders of the bile hypertension theory, Koroleov B A. and Picovschi D L. (1990) hypothesize that the pathogenesis of acute obstructive cholecystitis (AOC) includes a number of succesive components:

1. The major inciting factor is mechanical obstruction, represented by a calculus impacted in the infundibulum of the gallbladder and rarely in the cystic duct.
2. Sudden increase of intravesicular pressure.
3. Increase in bile concentration by means of increased water reabsorption and mucous production in the gallbladder lumen.
4. Chemical irritation, edema and aseptic changes in the gallbladder wall.
5. Stasis in the cholecystic vasculature causing microcirculation impairments and secondary ischemia.
6. Secondary contamination with microbial infection.
7. Cholecyst wall destruction from purulent inflammation and ischemia.
8. Infiltration development.
9. Local and general peritonitis.

Material and methods

A group of 403 patients with acute cholecystitis and cholecysto-pancreatitis were included in the study. Clinical, ultrasonographic, endoscopic and radiological parameters referring to the efficiency of bile system drainage were collected.

There were 116 (28.8 ± 2.3%, $p < 0.001$) cases of obstructive catarrhal acute cholelithiasis, phlegmonous cases – 254 (63.0 ± 2.4%, $p < 0.01$), gangrenous – 33 (8.2 ± 1.4%, $p < 0.001$).

The study was based on the following criteria:

1. Ultrasonographic examination of the biliary system.
2. Assessment of intravesicular pressure in different subtypes of acute cholecystitis – catarrhal, phlegmonous and gangrenous.
3. Bacteriological examination of bile.
4. Gallbladder and biliary duct decompression, and its efficiency in the evolution of catarrhal and destructive forms of acute cholecystitis.
5. Assessment of the viscosity of bile collected from the biliary system in catarrhal and destructive cholecystitis.
6. Degree of calculus impaction at the time of its lithoextraction. According to our understanding, we distinguish 3 stages of calculus impaction:

a) Total calculus impaction (TCI) of the gallbladder –during lithoextracion, one or more gallstones were found in the infundibulum/neck of the gallbladder, resulting in complete blockade.

b) Partial calculus impaction (PCI), or the process of its loosening. The calculus is lodged in the neck but allows for bile flow, without completely blocking the cystic duct.

c) Free calculi (FC), when calculi, "float" in the gallbladder without impeding the passage of bile.

8. Presence or absence of bile in the gallbladder lumen at the time of cholecystostomy or after it – presence of bile indicates patency of the cystic duct.
9. Cholecystoscopy of the biliary ducts to control lithoextraction and to inspect the infundibular-cystic junction.
10. Intraoperative and postoperative anterograde fistulocholecystocolangiography (FCCGA) (through the cholecystostomy site drain) that gives an objective assessment of permeability in the cystic duct, as well as the condition of intrahepatic and extrahepatic bile ducts.

Results obtained by the laproscopic technique regarding the above criteria led to the observation of several novel components regarding the pathogenesis of AOC (Author's certificate OS No. 576/1845 from February, 29, 2008).

Results

Of a total of 403 patients, 150 with different forms of acute cholecystitis had the intravesicular pressure measured during the surgical procedure (tab. 1).

Table 1

Manometric values of biliary hypertension in acute cholecystitis

Gallbladder morphology	Intravesicular pressure
Catarrhal	200-250
Phlegmonous	260-450 mm of water
Gangrenous	500-900 mm of water

Manometric values in catarrhal acute cholecystitis were within 200-250 mm H2O, in phlegmonous form – 260-450 mm H2O, in phlegmonous – 500-900 mm H2O. The level of hypertension correlated directly with the pathomorphological changes: the higher the pressure, the more severe the morphological changes.

We performed the bacteriological investigation of the gallbladder fluid in 126 cases (fig. 1).

Bacterial infection of the bile was confirmed in 65 (51.6%) cultures. In most cases the microbial pathogen was a Gram-negative aerobic organism (*E. coli, Klebsiella pneumoniae*) and occasionally a Gram-positive organism (enterococci). The time elapsed from the onset of the disease is important i. e. the longer the period, the more frequently bacteria are detected The low rate of positive cultures (51.6%) and the fact that their detection increases with increased latency from the onset of obstruction, both confirm the hypothesis that infection in acute cholecystitis as a secondary factor.

During laparoscopic cholecystostomy with lithoextraction, not all patients with catarrhal acute cholecystitis had impacted calculi (tab. 2). A total calculus impaction (TCI) was detected in 46 cases (39.7 ± 4.5%, $p < 0.001$), partial calculus impaction (PCI) – in 32 cases (27.6 ± 4.2%, $p < 0.001$) and free calculi (FC) in 38 cases (32.7 ± 4.4%, $p < 0.001$). Thus, if we assume that the trigger for all of these acute cholecystitis events was an impacted calculus, we suggest that the bile sequestered in the gallbladder, as well as the additional secreted mucous, distended the gallbladder volume leading to spontaneous or gradual calculus dislodgement.

In TCI group, after lithoextraction surgery, bile drainage from the cystic duct into the gallbladder was present in 34 (73.9%) cases, whereas in 12 (26.1%) cases bile was not detected in the gallbladder because of continued cystic duct obstruction, confirmed by an intra-operative and an immediately post-operative FCCGA.

In PCI continued gallbladder blockage was noted in 6 (18.7%) cases, and in 4 (10.5%) cases of FC. The residual obstruction after calculus extraction is likely secondary to inflammation of the mucosa at the junction of the gallbladder neck and cystic duct. Mucosal inflammation and the resulting functional obstruction occurred in 22 cases (19%) of the catarrhal group.

The mechanism of gallbladder obstruction by an impacted calculus is clear. It is more difficult to explain the phenomenon of bile passage disturbance in the cystic duct that persists after the spontaneous calculus dislodgement or lithoextraction. Our hypothesis for the functional obstruction is to regard the inflammation of mucosa in the infundibular-cystic

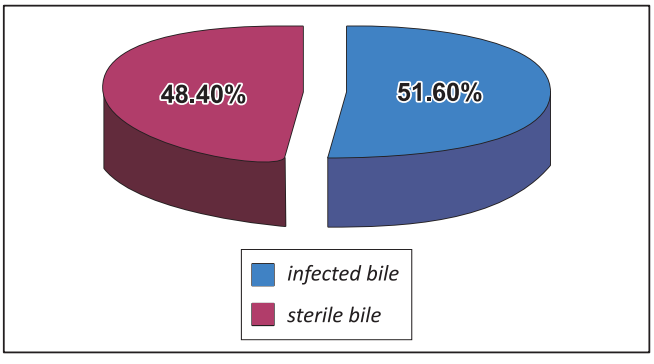

Fig. 1. Bacteriological investigation of bile in the bile cyst.

junction and the proximal cystic duct as a local manifestation of diffuse inflammation in the gallbladder aggravated by an impacted calculus and the resulting intravesicular hypertension. All of this leads to the luminal narrowing and decreased patency of the cystic duct, resulting in the complete blockage detected by cholecystoscopy and FCCGA. Another cause for the persistent obstruction could be prolonged spasms, detected by FCCGA in 3 cases, of the Lutkens sphincter situated in the proximal half of the cystic duct. Yet another cause is mucus secretion which, along with water reabsorption from the bile in the blocked gallbladder, increases the bile viscosity and impairs its evacuation. Our studies showed that the bile viscosity increased in acute catarrhal cholecystitis to 1.2 Pa.s., less frequently to 1.4 Pa.s. Normal value of cholecyst bile viscosity being 1.0 Pa.s.

It should be mentioned, that during laparoscopy more than half of the cases in the PCI group were noted to have a less tense gallbladder morphology compared to those in the TCI group, suggesting the presence of an intermediate stage of restoring bile flow through the cystic duct after calculus dislodgement.

In the FC group, laparoscopy revealed mild gallbladder tension with hyperemic mucosa – a finding confirming increased bile flow into the gallbladder with a gradual decrease in intravesicular pressure.

Analyzing this phenomenon from the clinical perspective, the positive response to conservative treatment in obstructive catarrhal acute cholecystitis is perfectly explicable in a considerable number of cases. Conser-

Table 2

Evaluation of gallbladder and bile duct decompression after laparoscopic cholecystolithostomy (CLSL) in catarrhal obstructive acute cholecystitis

Type of calculus impaction	Number of patients (%)	Cystic duct patency after lithoextraction	Cystic duct obstruction after lithoextraction	Cystic duct patency restoration in progress after CLSL						Cystic duct with patency unrestored
				0-6 hrs	6-12 hrs	12-24 hrs	24-48 hrs	48-72 hrs	Later	
Total calculus inclavation (TCI)	46 39.7 + 4,5%	34 73.9%	12 26.1%	9 75.0%	1 8.3%	-	-	-	-	2 16,7%
Partial calculus inclavation (PCI)	32 27.6 + 4,2%	26 81.3%	6 18.7%	5 83.3%	1 16.7%	-	-	-	-	-
Free calculi (FC)	38 32.7 + 4,4%	34 9.5%	4 10.5%	4 100.0	-	-	-	-	-	-
Total	116 100%	94 81%	22 19%	18 15.5%	2 1.7%	-	-	-	-	2 1,7%

Table 3

Evaluation of gallbladder and bile duct decompression after laparoscopic cholecystolithostomy (CLSL) in phlegmonous obstructive acute cholecystitis

Type of calculus impaction	Number of patients (%)	Cystic duct patency after lithoextraction	Cystic duct obstruction after lithoextraction	Cystic duct patency restoration in progress after CLSL						Cystic duct with patency unrestored
				0-6 hrs	6-12 hrs	12-24 hrs	24-48 hrs	48-72 hrs	Later	
Total calculus inclavation (TCI)	53 20.9 + 2.6%	20 37.7%	33 62.3%	21 63.6%	6 8.2%	3 9%	1	-	-	2 6%
Partial calculus inclavation (PCI)	66 26 + 2.8 %	27 40.9%	39 59.1%	28 71.8%	7 18%	2 5.1%	-	-	-	2 5.1%
Free calculi (FC)	135 53.1 + 3.1%	65 44.8%	70 55.2%	60 85.7%	7 10%	2 2.9%	-	-	-	1 1.4%
Total	254 100%	112 44.1%	142 55.9%	109 42.%	20 7.9%	7 2.8%	1 0.4%	-	-	5 2.0%

vative treatment is ineffective when calculi do not dislodge or when, after calculus dislodgement, the blockage persists because of presence of inflammation or, in rare cases, because the calculi passed into the cystic duct where it again became lodged.

Persisting functional obstruction after laparoscopic lithoextraction and decompression occured most frequently in the TCI group – 12 (26.1%) cases, followed by the PCI group – 6 (18.7%) cases and finally the FC group – 4 (10.5%) cases. A correlation between ductal patency and degree of calculus dislodgement is evident.

Following decompression, the inflammatory processes in the gallbladder begins to regress soon after cystic duct patency is reestablished. Thus, in 18 of the 22 patients (81.8%) in whom residual obstruction remained after lithoextraction, cystic duct patency restored during the first 6 hours, and only in 2 patients (9%) after 6-12 hours. Patency was established by presence of bile in the percutaneous stoma and confirmed by FCCGA. In 2 of the patients (1.7%) patency was not resotred because the gallstones passed and became lodged in the cystic duct:

- The mechanical factor: impacted calculi – dominant factor – in 39.7% cases;
- The inflammatory factor - inflammation of the mucosa of the gallbladder infundibulum junction with cystic duct – in 19% cases;
- The rise in bile viscosity, in most cases up to 1.2 Pa. s;
- The prolonged spasm of Lutkens sphincter – in 2.6% cases.

An interesting finding that can be mentioned is the proportion in the number of patients with TCI in 2 different types of AOC: 39.7 ± 4.5% cases in the phlegmonous group and approximately half the number, 20.9 ± 2.6% in the catarrhal group.

PCI was observed in 66 (26.0 ± 2.8%) cases with phlegmonous cholecystitis, while the number of patients with FC increased considerably to 135 (53.1 ± 3.1%).

The number of cases of phlegmonous cholecystitis in which cystic duct patency was restored after calculus dislodgement was as follows: TCI – 20 (37.7%), PCI – 27 (40.9%) and FC – 65 (44.8%) cases, mean value being 112 (44.1 ± 3.1%). This was seen in fewer cases as compared to the number of patients in the catarrhal cholecystitis group, mean 81.0 ± 3.6% ($p < 0.001$).

Following lithoextraction, residual obstruction occurred in 33 (62.3%) with TCI, in 39 (59%) patients with PCI and 70 (55.2%) with FC; mean value being 142 (55.9%), approximately three-fold higher frequency than in catarrhal cholecystitis.

Despite dislodgement, residual gallbladder obstruction persists in a considerable number of cases, most likely caused by persistent inflammation. This contributes to the increase in intravesicular hypertension and can progressively develop into gangrene and perforation.

The FC group of patients with restored patency after surgery, 65 (44.8 ± 4.3, $p < 0.001$) in number, are particularly interesting. The question arises as to why the gallbladder does not empty, and it is intereting to note that the inflamed gallbladder proves to be tense and hypertensive at time of laparoscopy.

In such cases the proximal part of the cystic duct is inflamed. FCCGA shows a difficult passage of contrast dye through the cystic duct. Given no mechanical obstruction, the likely cause of the maintained cholecystic hypertension and inflammation is the high frequency of infected bile and its raised viscosity – up to 1.8 Pa.s. These properties hamper bile drainage through the cystic duct, as well as the resolution of the inflammatory process.

Thus there are three factors contributing to the pathogenesis of phlegmonous AOC, characterized by worsening hypertention and inflammation:

1. The mechanical factor (impacted calculi) – 20.8% cases.
2. The inflammatory factor (inflammation of the infundibular-cystic junction mucosa), this factor dominates after calculus dislodgement – 55.9% cases;
3. The colloidal factor (increased bile viscosity) – 1.8 Pa.s.

After laparoscopic lithoextraction and cholecystic decompression, bile drainage is restored within the first 6 hrs in 109 (76.8 ± 2.6%) cases, within 6 to 12 hrs in 20 (14 ± 2.2%) cases, 12 to 24 hrs in 7 (4.9 ± 1.4%) cases and after 24 hrs in only one case. After decompression the gallbaldder inflammation begins to decrease, hence the essential importance of decompression as a first step in the surgical procedure. Cystic duct patency was not restored in 5 (2.0 ± 0.7%) cases because of cystic duct calculi and/or persistent inflammation.

Table 4

Evaluation of gallbladder and bile duct decompression after laparoscopic cholecystolithostomy (CLSL) in gangrenous obstructive acute cholecystitis

Condition of calculus inclavation	Number of patients (%)	Cystic duct permeability after lithoextraction	Cystic duct impermeability after lithoextraction	Cystic duct permeability restoration in progress after CLSL						Cistic duct permeability unrestored
				0-6 hrs	6-12 hrs	12-24 hrs	24-48 hrs	48-72 hrs	Later	
Total calculus inclavation (TCI)	6 18.2 + 6,7%	1 16.7%	5 83.3%	1 20%	1 20%	2 40%	1 20%	-	-	-
Patrial calculus inclavation (TCI)	9 27.3 + 7,8%	2 22.2%	7 77.8%	1 14.3%	2 28.6%	2 28.6%	1 14.3%	-	-	1
Free calculi (FC)	18 54.6 + 8,7%	5 27.8%	13 72.8%	3 23%	3 23%	4 30.8%	2 15.4%	-	-	1
Total	33 100%	8 24.2%	25 75.8%	5 15.5%	6 18.2%	8 24.2%	4 12.1%	-	-	2 6%

We have made the following clinical conclusions: in pre-laparoscopy ultrasound evaluation of acute cholecystitis with the detection of free or dislodged calculi does not necessarily means the resolution of an acute attack, as cholecystic hypertension and inflammation may be maintained by the cystic duct obstruction secondary to inflammation and/or raised bile viscosity. In such cases laparoscopy is indicated to evaluate the gallbladder condition and morphology.

Surgical treatment is imperative in phlegmonous AOC. High-risk patients undergo laparoscopic decompression and medical treatment aiming to target infection and optimize the circulating blood volume.

In gangrenous AOC (tab. 4) the number of TCI cases is even less – 6 (18.2 ± 6.7%, $p < 0.05$), PCI – 9 (27.3 ± 7.8%, $p < 0.01$) cases and FC – 18 (54.6 ± 8.7%, $p < 0.001$) cases.

We note that the severity of calculus impaction is inversely proportional to the degree of inflammation (cattarhal, phlegmonous, or gangrenous). Cystic duct patency after laparoscopy in gangrenous cholecystitis was present in only 8 (24.4%) cases, while in 25 (75.8%) patients the obstruction persisted. Bile viscosity in gangrenous cholecystitis was as high as 2 Pa. s. The causative factors contributing to gangrenous cholecystitis are:

1. The mechanical factor (impacted calculi) – 18.2% patients.
2. The inflammatory factor (inflammation of the infundibular-cystic junction) – 75.8% patients.
3. The colloidal factor (considerable bile viscosity) – 2.0 Pa. s.

Bile drainage from the gallbladder was restored in the first 6 hrs in 5 (15.5%) patients, within 6-12 hrs in 6 (18.2%) patients, within 12-24 hrs in 8 (24.2%) patients and after 24-48 hrs in 4 (12.1%) patients. Overall, bile drainage rsumed in most cases within the first 24 hrs, predominantly at 12-24 hrs, but in 16% of cases drainage was restored after 24 hrs. In no cases did laparoscopic decompression and lithoextraction aggravate the inflammatory process and cause perforation. On the contrary, after the surgical intervention, the morphological changes in the gallbladder improved to resemble those of chronic cholecystitis.

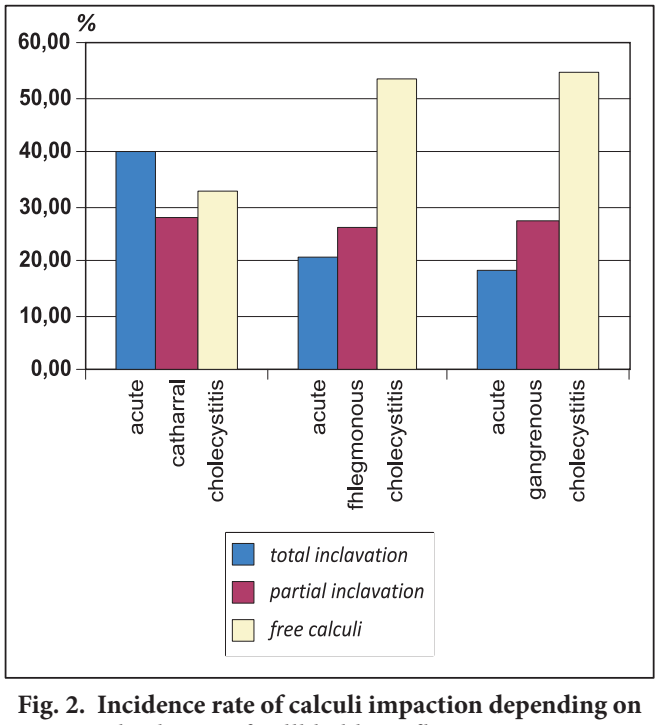

Fig. 2. Incidence rate of calculi impaction depending on the degree of gallbladder inflammation.

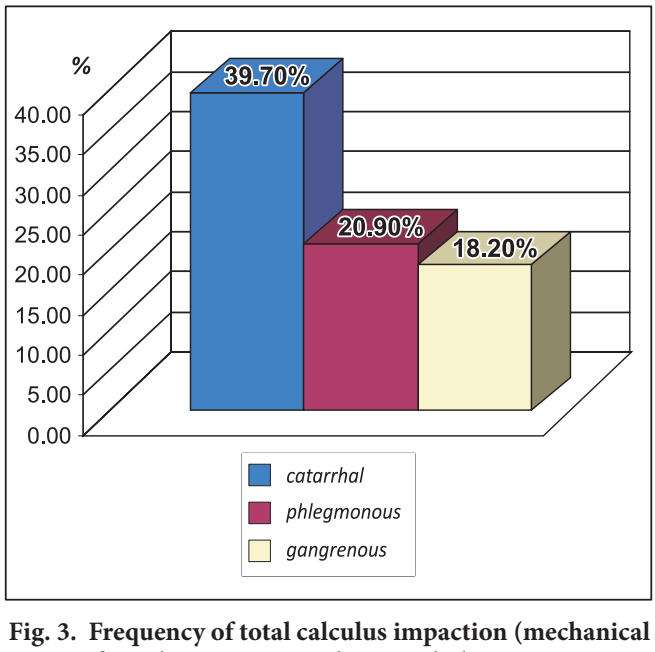

Fig. 3. Frequency of total calculus impaction (mechanical factor) in patients with acute cholecystitis.

In summary, we can conclude that impacted calculi are the leading factor in triggering biliary hypertension. However, after the onset of an acute attack, impacted calculi may start to gradually loosen and become dislodged, yet the inflammatory process and obstruction may continue for some residual time. Correlation between the degree of calculi impaction and the process of their dislodgement is shown in fig. 2.

Despite expectations, the TCI incidence decreases gradually from 39.7% in catarrhal cholecystitis to 20.9% in phlegmonous cholecystitis and to 18.2% in the gangrenous form (fig. 3).

According to Koroliov B A. and Picovschi D I. (1990), if the cause of acute cholecystitis attacks was just the mechanical impaction of calculi, then spontaneous resolution due to gradual calculi dislodgement would be much higher. But this does not happen because the pathogenic chain of events leads to the inflammation of the infundibular-cystic junction mucosa (fig. 4). This secondary cause of obstruction increases from 19% in catarrhal cholecystitis to 55.9% in the phlegmonous form and up to 75.8% in gangrenous cholecystitis, becoming the dominant factor of blockage that in turns contributes to worsening intravesicular hypertension and inflammation. In addition, the colloidal factor of increased bile viscosity increases from 1.2 Pa. s in catarrhal cholecystitis, 1.8 Pa. s in the phlegmonous and 2 Pa. s in the gangrenous form (fig. 5).

The increased viscosity component hampers gallbladder drainage aggravating both the vesicular hypertension and the inflammation of the gallbladder walls.

An additional factor maintaining bile stasis in the gallbladder may be the highly varied anatomical structure of the cystic duct – a long cystic duct, with a lumen that is narrow, convoluted, twisted, etc. (fig. 6-10) impedes, to some extent, bile drainage into the biliary duct system.

The clinical value in laparoscopic cholestostomy is biliary system decompression and the external drainage of the inflammatory focus. This contributes to the overall control of the acute inflammatory process by decreasing biliary tension, evacuating infected bile and limiting gallbladder necrosis, Despite many existing opinions, the gallbladder has a good capacity to regenerate and is mostly able to recover its morphological and functional properties even in cases of inflammations with small necrotic foci however, only if efficient decompression, calculi removal and external drainage of the infected contents (through an open stomy left after lithoextraction) have been performed.

Mucosal necrotic areas desquamate in the gallbladder lumen and the remaining ulcerations scar over. Small foci of necrosis affecting all layers of the gallbladder wall recover by forming an inflammatory infiltrate with subsequent fibrosis and deformation of the gallbladder morphology. On the basis of these studies laparoscopic decompression is feasible and recommended in gangrenous cholecystitis, the exception being complete gangrene of the gallbladder.

Conclusions

1. Calculus impaction in the infundibulum of the gallbladder and/or cystic duct, with resulting gallbladder obstruction

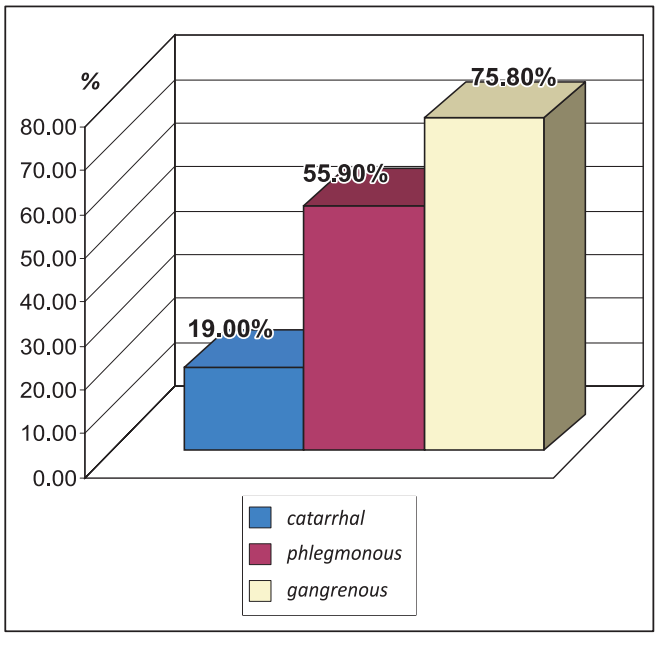

Fig. 4. Incidence of residual obstruction secondary to inflammation of the infundibular-cystic junction mucosa (inflammatory factor) in acute cholecystitis patients.

is the leading factor in the onset of acute cholecystitis. As inflammation develops, increased secretions into the gallbladder lumen contributes to its increased volume which in turn promotes dislodgement of the impacted calculus; but only in some patients (catarrhal > phlegmonous > gangrenous) does this lead to immediate resolution of symptoms.

2. After decompression and laparoscopic lithoextraction, remaining gallbladder obstruction is seen in catarrhral cholecystitis in 19.0 ± 3.6% of patients, in phlegmonous in 55.9 ± 3.1 % of patients, and in gangrenous in 75.8 ± 7.5% of patients. Residual obstruction remains the main cause of progressive biliary hypertension and inflammation of the gallbladder wall.

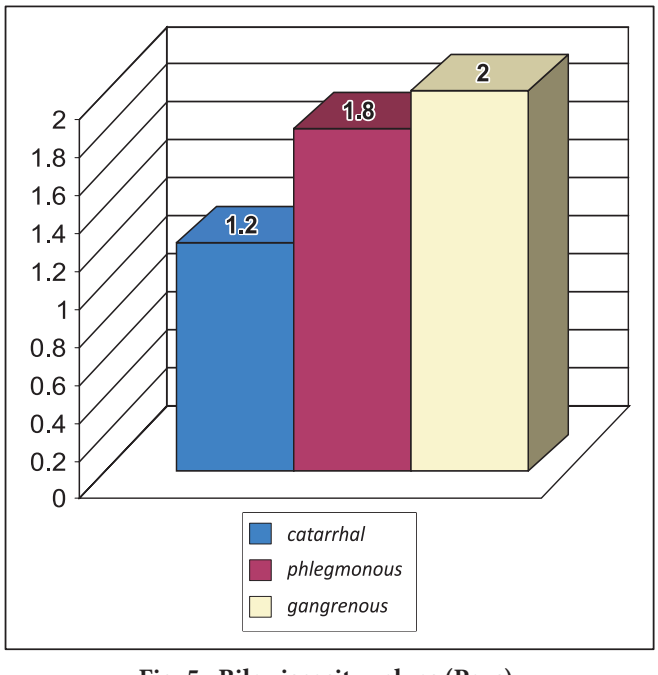

Fig. 5. Bile viscosity values (Pa. s).

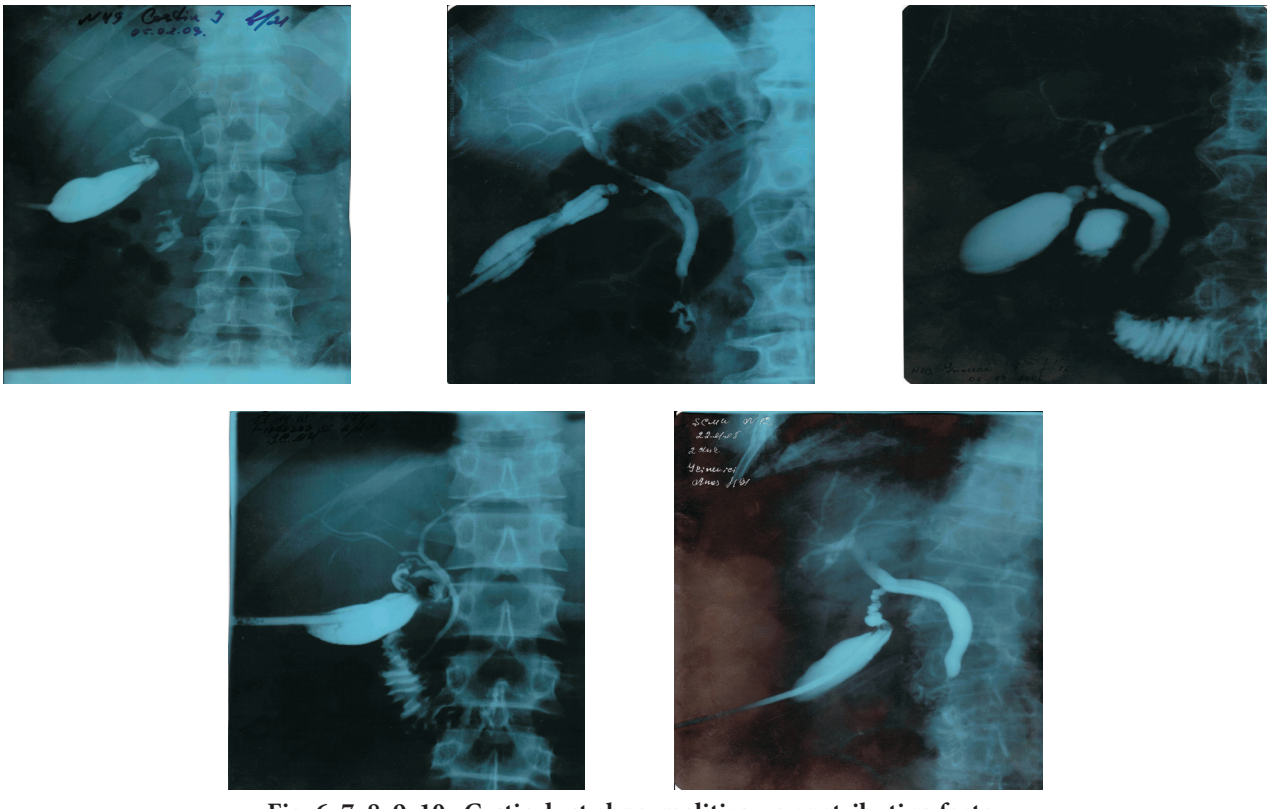

Fig. 6, 7, 8, 9, 10. Cystic duct abnormalities – a contributing factor in the development of obstructive cholecystitis as detected by FCCGA.

3. The increase in bile viscocity is another aggravating factor in the progressive intravesicular hypertension and inflammation. In the catarrhal cholecystitis viscosity is 1.2 Pa. s, in the phlegmonous it increases to 1.8 Pa. s and in gangrenous it is 2.0 Pa. s.

4. In catarrhal AOC the cause of obstruction is often an impacted calculus, with functional obstruction secondary to residual inflammation being a secondary cause. The growing bile viscosity and, in some cases, the prolonged Lutkens sphincter spasm have an additional importance in persistence of bile stasis. In this type of AOC conservative treatment initiated in a timely manner may be effective for many patients.

5. In phlegmonous AOC there are three equally important factors maintaining gallbladder obstruction: impacted calculi, the increasingly-becoming dominant factor of inflammation and the increased viscosity of bile. When the latter two factors predominate, cystic patency is not seen even after calculus dislodgement. Inflammation progresses and medical treatment is ineffective. In gangrenous AOC the dominating mechanisms of biliary obstruction, hypertension and inflammation are similar.

6. All the above mentioned factors contributing to cholecystic obstruction lead to intravesicular hypertension, persistent acute inflammation and subsequent gangrene and perforation.

7. Lithoextraction and decompression of the concentrated, high-viscocity bile decrease the intravesicular hypertension and inflammation (both the catarrhal and the destructive forms) and eventually restore cystic duct permeability in most cases.

8. After decompression, cholecystic inflammation decreases rapidly and the patency of the cystic duct is restored. In catarrhal cholecystitis most of the patency restoration occurs within the first 6 hours, after 6-12 hrs in phlegmonous and after 12-24 hrs in most cases of gangrenous cholecystitis. Furthermore, our studies confirmed the safety of laparoscopic cholecystostomy in gangrenous cholecystitis, with the exception of cases with total gangrene of the gallbladder.

9. Despite many existing opinions, the gallbladder – as a result of an efficient decompression with lithoextraction and external lavage – shows good capacity to regenerate, recovering its morphological and functional properties. This occurs even in cases of inflammations with small necrotic foci.

10. Thanks to the positive effect of laparoscopic decompression and minimal trauma, the surgical treatment of high-risk patients may be divided into 2 steps: laparoscopic cholecystostomy with lithoextraction and subsequent cholecystectomy. For those patients with significant comorbid diseases who are contraindicated to receive general anesthesia, laparoscopic cholecystolithostomy remains the only method of treatment.

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Терапевтическая эффективность комбинации препаратов Гепафил и Мекоморивитал Ф у больных хроническими вирусными гепатитами

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Therapeutic Efficacy of Combination Drugs Hepaphyll and Mekomorivital F in Patients with Chronic Viral Hepatitis

The therapeutic efficacy of a combination of drugs "Hepaphyll" and "Mekomorivital F" was evaluated in the treatment of patients with chronic hepatitis of viral etiology. A comparative study involved 63 patients who were diagnosed with chronic hepatitis of viral etiology: patients from the main group (32 pers.) treated with drugs "Hepaphyll" and "Mekomorivital F" in therapeutic doses for 24 days, and patients of the comparison group (31 pers.) during this period were under clinical and laboratory observation. Effectiveness of therapy was evaluated by the dynamics of the main indicators of clinical and laboratory hepatic syndromes. After 4 weeks of the administration of the combination of drugs "Hepaphyll" and "Mekomorivital F", patients diagnosed with chronic viral hepatitis were noted as feeling better, and most biochemical parameters improve.

Key words: Hepaphyll, Mekomorivital F, hepatoprotective drug, chronic hepatitis of viral etiology.

Реферат

Оценена терапевтическая эффективность комбинации препаратов Гепафил и Мекоморивитал Ф в терапии больных хроническими гепатитами вирусной этиологии. В сравнительном исследовании принимало участие 63 пациента с диагнозом хронический гепатит вирусной этиологии: пациенты основной группы (32 чел.) получали лечение препаратами Гепафил и Мекоморивитал Ф в терапевтических дозах в течение 24 дней, а пациенты группы сравнения (31 чел.) в течение данного периода находились под клинико-лабораторным наблюдением. Эффективность терапии была оценена по динамике показателей основных клинико-лабораторных печеночных синдромов. При приеме, в течение 4 недель, комбинации препаратов Гепафил и Мекоморивитал Ф у пациентов с диагнозом хронический вирусный гепатит было отмечено улучшение самочувствия и биохимических показателей.

Ключевые слова: Гепафил, Мекоморивитал Ф, гепатопротекторы, хронический гепатит вирусной этиологии.

Введение

Широкое внедрение современных методик лечения хронических вирусных гепатитов с использованием противовирусных препаратов в Республике Молдова является для отечественной системы здравоохранения весьма проблематичной задачей. Сложность ситуации обусловлена целым рядом объективных факторов, не