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Improvement of the Method of Treatment of Patients with Acute Calculous Cholecystitis Complicated by Choledocholithiasis

Radjabov Anvar Islomovich, Safoev Bakodir Barnoevich, Boltaev Timur Shavkatovich

Bukhara State Medical Institute, Bukhara, Uzbekistan

Abstract This scientific article is devoted to improving the treatment results of patients with acute calculous cholecystitis complicated by choledocholithiasis by improving minimally invasive methods. The results of the study led to the development of a more effective method for treating patients with choledocholithiasis, which contributed to a decrease in intraoperative and postoperative complications, as well as a decrease in the duration of surgery and the length of stay of patients in the hospital. The article is based on a retrospective and prospective study of patients with acute calculous cholecystitis complicated by choledocholithiasis, who were treated in the general surgery department of the Central Hospital of the Medical Department of the Ministry of Internal Affairs of the Republic of Uzbekistan, for the period 2018-2023.

Keywords Cholelithiasis, Choledocholithiasis, Endoscopic retrograde cholangiopancreatography, Endoscopic papillosphincterotomy

1. Introduction

All over the world, cholelithiasis is rightfully considered one of the most common diseases and is second only to atherosclerosis, leaving behind peptic ulcer of the stomach and duodenum. In this regard, the treatment of well-being disease, as cholelithiasis was figuratively called, is one of the most important problems of modern surgeons [3,7]. According to various authors, gallstone disease affects from 10 to 40% of the population of various ages. Mortality in different age groups in acute calculous cholecystitis in emergency surgery varies from 1 to 50% or more. In planned and delayed operations performed against the background of relieved acute inflammatory phenomena, after a comprehensive examination and preparation of patients, it does not exceed 0.5-1% [4,10].

In all countries of the world, the number of patients increases approximately twice over the past decade. The increase in the incidence of cholelithiasis is accompanied by an increase in the frequency of its complicated forms. In women, cholelithiasis occurs 2-6 times more often than in men. Large-scale epidemiological studies have established that the main risk factors for developing cholelithiasis are heredity, overweight, hyperlipidemia, and belonging to the female sexy. The incidence increases with age. About 2.5 million biliary tract surgeries (mainly cholecystectomy) are performed annually in the world [1,5].

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This dissertation research serves to a certain extent to fulfill the tasks stipulated in the Decree of the President of the Republic of Uzbekistan No. UP-6110 of November 12, 2020 "On measures to introduce fundamentally new mechanisms in the activities of primary health care institutions and further improve the effectiveness of reforms in the health system", as well as in other regulatory documents, taken in this direction [2,6].

In our country, among the large-scale measures implemented to improve the health care system, special attention is paid to early diagnosis of diseases, prevention and reduction of their complications. In this regard, 4 out of 7 priority areas indicated in the development strategy of the new Uzbekistan for 2022-2026 were noted: comprehensive measures aimed at implementing the program on public health, increasing the capacity of medical workers and developing the health system for 2022-2026 [8,9].

Objective: to improve the results of treatment of patients with acute calculous cholecystitis complicated by choledocholithiasis by using minimally invasive methods of treatment with nitroglycerin and electroactivated aqueous solution-A (EAS-A).

2. Material and Research Methods

The clinical characteristics of patients are given and are described the means used, clinical and laboratory, instrumental research methods and methods of treatment of patients are described.

The work is based on the results of examination and treatment of patients with acute calculous cholecystitis complicated by choledocholithiasis who were treated in the General Surgery Department of the Central Hospital of the Medical Department of the Ministry of Internal Affairs of the Republic of Uzbekistan for the period 2018-2023.

All 46 patients examined had acute calculous cholecystitis complicated by choledocholithiasis, in the treatment complex of which, in addition to the methods used, retrograde lavage of the lumen of the common bile duct with an electroactivated solution of EAS-A was used in order to accelerate the time of stopping the cholangitis process.

All examined patients had their body temperature and respiratory rate urgently measured on the day of admission, objective liver examination (palpation, percussion), ultrasound, and, if necessary, multislice computed tomography or computed tomography of the abdominal organs were performed. Laboratory blood tests, conservative general strengthening and symptomatic therapy, and preparation for minimally invasive surgical intervention - endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction were performed.

Endoscopic retrograde cholangiopancreatography was performed if choledocholithiasis was suspected, to determine the nature of mechanical jaundice, and to study the anatomy of the ducts before surgery. If a blockage or narrowing of the ducts was detected, additional procedures were performed:

1) insertion of a catheter to remove excess bile;
2) removal ofgallstones from the bile ducts;
3) sphincterotomy: a small incision in the area of the external opening of the common bile duct, which ensures the normal outflow of bile and the exit of small gallstones.

Endoscopic papillosphincterotomy was performed in an operating room equipped with modern X-ray equipment used for additional monitoring.

The procedure was performed using endoscopic equipment and a special instrument, which is a thin tube with a cutting tip.

After completing the main manipulations, stones were removed according to the indications, and a biopsy was performed if necessary.

To prepare an electroactivated aqueous solution, we used the Espero-1 NPF device, developed in 1998 by S. A. Alekhin, an employee of the Tashkent medical Institute. Bioelectroactivator type "Espero-1" is approved by the Pharmaceutical Committee of the Republic of Uzbekistan for obtaining drugs used in medical and clinical practice, and was widely used by employees of the V.Vakhidov Research Institute.

All examined patients were admitted in satisfactory condition up to 30% and in moderate condition up to 70%. In most cases, patients were admitted with complaints of increased body temperature, general weakness and malaise, sweating, lack of appetite, pain in the right hypochondrium.

During retrograde cholangiographic intervention, materials were taken from the bile duct contents for bacteriological examination. Antibiotic therapy was carried out taking into account the sensitivity of the identified microflora. The sensitivity of microorganisms was determined by the "disk-diffusion" method.

The leukocyte intoxication index (LII) was also assessed separately - the ratio of neutrophilic leukocytes to lymphocytes, monocytes and eosinophils and the lymphocyte index (LI). The level of endogenous intoxication was assessed by the volume (degree) of medium molecular weight peptides (MMP), spectrometry at a wavelength of 210 nm.

All patients had their total bilirubin, ALT and AST levels determined in the blood from the moment of admission. The bilirubin level in the blood serum was determined using the Van den Berg method.

Mathematical processing of the obtained data results was carried out by methods of variation statistics. Using the method of variation statistics, the arithmetic mean (M), its error (±m), 95% confidence interval CI, Student's criterion (t) at different levels of significance (P) were determined. Results were considered reliable at $P<0.05$.

3. Results and Their Discussions

In order to speed up the time of stopping the cholangitis process, the treatment complex was supplemented with retrograde lavage of the lumen of the common bile duct with an electroactivated aqueous solution of EAS-A, which has the following properties, expressed by antimicrobial, anti-inflammatory, antibacterial actions.

Of the 46 patients examined, the first stage of the operation was successful in 41 (89.1%) patients and resulted in complete removal of stones from the common bile duct. The duration of the first stage of operations with successful completion of ERCP and endoscopic papillosphincterotomy with lithoextraction averaged 35.4±1.9 minutes.

All such patients underwent the second stage of surgical intervention – cholecystectomy – after the acute inflammatory process in the lesion had been stopped and the intoxication indices and blood bilirubin had been normalized by the 5th-6th day. In 5 (10.8%) patients, due to dense wedging and high location of the calculus against the background of severe spasm of the muscular structures of the common bile duct, the first stage of the operation was unsuccessful – it was not possible to remove the calculi by endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction. In 1 (2.1%) case, intraoperative bleeding from the vessels of the common bile duct was observed during the first operation due to technical difficulties. In 5 patients (10.8%), removal of common bile duct stones by antegrade route with drainage of the common bile duct lumen and one-stage cholecystectomy was forcedly performed against the background of acute cholecystitis with high intoxication of the body. Of the 41 patients (89.1%) in whom stones were successfully removed at the first stage using endoscopic retrograde cholangiopancreatography

and endoscopic papillosphincterotomy with lithoextraction, in 40 patients (97.5%) after general detoxification and anti-inflammatory conservative therapy, delayed operations were performed by the 5-6th day: laparoscopic cholecystectomy. In 1 (2.1%) patient, due to the presence of a contraindication to laparoscopic surgery at the second stage, on the 6th day after successful endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction, cholecystectomy was performed using an open laparotomy method.

Thus, in patients of the third group, in only 7 cases (15.2%), open surgeries were performed using a midline laparotomic approach (Figure 1).

Analysis of the results of intoxication indicators in patients revealed the following changes: on the first day of treatment, body temperature varied in the range of 38.8±-0.06. In the general blood test, the content of leukocytes averaged 8.7± 0.17. The volume of average molecules varied in the range of 0.192±0.011. An increase in ESR and LII was also observed.

In most cases, 44 (95.6%) patients showed signs of cholangitis and hyperbilirubinemia against the background of mechanical jaundice.

Taking into account the peculiarities of clinical and surgical tactics, patients distributed by reasons of surgery performed at the first stage have open laparotomy access.

Analysis of the treatment results of patients operated by an open method due to the impossibility of removing the calculus during endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction at the first stage.

Of the 4 patients in whom it was not possible to remove a calculus during endoscopic retrograde cholangiopancreatography, in 2 (50%) the common bile duct calculus was localized in the upper third of the common bile duct, in 1 (25%) patient the calculus was localized in the middle third of the common bile duct, in 1 (25%) patient the obstructing calculus was located in the lower third of the common bile duct.

In all these patients, the stone sizes were not less than 7-8 mm, which was the main reason for the unsuccessful performance of endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction within 30-40 minutes. In this connection, it was decided to suspend the procedure and move on to emergency-deferred laparotomy after appropriate preoperative preparation.

The average duration of open operations in patients of this group was 65±3.1 minutes.

Drainage tubes were removed from the abdominal cavity on the 5th-6th day. Drainage from the common bile duct was removed by days 8-9 of treatment.

Analysis of the results of intoxication parameters of the examined patients revealed the following changes: on the first day of treatment, the body temperature of the patients averaged 38.8 ± 0.06. The content of leukocytes in the blood averaged 8.7 ± 0.17 x 109 / l. The volume of medium molecules averaged 0.192 ± 0.011 units. Similarly, an increase in LII and ESR was noted.

Table 1. Dynamics of biochemical blood parameters in patients operated by open method due to impossibility of removing calculus during endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction at the first stage (n=6)

Indicators	1-day	3-day	5-day	8-day	12-day
Total bilirubin	99,3±2,7	28,3±1,9**	19,4±1,1**	17,9±1,3**	17,7±1,1**
Direct bilirubin	80.2±2,6	11,4±1,2*	5,7±0,9**	3,3±0,3**	2,1±0,1**
Indirect bilirubin	19.1±1.8	16.9±1,3*	14,9±1,1**	14,6±1,3**	14,6±0,4**
ALT	49,9±2,9	41,1±2,3**	35,7±0,8**	34,1±1,3**	33,7±0,8*
AST	48,1±1,9	39,1±1,1**	29,8±0,8**	36,7±1,2**	26,4±0,7**

*Note: * - significance differences relative to the previous day's data are significant (*- P<0.05, * * - P<0.01, * * * - P<0.001).*

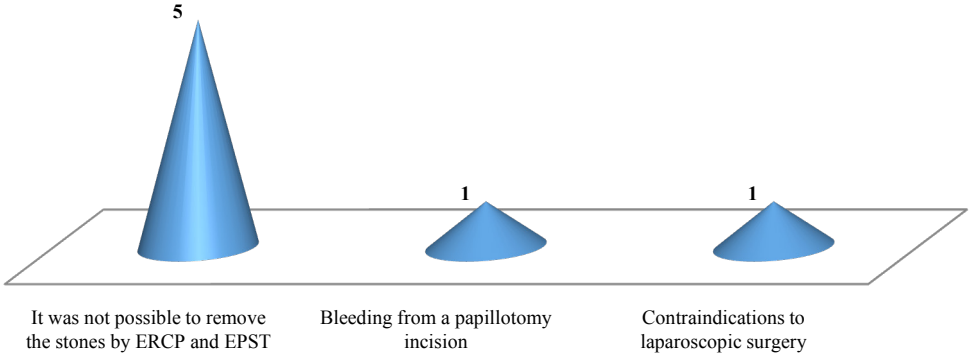

Figure 1. Distribution of patients operated by open method at the first stage according to reasons of conversion

With further treatment and observation by the eighth day, all analyzed intoxication parameters, except for ESR in the blood, were within normal limits. This was ahead of the corresponding indicators of patients of the first and second groups by an average of two days.

The next laboratory criteria for assessing the condition of patients were the study of biochemical parameters: bilirubin, ALT, AST in the blood (Table 1).

All biochemical parameters by the fifth day and thereafter tended to normalize, and by the 7-8th day were within the normal range.

The average duration of inpatient treatment for this category of patients was 12±1.2 days.

Despite the successful first stage of endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction with removal of gallstones, due to the existing contraindications to laparoscopic interventions in the abdominal cavity, one patient underwent open-ended cholecystectomy one day after endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction preoperative preparation. The operation was performed under general anesthesia, upper median access. The operation duration was 65±3.1 minutes. The early postoperative period was uneventful. Drainage tubes were removed from the abdominal cavity on the 5th day after surgery. The patient was discharged on the 9th day of treatment.

It should be noted that in the comparative analysis, the duration of operations of patients did not significantly differ from the duration of operations of patients in the previous groups. Since all patients in this category had identical surgical tactics, due to the failure of endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction at the first stage.

Analysis of the treatment results of patients operated on laparoscopically at the second stage.

Of the 41 (89.1%) patients who successfully removed stones at the first stage using endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction, after general detoxification and anti-inflammatory conservative therapy, 40 (86.9) patients underwent delayed operations on the 5-6th day: cholecystectomy by laparoscopic method.

Table 2. Dynamics of biochemical blood parameters in patients operated by laparoscopic method (n=22)

Indicators	1-day	3-day	5-day	8-day	12-day
Total bilirubin	98,9±2,9	22,2±1,3***	18,1±1,1**	17,3±1,2**	17,1±1,46**
Direct bilirubin	79,9±1,9	6,7±0,8*	3,1±04**	2,7±0,3**	1,8±0,3**
Indirect bilirubin	19.0±1.1	15,5±1,1*	15,0±0,12**	14,6,0,3±**	15,8±0,4**
ALT	40,7±1,3	39,4±1,1**	33,4±2,1**	30,0±1,2**	30,0±1,3*
AST	46,1±2,3	32,1±1,8***	26,9±1,3***	26,7±0,9***	26,4±1,1***

*Note: * - significance differences relative to the previous day's data are significant (*- P<0.05, * * - P<0.01, * * * - P<0.001).*

Table 3. Results of the main indicators of patients

#	Indicators	Patient groups
		III gr (n=46)
1	Stone removal by endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy failed	5 (10.8%)
2	The number of successful endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction	41(89.1%)
3	Bleeding from a papillotomy incision	1(2.1%)
4	Forced single-stage cholecystectomy with open	choledochotomy 5(10.8%)
5	Contraindications to laparoscopic cholecystectomy	1(2.1%)
6	Mean duration of successful ERCP and endoscopic papillosphincterotomy with lithoextraction	35.4±1.9 min
7	Number of open operations of cholecystectomy at the second stage	1 (2.1%)
8	Number of laparoscopic cholecystectomies	40 (86.9%)
9	Average duration of operations performed by open method	65±3.1 min
10	Time of removal of drainage tubes from the abdominal cavity.	5-6 days
11	Average duration of operations performed by laparoscopic method	46.3±2.7 min
12	Number of patients with prolonged cholangitis	-
13	Time of normalization of bilirubin	3-day
14	Time of normalization of intoxication parameters	3-4 days
15	Average duration of hospital days	8.4±1.7

In one patient, due to the presence of a contraindication to laparoscopic surgery, open cholecystectomy was performed on a delayed basis.

Analysis of the results of intoxication indices of the examined patients operated on laparoscopically showed that on the first day of treatment, the body temperature of the patients averaged 38.8 ± 0.060 C. The content of leukocytes in the blood averaged 8.7 ± 0.14 x 109 / l. The volume of medium molecules averaged 0.192 ± 0.016 units. Similarly, an increase in LII and ESR was noted.

During further treatment and observation on the tenth day, all analyzed intoxication indices, except for ESR in the blood, were within normal limits.

The next laboratory criteria for assessing the condition of patients were the study of biochemical parameters: bilirubin, ALT, AST in the blood (Table 2).

These indicators by the fifth day and subsequently had a tendency to normalize, and by the 5-6th day were within the normal range.

Thus, the study we conducted on patients, when analyzed with the results of treatment of patients, revealed the following features, which are of great practical importance: (Table 3).

The use of retrograde sanitation and lavage of the common bile duct using EAS-A for 3-4 days after removal of a stone from the common bile duct by endoscopic retrograde cholangiopancreatography and endoscopic papillosphincterotomy with lithoextraction reduces complications of prolonged cholangitis by 17.7%, accelerating the time of normalization of total bilirubin and body intoxication indicators from 8 to 3-4 days.

In the treatment of patients with acute cholecystitis complicated by choledocholithiasis, the use of nitroglycerin and retrograde sanitation and lavage of the common bile duct with an electroactivated aqueous solution of EAS-A helps to improve treatment results and reduce the duration of inpatient treatment for this category of patients from 12.6 to 8.4 days. All this allows us to widely recommend the use of the treatment method we propose in clinical practice, which is cost-effective.

4. Conclusions

The use of minimally invasive methods in combination with nitroglycerin and EAS-A in the treatment of patients with acute calculous cholecystitis complicated by choledocholithiasis during endoscopic retrograde cholangiopancreatography, endoscopic papillosphincterotomy and lithoextraction more effectively affects the treatment results, while the number of unsuccessful endoscopic retrograde cholangiopancreatography decreases from 25.8% to 10.8%, forced one-stage cholecystectomies with choledochotomy from 35.5% to 10.8%. The average duration of successful endoscopic retrograde cholangiopancreatography is reduced from 52.2±2.8 min to 35.4±1.9 min. The number of two-stage operations increases from 64.5% to 89.1%. Intraoperative bleeding complications are reduced from 9.7% to 2.1%. The periods of normalization of bilirubin and normalization of intoxication indices are 3-4 days. The average length of hospital stays for such patients is 8.4±1.2 days. Taking into account the comparative analysis of the obtained research results, an optimal method for treating patients with acute calculous cholecystitis complicated by choledocholithiasis has been developed using minimally invasive surgical treatment methods with nitroglycerin and EAS-A.

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