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BIOLOGICAL TISSUES HIGH-FREQUENCY ELECTRIC WELDING IN BILIODIGESTIVE ANASTOMOSES FORMATION IN THE EXPERIMENTAL AND CLINICAL CONDITIONS

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Resume

The aim of the study - to improve the treatment results of patients with main bile duct disturbances, using the modern method of tissues high-frequency electric welding (HFEW) for the hepaticojejunic anastomoses formation.

Material and methods. The formation of 15 models of termino-lateral hepaticojejunic anastomoses were performed experimentally. The modelings were done using "bioimitators" in the form of both hepaticocholedochus and small intestine fragments, removed during pancreatoduodenal resections. The HFEW method was used in 14 patients with the main biliary outflow disturbances for hepaticojejunic anastomoses formation: 6 patients were operated as the result of a periampular zone malignant tumor complicated by mechanical jaundice, 2 patients with chronic pancreatitis presented tubular stenosis of the distal part of the common bile duct, 6 patients presented scars and bile ducts iatrogenic lesions. The control group consisted of 60 patients in whom hepaticojejunic anastomoses was formed traditionally.

Results. Hepaticojejunic anastomoses formed by biological tissues radio-frequency (RF)-welding method were passable, completely sealed and had sufficient strength (706.9±70.0 H_2O mm). The primary narrowing of anastomoses lumen, formed by the HFEW method, was smaller (13.6±2.1%), compared to the same in the anastomoses formed by the suture method (49.1±3.4%). It was proved histologically that a coagulation suture was formed during electrowelding, and tissue joining was due to changes in the protein conformation of the intercellular substance and the destructed cells. The comparative analysis of clinical and laboratory data in patients of both main and control groups, provided during the postoperative period, revealed better results in the main group patients compared to the control group – the duration of anastomoses formation in case of RF-welding was averagely by 19 minutes (43.2%) shorter comparing to the duration in case of ligature use; the total bilirubin level throughout the postoperative period decreased quicker in the main group (40.4±6.2 μmol/l) comparing to the decrease in the control group (55.0±8.0 μmol/l); one could register both AlAT and AsAT levels quicker. Ultrasound investigation and Magnetic Resonance Cholangiopancreatography, performed at different times of the postoperative period, also proved HFEW anastomoses good patency and tightness.

Conclusions. HFEW method for soft biological tissues in clinical practice allows to create reliable biodigestive anastomoses, especially in conditions of inflammation. One could see decrease in early postoperative complications frequency and both bilirubin and transaminases levels faster normalization while using HFEW methods, which indicates liver function rapid recovery.

Keywords: high-frequency electric welding, hepaticojejunic anastomose, bile ducts, hepatopancreatoduodenal area, strictures, bile peritonitis, tumors, chronic pancreatitis, pancreatoduodenal resection.

Introduction

The problem of biliodigestive anastomoses (BDA) formation, with the purpose to restore the main bile outflow, remains urgent in the current surgical practice. Hepaticojejunostomy is dominant among the methods of its recovery and is a standard operation for extrahepatic biliary tract, both benign and malignant lesions [1-3]. Early postoperative complications, such as the sutures insufficiency and bile outflow, abscesses and cholangitis occur in about 10% of patients, mainly throughout the delayed postoperative period in the form of strictures – 7-20% [4, 5].

The high level of postoperative complications compels surgeons to investigate new methods of biliodigestive anastomoses formation [6-8]. In addition to stapler, compression and adhesive methods for hepaticojejunoanastomoses (HJA) formation, high-temperature methods recently were introduced into surgical practice – these methods allow to combine the stage of tissue dissection with a bleeding termination and then perform their direct welding. These methods' advantages are the absence of foreign suture material at the junction of tissues, which leads to a decrease in the inflammatory response, shortening the healing time and, as a result, allows to reduce the incidence of anastomoses failure in the early postoperative period and the formation of strictures in the later postoperative period [9, 10].

The aim of the study was to improve the treatment results of patients with main bile duct disturbances, using the modern method of tissues high-frequency electric welding (HFEW) for the hepaticojejunic anastomoses formation.

Material and methods. The experimental part of the work was performed on rabbits by a single-stranded BDA using HFEW method [11]. The positive results obtained experimentally allow to introduce this method of BDA formation into clinical practice.

All experimental investigations, patient recruitment, surgery, clinical and laboratory examinations were conducted at the O.O.

Shalimov National Institute of Surgery and Transplantology of National Academy of Medical Sciences of Ukraine. All therapy protocols were applied according to the patient's informed consent with all safety and bioethical aspects, as well as the legislation of Ukraine.

Before use in clinical conditions, a number of experiments on bioimitators were conducted to select the optimal mode of high-frequenced welding (HFEW), a more detailed study of the properties and strength of the weld. The used "bioimitators" were in the form of both hepaticocholedochus and small intestine fragments, removed during pancreatoduodenal resections. These parts of the material were not subjected to histological examination and were subject to disposal.

During the investigation the 15 models of termino-lateral HJA were formed. The method of HF welding resulted in 10 single-row HJA formation, 5 anastomoses were applied for comparison using the traditional ligature method.

HJA model's formation began with 3 U-shaped seams-holders imposition so that, after their extension, an equilateral triangle was formed. These sutures mapped the joint organs, performed the function of holders, and, also, provided the edges of the hepaticocholedochus and small intestine, which greatly facilitated and accelerated the welding process. The next step was the imposition of spot welds (seams) around the anastomosis perimeter. Welding was performed using the "Patonmed EKVZ-300" device with direct bipolar forceps in manual welding mode. The welds were applied one after the other in the intervals between the hold-seams, all welds were avertable – mucous to mucous. Thus, we received a weld around the anastomosis perimeter.

The second row of seams was not imposed (Fig. 1, 2). This method of BDA forming received the Ukrainian Patent (No. 116410 from 10.01.2018).

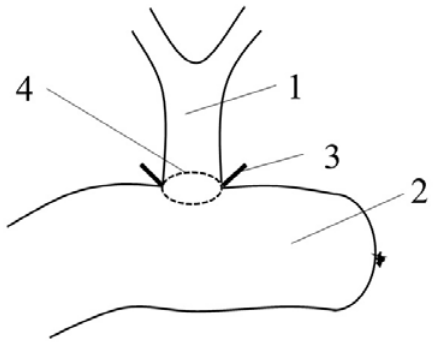

Fig. 1. *Termino-lateral welding HJA: 1) common hepatic duct, 2) small intestine, 3) welding seam, 4) connection line*

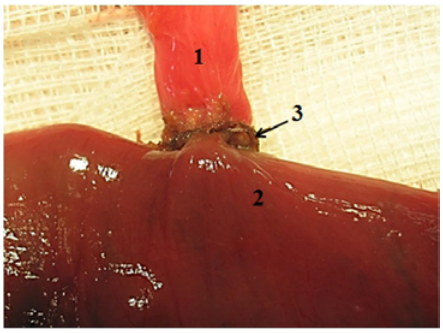

Fig. 2. *HJA welding model: 1) hepaticocholedochus, 2) small intestine, 3) welding seam.*

RF welding was used in 14 patients for reconstructive interventions in extrahepatic biliary tract. Using this method BDAs were formed in all patients: term-lateral HJA were formed in 11 cases, and lateral-lateral choledochal jejunoanastomoses – in 3 cases. Adhesions separation, tissue dissection, hepato-duodenal ligament mobilization and hemostasis were also performed using RF welding.

The age of patients ranged from 37 to 70 years, with an average of 59.1±2.7 years. There were 7 (50%) men and 7 women (50%). According to the pathology that led to the main bile duct disturbance nature, patients were divided into 2 groups: the 1st group consisted of patients with oncopathology, the 2nd – patients with benign diseases.

The 1st group consisted of 8 patients, 6 of them were with pancreatic gland, Fater papilla and common bile duct malignant tumors, resulted in the distal biliary tree occlusion and mechanical jaundice development. According to the volume of surgical intervention, this group of patients was divided into 2 subgroups: one subgroup included 4 patients who had palliative BDA, the other – 2 patients who managed to perform radical surgery in the volume of pancreatoduodenal resection, during which the termino-lateral HJA was formed. In addition, we included 2 patients with chronic pancreatitis with distal common bile duct complicated tubular stenosis. These patients also underwent termino-lateral HJA to eliminate obstruction.

The 2nd group consisted of 6 patients with bile duct lesions and benign tumors. This group was also divided into 2 subgroups, but the division was done not by the volume of the performed operation, but according to conditions in which this surgery was performed. One subgroup consisted of 3 patients with impaired bile flow and mechanical jaundice development without the inflammatory phenomena in the abdominal cavity: in one case there was a hepaticocholedochal scar stricture, occurred after 9 months after cholecystectomy, 2 were diagnosed with HJA scarring 10 months and 5 years, correspondently, after the anastomoses formation. The second subgroup included 3 patients with hepatoduodenal ligament acute inflammatory changes: 2 patients with impaired bile duct were diagnosed with acute purulent cholangitis and one patient was diagnosed with biliary peritonitis on the 8th day after iatrogenic injury (Bismuth II type).

All patients of the 2nd group underwent simultaneous reconstructive surgical interventions in the volume of HJA formation using HFEW method.

The control group consisted of 60 patients in whom the traditional methods were used for tissue dissection, haemostasis and BDA formation. Similar to the main group, by nature of the pathology and conditions in which the surgery was performed, these patients were also divided into 2 groups, each of which is divided into 2 more subgroups (15 patients in each). BDA in patients of the control group was formed by the traditional ligature method – continuous two-row suture, which was applied with a thread PDS 4/0.

Data reliability and statistical analysis. The patients of the main group and the control group had statistically the same indexes, i.e. they were comparable in terms of the main indicators – sex, age, disease prevalence and clinical laboratory data.

The methods of variational statistics used for obtained data calculations were the following – the investigated parameters frequencies characteristics (n, %), the average values (M) and the standard deviation of the average error (m).

The Chi-square test (χ^2) was used to compare the frequency distributions of qualitative characteristics and to evaluate the statistical significance of the difference between the compared groups, in frequency characteristics, and in the case of a small number of individual observations (<5) the Fisher exact test was used. The normality of distribution for the quantitative indicators was estimated using the Shapiro-Wilk test. Given the number of observations in the subgroups and the characteristics of the type (normality) of the data distribution, the Wilcoxone test (estimation of changes in dynamics) and the Mann-Whitney test (comparison between groups) were used to compare the averages.

The calculation of the prognostic assessment of the likelihood (risk) of complications was based on the determination of relative risk with the calculation of odds ratio (ORs) and 95% confidence interval.

The statistical significance of the results of the analysis was evaluated at a given threshold level of error of the first kind (α) not higher than 5% ($p < 0.05$).

The primary research base was created in Microsoft Excel. Statistical processing was performed using a licensed statistical package Stata 12.

Results and discussion. After HJA formation in the experimental conditions we checked their macro- and microscopic features and determined their strength. The macroscopical color of the welded seam was light gray, with no visible areas of necrosis and looked like a roller about 2 mm wide and about 4 mm high (from the edge of the wall of the organs to the free edge of the weld), which circularly covered the anastomoses (Fig. 2). From the side of the lumen of the anastomoses, the suture had the appearance of a thin strip of light gray color with a width of 1.0–2.5 mm, no thermal lesions of the mucous membrane outside the suture were observed.

All models of anastomoses formed using HFEW method were passable, their inner diameter almost corresponded to the initial diameter of the hepaticocholedoch. In contrast to welding, the formation of the HJA with suture method, due to the twisting nature of the seam, noted the penetration into the lumen of the anastomoses of the edges of the walls of the connected organs and, accordingly, narrowing of the anastomoses. Five welding and five ligature models made a series of measurements to determine the initial narrowing of the HJA.

The average initial of hepaticocholedoch diameter in sutured HJA models was equal to 11.0±1.5 mm, with one row of sutures the lumen of the anastomosis narrowed by an average of 31.6±3.2%, with two rows – 49.1±3.4%. Hepaticocholedoch average initial diameter at welding HJA was equal to 10.8±1.5 mm, the percentage of narrowing at the weld – 13.6±2.1%. Thus, the degree of initial narrowing in conditions of HJA models formed by the HFEW method was lower comparing the same in HJA modeling using ligature method.

After macroscopic evaluation we determined the tightness and strength of models HJA welding using the pneumopression method. Thus, it was found that the loss of HJA leakage occurred at a pressure of 40 to 70 mm Hg, an average of 52.0±5.1 mm Hg, which is equal to 706.9±70.0 H_2O mm.

Histological examination of the areas of the weld and surrounding tissues was performed to determine changes occurring in the tissues during electrical welding. To determine structural changes in the tissues, microscopy was performed under magnifications of different multiplicities, starting from x40, then x100 (Fig. 3) and x400, and ending with magnification x1000 (Fig. 4).

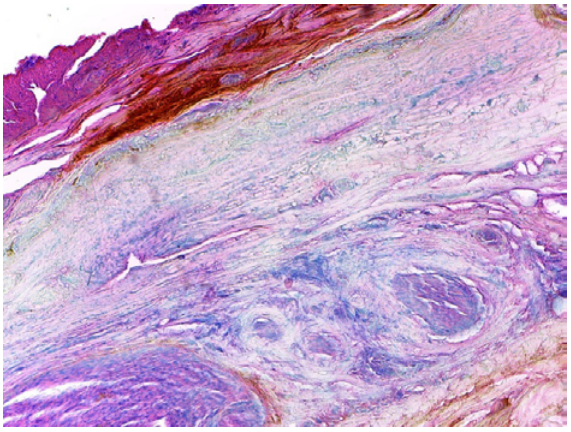

Fig. 3. *The model of HJA welding, coagulation seam. Azur-2-eosin staining. Increase: x100.*

Histological examination revealed that a coagulation suture was formed during the welding of the connective tissue. The tissues in the suture area were tightly sealed and dehydrated. On the periphery of the weld zone, there was a pronounced eosinophilia of collagen fibers, and deeper – moderate carbonization. The nuclei of the cells in this region underwent pycnosis and karyorexis (Fig. 3).

At the depth of the seam, homogenization of collagen fibers, caused by their fragmentation and disruption of the regular placement of fibrils, was noted. Enlightenment was observed, caused by the weakening of the interaction of dyes with the structural elements of this zone and the change in the tinctorial properties of collagen fibers (they showed weak or moderate metachromasia), in addition in the deep layers there was fragmentation of collagen beams and their fragments were split contoured (Fig. 4).

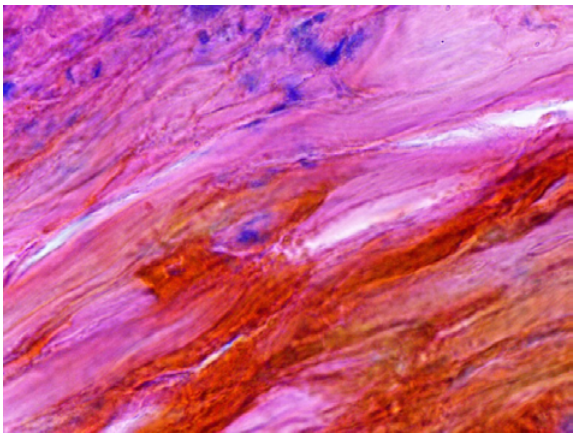

Fig. 4. The model of HJA welding, coagulation seam. Azur-2-eosin staining. Increase: x1000.

After welding, the tight muscle was preserved in the joint area and the submucosa, mucosa and serosa were not identified. The collagen fibers of the welding zone have undergone significant changes, and their disruption of their regular structure has led to the fragments of these fibers forming a felt impregnated with globular coagulated proteins. Such restructuring contributed to the tight adhesion of the tissues. The surrounding fabrics did

not undergo significant thermal changes.

The evaluation of the effectiveness of the proposed surgical treatment in patients with violation of the main bile duct was performed in several directions.

In 5 cases, timing of the formation of term-lateral welding HJA was performed, and similarly in 5 cases, term-lateral double-row suture HJA. Time from the moment of the first suture to the complete completion of the formation of the anastomosis was recorded in both groups. The duration of HJA formation by HFEW method ranged from 20 to 32 min, with an average of 25±2 min. The duration of HJA formation by the ligature method ranged from 37 to 52 min, with an average of 44±3 min. Thus, the duration of HJA formation by HFEW method was averagely by 19 minutes (43.2%) faster than ligature method (P<0,05).

To evaluate the reliability and efficiency of the HJA formed by the RF-welding method, a clinical evaluation of patients was performed, instrumental examinations were performed, such as Ultrasound investigation and Magnetic Resonance Cholangiopancreatography as well as analysis of a number of laboratory data.

To determine the adequacy of bile flow through the anastomosis, an assessment of bilirubin and transaminases was performed. The level of total bilirubin was monitored at all stages of treatment – at admission, in the first 2 days after surgery and before discharge from the hospital, the levels of AlAT and AsAT – at admission and before discharge (Table 1).

Table 1

Dynamics of the total bilirubin concentration and transaminases activities

Total bilirubin (μmol/l)	Main group (n=14)	Control group (n=60)
At admission	134,2±18,8	151,1±18,5
1-2 days after the operation	100,6±22,5	107,3±17,7
Before discharge	40,4±6,2	55,0±8,0
AlAT (U/l)		
At admission	165,1±33,3	146,9±14,3
Before discharge	63,3±9,4	65,6±6,5
AsAT (U/l)		
At admission	129,0±23,0	109,6±9,1
Before discharge	44,6±5,4	57,0±5,1

One could see from the table, the level of total bilirubin during the postoperative period decreased dynamically both in the main and in the control groups. Overall, it can be stated that the decrease in bilirubin levels were proportional to the initial level, but in the main group the final results were better (40.4±6.2 vs 55.0 ± 8.0 μmol/l).

Transaminase levels in the postoperative period were also decreased in all patients, as was the level of total bilirubin. At the same time, the initial level of both AlAT and AsAT in the main group was higher than in the control group, and the levels of both indicators before discharge were lower. Thus, in the main group there was a faster decrease in the levels of AlAT and AsAT than in the control group.

The reliability of the HJA done using HFEW method was confirmed not only by clinical observation, but also by the data of instrumental methods of examination, such as ultrasound and Magnetic Resonance Cholangiopancreatography (MRPCG) conducted at different times of the postoperative period, which showed good patency and tightness of these anastomoses (Fig. 5).

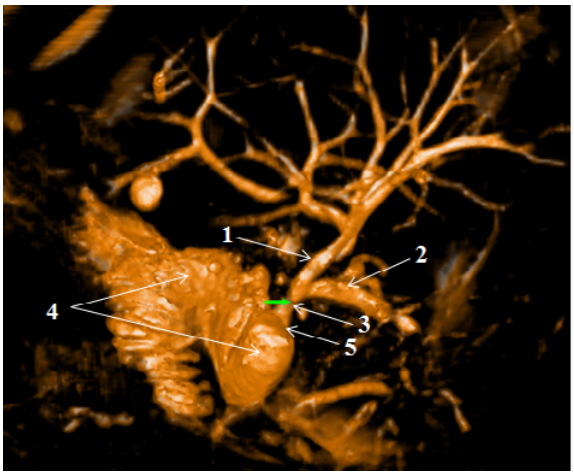

Fig. 5. *Patient B. (ICSW No. 1691): Magnetic Resonance Cholangiopancreatography, the 14th postoperative day: 1) right lobular duct, 2) left lobular duct, 3) common hepatic duct, 4) loop of the small intestine is excluded by Ru, 5) GJA.*

To determine the reliability of HJA welding a comparative analysis of complications that occurred in both groups of patients was performed, and the average postoperative bedtime was determined (Table 2).

In the main group, partial failure of the HJA occurred in one patient, which is 7.1%. This patient suffered anastomotic dehiscence (AD), on the 6th day, on the background of hypoproteinemia (total protein 49.5 g/l), there was a partial failure of pancreaticojejunoanastomoses with the release of pancreatic juice drainage. After that, on the 9th day, probably due to the lytic action of pancreatic enzymes, a partial failure of the HJA occurred. Conservative therapy for 12 days led to the elimination of complications.

Table 2

Distribution of patients according to the number of complications and postoperative bed days

	Main group (n=14)		Control group (n=60)	
Complications	Number	%	Number	%
Partial failure	1	7,1	6	10,0
Others	3	21,4	12	20,0
Average postoperative bedtime	11,4±1,1		12,7±0,7	

In the control group, partial failure of the anastomoses was in 6 patients (10.0%). All cases of anastomoses failure in the control group were also cured by conservative methods, without recurrent surgery.

Other, less severe, complications occurred in 3 (21.4%) patients of the main group – 2 had moderate lymphorea and 1 – suppuration of p/o wounds. In the control group, the other complications were in 12 (20.0%) patients: one after the AD had acute postoperative pancreatitis, in 1 case there was bleeding, in 1 case – cholangitis, in other cases there were milder complications – lymphorea occurred in 4 patients, suppuration of the postoperative wound in 3.

It should also be noted that in the postoperative period, the therapy, antibiotics and other drugs used in the main group

were identical to those used in the control group in the main group. The mean postoperative hospital stay in the main group was less than one day (11.4 ± 1.1) compared to the control group (12.7 ± 0.7).

Conclusions

1) BDA formed by HFEW method are sealed and have sufficient strength.

2) The primary constriction in the formation of BDA models by HFEW method is statistically significantly less than in the traditional suture method of forming anastomosis data.

3) Tissue bonding during electrowelding is provided by a thin layer of coagulated substance that is formed as a result of changes in the conformation of proteins, both intercellular matter and proteins of destroyed cells. Collagen fibers play a major role in the adhesion of tissues.

4) The use of HFEW method allows to reduce the duration of surgery.

5) The HFEW method allows to form reliable BDA in the conditions of acute cholangitis and certain forms of bile peritonitis.

6) The formation of BDA using HFEW method reduces the frequency of early postoperative complications and faster normalization of bilirubin and transaminases, which indicates a better restoration of liver function.

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