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Research Article

OUR PRACTICE EXPERIENCE IN APPLYING "FAST-TRACK" PROGRAM FOR THE PATIENTS' TREATMENT WITH PERFORATED GASTRODUODENAL ULCERS

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Abstract:

Aim. To study the «Fast-track» program effectiveness of accelerated recovery for the treatment of the patients with perforated gastroduodenal ulcer complicated by the extended peritonitis.

Materials and methods. During our research work, we performed prospective analysis of surgical treatment of 24 patients (index group) with perforation of gastroduodenal ulcer, and also comparative retrospective analysis of surgical treatment of 35 patients (experimental group) with the same diagnosis. All patients had been treated in the inpatient surgical department of the State budgetary institution of health care in Crimea Republic State clinical hospital N^{27} in Simferopol during the period from 2016 to 2017, and from 2015 to 2016 respectively. Treatment of all patients from both groups was performed in line with generally accepted peritonitis management plan.

Treatment of index group patients was made in accordance with "Fast-track" program. Clinical, laboratory and instrumental data received by us in post-operative period demonstrate quick restoration of the intestinal peristalsis, of the protein indicators; less complication frequency in the main group as to an experimental one.

Results. Pain syndrome level in the post-operative period at index group patients didn't exceed 4 points; in the experimental one pain level according to VAS (Visual Analog scale) didn't exceed 4 points at 24 patients, it was more than 4 at 9 patients and 5 of them had it more than 5 (p<0,05). By the 3-rd day Leukocyte index of intoxication (LII) was $3,2\pm0,1$ in the index group patients and $3,6\pm0,2$ - in the experimental group patients. Total protein level in the index group patients has grown up till $48,9\pm1,2$ grams per liter and up till $46,8\pm1,65$ grams per liter (p<0,05) - in the experimental group patients.

By the 5-th day LII was $2,7\pm0,3$ in the index group patients; $3,9\pm0,1$ - in the experimental one. Total protein level in the experimental group patients has increased up to $53,52\pm1,60$ grams per liter; in the index one- up to $61,70\pm1,77$ grams per liter (p<0,05). Restoration of motor-evacuation function of the intestine was noted on average in $18\pm2,5$ hours. In the experimental group of the patients it was observed in $38,5\pm6,5$ hours (p<0,05).

The average duration of inpatient treatment of the experimental group patients was $14,1\pm2,2$ days, in the index group patients - $7,9\pm1,1$ days (p<0,05).

Conclusions. "Fast-track" program applying increases the treatment effectiveness contributing to reduction of pain syndrome in the postoperative period, to the earlier restoration of motor-evacuative intestinal function, accelerated endotoxicosis reduction, decreases risk of the post-operative complications development. This point significantly reduces time spent in the hospital and accelerates the patients' rehabilitation process.

Key words: extended peritonitis, perforated ulcer, «Fast-track».

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INTRODUCTION:

Treatment problem for the patients with perforated ulcer of the stomach and duodenum is considered to be actual. It's on the 5-th place in the structure of urgent diseases of the abdominal cavity organs and makes up about 5-7% [1]. According to the data of native authors mortality in case of perforated gastroduodenal ulcer is from 6,2% up to 42,2% [2].

The choice of treatment tactics for the patients with perforated gastroduodenal ulcer complicated by extended peritonitis is still controversial today.

According to modern literature in 80-90% of cases peritonitis course is accompanied by the multiple organ insufficiency development including respiratory distress-syndrome, by coagulopathy, stress ulceration, renal failure, central nervous system damage and bacterial toxic shock [3].

In the complex of irregularities caused by extended peritonitis, enteral insufficiency is on the special place and accompanies intestinal paresis developing in 85-90% of patients and it serves as one of the main triggers for endotoxicosis. It was proved that exactly the enteral insufficiency syndrome plays the leading role in multiple organ dysfunction development at extended peritonitis where intestinal paresis is the key pathogenetic link [4].

Standard commonly used treatment plan in case of extended peritonitis includes the earliest surgical removal of the inflammation source of the peritoneum, an adequate sanitation of the abdominal cavity and the choice of arrangement tactics of the perioperative period what is the main factor for achieving a favorable outcome of the disease [5].

Early and appropriate antibiotic therapy, endotoxicosis correction, basic and drug therapy, immunocorrection also play a great role in the complex of therapeutic procedures taken at the common forms of peritonitis [6,7]. Midline laparotomy had been a common surgical approach in extended peritonitis for many years permitting to make an adequate examination of the abdominal cavity organs, to eliminate the cause of peritonitis; in case of gastroduodenal ulcer perforation it permits to suture or excise perforation, to senate and drain the abdominal cavity.

However, laparotomy is a traumatic procedure, which can aggravate stress disorders, loss of protein and electrolytes; it can suppress the immune defense mechanisms in postoperative period and cause a number of serious complications [8].

Today the most relevant is the search for measures that would prevent the complications development and reduce the period of inpatient treatment. Search for techniques permitting to improve the efficiency of the patients' surgical treatment led to the creation of the accelerated recovery concept «Fast-Track». This technique was developed by professor, anesthesiologist - resuscitator from Denmark H. Kehlet in the middle 90s of the XX century. Notion «Fast-track» covers all phases of perioperative preoperative, intraoperative treatment: and postoperative ones and provides minimizing the stress effect of the surgical treatment on the patient's body. which includes rational preoperative preparation, the use of minimally invasive and hightechnological surgical methods, applying of shortacting anesthetics and multimodal analgesia with subsequent early rehabilitation [9].

The following elements are the most frequently used:

premedication refusal: due to the fact that premedication increases the time of the patient's awaking after the completion of the surgical manipulation, its performing doesn't correspond with FTS concept [10];

prevention of carbohydrate metabolism disorders: decreasing of blood glucose levels before surgery reduces glycogen reserves and causes postoperative insulin resistance in the postoperative period. But increasing of the blood glucose in the postoperative period leads to breaking of oxygen delivery to the tissues, which leads to the impairment of the postoperative wound regeneration, zones of intestinal anastomoses. As a result, the use of glucose solution is justified in the preoperative preparation [11];

• minimal surgical invasion: it was proved that in contrast to laparotomic approach, in laproscopy as a result of a smaller area of peritoneal damage, the number of adhesive complications is less in postoperative period. Also minimal injury contributes to the early restoration of the small intestine motility [12];

• vomiting and nausea prevention;

• adequate infusion volume: uncontrolled infusion therapy can lead to both hyper and hypovolemia. Targeted therapy has been established to make it possible to optimize the intravascular sector condition, thereby maintaining tissue perfusion and oxygenation at an appropriate level, helping to improve outcomes after great surgical interventions [13];

• intestinal oxygenation: perspective method for improving intestinal wall perfusion is intestinal oxygenation. Nowadays the effectiveness of introducing oxygen into the small intestine of the seriously ill patients has been proven. This method permits to stimulate its motor function and leads to systemic oxygenating effect [14];

• refusal from narcotic analgesics: narcotic analgesics application can lead increasing of frequency of nausea and vomiting attacks, intestinal paresis in the postoperative period. In its turn, application of Nonsteroidal anti-inflammatory drugs (NSAIDs) combination allows to reduce the incidence of postoperative nausea and vomiting; to decrease sedation degree; to provide immediate mobilization and enteroalimentation (EA) [15];

• early enteral nutrition (EN): in postsurgery period, seriously ill patients frequently have conditions that result in blood flow redistribution. Therefore, an adequate perfusion and oxygenation of the gastrointestinal tract is impaired. At the same time, the degenerative changes in the intestinal wall occur in a few days of rest, and they are progressing, despite on carrying out an adequate parenteral feeding in full [16]. Disorders are exacerbated in the absence of nutrients in the lumen of the gastrointestinal tract, since the mucous cells get their nourishment largely directly from the chyme. It was proved that early enteral nutrition allowed to decrease recovery time of the intestinal functions what also led to risk reduction of the post-operative complications [17];

• early body moving activity: long term staying in bed leads to the rise in frequency of the thromboembolic complications, respiratory distress, decreases muscle strength and increases the risk of hemodynamic disorders. While immediate body moving permits to improve tissue oxygenation, to reduce muscle weakness, to decrease the risk of deep venous thrombosis and pulmonary embolism [18].

Advanced research direction in modern surgery is the study of the role of using «Fast-track» program for treatment of the patients with acute pathology of the abdominal cavity complicated by extended peritonitis.

Aim of the research is to study the «Fasttrack» program effectiveness of accelerated recovery for the treatment of the patients with perforated gastroduodenal ulcer complicated by the extended peritonitis.

MATERIAL AND METHODS:

Our research is based on the prospective analysis of the surgical treatment of 24 patients (index group) with acute extended peritonitis caused by perforation of gastroduodenal ulcer. Comparative retrospective analysis was also performed of the surgical treatment of 35 patients (experimental group) with acute extended peritonitis caused by perforation of gastroduodenal ulcer. All patients had been treated in the inpatient surgical department of the State budgetary institution of health care in the Crimea Republic State clinical hospital № 7 in Simferopol during the period from 2016 to 2017, and from 2015 to 2016 respectively. Patients from both groups were provided with management according to common treatment regimen in extended peritonitis: early surgical elimination of the inflammation source in the peritoneum, an appropriate sanitation of the abdominal cavity, therapy for replacing fluid loss; stopping of microcirculation disorders; correction of the respiratory and cardiovascular system disorders. Grouping of the patients according to peritonitis etiology is represented in the table 1.

Table 1. Peritonitis etiology

Peritonitis causes	I group (n=24)	II group (n=35)
Perforated stomach ulcer	11 (45,8%)	14 (40%)
Perforated duodenal ulcer	13 (54,2%)	21 (60%)

On admission to the hospital, severity of the patients' condition was rated on SAPS scale. Grouping of the patients according severity of their condition is represented in the table 2.

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Points accroding to SAPS	I group (n=24)	II group (n=35)
10-12 points	13 (54,2%)	21 (60%)
13-16 points	8 (33,3%)	8 (22,9%)
17-20 points	2 (8,3%)	6 (17,1%)
21 and more points	1 (4,2%)	-

Table 2. Severity of the patients' condition according to SAPS scale on admission

Patients' age ranged from 24 to 64 years. An average age in the index group was 39.8 ± 1.8 years, in the experimental group it was 40.1 ± 1.6 years. There were 38 (64,4%) females and 21 (35,6%0 of males among our patients. The groups are similar in all cohort characteristics.

Complete preoperative assessment was performed in preoperative stage in both groups in order to stabilize hemodynamic and electrolyte disorders. Elimination of peritonitis cause, abdominal sanitation and drainage were carried out during surgery. Antibiotic therapy, correction of electrolytes impairments, analgesia, fluid loss recovery, stopping of microcirculation disorders, management of the vital functions damage were made in postoperative period.

At this, treatment of the patients from the index group was carried out in accordance with the program «Fast-track»:

• premedication refusal;

• prevention of carbohydrate metabolism: when having preoperative assessment in order to prevent carbohydrate metabolism disorder all patients from the main group were given intravenous infusion of 5% glucose solution in the quantity of 800 ml (except diabetic patients).

Preventive measures for carbohydrate metabolism were not performed for the patients in the experimental group as it wasn't specified in the National clinical recommendations.

• vomiting and nausea prevention: for this purpose during anesthetic induction 4-8 mg of dexamethasone and 25-50 mg of metoclopramide were injected intravenously at 30-60 minutes before the end of the operation.

• minimal invasive approach: in the beginning survey video-laparoscopy with further intraoperative determination of the operation extent was made to the patients from the study group. At the same time, 18 patients were made suturing of the perforated hole, nasogastric intubation, abdominal sanitation and drainage laparoscopically. Conversion was performed in 6 cases: suturing of the perforated hole, nasogastric intubation, abdominal sanitation and drainage laparoscopically.

drainage. As for the experimental group, laparotomy, suturing of the perforated hole, nasogastric intubation of the small intestine, abdominal sanitation and drainage was made to all patients there.

• sanitation of the abdominal cavity with antiseptic solution: an average of 4.3 ± 1.8 liters were used for sanitation. Cleansing solution contained 0,9% solution of sodium chloride, 0,25% novocaine solution (in order to reduce pain impulsation from the inflamed peritoneum), 3% hydrogen peroxide solution (in order to clean peritoneum mechanically and to have an impact on the anaerobic microflora). Its temperature was 37,0-38,0 C.

• intestinal oxygenation: this procedure was carried out in the following way: 100% oxygen was being injected slowly into the tube in the different dosage portions. During the first procedure (in 12 hours after the surgery) 100% oxygen was injected in the dosage of 500 ml; later 100% oxygen was being injected every 25 minutes for 3 hours. Other repeated oxygen injections (300 ml) were carried out with an interval of 4 hours during the first 48 hours of the days of the postoperative period.

• targeted infusion therapy: in the postoperative period the intravenous infusion of 4% solution of potassium chloride was made in order to correct water-salt metabolism starting from the 2-nd day after the surgery depending on the biochemical blood parameters of each patient. This reduced intracellular potassium deficiency that contributed to recovery of intestinal peristalsis.

• refusal from narcotic analgesics: in order to stop pain syndrome in post-operative index group patients we used the following NSAIDs combination according the next plan: 100,0 of 1% Paracetamol solution was injected intravenously at the first hour after the surgery; 1,0 - 30 mg/ml of Ketorolak Trometamol were injected intramuscularly in an hour and then it was injected 3 t/per day during 3-4 days of the post-operative period. In order to receive pain level not more than 3 points in VAS we started to inject 1,0 - 30 mg/ml of Ketorolak Trometamol intramuscularly 2 t/per day. But for the experimental group patients in the early postoperative period we used 1,0- 20 mg/ml of Promedol solution intramuscularly immediately after the surgery and then every next 6 hours during 2 days. After then we started injecting 1,0 - 30 mg/ml of Ketorolak Trometamol intramuscularly 3 t/per day.

• early enteral nutrition: according to EGEG (electrogastroenterography) data, the beginning of indexes resetting of electrical activity of the small intestine suggested about restoration of the motor intestinal function. Enteral nutrition for all patients from the index group was started on average in $18,3\pm2,5$ hours after the surgery. For this purpose, we used glucose- salt mixes at the ratio of 1:1 +specialized formula which contained pharmaconutrients (glutamine, arginine, Omega-3 fatty acids, antioxidants and tributyrin); on the first day up to 500 ml of these mixes were allowed to inject with the speed of 25-50 ml/per hour; infusion technique was used to give this medication in all cases. Duration of mixture supply for the enteral nutrition was 16,2±4,3 hours. At high tolerability (in absence of vomiting, diarrhea, allergic reactions) the volume of the feeding formula was increased up to 1500 ml on the 2-nd day, rate of administration was also raised up to 50-75 ml/per hour. In 48 hours after the surgery the patients were switched to oral food dosing.

• early body activity: at the condition of the appropriate analgesia patients were made to move in the first 48 hours after the operation. It meant that they needed to stand up from the bed and to walk in the ward. Targeted point was to have the patient being awaken and not in the bed not less than 1 hour on the 2-nd day after the surgery and not less than 4 hours of being in normal consciousness during the following days.

We determined the effectiveness of the treatment from the clinical and laboratory data: intensity of the pain syndrome as for VAS (Visual Analog Scale), vomiting in post-operative period, periods of beginning of passing of flatus, biochemical blood test (total protein level), dynamics of the systemic endotoxicosis, information received from the electrogastroenterography.

Leukocytosis was calculated according to the standard technique in the clinical laboratory of the 7-the municipal clinical hospital in Simferopol at the day of surgery, on the 1-st, 3-rd, 7-th and 10-th days of the postoperative period. Leukocytal intoxication index (LII) by Kalf-Kalypf was performed according to the data from the differential leukocyte count at the days of operation, on the 1-st, 3-rd, 7-th, 10-th day of the post-surgery period. Estimation of the total protein level was made on the 1-st, 3-rd, 7-th, 10-th day of the post-operation period.

Electrogastroenterography was made during the first 24 hours after the operation continuously, then every 4 hours for 2 days of the post-operative period. All received results were processed and saved in the in electronic form in the PC memory.

Statistical processing of the received data was performed having used the methods of variation statistics with average determination (M), assessment of probability of discrepancies (m), reliability of estimate of changes based on Student's t-test. Significant point was considered to be the difference in average when p<0,05.

RESULTS AND DISCUSSION:

In 4, 6 and 12 hours, and also on the 2-nd day of the postoperative period 100% of the patients from the index group had pain level according to VAS not more than 4 points that was an acceptable one for this period and it didn't have a negative effect on its course. In the experimental group 24 patients had pain level according to VAS not more than 4 points, 9 patients had it more than 4 points.

8 (22%) patients from the experimental group were noticed to have vomiting on the 1-st day of the postoperative period; when 2 (8,3%) patients from the index group were noticed to have vomiting on the 1-st day.

During the first 2 days of the postoperative period changes dynamics of the laboratory indexes in both groups was the same having the high level of systemic endotoxicosis; received results didn't change significantly. Absence of active peristalsis and passing of flatus, growing hypoproteinemia, increasing of leukocytosis level in both groups showed severity of the systemic inflammatory reaction that corresponded to the volume and terms of the surgical procedure.

However, starting from the 3-rd day of the postoperative period improvements in the biochemical and blood test indexes were observed as an evidence of the positive change in the patients' condition. LII in the index group was $3,2 \pm 0,15$, in the experimental group it was $3,8 \pm 0,2$ (difference is significant, p<0,05). The level of total protein at the patients from the index group was $48,9 \pm 1,2$ gr/l by this period, but in the experimental group to $45,8 \pm 1,5$ gr/l (difference is significant, p<0,05).

By the 5-th day LII in the index group was $2,7\pm0,3$; in the experimental one it was $3,9\pm0,1$. (p<0,05). By this period total protein level increased up to $53,52\pm1,60$ gr/l at the experimental group patients, when it increased up to $61,70\pm1,77$ gr/l (p<0,05) in the index group.

Results received from the electrogastroenterography evaluation suggested that restoration of the gastrointestinal tract function was noticed in 12-25 hours (at average $18,3\pm2,5$ hours) at the patients from the index group, but the patients from the experimental group had it in 36-44 hours (at average $38,5\pm6,5$ hours).

8 (22,9%) of experimental patients showed postoperative wound infection as compared with index group patients where postoperative wound infection was registered in 3 cases (12,5%) only. 5 experimental patients (14,3%) developed early adhesive intestinal obstruction resulted in revision, and 3 fatal outcomes. As for index in-patients cases of adhesive intestinal obstruction were not registered.

Mortality in the experimental group made up 11,4% (4 patients). As to the index group, the death rate was 4,2% (1 patient). The average length of stay for experimental patients was 12-16 days (on average, 14,1 \pm 2,2 days), while that for index group patients was 7-9 days (7,9 \pm 1,1 days).

According to PubMed Internet resource, from January, 1998 till January, 2013 postoperative pain syndrome was observed in 10 - 50% patients after 8 weeks from previous surgery [19]. It's also necessary to note that narcotic analgesics following major surgery remain to be the agent of choice. According to ORADE (opioid-related adverse drug events) study, 20% of patients taken narcotic analgesics in post-operative period developed skin itch, retention of urine, postoperative intestinal paralysis, and delirium. Elderly patients showed respiratory failure and apnoea [20]. Data resulting from our studies of post-operative period showed that combination of NSAID instead of narcotic analgesics allowed to relieve pain syndrome in index patients as effective as in experimental patients. According to VAS (Visual Analogue Scale), the factor in index group did not exceed 4 points during the entire postoperative course. It allowed not only reduce early post-operative vomiting but also promoted early restoration of the intestinal motor function in index group patients relative to experimental group.

During the post-operative course, primary attention should be paid to get rid of intoxication, correct electrolyte disturbances, eliminate tissue hypoxia and restore the intestinal motor function. The earlier intestinal motor function is restored in post-operative course, the less complications are probable [21]. At present there are data about successful use of "fasttrack" program aimed to restore the intestinal motor function in patients after previous colorectal surgery. Intestinal peristalsis was restored on the 2nd postoperative day [22]. According to Malkov I. S. and colleagues [23], in connection with laparoscopic approach with the following laparoscopic closure of perforated duodenal ulcer, restoration of peristalsis and passage of flatus were registered on the 2nd - 3rd days of the post-operative course. According to EGEG data, during the study in connection with the use of fast recovery program, the intestinal eclectic activity in the index group had been restored on average in $18 \pm 2,5$ hours, whereas in experimental group this factor was $38,5 \pm 6,5$ hours. It was confirmed by laboratory blood tests.

In connection with the use of fast recovery program, post-operative dynamic pattern of laboratory data indicated more impetuous endotoxemia control in index group patients as compared with those of experimental group. Comparative analysis of the start of active peristalsis and start of passage of flatus testify the efficiency of "fast-track" program aimed to speed-up the recovery time of intestinal activity. In the index group it took twice less time as compared with the experimental group. The use of this method allowed to decrease the amount of complications within the early post-operative course and to shorten the post-operative stay.

CONCLUSION:

The obtained data argue the applicability and efficiency of "fast-track" program in case of perforated gastroduodenal ulcers. As a result of its use during the post-operative course, the factor in index group did not exceed 4 points promoting early activation. According to VAS, in 24 patients from the experimental group it did not exceed 4 points, in 9 patients it was higher than 4, and in 5 patients – higher than 5 (p < 0.05).

Restoration of intestinal motor function in patients of index group occurred on average in $18 \pm 2,5$ hours, whereas in experimental group this factor was 38,5 $\pm 6,5$ hours (p<0,05).

By the 3rd day, LII in the index group was $3,2 \pm 0,1$ whereas in the experimental group it was estimated as $3,6 \pm 0,2$. Total protein (TP) in index group increased to $48,9 \pm 1,2$ g/l, and in experimental group it was $46,8 \pm 1,65$ g/l (p < 0,05). By the 5th day, LII in the index group was $2,7 \pm 0,3$, and in the experimental group it was $3,9 \pm 0,1$. TP in experimental group increased to $53,52 \pm 1,60$ g/l, whereas in the index group it was $61,70 \pm 1,77$ g/l (p < 0,05).

The average in-hospital stay for the patients from experimental group was $14,1 \pm 2,2$ days; in the index group it was $7,9 \pm 1,1$ days (p < 0,05).

List of symbols and Abbreviations

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EA - enteroalimentation
EGEG - electrogastroenterography
FTS – fast-track surgery
LII - leukocytal intoxication index
ORADE - opioid-related adverse drug events
NSAID - nonsteroidal anti-inflammatory drugs
SAPS - scale for the assessment of positive
symptoms
TP - total protein
VAS - Visual Analogue Scale
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