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## Evaluation of the efficacy of antiseptic gel solution for peritoneal lavage in generalized peritonitis

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### Abstract

In 80-85% of cases successful management of generalized peritonitis depends on the effect of intraoperative and postoperative peritoneal cavity lavage.

**The aim of the study** is to improve the effectiveness of peritoneal lavage with antiseptic gel solution in patients with generalized peritonitis.

**Materials and methods.** The analysis of the comprehensive treatment was performed in 96 cases diagnosed as generalized peritonitis at the clinic of the Department of Surgery and Proctology of P.L. Shupyk National Medical Academy of Postgraduate Education from 2016 to 2020. The patients were 23 to 76 years old (the mean age was  $54.3 \pm 2.1$ ). Among them there were 63 males (65.6%) and 33 females (34.4%). Depending on the method of peritoneal cavity lavage, patients were categorized into two groups. Group I or main group, including 47 (48.96%) patients, underwent peritoneal lavage with an antiseptic gel solution in compliance with the method of our invention (patent of Ukraine № 123924 for the utility model as of 12 March 2018). Group II or comparison group, including 49 (51.04%) patients, underwent peritoneal lavage with 0.02% chlorhexidine bigluconate.

**Results.** In group I, the use of antiseptic gel solution for peritoneal lavage reduced the number of strains from 94 to 49 ( $p < 0.01$ ), the number of colonies - from 43.69 Lg CFU / mL to 20.08 Lg CFU / mL,  $\Delta = 23.61$  Lg CFU / mL ( $p < 0.01$ ), whereas in group II, the number of strains decreased from 93 to 68 ( $p < 0.01$ ) and the number of colonies from 42.68 Lg CFU / mL to 30.87 Lg CFU / mL,  $\Delta = 11.81$  Lg CFU / mL ( $p < 0.01$ ). The study found significant reduction of the number of E. Coli strains to 28 in group I compared with 41 in group II and the number of colonies to 3.35 Lg CFU / mL in group I compared with 5.28 Lg CFU / mL in group II. The number of leukocytes in patients of group I was lower and amounted to  $7.2 \pm 0.9$  comparing to  $10.5 \pm 1.2$  in patients of group II ( $p_{I-II} < 0.05$ ). Dynamics of procalcitonin concentration before and after peritoneal lavage: from  $5.7 \pm 0.4$  ng / ml to  $1.1 \pm 0.1$  in group I, from  $5.9 \pm 0.5$  ng / ml to  $3.54 \pm 0, 4$  ng / ml in group II ( $p_{I-II} < 0.05$ ). The clinical results of the complex treatment of patients with generalized peritonitis showed that in group I the complications occurred in 10.6% (5/47) of peritonitis cases, and in group II - in 26.5% (13/49) of peritonitis cases. In group I, the average length of hospital stay was  $9 \pm 1.4$  days comparing to  $14 \pm 2.2$  days in group II ( $p < 0.01$ ).

### **Conclusions**

In generalized peritonitis, an antiseptic gel solution for peritoneal lavage showed higher efficacy than water-based antiseptic due to its ability to cover the entire parietal and visceral peritoneal surface as well as maximum exposure, thus reducing the number of strains of microorganisms from 94 to 49, the number of colonies from 43,69 lg CFU / ml to 20.08 lg CFU / ml, whereas the use of water-based antiseptic helped to decrease the number of strains of microorganisms from 93 to 68, the number of colonies from 42.68 lg CFU / ml to 30.87 lg CFU / ml.

In the comprehensive surgical treatment of patients with generalized peritonitis, peritoneal lavage with antiseptic gel solution helped to reduce the overall incidence of postoperative complications to 10.6% in group I comparing to 26.5% in group II, the occurrence of abdominal abscesses to 2.13% in group I comparing to 8,16% in group II, early adhesive intestinal obstruction to 2.13% in group I comparing to 8.16% in group II, postoperative wound suppuration to 6.38% in group I comparing to 10.2% in group II. Peritoneal lavage with antiseptic gel solution also decreased the average length of in-hospital stay to  $9 \pm 1.4$  in group I comparing to  $14 \pm 2.2$  days in group II.

**Key words: peritonitis; abdominal abscesses; peritoneal cavity lavage; antiseptic solutions.**

Despite advances in abdominal surgery, peritonitis is still one of the most serious complications of inflammatory diseases of the abdominal cavity. Mortality in this pathology remains at a high level and, according to various authors, is from 6 to 60% [1, 2, 3]. The technological advances in abdominal surgery and the use of modern antibacterial drugs have not contributed to the reduction in mortality from peritonitis, thus indicating the urgency of this problem.

In generalized peritonitis, special attention is paid to the intraoperative and postoperative peritoneal cavity lavage as in 80-85% of cases the success of treatment depends on this procedure [3, 4, 6, 7]. After the elimination of the source of infection, the water-based antiseptic solutions, such as 0.02% chlorhexidine bigluconate and 0.02% decamethoxine, are mainly used for the peritoneal cavity lavage [3, 9]. It must be noted that the antiseptic effect of these solutions becomes minimal 24 hours after peritoneal lavage due to the process of adhesion in the abdominal cavity. The antiseptic solution fails to cover the entire surface of the parietal and visceral peritoneum, as separate adhesions, as well as adhesions between the loops of the intestine, omentum, parietal peritoneum and anterolateral abdominal wall, are formed. The antiseptic solution flows through the lateral canals of the abdominal cavity, and separate clusters of peritoneal exudate additionally develop, leading to the formation of inter-loop abscesses [2, 8, 10]. As a result, peritoneal lavage with a traditional water-based solution becomes ineffective.

In our opinion, it would be expedient to use an antiseptic gel solution for intraoperative and postoperative peritoneal cavity lavage, which would prevent the formation of adhesions in the abdominal cavity and provide the maximum antiseptic effect. [11, 12].

**The aim of the study** is to improve the effectiveness of peritoneal lavage with antiseptic gel solution in patients with generalized peritonitis.

### **Materials and methods**

The analysis of the comprehensive treatment was performed in 96 cases diagnosed as generalized peritonitis at the clinic of the Department of Surgery and Proctology of P. L. Shupyk National Medical Academy of Postgraduate Education from 2016 to 2020. The patients were 23 to 76 years old (the mean age was  $54.3 \pm 2.1$ ). Among them there were 63 males (65.6%) and 33 females (34.4%).

Generalized peritonitis was diagnosed in patients with the following diseases: perforated duodenal ulcer in 38 (39.58%) patients, perforation of malignant tumours of the colon in 22 (22.92%) patients, gangrenous-perforated appendicitis in 21 (21.88%) patients,

strangulated hernias with necrosis of the loops of the small intestine in 10 (10.42%) patients, perforation of the diverticulum of the colon in 5 (5.21%) patients.

The patients with end-stage peritonitis, who were prescribed a programmed laparostomy, were excluded from the study.

Depending on the method of peritoneal cavity lavage, patients were categorized into two groups.

Group I or main group included 47 (48.96%) patients who underwent peritoneal cavity lavage with 250 ml of an antiseptic gel solution containing sodium hyaluronate 1250 mg, decamethoxine 50 mg, succinate buffer pH 7.3 from 2018 to 2020. The peritoneal lavage was performed in compliance with the method of our invention (Ukrainian patent № 123924 for a utility model as of 12 March 2018) and included some consecutive steps.

Laparotomy, elimination of the source of peritonitis, peritoneal cavity lavage with decamethoxine 1600-2000 ml, accompanied by active irrigation, drainage from 4 points, in particular, from subhepatic space, left subphrenic space, right lateral canal and pelvis, and closure of the laparotomy incisions were followed by the injection of 250 ml of an antiseptic gel solution through the upper drainages. The procedure was repeated (fractionally) every 8 hours for 4-5 days.

From 2016 to 2017, 49 (51.04%) patients of group II (comparison group) underwent peritoneal lavage with 250 ml of 0.02% chlorhexidine bigluconate every 8 hours for 4-5 days. The procedure was performed after laparotomy, elimination of the source of peritonitis, peritoneal cavity lavage with 0.02% chlorhexidine bigluconate 1600-2000 ml, and drainage of the abdominal cavity from 4 suturing points of the laparotomy incisions.

The patients of both groups were comparable in age and gender.

In the postoperative period, the patients of both groups received antibacterial and detoxification therapy as well as underwent the correction of protein and water-electrolyte metabolism. There were no differences in the postoperative treatment of patients in group I and group II.

The effectiveness of peritoneal lavage was evaluated by microbiological examination of the contents of the abdominal cavity and the content of drainage before and after peritoneal lavage. The contents of the abdominal cavity were taken in special sterile tubes, according to the rules of antiseptics, and immediately delivered to the bacteriological laboratory. After 4-5 days, a control bacterial culture of the contents of the drainages was performed in two groups identically. The material for microbiological examination was taken and analysed on the same day. The criterion for the etiological role of bacterial pathogens of peritonitis included the

titres of the colony-forming units (CFU / ml), indicated in the “Appendices to the order of the Ministry of Health of Ukraine № 4 as of 05 January 1996” [5]. To determine the quantitative composition of the microflora of peritoneal exudate, the method of sectoral cultures, based on incubation of diluted concentrations of microorganisms, was used. The time of determination of the microbial count was 18-36 hours. The inflammatory response of the body was also taken into account by determining the leukocyte formula and procalcitonin before and after peritoneal lavage, the length of the in-hospital stay and the presence and frequency of postoperative complications [16 - 22].

Statistical processing of the findings was performed using a licensed version of the software package STATA 12 (USA). Before choosing the method of intergroup comparison of parametric parameters or in repeated studies, the normality of the distribution was checked according to the Shapiro - Wilk criterion. Wilcoxon's criterion and McNemar's Chi-square test were used to compare the dynamics (related aggregates), and the chi-square test (Fisher's exact test) and Mann-Whitney test (comparison of groups I-II) were applied to compare the findings in both groups.

### **Results and discussion**

The results of microbiological studies of the contents of the abdominal cavity in patients of groups I-II before and after peritoneal lavage are presented in table 1.

As can be seen from the table, the contents of the abdominal cavity in generalized peritonitis are polymorphic in nature of pathogens, both aerobic and anaerobic gram-positive and gram-negative microorganisms. The non-sporing obligate anaerobes and their associations with aerobes are dominant in peritonitis. Literature data confirm the obtained results and indicate that among them etiologically significant in the development of peritonitis are gram-negative bacteria of the family Enterobacteriaceae (*Escherichiacoli*, *Proteusspp.*, *Klebsiella - Enterobacter - Serratia*). [11 - 15].

The species composition of cultures taken before peritoneal cavity lavage with antiseptic solutions was similar in the number of strains and colonies in both groups.

Thus, after peritoneal lavage with an antiseptic solution of decamethoxine in combination with hyaluronic acid in group I, the number of strains decreased from 94 to 49 ( $p < 0.01$ ), the number of colonies - from 43.69 lg CFU / ml to 20.08 lg CFU / ml,  $\Delta = 23.61$  lg CFU / ml ( $p < 0.01$ ). In group II, after peritoneal lavage with 0.02% chlorhexidine bigluconate, the number of strains decreased from 93 to 68 ( $p < 0.01$ ) and the number of colonies from 42.68 lg CFU / ml to 30.87 lg CFU / ml,  $\Delta = 11.81$  lg CFU / ml ( $p < 0.01$ ).

Table 1

The results of microbiological examination of the contents of the abdominal cavity of patients before and after peritoneal lavage

Groups (number of patients)	Infectious agents	Number of strains		P (McN)	Microbial load (lg CFU/ml)		P (W)
		Before lavage	After lavage		Before lavage	After lavage	
Group I (n=47)	Staphylococcus aureus	4	0	0,045*	3,88	0	0,0001*
	Staphylococcus spp.	1	0	0,317	3	0	0,0001*
	Streptococcus spp.	7	1	0,014*	2,42	1	0,0001*
	Enterococcus spp.	6	2	0,045*	4,75	2,5	0,0001
	Corynebacterium spp.	2	0	0,157	4,5	0	0,0001*
	Escherichia coli	41	28	0,0003*	5,28	3,35	0,003*
	Klebsiella spp.	8	3	0,025*	5,69	2,4	0,0001*
	Enterobacter spp.	3	3	1	6,67	2,33	0,0001*
	Citrobacter spp.	0	0	-	-	-	-
	Proteus spp.	3	1	0,157	4	1	0,0001*
	Pseudomonas aeruginosa	4	3	0,317	3,25	2	0,002*
	Acinetobacter spp.	1	1	1	4	3,5	0,328
	Anaerobes	13	6	0,008*	-	-	-
	Candida albicans	1	1	1	3,5	2	0,0005*
	Yeasts	0	0	-	-	-	-
<b>Total</b>	94	49	0,0001*	43,69	20,08	0,0001*	
Group II (n=49)	Staphylococcus aureus	5	1	0,045*	4,7	2,5	0,0001*
	Staphylococcus spp.	1	0	0,317	1		0,0001*
	Streptococcus spp.	6	3	0,083	2,83	1,5	0,0001*
	Enterococcus spp.	8	4	0,045*	4,56	3,38	0,037*
	Corynebacterium spp.	0	0	-	-	-	-
	Escherichia coli	43	36	0,008*	5,17	4,22	0,144
	Klebsiella spp.	6	5	0,317	6,25	4,1	0,005*
	Enterobacter spp.	1	1	1	4,5	3	0,007*
	Citrobacter spp.	1	1	1	3,5	1	0,0001*
	Proteus spp.	3	2	0,317	4,5	2,5	0,0003*
	Pseudomonas aeruginosa	3	3	1	2,67	2,5	0,6251
	Acinetobacter spp.	1	1	1	4,5	4	0,3868
	Anaerobes	11	7	0,045*	-	-	-
	Candida albicans	3	3	1	2,67	1,17	0,0001*
	Yeasts	1	1	1	3	1	0,0001*
<b>Total</b>	93	68	0,0001*	42,68	30,87	0,0008*	

Note: P (W) - Statistical significance of the manifestation of the effect of reducing the load (a score by Wilcoxon test), P (McN) - the criterion of the McMiari Chi-square (a score for related populations); P ( $\chi^2$ ) - criterion Chi-square (comparison of groups I-II); P (MW) Mann-Whitney test (comparison of groups I-II); \* - the difference is statistically significant ( $p < 0,05$ ).

An antiseptic solution of decamethoxine in combination with hyaluronic acid proved to be more effective for peritoneal cavity lavage in comparison with chlorhexidine solution.

Among all the isolated bacterial pathogens that were cultured in groups I and II, the most characteristic pathogen was E. Coli. The number of isolated strains of E. coli, found in the peritoneal exudate of patients in groups I and II, is presented in table 2.

Table 2

The number of E. Coli found in groups I-II before and after peritoneal cavity lavage

Parameters	Periods	Group I	Group II	P (I-II)
Number of strains	before lavage	41	43	$P(\chi^2) = 0,938$
	after lavage	28	36	$P(\chi^2) = 0,520$
	P (McN)	0,0003*	0,008*	-
Number of colonies (lg CFU/ml)	before lavage	5,28	5,17	$P_{(MW)} = 0,850$
	after lavage	3,35	4,22	$P_{(MW)} 0,038^*$
	$\Delta$ (before-after)	1,93	0,95	$P_{(MW)} 0,0001^*$
	P (W)	0,0005*	0,082	-

Note: P (W) - Statistical significance of the manifestation of the effect of reducing the load (a score by Wilcoxon test), P (McN) - the criterion of the McMiari Chi-square (a score for related populations); P ( $\chi^2$ ) - criterion Chi-square (comparison of groups I-II); P (MW) Mann-Whitney test (comparison of groups I-II); \* - the difference is statistically significant ( $p < 0,05$ ).

Peritoneal lavage with an antiseptic solution of decamethoxine in combination with hyaluronic acid provided better outcomes than when 0.02% chlorhexidine bigluconate was used for the procedure. A significant reduction in the number of E. Coli strains from 41 to 28 and the number of colonies from 5.28 lg CFU/ ml to 3.35 lg CFU/ ml was achieved after peritoneal lavage due to more effective action of an antiseptic gel solution compared with water-based antiseptics. Better outcomes of peritoneal lavage can be explained by specific characteristics of the substance. Thus, due to the gel form of antiseptic, in contrast to water, it covers the maximum surface of the perietal and visceral peritoneum, prevents sticking and adhesion between the loops of the intestine, parietal peritoneum, and anterolateral wall of the abdomen.

The number of leukocytes and the level of procalcitonin in group I and group II before and after peritoneal lavage is shown in table 3.

Table 3

Leukocyte count and procalcitonin levels in group I and group II before and after peritoneal lavage

Parameters	Periods	Group I	Group II	P (I-II)
Leucocytes	Before operation	18,6±2,3	17,9±3,8	P (MW) = 0,280
	5 days after	7,2±0,9	10,5±1,2	P (MW) = 0,0001*
	Δ (95%ΔI) (before-after)	11,4 (10,6-12,1)	7,4 (6,2-8,5)	P (MW) = 0,0001*
	P (W)	0,0003*	0,008*	-
Procalcitonin (ng/ml)	Before operation	5,7±0,4	5,9±0,5	P (MW) =0,850
	5 days after	1,1±0,1	3,54±0,4	P (MW) 0,038*
	Δ (95%ΔI) (before-after)	4,6 (4,5-4,7)	2,36 (2,2-2,5)	P (MW) 0,0001*
	P (W)	0,0001*	0,0001*	-

Note: P (W) - Statistical significance of the difference between the indicators in the dynamics (assessment by Wilcoxon test), P (MW) Mann-Whitney test (comparison of groups I-II); \* - the difference is statistically significant (p <0,05).

The number of leukocytes in patients of both groups was comparable (p = 0.280) before peritoneal lavage. After surgical treatment, including elimination of the source of infection and peritoneal cavity lavage, the number of leukocytes in patients of group I was lower than 7.2 ± 0.9 in comparison to 10.5 ± 1.2 in group II. The statistical significance of the improvement of the laboratory parameters (pI-II <0.05) is observed in group I compared with group II.

The dynamics of the concentration of procalcitonin before and after peritoneal lavage with different antiseptic solutions was different. Significant reduction of procalcitonin was observed in patients of group I, who underwent peritoneal lavage with antiseptic gel solution, from 5.7 ± 0.4 ng / ml to 1.1 ± 0.1 ng / ml, whereas in patients of group II, who received a water-based antiseptic solution, this reduction was slightly smaller, but also statistically significant - from 5.9 ± 0.5 ng / ml to 3.54 ± 0.4 ng / ml. Thus, procalcitonin levels in patients of both groups, as expected, also had statistically significant differences (pI-II <0.05) at



admission and on day 5. Postoperative decrease in procalcitonin levels was observed on the 5th day, indicating successful elimination of the septic source in the abdominal cavity, which was also confirmed by the studies [20].

Clinical results of the complex treatment of patients with generalized peritonitis showed that among patients of group I (n = 47), in the early postoperative period on the 4th day after surgery 1 (2.13%) patient was diagnosed with subphrenic abscess, which was eliminated by ultrasound-guided puncture. The signs of early adhesive intestinal obstruction were also observed in 1 (2.13%) patient on the 6th day after surgery. Postoperative wound infection was seen in 3 (6.38%) patients. The total number of complications amounted to 5/47 (10.6%).

Among patients of group II (n = 49), 4-5 days after surgery 4 (8.16%) patients were diagnosed with abdominal abscesses (subphrenic, on the left - 1, between the loops of the intestine - 2, pelvic - 1), which were successfully eliminated by ultrasound-guided puncture. Moreover, 4 (8.16%) patients had early adhesive intestinal obstruction, one of whom underwent relaparotomy to eliminate the intestinal obstruction. Postoperative wound infection was observed in 5 (10.2%) patients. In group II, the total number of complications was 13/49 (26.5%). In general, the difference between the groups in the frequency of complications is statistically significant ( $p = 0.046$ ) and indicates a decrease in the probability of complications in group I by 67% compared with group II - ORI-II = 0.33 (0.11-1.0).

The average length of in-hospital stay was  $9 \pm 1.4$  days in group I, which is significantly less ( $p < 0.01$ ) compared with the average length of in-hospital stay in group II -  $14 \pm 2.2$  days.

The obtained findings confirm the higher effectiveness of the treatment in group I in comparison to group II due to the use of antiseptic gel solution for peritoneal lavage in the complex treatment of generalized peritonitis, which prevents the formation of adhesions, separate canals and provides maximum antiseptic effect on the entire peritoneal surface.

## **Conclusions**

In generalized peritonitis, the antiseptic gel solution for peritoneal lavage showed higher efficacy than water-based antiseptic due to its ability to cover the entire parietal and visceral peritoneal surface as well as maximum exposure, thus reducing the number of strains of microorganisms from 94 to 49, the number of colonies from 43,69 lg CFU / ml to 20.08 lg CFU / ml, whereas the use of water-based antiseptic helped to decrease the number of strains

of microorganisms from 93 to 68, the number of colonies from 42.68 lg CFU / ml to 30.87 lg CFU / ml.

In the comprehensive surgical treatment of patients with generalized peritonitis, peritoneal lavage with antiseptic gel solution helped to reduce the overall incidence of postoperative complications to 10.6% in group I comparing to 26.5% in group II, the occurrence of abdominal abscesses to 2.13% in group I comparing to 8,16% in group II, early adhesive intestinal obstruction to 2.13% in group I comparing to 8.16% in group II, postoperative wound suppuration to 6.38% in group I comparing to 10.2% in group II. Peritoneal lavage with antiseptic gel solution also reduced the average length of in-hospital stay to  $9 \pm 1.4$  days in group I compared with  $14 \pm 2.2$  days in group II.

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