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Preventive effect of probiotics to the postoperative infection for surgical patients with obstructive jaundice.

Wei-Feng Yao, Jun-Wei Liu, Dongsheng Huang*

Department of Hepato-Biliary-Pancreatic Surgery, Zhejiang Provincial People's Hospital, Hangzhou, PR China

Abstract

Objectives: To investigate the perioperative application of probiotics on postoperative infectious complications.
Patients and methods: A total of 58 cases of upper abdominal surgery patients with obstructive jaundice were collected and divided into two groups, the control group B routinely get preoperative preparation before surgery 3 days, and the probiotics group A get oral intestinal microbial agents 2.0 g, 3 times per day in the preoperative 5 days, the inflammation indicators and postoperative infection complications were observed after treatment.
Results: After treatment for 1 week, the inflammation indicators include CRP, IL-6, and endotoxin in Probiotics Group were significantly lower than control group B after operation, the level of CRP, IL-6, endotoxin were 14.90 ± 3.99, 151.14 ± 26.62 and 0.034 ± 0.007 in group A respectively, while in group B which is 17.00 ± 3.94, 172.07 ± 41.29, 0.039 ± 0.011 respectively (P<0.05). The overall incidence of complications was 58.6% in control group and 27.6% in observation group (P<0.05), respectively.
Conclusion: Perioperative administration of probiotics can reduce postoperative inflammatory reaction, inhibit infection and reduce postoperative complications associated with infections.

Keywords: Intestinal probiotics, Inflammation, Obstructive jaundice, Infectious complication.

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Introduction

The intestinal flora, also known as the intestinal microflora system is the most important and complex micro-ecosystem, composed with anaerobic, aerobic and facultative anaerobic bacteria, including bifidobacterium and bacteroides, which account for 90% of the total number of bacteria [1]. There are about 100 trillion cells of microbes in the human body, which is about 10 times as much as the human cell [2,3]. Most of the microbial colonization in the human gut, can affect the human physiological and nutritional status, which is essential to human life [4,5].

Under physiological conditions the bile salts flow into the intestine and inhibit bacterial growth, free bile acids in the colon can adjust the balance of intestinal flora. Bile salts can combine with Lipopolysaccharide (LPS) into binding complexes which are difficult to absorb, preventing their migration through the intestinal tissue, the secreted IgA (sIgA) can neutralize endotoxin, and split LPS into non-toxic subunits and polymers. In obstructive jaundice patients, the way into intestinal is blocked and the intestinal bacteria blooms, gastrointestinal mucosal barrier damage and a large number of bacteria and LPS migrate into the blood. When in obstructive jaundice patients, the reticuloendothelial system reduces endotoxin clearance, endotoxin cannot be detoxify by the liver and then get into the systemic circulation endogenous formation of intestinal endotoxemia, causing damage to liver cells, leading to liver cell necrosis [6].

The microbiota can have multiple interactions with the host, and have several functions, including prevention the pathogenetic organisms from colonization, regulation of immunity, to maintain the intestinal movement and mucosal secretion. [7]. Reduced gut microbial content may be associated with an impaired defense mechanism against pathogens and less environmental stimulation of the developing immune system of the digestive tract. Therefore, those submitted to extensive abdominal surgical procedures are at a particular risk [8,9]. Major abdominal surgery tends to make patients at several risks which will disturb the intestinal microbiota, leading to trans-location of pathogens, such as decreased postoperative intestinal motility; overuse of pharmacologic interventions, mucosal dysfunction, malnutrition, and bowel manipulation [10-12]. In certain circumstances, however, various factors such as malnutrition, major abdominal surgery, or the use of long-term antibiotics can lead to intestinal flora imbalance [13]. In such situation, translocation of intestinal bacterial or their toxins will happen after the excessive reproduction of bacteria, loss of intestinal epithelial cells and immune deficiency, then lead to bacteremia and infective complications [14,15].

Patients and Methods

Eligible patients were consecutively enrolled between June 2015 and August 2016, aged 34 to 78 years, one patient was included if he or she had been diagnosed as obstructive jaundice, Patients with other important organ failure, taking antibiotics and micro ecological regulating drug and yogurt gastrointestinal motility drug in 4 weeks were excluded. The study protocol was approved by the ethics committee of Zhejiang Provincial People's hospital; all the participants give informed consent voluntarily. A computer-generated number list was created randomly, and patients were included consecutively. Patients were randomized on the day of hospitalization. Sequence was concealed-opaque consecutively numbered envelopes-until intervention was assigned; a study nurse generated the allocation sequence, enrolled the participants, and assigned participants to their group. In our study, care managers were responsible for the reception and education of patients.

All the patients (n=58) were divided into 2 groups randomly: the control group B routinely get preoperative preparation before surgery 3 days, and the probiotics group A get oral intestinal microbial agents 2.0 g, 3 times per day in the preoperative 5 days.No conventional bowel preparation was performed.

Peripheral blood assay

Peripheral venous blood samples were collected preoperative day 5 postoperative day 9. Serum was centrifuged for and interleukin-6, C-Reactive Protein (CRP) assays using commercially available enzyme-linked immunosorbent assay kits (CRP: RayBiotech, Norcross). Endotoxins were quantified with a limulus amebocyte lysate assay kit (Yihua Bio, Shanghai, China). The blood bacterial cultures were carried out when the temperature exceeding 38.5˚C.

Statistical analysis and sample size calculation

All data were expressed as mean ± standard deviation, Homogeneity of variance was tested by Levene's statistic, the two groups' characteristics were compared by the independent t test, and differences among proportions were tested by the chi-square test. Statistical analysis was performed using SPSS for Windows version 16.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was inferred at a two-tailed P value of <0.05.

Results

Characteristics of patients

As we can see in Table 1, fifty-eight patients were enrolled, and there is no differences were observed between groups A and B in baseline characteristics, including age, gender, total bilirubin, haemoglobin, peripheral white blood cell count.

Changes of CRP, endotoxin and IL-6

As seen in Table 2, regardless of the experimental group A or the control group B, The level of CRP, IL-6, Endotoxin, were significantly higher than preoperative after operation except for the level of IL-6 in group A, and there were significant differences statistically between the two groups. But not in IL-6, Endotoxin, and CRP in the detection of peripheral blood before surgery. While in peripheral blood on ninth days postoperatively. The level of CRP, IL-6, endotoxin were 14.90 ± 3.99, 151.14 ± 26.62 and 0.034 ± 0.007 in group A respectively, while in group B which is 17.00 ± 3.94, 172.07 ± 41.29, 0.039 ± 0.011 respectively, there were significant differences between the two groups.

Table 1. *Baseline characteristics of patients.*

	Group A (n=29)	Group B (n=29)	P value
Average age	54.8 ± 10.6	51.2 ± 11.3	0.228
Gender (male: female)	12:17	14:11	0.28
Total bilirubin	39.52 ± 9.76	36.17 ± 10.86	0.22
Albumin	40.85 ± 7.03	38.03 ± 6.53	0.120
WBC count	6.07 ± 2.13	5.61 ± 1.82	0.386
Haemoglobin	138.07 ± 15.37	130.76 ± 14.53	0.068

Table 2. *Variation in CRP, endotoxin and IL-6.*

		Preoperation	Postoperation	
CRP	Group A	3.93 ± 0.88	14.90 ± 3.99	P<0.01
	Group B	3.75 ± 1.09	17.00 ± 3.94	P<0.01
		P=0.511	P=0.048	
IL-6 (ng/L)	Group A	141.93 ± 19.95	151.14 ± 26.62	P=0.142
	Group B	137.48 ± 26.12	172.07 ± 41.29	P<0.0001
		P=0.469	P=0.026	
Endotoxin (EU/ml)	Group A	0.028 ± 0.011	0.034 ± 0.007	P=0.01
	Group B	0.030 ± 0.009	0.039 ± 0.011	P<0.01
		P=0.472	P<0.031	

Changes of postoperative infection in the two groups

As showed in Table 3, the incidence of bacteremia and abdominal infection in Group A decreased compared with Group B, But there was no difference significantly. However, the overall incidence of complications was 58.6% in control group and 27.6% in observation group, respectively (P<0.05).

Table 3. *Changes of postoperative infection in the two groups.*

	Group A (n=29)	Group B (n=29)	P value
Pneumonia	2	4	0.666
Biliary tract infection	2	2	1

Urinary infection	0	1	1
Abdominal infection	1	3	0.526
SSI	2	1	1
Bacteremia	1	6	0.107
total	8	17	0.017

Discussion

Postoperative infection is a common complication in abdominal surgery; most infections are caused by bacteria. During the abdominal surgery, the gut microbial flora and mucosal permeability were affected, leading to intestinal barrier dysfunction and micro ecological imbalance. As a result of this, it will suppress the immune function and aggravate the inflammation of the body [16]. All of these factors will increase the risk of postoperative infection and sepsis. For a long time, several measures such as bowel preparation, application of antibiotics in preparing patients for abdominal surgery are applied; furthermore, recent studies report that the use of probiotics perioperative could reduce the influence of these factors. Several clinical trials have been presented in which probiotics has been used. It seems that in patients undergoing upper abdominal surgery prophylactic administration of different probiotics will reduce postoperative infections. While other studies failed to get positive results in colorectal surgery using the similar strategies. In one study, Sugawara treated two groups of patients undergoing hepatobiliary resection by oral synbiotics to investigate the effect on gut barrier function, immunity, systemic inflammation, and postoperative complications, and they found that after treatment with synbiotics, the serum IL-6, white blood cell counts, and C-reactive protein were significantly lower than the other group who get routinely preparation. Moreover, during the treatment period, the bifidobacterium extracted from the stool increased significantly in the synbiotics group, and the incidence of postoperative infectious complications decreased significantly ($P<0.05$) [17]. Also Rayes et al. found that addition of probiotics seemed to increase the benefits in patients with gastric resections and liver transplantation and Pylorus-Preserving Pancreatoduodenectomy (PPPD), furthermore, the time of antibiotics application was significantly shorten, in the probiotics group, and patients can be well tolerated with probiotics [11,18,19]. And in patients undergoing living donor liver transplantation, similar results have found that postoperative sepsis was significantly reduced from 24% to 4% [20].

Up to now, the application of micro ecological preparation in patients with obstructive jaundice had not been reported, and the intestinal microflora imbalance is more common in these patients, and which will increase the abdominal infections and infections of the other sites of the body after operation.

In our study, we found that after surgery, the level of CRP, endotoxin and IL-6 are significantly increased in both groups, indicating that during the operation, the intestinal barrier function and immune function are reduced in two groups of patients with obstructive jaundice. In this situation, the intestinal bacteria will translocate more easily, and then induce to endotoxemia and bacteremia, thereby increasing the incidence of postoperative infection. After the application of probiotics, the level of serum CRP, endotoxin and IL-6 were decreased significantly, and there are significant differences in statistic, our results show that the application of probiotics can improve the intestinal barrier function and intestinal immune function significantly.

In our study, there were care managers who in charge of the education for patients enrolled, act as a bridge between doctors, experts and patients, according to the doctors and patients of the hospital to develop individualized, psychological nursing of patients, and provide the necessary information and help [21].

However, several studies failed to obtain meaningful results in the administration of probiotics [22-25], in these studies, the number of probiotics was rather low, moreover, and the study population included both all the gastrointestinal surgery, especially colorectal resections. Small intestine and liver immune system and the immune modulation effects play a more important role in the upper abdomen surgery. And bacteria content is relatively low of the organs, and more likely to benefit from the influence of living bacteria, while in colorectal surgery, intestinal flora is much more, so in patients with colorectal surgery, therefore, need a higher dose of probiotics can achieve this effect. Although most researchers have pointed out the potential application of intestinal micro ecological agents, few have analysed the mechanism. Management of probiotics is generally considered safe and have been used for many years, the side effects reported rarely. However, the live bacteria on the patient management, safety should be carefully evaluated.

So far, we have enrolled 58 cases, and this is the limitation of our research, we need to do more effort to improve our research. In the follow-up study, we should enrol more suitable patients; maybe we can get better results.

Conclusion

Despite some controversy, the current study showed that in abdominal surgery patients, especially in patients with obstructive jaundice, the application of probiotics can reduce the risk of postoperative abdominal infection. This strategy has the potential to decrease morbidity, length of antibiotic therapy, and duration of hospital stay. In different patient groups such research is difficult to present, because the application of probiotics dose and composition is different. Although some studies have reported the sepsis induced by synbiotics or probiotics, such risks can be effectively controlled. Controlled trials conducted so far, the results show that with probiotic therapy appears to be safe and no apparent serious side effects. Further research is warranted to elucidate the potential mechanism.

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*Correspondence to

Dongsheng Huang

Department of Hepato-Biliary-Pancreatic Surgery

Zhejiang Provincial People's Hospital

PR China