Original Article
Effect of dual plasma molecular adsorption system combined with hormone therapy on postoperative liver cancer

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Abstract: Objective: Effects of dual plasma molecular adsorption system (DPMAS) combined with hormone therapy on liver function (LF), coagulation function (CF) and inflammation indexes in patients with hepatic failure after liver cancer (LC) surgery. Methods: Altogether 108 patients with liver failure admitted to our hospital for liver cancer resection were selected as the research participants, 58 of whom were treated with dual plasma molecular adsorption system combined with hormone therapy as the research group, and 50 of whom were treated with single dual plasma molecular adsorption system as the control group. The clinical effects of the two groups were compared. The changes of liver function before and after treatment were detected by an automatic biochemical analyzer, coagulation function was detected by a hemagglutination analyzer, inflammatory index was detected by ELISA, and immunoglobulin levels before and after treatment were compared between the two groups. The average hospital stay and adverse reactions after treatment were observed. Results: The efficacy in the research group (RG) was clearly higher than that in the control group (CG) (P<0.05). AST, ALT and TBIL expressions in RG were lower than those in CG (P<0.05). After treatment, prothrombin activity, coagulation factor X and platelets in the RG were higher than those in the CG (P<0.05). After therapy, the inflammatory level in the RG was significantly lower than that in the CG (P<0.05). After therapy, the levels of IgG, IgA and IgM in the RG were lower than those in the CG (P<0.05). There was no obvious difference in the average hospitalization time in both groups (P>0.05). The incidence of adverse reactions in the RG was clearly lower than that in the CG (P<0.05). Conclusion: DPMAS combined with glucocorticoids had significant therapeutic effect on patients with hepatic failure after LC surgery, which could effectively reduce inflammatory factors of patients and improve CF. It is worthy of clinical application.

Keywords: Dual plasma molecular adsorption system, glucocorticoid, hepatic failure, liver function, coagulation function, inflammation index

Introduction

For the past few years, the incidence rate of malignant tumors in China has increased annually [1]. LC, is one of the most familiar malignant tumors in clinical practice, and it has a high incidence rate and a high mortality rate [2]. LC is a malignant tumor occurring in liver cells or intrahepatic bile duct cells. The number of new cases of LC in China accounts for more than 50% of the global incidence every year [3]. With the increasing number of LC patients, optimiz-

ing the treatment of LC is a major focus of research [4]. At present, specific individual comprehensive therapy is carried out clinically according to the disease characteristics of different LC patients, but surgical resection is still one of the important methods for the treatment of LC in patients [5]. It can effectively reduce the patient's condition, prolong the survival period and improve the clinical prognosis [6]. Although the surgical treatment methods of hepatectomy are gradually improving, the trauma of hepatectomy is still relatively large. The

liver is the primary site for the inactivation of inflammatory factors. After operation, excessive release of inflammatory factors can cause systemic inflammatory reactions, which can further aggravate liver injury after hepatectomy, leading to hepatic failure. Hepatic failure is the main reason for death of patients undergoing hepatectomy [7, 8]. Therefore, the effective control of hepatic failure is also an important point in clinical research.

Glucocorticoid drugs are mainly used for anti-inflammation, anti-virus and immunosuppression related therapies in clinical practice [9], with significant clinical effects. Studies have shown that glucocorticoid therapy is applied to the treatment of various diseases, such as primary nephrotic syndrome [10]. At present, it is also applied to the treatment of hepatic failure after LC surgery [11]. However, its effect is still controversial [12]. In recent years, the treatment mode of DPMAS that has emerged to use the combination of two adsorbents of neutral macroporous resin and ion exchange resin for plasma adsorption therapy. Compared with plasma exchange therapy, this technology overcomes the shortcomings of plasma shortage and allergy. It can be used as a replacement therapy for plasma exchange [13]. At present, it is also applied to LC therapy [14]. The research of the author Zhong S et al [15] has shown that plasma exchange combined with dual plasma adsorption therapy can improve the prognosis of chronic hepatic failure. This indicates that the combined therapy may have better curative effects in hepatic failure after LC surgery. Currently, the treatment of hepatic failure by DPMAS combined with hormone therapy is still controversial. Therefore, this experiment aimed to explore the influence of DPMAS combined with hormone therapy on LF, CF and inflammatory indexes of hepatic failure patients after LC surgery; providing new ideas and reliable theoretical foundation for future clinical diagnosis and treatment of hepatic failure patients after LC surgery.

Materials and methods

Baseline data

From June 2017 to June 2019, 108 patients admitted to our hospital for LC resection and hepatic failure were selected as the research subjects, of which 58 patients were treated with DPMAS combined with hormone therapy (RG), and 50 patients were treated with single DPMAS (CG). This study was ratified by our hospital ethics committees. All of the subjects or immediate family members signed the informed consent form.

Inclusion and exclusion criteria

Inclusion criteria: All patients were diagnosed with LC through our hospital. All patients underwent hepatectomy in our hospital and developed hepatic failure. All patients participating in the experiment were primary LC patients. All patients received follow-up treatment in our hospital after diagnosis. They had complete case data. They agreed to cooperate with and assist the medical staff of our hospital.

Exclusion criteria were as follows: Concomitant with other tumors, concomitant with other cardio-cerebrovascular diseases, organ failure, mental illness, physical disability, long-term bed-ridden and inability to take care of themselves, pregnancy, concomitant with other autoimmune diseases, concomitant with other chronic diseases, transferred to another hospital, and surgical contraindications.

Methods

CG: DPMAS therapy: Blood pathway was established by femoral vein catheterization, and artificial liver was treated by DX-10 multifunctional blood purification treatment device after connecting with extracorporeal circulation blood pipeline. In advance, the pipeline and adsorption column were pre-flushed with 2500~3000 mL of 0.9% physiological saline to exhaust the gas. Next, heparinization was pre-flushed with 500 mL heparin sodium saline (containing 20 mg heparin sodium). The pipeline was sealed after heparin for 10~30 min. Twenty-five mL heparin sodium saline (containing 100 mg heparin sodium) was selected for micropump injection at 5 mL/h. The dosage was adjusted according to the conditions and CF. The intraoperative blood flow velocity was controlled to 100~120 mL/min. The plasma separation velocity was controlled to 20~24 mL/min. The adsorption time was 120~180 min. At the end of treatment, protamine sulfate was used for IV bolus, and this dosage was half of the total dosage of heparin (no more than 50 mg).

Table 1. Comparison of baseline data between the two groups [n (%)]

	RG (n=58)	CG (n=50)	t/X²	P
Age/years old	51.6±8.4	52.3±7.9	0.444	0.658
BMI (KG/cm²)	24.68±2.82	24.75±3.14	0.122	0.903
Gender			0.298	0.585
Male	40 (68.97)	32 (64.00)		
Female	18 (31.03)	18 (36.00)		
Smoking			0.074	0.785
Yes	38 (65.52)	34 (68.00)		
No	20 (34.48)	16 (32.00)		
Alcoholism			0.061	0.805
Yes	35 (60.34)	29 (58.00)		
No	23 (39.66)	21 (42.00)		
Exercise habits			0.109	0.742
Yes	26 (44.83)	24 (48.00)		
No	32 (55.17)	26 (52.00)		
Place of residence			0.256	0.613
City	32 (55.17)	30 (60.00)		
Rural	26 (44.83)	20 (40.00)		
Nation			0.705	0.401
Han nationality	45 (77.59)	42 (84.00)		
Minority nationality	13 (22.41)	8 (16.00)		
Family history			0.057	0.811
Yes	21 (36.21)	36 (34.00)		
No	17 (63.79)	66 (66.00)		
Course of disease	1.6±1.1	1.8±1.2	0.903	0.368

RG: Patients were treated with glucocorticoids in addition to the treatment in the CG. One day prior to treatment with DPMAS, the patients were given 1 mg (/kg·d) of methylprednisolone sodium succinate for injection (Nanguang Chemical Pharmaceutical Co., Ltd., SFDA Approval No. HC20160039). After treatment for one week, the dose was reduced to ½-3/4 of the original dose. After continuous treatment for one week, the injection was changed to prednisone acetate tablets 10 mg orally, taken three times a day, and the dosage was reduced by 5 mg every 7 days until the drug was discontinued.

Note: Automatic biochemical analyzer (Beijing Gene &I Scientific Co., Ltd., AU5800) was used for LF test. Blood coagulation analyzer (Shanghai Hanfei Medical Devices Co., Ltd., RAC-060) was used for blood coagulation function test. ELISA was used to detect inflammatory indexes.

Outcome measures

Main outcome measures: The clinical effects between the two groups were compared [16]. An automatic biochemical analyzer was used to detect the changes of liver function before and after treatment of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin (TBIL) in the two groups. A hemagglutination analyzer was used to detect the changes of prothrombin activity, coagulation factor X and platelet index in the two groups before and after treatment. ELISA was used to detect the changes of inflammatory factors IL-2, IL-6, IL-10 and TNF-α indexes in the two groups before and after treatment. IgG, IgA and IgM immunoglobulin levels were compared in the two groups before and after treatment.

Secondary observation indexes: The average hospitalization time of patients were compared in the two groups. After treatment, the adverse reactions were observed in both groups.

Statistical methods

SPSS 22.0 software was used to process the data. Graphpad7 was used to illustrate figures. Enumeration data was represented by (rate). Chi-square test was applied for comparison between groups. Measurement data were represented as (mean number ± standard deviation). A t test was applied for data conforming to a normal distribution. The Wilcox test was applied for data conforming to a non-normal distribution. The difference was statistically significant with P<0.050.

Results

Comparison of the baseline data

There were no differences in age, BMI, gender, smoking, drinking, exercise habits, place of residence, nationality, family history, and course of disease between groups (P>0.050) (**Table 1**).

Table 2. Clinical efficacy

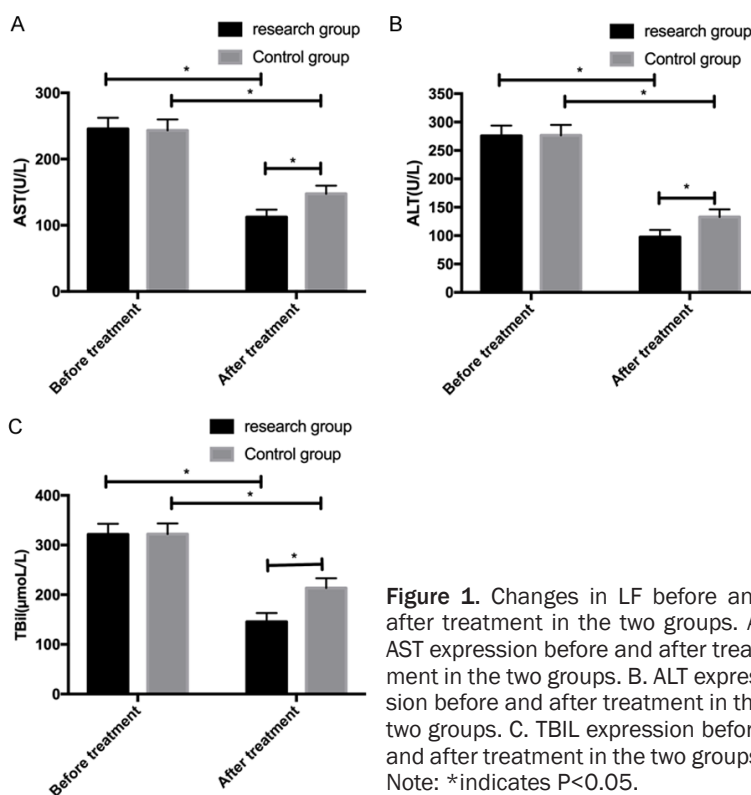|	RG (n=58)	CG (n=50)	X^2	P
Markedly effective	42 (72.41)	16 (32.00)		
Effective	14 (24.14)	27 (54.00)		
Ineffective	2 (3.45)	7 (14.00)		
Total effective rate (%)	56 (96.55)	43 (86.00)	3.914	0.048

Figure 1. Changes in LF before and after treatment in the two groups. A. AST expression before and after treatment in the two groups. B. ALT expression before and after treatment in the two groups. C. TBIL expression before and after treatment in the two groups. Note: *indicates P<0.05.

of AST, ALT and TBIL was decreased in both groups, and the expression of AST, ALT and TBIL in the RG were lower than those in the CG. The difference was statistically significant (P<0.05) (**Figure 1**).

Changes of CF

Before and after therapy, the changes of CF were analyzed in both groups. The results revealed that there was no significant difference in prothrombin activity, coagulation factor X, platelets and other indexes in both groups before therapy. After treatment, the prothrombin activity, coagulation factor X, platelets and other indexes in both groups were higher than before therapy, and the levels in the RG were higher than of the CG (P<0.05) (**Figure 2**).

Changes of inflammatory indexes

The changes of inflammatory indexes of patients were analyzed in both groups. The results revealed that the levels of IL-2, IL-6, IL-10 and TNF-α in the two groups had no significant changes before treatment. The levels of inflammatory indicators of patients in both groups were significantly declined after treatment, and those in the RG was clearly lower than in the CG (**Figure 3**).

Comparison of immunoglobulin level before and after treatment

Comparing the immunoglobulin levels in the two groups before and after therapy, the results revealed that there was no obvious difference in the levels of IgG, IgA and IgM in both groups before treatment. After treatment, the levels of IgG, IgA and IgM declined in both groups, and the levels in the RG were significantly lower than in the CG, with statistical difference (P<0.05) (**Figure 4**).

Clinical efficacy

After therapy, the clinical efficacy of patients was compared in both groups. The results revealed that the total effective rate was 96.55% in the RG, and the total effective rate was 86.00% in the CG. The RG was significantly higher than the CG, with statistical difference (P<0.05) (**Table 2**).

Changes of LF of patients before and after treatment

Before and after therapy, the changes of LF were analyzed in both groups. The results revealed that there was no significant difference in aspartate aminotransferase (AST), alanine aminatransferase (ALT) and total bilirubin (TBIL) expression in both groups before treatment (P>0.05). After treatment, the expression
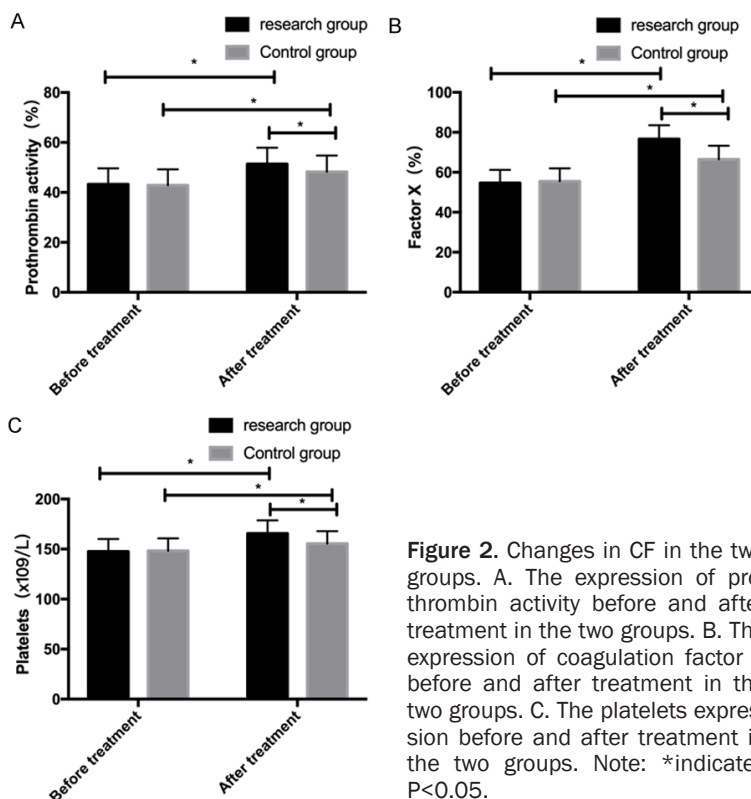
Figure 2. Changes in CF in the two groups. A. The expression of prothrombin activity before and after treatment in the two groups. B. The expression of coagulation factor X before and after treatment in the two groups. C. The platelets expression before and after treatment in the two groups. Note: *indicates P<0.05.
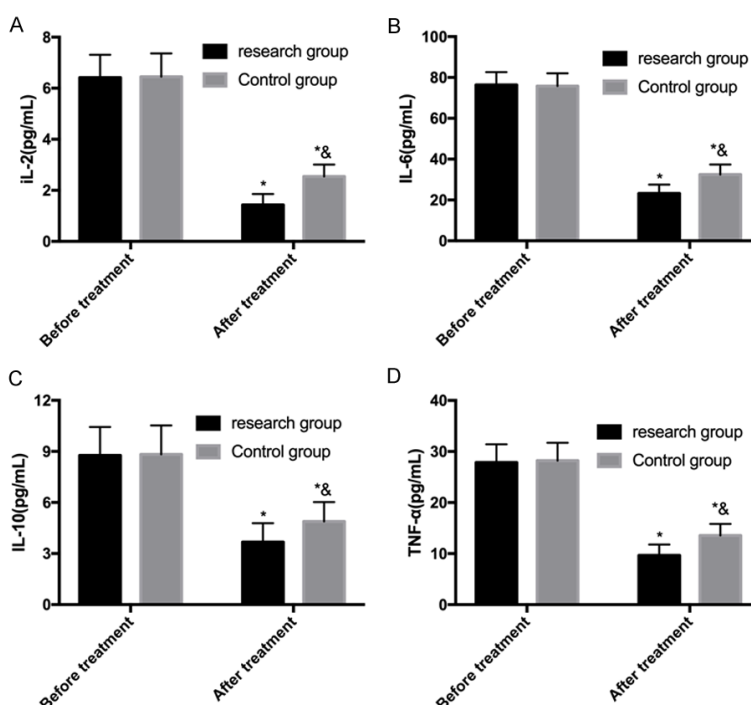

Figure 3. Changes of inflammatory indexes of patients in the two groups. A. IL-2 expression before and after treatment in the two groups. B. IL-6 expression before and after treatment in the two groups. C. IL-10 expression before and after treatment in the two groups. D. TNF-α expression before and after treatment in the two groups. Note: *indicates the comparison with before treatment. &indicates comparison with the RG.

Average hospitalization time

The average hospitalization time of patients were observed in the two groups. It was found that there was no obvious difference in the average hospitalization time of patients in either group (**Figure 5**).

Adverse reactions

After therapy, the incidence of adverse reactions was analyzed in both groups. The results revealed that the incidence of adverse reactions in the RG was 3 (5.17) and that in the CG was 10 (20.00). The incidence of adverse reactions in the RG was obviously lower than that in CG (**Table 3**).

Discussion

At present, with the increasing incidence of LC worldwide, the number of patients with hepatic failure after LC surgery is also increasing [17]. The application of DPMAS may significantly improve the treatment of hepatic failure [18]. However, the therapeutic effect of glucocorticoids combined with double plasma molecular adsorption system on hepatic failure is still controversial. Therefore, this research aimed to provide a reliable theoretical basis for future clinical treatment of hepatic failure by exploring the application of glucocorticoids combined with double plasma molecular adsorption system.

The experimental results revealed that the clinical efficacy of patients in the RG treated with DPMAS combined with hormone therapy was better than that of patients in the CG treated with DPMAS only; sug-

Figure 4. Immunoglobulin level in both groups before and after treatment. A. IgG level before and after treatment in the two groups. B. IgA level before and after treatment in the two groups. C. IgM level before and after treatment in the two groups. Note: *indicates the comparison with before treatment. &indicates comparison with the RG.
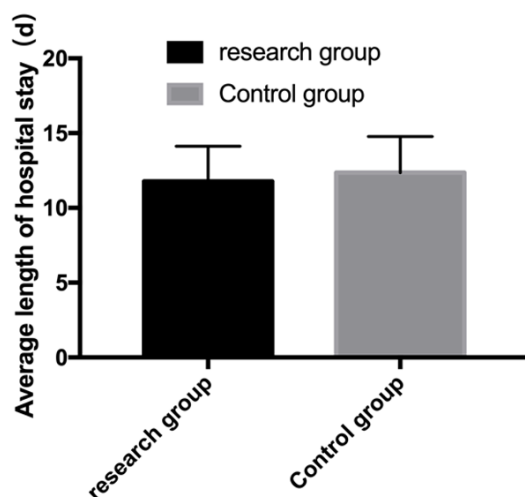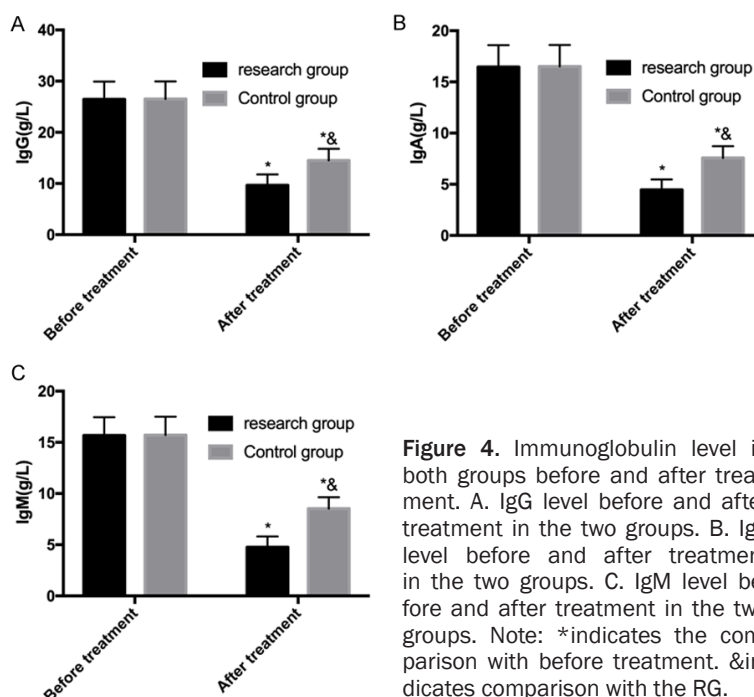

Figure 5. The average hospitalization time of patients in the two groups.

gesting that hormone therapy could effectively improve the efficacy of DPMAS for hepatic failure after LC surgery. This point was also consistent with results from previous studies [19], which support this experiment. By comparing LF in patients of both groups, we also found that LF in the RG was markedly higher than that in the CG after therapy, which also confirmed that the use of DPMAS combined with hormone therapy was more significant for the prevention of LF. Studies have shown that glucocorticoids

could prevent or delay excessively strong cellular immunity by inhibiting the function of T lymphocytes and adhesion molecule-1 in hepatocyte membrane cells [20]. In liver cells, we speculated that the role of glucocorticoids might be related to inflammatory factors. Studies have pointed out that the concentrations of inflammatory factors increased greatly in the process of liver injury [21]. In this study, we tested IL-2, IL-6, IL-10 and TNF-α levels in both groups of patients and found the same situation. It was confirmed that inflammatory factors play a certain role in hepatic failure. Glucocorticoids can induce apoptosis of inflammatory cells and inhibit their expression [22]. Therefore, we speculated that glucocorticoids can prevent or delay the disturbance of microcirculation in liver by reducing the inflammatory factor expression, thus reducing the ischemia and hypoxia of liver cells. This was also the reason why IL-2, IL-6, IL-10 and TNF-α in the RG were lower than those in the CG after treatment. Comparing the CF in the two groups of patients, we found that the CF in the RG was significantly improved after treatment, which also confirmed that the use of glucocorticoids could improve the CF of patients with DPMAS. Some studies have pointed out that coagulation dysfunction was a very common complication in the treatment of hepatic failure by DPMAS [23]. However, glucocorticoid adjuvant therapy can effectively improve this point. This further revealed the application value of glucocorticoids combined with DPMAS. Compared with the immunoglobulin level in the two groups of patients, we found that the immunoglobulin in the RG was also significantly reduced after treatment, which also suggested that glucocorticoids might enhance the efficacy of patients by suppressing inflammatory cytokines or immunosuppression. Some studies have pointed out that glucocorticoids have a strong immunosuppressive ability, reducing protein leakage and decomposition [24]. The results of this experiment were also in accor-

Table 3. The adverse reactions of patients in the two groups

	RG (n=58)	CG (n=50)	X^2	p
Nausea and vomiting	1 (1.72)	2 (4.00)		
Fever	0 (0.00)	1 (2.00)		
Hypotension	0 (0.00)	3 (6.00)		
Allergic reaction	1 (1.72)	2 (4.00)		
Infection	1 (1.72)	2 (4.00)		
Overall incidence (%)	3 (5.17)	10 (20.00)	5.576	0.018

dance with this point. Immunoglobulin has been shown to be involved in hepatic failure. With the increasing severity of the patient's condition, the regulation of immunoglobulins was reduced and the ability to remove antigens absorbed from intestinal tract and autoantigens was reduced due to the pathological changes of liver cells. On the other hand, with the aggravation of the patient's condition, necrosis of liver cells was constantly increasing. As a result, immunoglobulins are not able to perform their original phagocytic role and lose the ability to process antigens, thus infiltrating into blood and tissues in large quantities. The decrease of immunoglobulins also indicated that the immune metabolic function in the liver tissue of the patient has been improved and returned to normal. Similarly, we also found that the incidence of adverse reactions in the treatment process of the RG was lower than that of the CG, which also showed that glucocorticoid combined with DPMAS has good safety. It can be widely used in clinical practice. By comparing the hospitalization time in the two groups of patients, we found that there was no difference in both groups, revealing that the application of glucocorticoids might need more in-depth research to shorten the rehabilitation period of patients. This might be related to the dosage. Some studies have pointed out that large doses of glucocorticoids had side effects on human body. Therefore, strict control of the dosage when using glucocorticoids is important.

This experiment explored the clinical effect of DPMAS combined with glucocorticoids in the treatment of hepatic failure patients after LC surgery. Because of the limited experimental conditions, there are still shortcomings. For instance, due to the short experimental period, we cannot evaluate the long-term prognosis in the two groups of patients. At present, we still need to conduct more in-depth experiments to confirm the relevant mechanism of glucocorticoids enhancing DPMAS in the treatment of hepatic failure. We will carry out more experimental analysis to obtain the best experimental results for clinical reference.

In short, DPMAS combined with glucocorticoids had significant therapeutic effects on patients with hepatic failure after LC surgery, which could effectively reduce inflammatory factors of patients and improve CF. Thus, i is worthy of clinical application.

Disclosure of conflict of interest

None.

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