International Journal of Medicine and Life Sciences
ISSN: 2518-0223, Volume 3, Issue 1, June, 2018

Effect of Indexes of Liver Function and Indicators of Hepatic Fibrosis in Patients with Primary Liver Cancer after Interventional for Treatment of Postoperative with Magnesium Isoglycyrrhizinate

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Abstract: Objective Observe the effect of indexes of liver function and hyaluronic acid (HA), type IV collagen (IV-C)and laminin (LN) in patients with primary liver cancer after interventional for treatment of postoperative with magnesium isoglycyrrhizinate. Methods They were randomly divided into treatment group (40 cases) and control group (40 cases) that 80 patients with primary liver cancer after international therapy. The control group was given routine therapy (mainly tiopronin), the treatment group was received magnesium isoglycyrrhizinate. Compared alanine aminotransferase (ALT), prothrombin time (PT), total bilirubin ((TBIL), hepatic pro-thromboplastin test (HPT) ,Hyaluronic acid (HA), type IV collagen (IV-C)and laminin (LN)of livers between two groups, the dosage of diuretic and relevance safety. Results There were statistically significant that in the ALT, TBIL, PT, HPT HA,IV-C and LN between treatment group and control group after ten days. It was not found that drug allergies, heart palpitations, dizziness, skin rashes and other adverse reactions with magnesium isoglycyrrhizinate. The efficacy of magnesium isoglycyrrhizinate about liver injury and liver fibrosis after interventional treatment is relatively safe for widespread clinical application.

Keywords: Magnesium isoglycyrrhizinate; Primary liver cancer; Intervention therapy; Lliver fibrosis; Liver function

1. Introduction

At present, It was increasing year by year that the incidence of primary liver cancer in China and it was in the mid -late stages and missed the operative period when they Visited to the hospital . Trans-catheter hepatic artery chemoembolization (TACE) has become one of the main methods for patients with advanced primary liver cancer with the rapid development of interventional radiology ［1］. However, chemotherapy drugs also caused damage to liver function after interventional treatment, and quality of life and the prognosis of patients seriously affected by anti-tumor drugs caused liver injury (DILI) . The new generation of magnesium isoglycyrrhizate has been used in the prevention and treatment of anti-tumor drugs caused by DILI as a multifunctional preparation for anti-inflammation and liver protection drug glycyrrhizic acid in recent years.

2. Materials and methods

2.1. Materials

Collect 80 cases of primary hepatocellular carcinoma patients in hospital from January 2015 to December 2017. Age: 40-72(mean: 54.1± 6.2), including 46 males (62.2%) and 28 females (37.8%). All the patients were diagnosed as the primary liver cancer treated by hepatic artery chemoembolization on the basis of the elevated alpha-fetoprotein in blood test, histopathology or imaging (enhanced CT or MR). 16 cases were complicated with portal cirrhosis. 34 cases with retroperitoneal lymph node and lung metastasis by imaging examination revealed, 36 cases with ALT greater than 40U/L, and 40 cases with

AFP greater than 400 g/L, 28 cases of HBsAg, HBeAg and HBcAb test positive and 44 cases of HBsAg, HBeAb and HBcAb test positive by the hepatitis index examination showed , 40 patients in the left liver and 32 patients with tumors in the right liver among the 80 patients with primary liver cancer. All of the above are in accordance with the primary liver cancer diagnostic criteria.

2.2. Research methods

Seldinger technique was used. First, peritoneal artery and hepatic intrinsic artery angiography were performed through femoral artery puncture and intubation. Secondly, the location, size, portal vein condition, blood supply of the tumor were determined, and the artery of the catheter was slowly injected with chemotherapeutic drugs and embolism after the blood supply of the tumor was determined. Chemotherapeutic drugs: mitomycin 10mg, pirobicin 70mg, 5-fluorouracil 1.0g and ultra-liquid iodine oil 10-25ml.The control group was treated with western drug tiopronine after intervention. The treatment group was treated with magnesium isoglycyrrhizate.
Both groups of patients were fasting bleeding test liver function indicators which included TBIL, ALT, PT and HPT with liver fibrosis indicators which included HA, IV-C and LN at preoperatively, 2 days ,10 days after surgery. adverse reactions were recorded in both groups.

2.3. Method of administration

Medicine: magnesium isoglycyrrhizin (product name: tianqing, ganmei, zhengda tianqing pharmaceutical company production; Approval number: H20051942). Test group: magnesium isoglycyrrhizinate 200mg+ 10% glucose injection 250mL, qd, continuous use for 10d; Control group: tiopronine 2.0g+ 10% glucose injection 250mL, qd, continuous use for 10d. Liver function was reassessed at day 2 and 10 after surgery.

2.4. Efficacy evaluation index

Main observation indexes: liver cell damage index: ALT; Liver excretion function index: TBIL. Liver synthetic coagulation factor function index: PT and HPT. Liver fibrosis indicators include HA, IV - C and LN. In addition, adverse reactions of patients in the treatment group were recorded in detail.

2.5. Statistical analysis

SPSS18.0 statistical software was used for data analysis. The comparison of the rates between the two groups was examined by x test, and the liver function indicators were examined by T test of various local mean Numbers.

3. Results

Incidence of adverse drug reactions in the two groups, 10 patients (27.7%), 8 patients (21.6%), 3 patients (0.08%) with abdominal pain and diarrhea occurred in the control group after surgery with varying degrees of nausea and vomiting. In the treatment group, there were 7 cases (18.9%) of postoperative nausea and vomiting, 3 cases of fever (0.08%), and 0 cases of abdominal pain and diarrhea (0%). The difference between the two groups was statistically significant ($P < 0.05$).
Changes in liver function indexes before and after surgery of the two groups of patients (see table 1). ALT, TBIL and PT indicators of the two groups of patients on day 2 after surgery were higher than those before surgery, and It was statistically significant differences that the ratio of HPT decreased ($P < 0.05$). After 10 days of treatment, there was a statistically significant difference between the control group and the treatment group ($P < 0.05$).

Table 1. Changes of indicators in liver function before and after treatment

Detection index	Treatment group			Control group		
	Preoperative	Postoperative	Postoperative	Preoperative	Postoperative	Postoperative
		2 days	10 days		2 days	10 days
ALT(u/L)	43±9	81±10	36±8 *	41±8	82±9	61±8
TBIL(umol/L)	16.7 ± 3.1	18. 2± 4.3	14.0 ± 3.1*	16.5 ± 3.0	18.4 ± 4.5	16.9 ± 3.7
PT	16.6±2. 1	18.7 ±2.4	13.1 ±1.9 *	15.5 ±2.1	18.6 ±2.3	17. 1 ±2.0
HPT%	96.1±13.4	80.2±11.7	95.8±12.6*	96.3±13.5	81.6±11.9	90.8±11.9

Note:*The comparison among groups was statistically significant, $P < 0.05$

Table 2 . Liver fibrosis indexes of two groups of patients after treatment

Case	HA(ng/mL)	IV—C(ng/mL)	LN(ng/mL)
Treatment 40 before	321.2±208.7	68.7±31.6	180.5±69.3
Treatment 40 after	174.5±143.5*	49.3±21.1*	113.8±54.8*
Control 40 before	319.6±206.2	66.2±30.8	176.3±69.6
Control 40 after	267.4±181.4*	55.2±26.7*	141.0±60.9*

Note: the treatment group compared with control group $p<0.05$

4. Discuss

Hepatocellular carcinoma (HCC) including primary liver cancer, metastatic liver cancer and mixed hepatocarci-

noma is one of the malignant tumors that seriously threaten human health. The mortality rate of liver cancer is only the third most common malignant tumor after gastric cancer and esophageal cancer, ranking the 6th in the incidence of malignant tumor worldwide and the 3rd in the cause of death [3]. Once most of them are found to be in the middle and late stage as the initial symptoms are not obvious and the opportunity of surgery is missed. The concentration of local chemotherapeutic drugs in hepatic tumor was dozens of times higher than that of intravenous chemotherapeutic drugs with the intervention of hepatic artery and the treatment of arterial embolization, and the abundant blood supply of tumor was cut of therefore chemotherapy drug side of the body is small, However, there is still damage to normal liver cells, and a few patients even have acute liver failure.

Magnesium isoglycyrrhizin (MgIG) is a hepatocyte protectant with anti-inflammatory, protective effects on liver cell membranes and improving liver function. Studies have shown that it can prevent the increase of serum transaminase in animals and reduce hepatocyte degeneration, necrosis and inflammatory cell infiltration[4]. Wang Pei, Liu xiaoyu [5] and other experiments confirmed that MgIG may play a role in combating chronic liver damage by suppressing inflammation and it can inhibit the secretion function of macrophages. It can reduce hepatocyte degeneration, clastic necrosis and inflammatory infiltration, inhibit the elevation of transaminase, reduce the level of NO, improve the hepatic cell metabolism disorder, and promote the synthesis of albumin. MgIG can reduce the sharp increase of serum transaminase in patients after hepatectomy, reduce the damage of surgery to liver cells, improve liver function, reduce complications, and have high clinical safety[6]

Laminin（LN） is an ingredient of collagen glycoprotein and distributes in the transparent layer of basement membrane of the outer cell mass. Type IV collagen is the main component of the basement membrane . The basement membrane is damaged and type IV collagen is deposited in the basement membrane in the process of collagen proliferation when liver fibrosis occurs. Hyaluronic acid(HA) is a kind of macromolecular amino polysaccharide. Its level gradually increases with the development of hepatitis due to the ability decreases to absorb and decompose HA when hepatic lesion is involved in endothelial cell work. LN IV-C and HA are powerful indicators for the diagnosis of liver fibrosis and are positively correlated with the degree of liver damage [7]. Antifibrotic therapy is of great significance to prevent the transformation from cirrhosis to liver cancer.

This study shows that it is demonstrated the anti-fibrosis effect of magnesium glycyrrhizin that is statistically significant between the two groups, because the indexes of liver fibrosis recovered of the treatment group was obvious after treatment. It's the same as qisheng-zhang's[8]. ALT is the most commonly used sensitive indicator of hepatic parenchymal injury in liver function indexes. Serum ALT level can be doubled when 1% of hepatic cells died. The results of this study show that it was significantly higher which serum ALT level of liver cancer patients after interventional treatment than that before interventional treatment. It indicating that chemotherapy drugs used in interventional treatment had a killing effect on tumor cells, but also damaged normal liver cells to a certain extent. Several experimental studies have shown that magnesium isoglycyrrhizate promote the proliferation of liver cells, protect and treat liver damage caused by various reasons, and improve the immune regulation function of regulatory T cells [9-10].

The results of this study showed that serum total bilirubin increased significantly after intervention compared with that before treatment, indicating that liver excretion function was also damaged, and TBIL recovered significantly after 10 days of treatment. The results were statistically significant compared with that before treatment ($P < 0.05$), which was consistent with those of qu jing and zheng Lin [11-12]. This indicates that magnesium isoglycyrrhizinate dredge the capillary bile duct in the liver, promote the secretion and excretion of bile, increase the velocity of bile in the intrahepatic bile duct, and promote the regression of jaundice. PT is a sensitive indicator to reflect the degree of hepatocyte damage and prognosis. HPT activity reflects the activity of plasma factor Ⅶ, Ⅱ, Ⅹ change, namely vitamin K dependent plasma levels of clotting factor. Ⅶ factor first decreases, factor Ⅱ, Ⅹ reduce times especially when the liver cell damage, so the HPT of liver disease severity and prognosis is sensitive to PT. The results of this study showed that the function of liver synthetic coagulation factor was affected by chemotherapy drugs, and PT prolonged and HPT decreased. Compared with the control group, the recovery of the treatment group was significant and statistically significant although both groups recovered somewhat after treatment. In addition, no adverse reactions, such as rash or drug allergy, have been found in clinical application. Magnesium isoglycyrrhizin can improve liver synthesis, bilirubin metabolism, coagulation and reserve function, and can be widely used in clinical treatment.

5. Acknowledgment

Key topics for medical science research in hebei province in 2018 (No. 20180803).

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