Effect of radiofrequency ablation combined with transcatheter arterial chemoembolization on inflammatory factors, oxidative stress response factors and tumor activity factors in patients with primary liver cancer

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Objective: To investigate the effects of radiofrequency ablation (RFA) combined with transcatheter arterial chemoembolization (TACE) on inflammatory factors, oxidative stress response factors and tumor activity factors in primary hepatocellular carcinoma (HCC) patients. Methods: A total of 100 cases of primary liver cancer patients from January 2014 to June 2016 were selected and randomly divided into observation group and control group with 50 cases in each group, the observation group was treated with RFA combined with TACE treatment, the control group was given TACE treatment, compared two groups before treatment (T0), 1 weeks of treatment (T1), 2 weeks (T2) inflammation factor, oxidative stress factor and tumor activity index. Results: (1) The hs-CRP, IL-6 and TNF-α levels of T1 in two groups were significantly increased, T2 decreased significantly, T1>T1>T2, but the observation group hs-CRP, IL-6, TNF-α levels of T1 were higher than the control group and the difference was statistically significant, hs-CRP, IL-6, TNF-α levels of T2 had no statistically significant; (2) The ROS level of T1 in the observation group was higher than the control group, while the SOD and T-AOC levels were lower than the control group, the ROS level of T2 in the observation group was lower than the control group, SOD and T-AOC were higher than the control group, there was significant difference. (3) Serum AFP, CA199 and MMP levels in T1 and T2 of the observation group were lower than the control group, the difference was statistically significant. Conclusion: RFA treatment of HCC may lead to inflammation and increased oxidative stress in the early stage. However, TACE combined with TACE can improve the micro inflammatory state, especially enhance the antioxidant function and decrease the level of tumor active factor.

1. Introduction

Transcatheter arterial chemoembolization (TACE) is one of the most popular non-surgical therapies for the treatment of advanced and primary hepatocellular carcinoma (HCC) at home and abroad. However, long-term clinical observation suggests that TACE treating HCC alone can not block the tumor blood supply and has a high recurrence rate, and need for repeated treatment[1]. In recent years, with the rise of percutaneous radiofrequency ablation (RFA), it has been widely used in tumor therapy, and the treatment on HCC combined with TACE has obtain significant results[2]. In this study, the use of RFA combined with TACE in the treatment of HCC in the early stage have a certain effect on the serum inflammatory factors, oxidative stress response factors and tumor activity factors, the report is as follows.

2. Data and methods

2.1 Clinical data

A total of 100 cases of HCC patients admitted to the Department of hepatobiliary surgery of the hospital from January 2014 June 2016 were randomly divided into observation group and control...
group with 50 cases in each group, the observation group: male 31 cases, female 19 cases, age 41-66, tumor diameter 4-10 cm, average (7+2) cm, Child-Pugh classification of liver function in 26 cases of Grade A, 24 cases of grade B; control group: male 29 cases, female 21 cases, age 42-69, tumor diameter 5-12 cm, average (7+2) cm, 25 cases of liver function Child-Pugh grade A, 25 cases of grade B, two groups had no statistically significant differences in gender, age, tumor size, liver function and other clinical data ($P>0.05$), comparable.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) The diagnosis was consistent with “the criteria of diagnosis and treatment of primary hepatocellular carcinoma (2011 version)”, CT scan and/or MRI enhanced scan showed HCC performance, AFP>400 μg/L; (2) TNM stage II-IV period; (3) Compliance with TACE, RFA surgery indications; (4) Informed consent was obtained from patients and family members, and informed consent was signed.

Exclusion criteria: (1) Coagulation dysfunction, surgical infection, severe heart disease, renal insufficiency and other TACE, HIFU treatment of contraindications; (2) Liver function Child-Pugh class C; (3) Other parts of malignant tumors.

2.3 Treatment methods

Observation group: the RFA combined with TACE treatment, the specific method is as follows: First TACE treatment, the use of percutaneous femoral artery puncture, the first hepatic artery angiography, to determine and catheter into the blood supply to the liver after the injection of saline diluted chemotherapy drug Osha 10-30 mg, hydroxyxycamptothecin (Harbin triple Pharmaceutical Co., Ltd. production, Zhunzi H20033506) 15-30 mg, and then injected into the pirarubicin (Shenzhen Wanle Pharmaceutical Co., Ltd., Zhunzi H10930105) 20 mg and 7-20 mL of iodized oil mixture embolization of blood vessels. RFA treatment was performed 4-5 d after TACE. All patients underwent RFA treatment guided by CT scan. Rita 1 500 X radiofrequency tumor treatment system was selected and the 15 G or 20 G RFA needle was percutaneously punctured to the tumor set the RF power, the target temperature was set at 105 °C, and the power was set at 150 W, and the ablation area was controlled at 5 cm. All the patients were treated by single point puncture and multi-direction superimposed ablation. According to the size of the lesion to set the scope and time of ablation, ablation of at least 0.5 cm beyond the lesion boundary. Postoperative hemostatic drugs to stop bleeding, antibiotics to prevent infection, and liver function protection drugs and other treatment.

The control group: TACE treatment alone, the specific methods and drugs with the observation group.

2.4 Observation indicators

Observe the two groups inflammatory factors, oxidative stress factor and tumor activity factors before treatment (T0), 1 weeks of treatment (T1), 2 weeks (T2), TNF-α, IL-6, high sensitive C reactive protein (hsCRP); Oxidative stress response factors including: serum reactive oxygen species (ROS), superoxide dismutase (SOD) and total antioxidant capacity (T-AOC); Antitumor activity index including alpha fetoprotein (AFP), carbohydrate antigen CA199, matrix metalloproteinase (MMP). TNF-α, IL-6, hsCRP, AFP, CA199, MMP were measured by enzyme-linked immunosorbent assay. ROS, SOD and T-AOC were detected by radioimmunoassay.

2.5 Statistical methods

Using SPSS 19 edition of statistical analysis, measurement data of multiple time points test using repeated measures analysis of variance + t test, $P<0.05$ said the difference was statistically significant.

3. Results

3.1 Comparison of serum inflammatory factors levels between two groups before and after treatment

The hs-CRP, IL-6, TNF-α levels of T0 in the two groups had no statistical significance difference ($^{hs-CRP} t=3.065$, $^{IL-6} t=4.012$, $^{TNF-\alpha} t=4.012$, $^{IL-6} t=3.065$, $^{TNF-\alpha} t=3.065$).
3.2 Comparison of oxidative stress response factor levels of the two groups before and after treatment

There was no significant difference in ROS, SOD, and T-AOC levels of T0 between the two groups (ROS T0 = 6.013, SOD T0 = 6.762, T-AOC T0 = 2.375, P > 0.05), but the ROS level of T1 was increased significantly, T2 decreased significantly, T1 > T0 > T2. The serum inflammatory factors hs-CRP, IL-6, TNF-α levels of T1 were higher than that of the control group, there was significant difference (hs-CRP T1 = 22.135, IL-6 T1 = 101.446, TNF-α T1 = 131.055, P < 0.05), hs-CRP, IL-6, TNF-α levels of T2 in two groups had no statistically significant difference (hs-CRP T2 = 5.856, IL-6 T2 = 2.461, TNF-α T2 = 2.584, P > 0.05), see Table 1.

3.3 Comparison of serum tumor activity factor levels between the two groups before and after treatment

The serum AFP, CA199 and MMP levels of T0 in the two groups had no statistical significance (AFP T0 = 4.126, CA199 T0 = 6.815, MMP T0 = 5.011, P > 0.05). The levels of AFP, CA199 and MMP were decreased significantly, T2 < T1 < T0. The serum AFP, CA199 and MMP levels in the T1 and T2 observation group were lower than those in the control group, the difference was statistically significant (AFP T1 = 263.754, CA199 T1 = 112.342, MMP T1 = 45.675, AFP T2 = 86.764, CA199 T2 = 42.376, MMP T2 = 37.352, P < 0.05), see Table 3.

4. Discussion

HCC is one of the most common malignancies of the digestive system. In recent years, the incidence of HCC is obviously higher. According to the literature, about one million new cases have been reported each year, which has become the second cause of cancer death[4]. A large number of clinical studies at home and abroad suggest that HCC can lead to micro-inflammatory state of the body, serum inflammatory factors hs-CRP, IL-6, TNF-α levels increased. In addition, HCC liver function decline, the body's antioxidant pose a serious impact, which can lead to increased ROS, SOD, T-AOC levels. AFP is an important tumor activity factor of HCC, which has a high sensitivity to reflect the severity of disease and relapse[6-8]. CA199 is an important marker of digestive system malignancy, domestic and international studies have confirmed that AFP can be used as assessment of treatment efficacy and risk of recurrence of the reference[9,10]. MMP is one of the active factors that have been shown to have a significant effect on tumor infiltration, invasion, and recurrence and metastasis in recent years. The higher the level of MMP, the more aggressive the tumor[11].

Currently the preferred method of treatment of HCC is still surgical resection, but the surgical trauma is relatively large, and the middle
and late stage HCC patients has poor surgical results. With the continuous development of TACE technology and chemotherapy drugs, its application in liver diseases accounted for more and more widely, TACE treatment of HCC can inject chemotherapy drugs directly into the tumor near, effectively kill cancer cells, improve the effect of chemotherapy, reduce adverse reactions, and can block HCC blood supply, lack of blood supply to tumor death. In recent years, its clinical application rate is getting higher and higher, and it has become the preferred treatment method. Domestic Jiang Fu Qiang[12] research found that TACE treatment of HCC can effectively control tumor growth and regulate the level of tumor activity factor. This study shows that serum inflammatory cytokines hs-CRP, IL-6, TNF-α levels decreased significantly in patients treated with TACE after 2 weeks operation, the level of oxidation stress response factor ROS decreased, SOD and T-AOC increased, serum tumor activity factor AFP, CA199 and MMP were decreased, basically the same with Jiang Fuqiang and other research results. However, a large number of literatures reported that TACE alone in the treatment of HCC is difficult to completely embolization tumor blood vessels, as well as the collateral circulation, some patients with poor tumor necrosis, postoperative recurrence and metastasis rate is higher[13,14].

In recent years, RFA has been widely used in the treatment of cancer, by thermal chemical reaction, the dissolution of tumor necrosis occurred in a short period of time, thus to achieve effective tumor cell killing effect, the clinical study showed that RFA patients with less surgical trauma, and the patients recovered faster. At present, many scholars at home and abroad consider which with TACE as the best combination therapy for the treatment of HCC[15,16]. This study shows that serum inflammatory factor level of RFA and TACE treatment patients were higher than those in patients treated with TACE of 1 weeks after surgery, and the serum oxidative stress factor ROS level is higher, while SOD and T-AOC levels lower than that of TACE treated patients, but after 2 weeks, despite there was no statistically significant differences in the level of inflammatory factors (P>0.05), the level of oxidative stress response factor ROS decreased, and SOD and T-AOC were higher than those of TACE alone. The reason was that postoperative 1 week serum inflammatory factors levels increased and increased oxidative stress factors may lead to increased early radiofrequency ablation of tumor and surrounding liver tissue necrosis, increased inflammation of the body, leading to a transient decline in liver function[17–19]. On the other hand, two weeks after the surgery, the results showed that the two treatment regimens could inhibit the microinflammatory state induced by the tumor of the body, but the combined treatment had better effect on the early improvement of the body's antioxidant function[20–22]. Further observation of changes in tumor activity factor levels found that the combined treatment of patients after 1 week and 2 weeks, the level of decline were higher than that in patients with TACE alone, suggesting that RFA combined with TACE has an advantage in the effective killing of tumor cells and improving the early treatment.

In summary, RFA treatment of HCC despite the early may lead to the phenomenon of increased inflammation and oxidative stress in the body, but the combination with TACE on the treatment of HCC can improve the micro-inflammatory state of the body, in particular, can improve the body's antioxidant function, reduce tumor activity factor level, suggesting that the combined treatment is better.

References


