Advances in Research of Post Embolism Syndrome after Transarterial Chemoembolization (TACE) for Hepatocellular Carcinoma

Jimusi[1], Sarengerile[2]*

1. Inner Mongolia Medical University, Hohhot 010110, China; 2. Inner Mongolia International Mongolian Hospital, Hohhot 010110, China

Abstract This article reviews the concept and clinical manifestations of post embolism syndrome after transarterial chemoembolization (TACE), and the prevention or timely intervention of post embolism syndrome in advance is expected to reduce its incidence and degree in clinical treatment, and to improve the quality of treatment of Hepatocellular Carcinoma Carcinoma (HCC).

Key words Hepatocellular Carcinoma (HCC), Transarterial chemoembolization (TACE), Post embolism syndrome (PES)

1 Introduction

Hepatocellular Carcinoma (HCC), also known as liver cancer, is one of the most common malignant tumors in clinic, accounting for the fifth incidence of malignant tumors and the second mortality in China[1]. Surgical treatment is the first choice for liver cancer, but the onset of liver cancer is insidious, the disease progresses rapidly, and most patients have developed to the middle and late stages when diagnosed, thus losing the chance of surgery[2]. At present, the transarterial chemoembol ization (TACE) is recognized as the most commonly used non-surgical treatment for Hepatocellular Carcinoma[3]. TACE has the characteristics of high safety and small trauma, but there are many adverse reactions while achieving curative effect, among which post embolism syndrome (PES) is the most common adverse reaction[4]. In this paper, we reviewed the concept of post embolism syndrome and the treatment of symptoms, in order to provide a reference for the treatment and research of post embolism syndrome.

2 Understanding of the post embolism syndrome

In 1981, post embolism syndrome was first mentioned[5], but so far there are still no clear diagnostic criteria for post embolism syndrome after TACE. It is generally believed that its main characteristics include pain, fever, nausea, vomiting, loss of appetite, fatigue, sleep disorders, depression, liver function damage, leukopenia and so on[6]. In one study, post embolism syndrome was described as a self-limiting symptom, including fever, persistent nausea, general malaise, loss of appetite, and abdominal pain[7]. Postoperative TACE syndrome has been defined as one of the five symptoms or signs of nausea, vomiting, fever, abdominal pain, and elevated alanine aminotransferase levels after TACE[8]. Some scholars also divide the clinical manifestations of TACE postoperative syndrome into specific and non-specific, specific including abdominal pain, nausea, vomiting and low fever, non-specific including loss of appetite, depression, leukopenia[9]. Because the pathological mechanism of the syndrome after TACE involves the systemic inflammatory response caused by hepatocyte lysis, hypoxia, ischemia or necrosis, or the systemic effects of chemotherapeutic drugs, the dose of chemotherapeutic drugs, the largest tumor size treated and female are potential risk factors for the occurrence of the syndrome after TACE[10], while cardiovascular and cerebrovascular diseases are important risk factors[11]. Studies have shown that more than 90% of liver cancer patients who have undergone TACE surgery have different degrees of post embolism syndrome[12]. Wang Xia *et al.*[13] selected 70 patients with post embolism syndrome after TACE, who had different degrees of fever within one week after TACE, the incidence rate was 59.74%, the incidence rate of gastrointestinal reactions was 50.29%, the incidence rate of hepatic encephalopathy was 3.09%, and the incidence rate of puncture site bleeding was 2.57%, the incidence of liver pain was 7.66%.

3 Clinical manifestations

3.1 Pain in the liver area Hepatic pain is the most common complication after TACE for liver cancer, which usually occurs 2 - 7 d after operation and often reaches its peak 24 - 48 h after operation[14]. Studies have reported that its incidence is as high as 80%, of which severe pain accounts for about 1/3[15], affecting the recovery of patients after surgery, and even unable to continue treatment in severe cases. Hepatic pain is mainly caused by cutting off the main hepatic artery of the tumor by embolization, which leads to ischemia and hypoxia of the liver, resulting in ischemic pain. In addition, the infusion of chemotherapeutic drugs causes necrosis of tumor cells, resulting in pain in the capsule, or the mixture of chemotherapeutic drugs and iodized oil stimulates the intima of blood vessels, resulting in pain in vasospasm. Besides, the embolization process mistakenly embolizes the blood vessels of normal organs such as the cystic artery, resulting in ischemic pain[16-17]. At present, it is generally believed that different intraoperative procedures, embolization materials, embolization degree, drug dosage and other factors may affect the occurrence of intervention-related pain[18].

Bian Lifang *et al.*[19] considered that multiple intrahepatic tumors (number of tumor lesions ≥3), history of abdominal pain after TACE, operation mode and number of TACE were risk factors for acute moderate to severe abdominal pain after TACE. A

Received: January 10, 2024 Accepted: March 5, 2024

* Corresponding author. E-mail: 2408909902@qq.com

retrospective study pointed out[20] that the incidence of pain in patients with advanced liver cancer treated with TACE alone was higher than that in patients treated with non-TACE, and the pain related to intervention could be relieved spontaneously after 3 – 4 weeks. However, the pain scores of patients with moderate and severe epigastric pain before operation were lower than those of the control group after 6 months, indicating that the long-term pain relief rate of TACE treatment was higher.

3.2 Fever The incidence of fever after TACE for liver cancer is as high as 75% – 100%[21], which is also a common complication after operation. The main reason is that the chemotherapy drugs and iodized oil infused by surgery inhibit and kill tumor cells locally, and at the same time, interventional embolization of the main blood supply arteries of the tumor causes ischemia and necrosis of the tumor tissue, and the absorption of necrotic substances into the blood causes fever. Studies have found that the larger the tumor volume of embolization, the more the volume of iodized oil used, the more severe the fever of patients, the longer the duration, the more ideal the embolization effect[22]. Wu Hao *et al.*[23] studied the relationship between the fever symptoms after TACE and the short-term curative effect, and confirmed that the fever symptoms after TACE mostly indicated that the short-term curative effect of tumor embolization was good, and the fever time after interventional therapy was positively correlated with the short-term curative effect. The clinical treatment of fever is mainly physical cooling or drug cooling[24]. Jiang Liya *et al.*[25] used 15% ethanol ice bag to cool patients with fever after TACE, and found that the overall cooling effect of 15% ethanol ice bag was better than that of ordinary water ice bag, which provided a new idea for physical cooling of patients with fever after TACE. After TACE, the immunity of patients will decrease, so the fever may also be caused by infection, and it is necessary to evaluate the body temperature and its accompanying symptoms in time for identification. The application of antibiotics can be guided according to the relevant infection indicators. Relevant research reports[26] that the transient infection rate of TACE is 4%, so antibiotics are generally not suitable for preventive anti-infection and antipyretic in clinic.

3.3 Nausea and vomiting Contrast media, chemotherapy drugs and embolic agents used in TACE can reach the relevant arteries of the gastrointestinal tract with blood circulation and stimulate the chromaffin cells of the gastrointestinal mucosa to release 5-hydroxytryptamine 3 (5-HT3), thus inducing nausea and vomiting symptoms[27]. This symptom may occur during the operation, even severe vomiting symptoms, affecting the operation process, at this time should reduce or stop the use of chemotherapy drugs, while actively giving acid suppression, antiemetic and other treatments to protect the gastric mucosa. In addition to chemotherapy drugs, necrotic tumor tissue and its decomposition products can also become a signal to stimulate the vomiting center of the body, leading to nausea and vomiting[28]. Studies have shown that postoperative abdominal distension and pain are also risk factors for nausea and vomiting, while age is a protective factor, and preventive use of antiemetic drugs can effectively reduce the incidence of nausea and vomiting[29]. Li Hongfu *et al.*[30] carried out clinical observation on 132 patients with liver cancer, and found that the control rate of nausea and vomiting in the preoperative antiemetic group was significantly higher than that in the postoperative group, which confirmed that the preoperative antiemetic had a good effect on preventing and controlling nausea and vomiting.

3.4 Abdominal distension and constipation The incidence of abdominal distension and constipation in patients with liver cancer after TACE was higher than that in patients with malignant tumors after intravenous chemotherapy alone. In addition to the neurotoxic effects of chemotherapy drugs used during the operation, post embolism syndrome such as nausea, vomiting, pain and fever occurred after the operation. The application of analgesic and antiemetic drugs in clinical symptomatic treatment caused slow gastrointestinal peristalsis, and the decrease of postoperative activity led to abdominal distension, constipation, loss of appetite and other symptoms[31]. Clinically, symptomatic treatment is mainly to relax the bowels and promote gastrointestinal motility. Relevant studies by Ding Aiping *et al.*[32] showed that cisapride could effectively prevent and treat abdominal distension and vomiting after chemotherapy, with an effective rate of 83.3%. Li Hailiang *et al.*[33] clinically observed 156 patients with abdominal distension after TACE. The effective rate of simethicone emulsion in the treatment group was 83.1% in 24 h and 91.6% in 48 h. Liu Liyun *et al.*[31] applied glycerol enema to 30 patients with abdominal distension and abdominal pain after TACE, and the constipation relief rate was as high as 100%, while the abdominal pain relief rate was 73.3%, which was significantly better than the general nursing of the control group.

4 Conclusions

The post embolism syndrome is the most common adverse reaction after TACE, which seriously affects the quality of life of patients after TACE. Scholars have managed the symptoms of post embolism syndrome through various intervention methods, and have achieved certain results. However, most of the studies focused on a single symptom in post embolism syndrome. At present, the research on the comprehensive management of post embolism syndrome is very limited, so it is necessary to formulate more comprehensive, scientific and feasible overall management measures. The applicability of existing specificity assessment tools needs to be verified. In the future, researchers need to further verify the reliability of the specific assessment tool for post embolism syndrome, and constantly improve the assessment tool according to the symptoms of post embolism syndrome. The purpose of this study is to provide a basis for clinical nurses to accurately assess post embolism syndrome, and to provide a reference for further research on symptom management of post embolism syndrome.

References

[1] LIU ZC, LI ZX, ZHANG Y, *et al.* Interpretation on the report of Global Cancer Statistics 2020[J]. Journal of Multidisciplinary Cancer Manage-

ment (Electronic Version), 2021, 7(2): 1 – 12. (in Chinese).
[2] ANWANWAN D, SINGH SK, SINGH S, *et al*. Challenges in liver cancer and possible treatment approaches[J]. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer, 2020, 1873(1): 188 – 314.
[3] MADDALA YK, STADHEIM L, ANDREWS JC, *et al*. Drop-out rates of patients with hepatocellular cancer listed for liver transplantation: Outcome with chemoembolization[J]. Liver Transplantation, 2004, 10(3): 449 – 455.
[4] LIMA M, DUTRA S, GOMES FV, *et al*. Risk factors for the development of postembolization syndrome after transarterial chemoembolization for hepatocellular carcinoma treatment[J]. Acta Médica Portuguesa, 2018, 31(1): 22 – 29.
[5] ARSLAN M, DEGIRMENCIOGLU S. Risk factors for postembolization syndrome after transcatheter arterial chemoembolization[J]. Current Medical Imaging Reviews, 2019, 15(4): 380 – 385.
[6] XU L, WANG S, ZHUANG L, *et al*. Jian Pi Li Qi decoction alleviated postembolization syndrome following transcatheter arterial chemoembolization for hepatocellular carcinoma: A randomized, double-blind, placebo-controlled trial[J]. Integrative Cancer Therapies, 2016, 15(3): 349 – 357.
[7] BLACKBURN H, WEST S. Management of postembolization syndrome following hepatic transarterial chemoembolization for primary or metastatic liver cancer[J]. Cancer Nursing, 2016, 39(5): e1 – e18.
[8] YANG H, SEON J, SUNG PS, *et al*. Dexamethasone prophylaxis to alleviate postembolization syndrome after transarterial chemoembolization for hepatocellular carcinoma: Arandomized, double-blinded, placebo-controlledstudy[J]. Journal of Vascular and Interventional Radiology, 2017, 28(11): 1503 – 1511.
[9] PISCAGLIA F, TOWOVOLI F, PINI P, *et al*. A new horizon in the prevention of the postembolization syndrome after transcatheter arterial chemoembolization for hepatocellular carcinoma[J]. Hepatology, 2018, 67(2): 467 – 469.
[10] LIMA M, DUTRA S, GOMES FV, *et al*. Risk factors for the development of postembolization syndrome after transarterial chemoembolization for hepatocellular carcinoma treatment[J]. Acta Medica Portuguesa 2018, 31(1): 22 – 29.
[11] MARCACUZCO QA, NUTU OA, SAN ROMAN MR, *et al*. Complications of transarterial chemoembolization (TACE) in the treatment of liver tumors[J]. Cirugía Española, 2018, 96(9): 560 – 567.
[12] CHENG ZW, CHENG W, XING DW. Progress in the application of traditional Chinese medicine in the treatment of embolism syndrome after transcatheter arterial chemoembolization[J]. Jilin Journal of Chinese Medicine, 2019, 39(11): 139 – 142. (in Chinese).
[13] WANG X, JI HX. Analysis of the effect of integrated traditional Chinese and western nursing intervention on complications and quality of life of patients with liver cancer after interventional operation[J]. China & Foreign Medical Treatment, 2020, 39(28): 146 – 148. (in Chinese).
[14] COLDWELL DM, LOPER KA. Regional anesthesia for hepatic arterial embolisation[J]. Radiology, 1989, 172(3 Pt2): 1039 – 1040.
[15] LIU KC, LV WF, ZHOU CZ, *et al*. Curative effect and influencing factors of hepatocellular carcinoma with portal vein tumor thrombosis treated with TACE[J]. Chinese Journal of Interventional Imaging and Therapy, 2018, 15(6): 331 – 336. (in Chinese).
[16] LI YH. Illustrated practical clinical interventional diagnostics[M]. Beijing: Science Press, 2007: 139. (in Chinese).
[17] LEE SH, HAHN ST, PARK SH. Intraarterial lidocaine administration for relief of pain resulting from transarterial chemoembolization of hepatocellular carcinoma: Its effectiveness and optimal timing of administration[J]. CardioVascular and Interventional Radiology, 2002 (24): 368 – 371.
[18] LUO J, SHAO GL, ZHENG JP, *et al*. The regularity of abdominal pain and its influence factors in patients with primary hepatocellular carcinoma after receiving TACE[J]. Journal of Interventional Radiology, 2017, 7(26): 613 – 617. (in Chinese).
[19] BIAN LF, GAO BL, ZHANG S, *et al*. Risk factors and predictive analysis of acute severe abdominal pain after transarterial chemoembolization[J]. Chinese Journal of Nursing, 2020, 35(4): 326 – 328. (in Chinese).
[20] HUANG Y, JING R, PAN LH. Analysis of the efficacy of simple hepatic artery chemoembolisation on pain in patients with middle and advanced hepatocellular carcinoma[J]. Chinese Journal of Oncology Prevention and Treatment, 2017, 9(5): 398 – 400. (in Chinese).
[21] WANG LF, WANG ZX, YANG HY, *et al*. Efficacy of TCM treatment on fever in hepatocellular carcinoma patients after transarterial chemoembolization[J]. Chinese Journal of Integrated Traditional and Western Medicine on Liver Diseases, 2011, 21(4): 214 – 215. (in Chinese).
[22] HUANG YD, ZHANG ZY, MAO J, *et al*. Diagnostic and therapeutic analysis of fever after primary liver cancer intervention[J]. Modern Interventional Diagnosis and Treatment in Gastroenterology, 2010, 15(5): 325 – 326. (in Chinese).
[23] WU H, HUANG M, ZHAO L. Clinical analysis of fever in patients with primary hepatocellular carcinoma after transcatheter arterial chemoembolization[J]. Journal of Medical Research, 2014, 43(10): 136 – 138. (in Chinese).
[24] LI J, JU CX. Effect of Orim self-care mode on patients with hepatic arterial chemoembolization(TACE) for its complications and self-management ability[J]. Chinese Evidence-Based Nursing, 2021, 7(1): 106 – 109. (in Chinese).
[25] JIANG LY, WANG XJ, WANG LM. Observation on the cooling effect of 15% ethanol ice packs used for patients with fever after TACE for primary liver cancer[J]. Journal of Nursing and Rehabilitation, 2015, 14(9): 899 – 900. (in Chinese).
[26] SHAWKER TH, KLUGE RM, AYELLA RJ. Bactermia associated wiht angiography[J]. JAMA, 1947, 229(8): 1090 – 1092.
[27] Chinese Anti-Cancer Association Tumour Clinical Chemotherapy Professional Committee, Chinese Anti-Cancer Association Tumour Support Therapy Professional Committee. Expert consensus on the prevention and treatment of nausea and vomiting related to anti-cancer drug treatment in China (2022 edition)[J]. National Medical Journal of China, 2022, 102(39): 3080 – 3094. (in Chinese).
[28] WANG SY, ZHU WH, VARGULICK S, *et al*. Nausea and vomiting after transcatheter arterial chemoembolization for hepatocellular carcinoma: Incidence and risk factor analysis[J]. Asian Pacific Journal of Cancer Prevention, 2023, 14(10): 5995 – 6000.
[29] ZANG S, XU Y. Non-chemotherapy influence factors for nausea and vomiting among hepatocellular carcinoma patients after transarterial chemoembolization[J]. Chinese General Practice, 2015, 18(3): 300 – 303. (in Chinese).
[30] LI HF, GAO WQ. Comparison observation on application of anti-vomiting drugs before and after TACE surgery of primary liver cancer[J]. Journal of Henan University of Science & Technology: Medical Science, 2012, 30(1): 55 – 56. (in Chinese).
[31] LIU LY, XU LZ. Observation on the effect of glycerol enema method on constipation and abdominal pain in patients after chemoembolisation for primary liver cancer[J]. World Latest Medicine Information, 2017, 17(50): 35. (in Chinese).
[32] DING AP, AN YH, ZHAO YY. Cisapride in the prophylaxis of constipation and abdominal distention caused by chemotherapy[J]. Acta Academiae Medicinae Qingdao Universitatis, 2006(3): 246 – 247. (in Chinese).
[33] LAI HL, HU HT, GUO CY, *et al*. Evaluation of the efficacy of simethicone emulsion on abdominal distension after TACF for primary hepatocellular carcinoma[C]//Professional Committee of Minimally Invasive Treatment of Tumour, Chinese Anti-Cancer Association. Proceedings of the Ninth Chinese Academic Conference on Minimally Invasive Therapy for Cancer. Department of Radiology, Henan Cancer Hospital, Interventional Ward, Affiliated Cancer Hospital of Zhengzhou University, 2013: 1. (in Chinese).