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ORIGINAL ARTICLE

Retrospective study of TACE in the treatment of lobaplatin-induced thrombocytopenia in primary hepatocellular carcinoma

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Summary

Purpose: *To discuss postoperative thrombocytopenia in the treatment of hepatocellular carcinoma (HCC) through transcatheter arterial chemoembolization (TACE) with single application of Lobaplatin as chemotherapy drug.*

Methods: *The study retrospectively analyzed 1,945 HCC patients treated with TACE in our hospital from May 2013 to May 2018. The number of first-time users of lobaplatin reached 128, the second-time users reached 417, the third-time and above users 239. The analysis examined various items of patients, including gender, age, multiple preoperative examination indicators (platelet level, liver function tests, AFP level), ascites, preoperative presence of peptic ulcer at the initial (3-7 days) and long-term (21-90 days) postoperative stages. Platelet levels were evaluated according to the WHO Grading System for Hematologic Toxicity for side effects of anticancer drugs.*

Results: *For HCC patients with normal pre-intervention platelet level, the incidences of mild decrease, moderate decrease and severe decrease after intervention were 16.50%, 10.47% and 4.88% respectively, the incidences of long-term platelet reduction after intervention were 13.25%, 4.73% and 1.65% respectively. The level of post-intervention thrombocytopenia was not correlated with the cycles of lobaplatin use. The initial thrombocytopenia was more obvious in female patients after intervention. The presence or absence of peptic ulcer and ascites before the intervention had an effect on the initial thrombocytopenia after the intervention. Platelet level before intervention was correlated with that after intervention. The liver function grading before intervention had no effect on the two levels of thrombocytopenia after intervention. There was a correlation between AFP level grouping before intervention and initial thrombocytopenia after intervention.*

Conclusions: *The long-term incidence of thrombocytopenia after interventional therapy was not high in TACE patients with HCC treated with LPT alone, which was relatively safe. Besides, the occurrence of thrombocytopenia after intervention had certain characteristics, which can be used to guide clinical practice, so as to reduce the incidence of thrombocytopenia or provide targeted symptomatic support treatment.*

Key words: *lobaplatin, primary hepatocellular carcinoma, TACE, adverse reactions, thrombocytopenia*

Introduction

Primary liver cancer has high incidence and mortality rates, and 85-90% is hepatocellular carcinoma (HCC) [1,2]. There are a variety of therapeutic methods for HCC, but most patients have lost the opportunity of surgery when they first visit a doctor. Transcatheter arterial chemoembolization (TACE) is one of the most commonly used methods for non-surgical treatment of HCC [1,2]. There are many choices of chemotherapeutic drugs in TACE, and the choice of these drugs is closely related to

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the efficacy of TACE. Low-dose TACE produces less liver function damage and less postoperative side effects, and the efficacy and survival are no different from that of conventional TACE dose [3]. Small doses of TACE mainly reduce the types and doses of chemotherapeutic drugs [3].

As third-generation platinum anticancer drug [4,5], Lobaplatin's single application as a chemotherapeutic agent in TACE has a good effect on median survival and therapeutic response [6,7]. The most common adverse reaction of Lobaplatin is myelosuppression, with thrombocytopenia and leukopenia [8]. The greatest risk of thrombocytopenia is spontaneous intracranial or gastrointestinal bleeding, which may lead to death in severe cases. At present, there are many reports on adverse reactions of platelet reduction caused by Lobaplatin, most of which are from intravenous chemotherapy. This study mainly studied and summarized the characteristics of thrombocytopenia caused by single application of Losplatin in TACE. A retrospective analysis was performed on 1,945 patients with HCC treated with TACE alone as a chemotherapeutic drug, and relevant information and laboratory indicators were recorded to explore the incidence and characteristics of thrombocytopenia after TACE.

Methods

Clinical data

This study was approved by the Ethics Committee of Tongji Hospital, Tongji Medical College Huazhong University of Science and Technology. Signed informed consents were obtained from all participants before the study entry. Data of HCC patients treated with TACE in Tongji Hospital, Tongji Medical College Huazhong University of Science and Technology from May 2013 to May 2018 were retrospectively analyzed.

Inclusion criteria were: (1) clinical diagnostic or pathological diagnostic criteria for HCC; (2) ECOG performance status to assess the patient's overall condition, with 0-2 scores for physical fitness, and Child-Pugh grade A or B for liver functions; (3) patients deemed as unsuitable for surgery after surgeon's decision or patient unwillingness to accept surgery; (4) TACE was the main treatment for the patients, who had not received liver cancer surgery or other local treatment, including surgical resection, liver transplantation, local ablation therapy (RFA, microwave intervention, alcohol injection, Argon-Helium knife, Hifu-knife) and radiotherapy, and patients who had not used targeted drugs for liver cancer; (5) In TACE treatment, Lobaplatin alone was used as a chemotherapeutic drug, and was mixed with ultra-liquefied iodine oil as an emulsion. No other chemotherapeutic drugs or targeted drugs were used.

Exclusion criteria: (1) HCC with extrahepatic metastasis; (2) before receiving TACE, the patient had been operated or had other local ablation treatment; (3) If in TACE treatment, in addition to Lobaplatin, other chemotherapeutic drugs or targeted drugs were used; (4) In TACE treatment, no granular substances were used, e.g. embolization of gelatin sponge particles, drug-loaded microspheres, polyvinyl alcohol (PVA) or PVA embolization microspheres. Eventually, 1,945 TACE patients were included in the study, including 1,711 males and 234 females aged 16-91 years, with an average age of 53.14±11.56 years.

TAC treatment

The patient's inguinal region was disinfected and covered with a disinfected sheet according to routine. Under local anesthesia with 2% lidocaine, the femoral artery sheath was inserted after successfully Seldinger's [9] puncture, a 5F Yashrio, Cobra catheter was inserted into the celiac artery and superior mesenteric artery for angiography. Lopramide injection was used as contrast agent, with a total volume of 15ml and a flow rate of 5ml/s, to search the blood supplying arteries of tumor and observe the portal vein. Then, 5F catheter or 2.7F microcatheter were placed to super-select the blood supplying arteries of the tumor. The more common ones included the right hepatic artery, right accessory hepatic artery, left hepatic artery and middle hepatic artery, while the less common ones included the inferior phrenic artery, left gastric artery, gastroduodenal artery, right renal artery branch, right adrenal inferior artery, intercostal artery or subcostal artery. Multiple branches of the tumor blood supplying arteries might exist, which should be searched according to the tumor location, size, CT enhancement range and degree, and whether the Digital Subtraction Angiography (DSA) staining was complete. If necessary, abdominal aorta, subphrenic artery, renal artery, intercostal arteries (or subcostal arteries) angiography should be performed to look for ectopic blood supply. The tumor blood supplying arteries were embolized one by one. The embolization agents were lipiodol ultra-fluid and emulsion of Lobaplatin, with the dosage of lipiodol ultra-fluid not exceeding 20 mL and the dosage of Lobaplatin not exceeding 50 mg. Lobaplatin was given at 50 mg/dose, which is suggested by Hainan Changan International Pharmaceutical Co. Ltd (Haikou, China),. The dose was from 20-50 mg, with the maximum dose 50 mg. After interventional surgery, patients were given symptomatic treatment, including nutritional support, antiemetic and analgesic treatment. If the patient developed fever, antipyretic drugs could be used.

Observation targets

1,945 patients had TACE for HCC with single application of Lobaplatin. Among them, the number of first-time users of Lobaplatin reached 1,289, the second-time users reached 417, the third-time and above users 239. General information of 1,945 patients with TACE treatment mentioned above was collected, including gender, age and whether there was a history of peptic ulcer before intervention. The patients were divided into four groups: those under 35 years old, those between 35 and 50 years old, those between 50 and 65 years old, and

those over 65 years old. WHO Grading System for Hematologic Toxicity for side effects of anticancer drugs according to platelet count: grade 0: 100×10^9/L, grade I: $75\text{-}99\times10^9$/L, grade II: $50\text{-}75\times10^9$/L, grade III: $25\text{-}50\times10^9$/L, grade IV: $<25\times10^9$/L. The platelet level was divided into four degrees: normal (WHO-grade 0), mild decrease (WHO-grade I), moderate decrease (WHO-grade II), and severe decrease (WHO-grade III and WHO-grade IV).The platelet levels were calculated and graded accordingly, namely the stage before the intervention, the initial stage after the intervention (3-7 days), and the long-term stage after the intervention (21-90 days). Before intervention, liver function indicators, grade, ascites and AFP level were statistically analyzed. The AFP level was divided into three ranges: negative, almost positive (> the upper limit of normal but < 400ng/mL), and strong positive (> 400 ng/mL).

Statistics

SPSS 23.0 software (IBM, Armonk, NY, USA) was used for statistical analyses. The correlation between the following four items and the grouping of thrombocytopenia after intervention is the counting data in which grouping variables are disordered but indicator variables are ordered. These four items are gender, presence or absence of ascites before intervention, Child-Pugh grade A or B for liver functions, and presence or absence of history of peptic ulcer before intervention. Kruskal Wallis test was used to test the correlation between the number of times of using Lobaplatin and the grouping of thrombocytopenia after intervention. The comparison between the initial stage and the long-term after intervention was classified as counting data with disordered grouping variables but orderly index

Table 1. Comparison of early and long-term thrombocytopenia levels in patients HCC (Normal pre-intervention platelet levels) treated with Lobaplatin

Lobaplatin use	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
First time using Lobaplatin	Early stage	791	130	16.43	75	9.48	39	4.93	
Second time using Lobaplatin	Early stage	209	34	16.27	28	13.40	11	5.26	
Third time using Lobaplatin	Early stage	127	22	17.32	15	11.81	5	3.94	0.440
First time using Lobaplatin	Forward	604	83	13.74	29	4.80	10	1.66	
Second time using Lobaplatin	Forward	151	20	13.25	6	3.97	4	2.65	
Third time using Lobaplatin	Forward	90	9	10.00	5	5.56	0	0.00	0.590

Table 2. The incidence of thrombocytopenia after intervention in patients with different platelet levels before Intervention and the comparison of early and long-term among groups after intervention

Platelet distribution width before intervention	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
0 degree	Early stage	1127	186	16.50	118	10.47	55	4.88	
	Forward	845	112	13.25	40	4.73	14	1.66	<0.001
I degree	Early stage	210	62	29.52	99	47.14	34	16.19	
	Forward	152	47	30.92	40	26.32	13	8.55	<0.001
II degree	Early stage	181	12	6.63	78	43.09	87	48.07	
	Forward	140	22	15.71	65	46.43	43	30.71	<0.001

Table 3. Comparison of thrombocytopenia levels between early and long-term after intervention in HCC patients of different genders (Normal platelet level before intervention)

Gender	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
Male	Early stage	994	158	15.90	102	10.26	46	4.63	
Female	Early stage	133	28	21.05	16	12.03	9	6.77	0.039
Male	Forward	753	101	13.41	36	4.78	12	1.59	
Female	Forward	92	11	11.96	4	4.35	2	2.17	0.792

variables, and Mann-Whitney *U* test was used. The relationship between platelet level before intervention and platelet level at two-time stages after intervention was a bidirectional ordered counting data with the same property, which was tested by Kappa test. The relationship between age groups and the groups of thrombocytopenia after intervention, the relationship between AFP level group before intervention and the group of thrombocytopenia after intervention were all bidirectional ordered counting data with different properties. Kendall's tau-b rank correlation analysis and Spearman rank correlation analysis were used. Statistically significant difference was set at $p<0.05$.

Results

Incidence and characteristics related to intervention

No statistically significant differences were found in the first time, second time, third time and the short-term and long-term thrombocytopenia after intervention in these three groups (Table 1) The study retrospectively analyzed 1,945 HCC patients with different levels of platelets before intervention, cases and different incidences of the normal, mild, moderate and severe decreases of platelets in initial and long-term stages after intervention, suggesting that the degree of thrombocytopenia was more serious in the early stage after intervention, and was relatively light in the long-term, with statistically significant difference (Table 2).

Characteristics of general conditions

For HCC patients with normal platelet level before intervention, the degree of thrombocytopenia in female patients was slightly heavier than that in male patients at the initial term after intervention, with statistically significant difference, but there was no statistically significant difference in the degree of thrombocytopenia in the long-term after intervention (Table 3). The patients' age had an influence on the difference of platelet levels in the early stage after intervention. Of the four age groups, the older the patient was, the more obvious the thrombocytopenia in the early and long-term after intervention was. The age groups had statistical correlation with the thrombocytopenia in the early and long-term after intervention (Table 4). The difference of thrombocytopenia in patients with or without peptic ulcer and ascites before intervention was statistically significant, but the difference of thrombocytopenia in the long-term after intervention was not statistically significant (Tables 5 and 6).

Thrombocytopenia and corresponding laboratory examinations

For different pre-intervention platelet levels, statistical correlation was found between the early and long-term thrombocytopenia levels before and after intervention (Table 7). There was no significant difference in the early and long-term thrombocytopenia between different Child-Pugh classifications before intervention (Table 8). The AFP level before intervention was statistically correlated with thrombocytopenia at the early stage after intervention, but not with long-term thrombocytopenia after intervention (Table 9).

Table 4. Comparison of thrombocytopenia levels between early and long-term after intervention in HCC patients of different age groups (Normal platelet levels before intervention)

Age groups	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
Below 35 years of age	Early stage	66	9	13.64	4	6.06%	3	4.55	<0.001
35-50 years of age (including 35)	Early stage	366	47	12.84	34	9.29%	10	2.73	
50-65 years of age (including 50)	Early stage	509	89	17.49	59	11.59%	25	4.91	
Over the age of 65 (including 65)	Early stage	186	41	22.04	21	11.29%	17	9.14	
Below 35 years of age	Forward	55	10	18.18	1	1.82%	0	0.00	0.021
35-50 years of age (including 35)	Forward	306	33	10.78	10	3.27%	11	3.59	
50-65 years of age (including 50)	Forward	386	49	12.69	22	5.70%	18	4.66	
Over the age of 65 (including 65)	Forward	118	20	16.95	7	5.93%	5	4.24	

Discussion

Primary liver cancer is the most common malignant tumor in the liver, with high incidence and mortality, ranking fourth in the incidence of malignant tumors in China and the third in the mortality. In China's hardest hit area for liver cancer, the annual new cases account for more than half of those in the world. Its pathological types include hepatocellular carcinoma (HCC), cholangiocarcinoma (intrahepatic) and mixed type, which are quite different in terms of pathogenesis, pathological morphology, treatment methods and prognosis. HCC is most common, accounting for over 85-90% of primary liver cancer. There are six main therapeutic methods for HCC: surgical excision, liver transplantation, local ablative therapy, TACE, radiotherapy and systemic therapy [1-3]. Only 20-30% of the patients can have the chance of surgical excision when seeing a doctor, and most patients have lost the chance of surgery. TACE is recognized as one of the most commonly used methods in non-surgical treatment of HCC [9], and one of the standard treatment methods for middle and advanced stage of HCC. In both the guidelines of Europe and the United States, TACE is recommended as the preferred treatment for patients in phase B clinical staging systems of liver cancer. The Barcelona Clinic Liver Cancer (BCLC) recommends TACE treatment for patients in clinical staging systems of liver cancer, while the Diagnostic and Therapeutic Guidelines for Primary Liver Cancer (2017 edition, China) recommends TACE treatment for some patients in clinical staging systems of liver cancer IIb, IIIa and IIIb. There are many choices of chemotherapeutic drugs in TACE, and the choice

Table 5. Effects with or without history of peptic ulcer on the levels of thrombocytopenia in the early and long-term after intervention (Platelet level is normal before intervention)

With or without peptic ulcer disease history before intervention	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
With	Early stage	42	12	28.57	4	9.52	4	9.52	0.037
Without	Early stage	1085	174	16.04	114	10.51	51	4.70	
With	Forward	35	6	17.14	1	2.86	2	5.71	0.338
Without	Forward	810	106	13.09	39	4.81	12	1.48	

Table 6. Effects with or without ascites on the levels of thrombocytopenia in early and long-term after intervention (Platelet level is normal before intervention)

With ascites before intervention	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
With ascites	Early stage	43	5	11.63	3	6.98	0	0.00	0.046
Without ascites	Early stage	1084	181	16.70	115	10.61	55	5.07	
With ascites	Forward	35	7	20.00	1	2.86	0	0.00	0.732
Without ascites	Forward	810	105	12.96	39	4.81	14	1.73	

Table 7. Influence of different platelet levels before intervention on thrombocytopenia levels in early and long-term after intervention

Platelet distribution width before intervention	*Time points after intervention*	*Total cases*	*Mild decrease*	*Moderate decrease*	*Severe decrease*	*p value*
			Cases	*Cases*	*Cases*	
0 degree	Early stage	1127	186	118	55	
I degree	Early stage	210	62	99	34	
II degree	Early stage	181	12	78	87	<0.001
0 degree	Forward	845	112	40	14	
I degree	Forward	152	47	40	13	
II degree	Forward	140	22	65	43	<0.001

Table 8. Comparison of thrombocytopenia levels between early and long-term after intervention in HCC patients with different Child-Pugh classifications (Normal platelet levels before intervention)

Child-Pugh before intervention	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
Level A	Early stage	997	164	16.45	102	10.23	54	5.42	
Level B	Early stage	83	17	20.48	9	10.84	0	0.00	0.610
Level A	Forward	744	91	12.23	38	5.11	13	1.75	
Level B	Forward	59	15	25.42	2	3.39	0	0.00	0.124

Table 9. Comparison of thrombocytopenia levels between early and long-term after intervention in HCC patients with different AFP levels (Normal platelet levels before intervention)

AFP before intervention	*Time points after intervention*	*Total cases*	*Mild decrease*		*Moderate decrease*		*Severe decrease*		*p value*
			Cases	*%*	*Cases*	*%*	*Cases*	*%*	
Negative	Early stage	296	53	17.91	33	11.15	19	6.42	
Positive	Early stage	371	71	19.14	44	11.86	20	5.39	
Strong positive	Early stage	329	48	14.59	29	8.81	12	3.65	0.016
Negative	Forward	203	17	8.37	7	3.45	8	3.94	
Positive	Forward	283	49	17.31	13	4.59	3	1.06	
Strong positive	Forward	260	32	12.31	18	6.92	2	0.77	0.395

of these drugs is closely related to the efficacy of TACE. Reducing the dosage of chemotherapeutic drugs, only a single small dose of mixed emulsion of these drugs and lipiodol ultra-fluid is embolized through arteries, while gelatin sponge and PVA particles are added if necessary. This is called low-dose TACE [3,9]. There is no significant difference in survival between low-dose TACE and conventional dose TACE, and low-dose TACE produces less damage to liver function and fewer postoperative side effects.

For low-dose TACE, it is more important to choose the appropriate chemotherapeutic drugs and use the appropriate dose. Lobaplatin, as third generation of platinum (Pt) compound [4,5], interferes with DNA replication and transcription process by forming cross-links in Pt-GG and Pt-AG chains, thus interfering with the function of tumor cell cycle [10,12]. It is characterized with good water solubility, wide anti-tumor spectrum, strong anti-tumor activity, no cross-drug resistance with other platinum-based categories, low toxic and side effects, etc [4,5], and has definite therapeutic effect in treating various tumors such as breast cancer [13,14], nasopharyngeal carcinoma [15], lung cancer [16], esophageal cancer [17,18], gastric cancer [19], colon cancer [20], malignant pleural effusion [21,22], etc. With regard to HCC, Lobaplatin is hardly metabolized by the liver, so it will not further aggravate liver parenchyma damage. Moreover, the interaction between Lobaplatin and other drugs is small, and Lobaplatin can be used in combination with chemotherapeutic drugs such as adriamycin/epirubicin, 5-fluorouracil, mitomycin and the like [23]. Lobaplatin has good solubility, can form stable "medicine-in-oil" suspension particles, and is not delaminated after long-term storage. It is the Platinum-based preparation most suitable for TACE treatment. *In vitro* experimental research proves that Lobaplatin has inhibitory effect on liver cancer cells [24], and can be recommended for clinical treatment of HCC. Shi Ming et al [25] have used Lobaplatin for TACE treatment of liver cancer, whose research results show that epirubicin hydrochloride combined with Lobaplatin and mitomycin is superior to epirubicin hydrochloride alone in the treatment of unresectable large liver cancer with good liver function. Lobaplatin alone as a chemotherapeutic agent in TACE has good effect on mean survival time and therapeutic response, which is superior to pirarubicin hydrochloride alone, with a statistically significant difference [26]. Some authors have combined TACE containing Lobaplatin and particle implantation therapy to treat HCC, and achieved good results [27].

The most common adverse reaction of Lobaplatin is myelosuppression [8], specifically manifested as thrombocytopenia, leukopenia, etc. Thrombocy-

topenia is a dose-limiting toxic reaction of Lobaplatin, and its greatest risk is spontaneous intracranial hemorrhage or digestive tract hemorrhage, which can cause death of patients. When platelets are lower than 30×10^9/L, the risk of hemorrhage is significantly increased. The characteristics of thrombocytopenia caused by Lobaplatin can be found in the literature, but the literature mostly comes from intravenous systemic chemotherapy, and the characteristics of thrombocytopenia caused by local use of Lobaplatin in TACE have been specially studied or summarized. In this study, it was found that patients with normal platelet level before intervention had 4.88% and 1.65% of severe thrombocytopenia in the early and long-term after intervention, respectively, which proved that Lobaplatin alone was relatively safe for TACE. However, the above two percentages were 16.19% and 8.55%, respectively, for patients with slight reduction of platelet level before intervention, and for patients with moderate reduction of platelet level before intervention, the above two percentages were 48.07% and 30.71% respectively, which were significantly higher. In the results of this study, the cycles of using Lobaplatin in TACE had no obvious relationship with thrombocytopenia after intervention. This conclusion is different from that of intravenous drug use. It is speculated that the reason may be related to the relative decrease in the number of cases using Lobaplatin for the third time and above in this study. The initial thrombocytopenia was more obvious than the long-term thrombocytopenia after intervention. This conclusion is similar to the characteristics of intravenous medication, and thrombocytopenia may gradually recover after 3 weeks. The difference of thrombocytopenia in the early-term after intervention between patients of different genders was statistically significant, suggesting that female patients may have more thrombocytopenia in the early-term after intervention, but without statistically significant difference between the two genders in the long-term after intervention. There was no statistical difference of the Child-Pugh classification before intervention on thrombocytopenia in the early and long-term after intervention. It is presumed that thrombocytopenia is mainly related to bone marrow function but not much to liver function.

The age group is correlated with the grade of thrombocytopenia in the early- and long-term after intervention, which may be related to the gradual decrease of the functional activity of bone marrow hematopoietic system with the increase of age.

The lower the level of AFP before intervention, the more thrombocytopenia in the early-term after intervention. There was a statistical correlation between the grouping of AFP before intervention and thrombocytopenia in the early-term after intervention. This conclusion has not been reported and the specific reason is unknown.

To sum up, we tried to summarize the characteristics of thrombocytopenia caused by Lobaplatin in TACE: 1. It has no obvious correlation with early treatment or retreatment, and has no obvious correlation with the frequency of using Lobaplatin. Repeated use does not increase the possibility of thrombocytopenia. It may also be related to our use of low doses, not exceeding 50mg each time; 2. Thrombocytopenia was obvious in the early-stage after intervention and recovered in the long-term. There was a difference between the two periods; 3. For patients with thrombocytopenia before intervention, the possibility and grade of thrombocytopenia after intervention are significantly increased; 4. The incidence of thrombocytopenia in female patients is slightly higher than in male patients at the initial stage after intervention, and there is no difference in the long-term after intervention, which needs to be verified by large-volume of samples and multi-center data; 5. The older the patient is, the higher the incidence of thrombocytopenia is in the early and long-terms after intervention. It may be that the bone marrow reserve function decreases with age, thrombocytopenia is easy to occur, and the recovery is slower; 6. For patients with previous history of digestive tract ulcer or ascites before intervention, thrombocytopenia is more obvious at the initial stage after intervention; 7. The lower AFP level before intervention, the more thrombocytopenia in the initial stage after intervention; 8. There is no obvious relationship between liver function level before intervention and thrombocytopenia after intervention. The above characteristics have the following indications for guiding us to use Lobaplatin in TACE: 1. For patients with normal platelet level before intervention, it is relatively safe to use Lobaplatin as chemotherapeutic drug in TACE; 2. The sensitive period of thrombocytopenia after intervention is within three weeks. This period is an important period for monitoring and prevention, and is also the main period for preventing complications caused by thrombocytopenia; 3. For patients with thrombocytopenia before the intervention, attention should be paid to avoid using Lobaplatin or reducing the dose of Lobaplatin. Platelet level should be closely monitored at the initial stage after the intervention, and platelet-elevating drugs should be given when necessary; 4. For female patients, older patients, especially those over 65 years of age, patients with ascites before intervention and patients with low AFP level before intervention,

the incidence of thrombocytopenia at the initial stage after intervention is relatively higher. For patients meeting one or more of the above conditions, attention should be paid to reducing the dose of Lobaplatin and closely monitoring the platelet level at the initial stage after intervention.

Conclusions

The long-term incidence of thrombocytopenia after interventional therapy is not high in TACE patients with HCC treated with Lobaplatin alone, which was relatively safe. Besides, the occurrence of thrombocytopenia after intervention has certain characteristics, which can be used to guide clinical practice, so as to reduce its incidence or provide targeted symptomatic support treatment.

Conflict of interests

The authors declare no conflict of interests.

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