
Significance of the Hepatic Artery Anatomy and Radionuclide Flow Data for the Technique and Results of Intraarterial Infusion Chemotherapy in Patients with Liver Neoplasms

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The aim of this study was to evaluate the impact of different variations of liver vascular anatomy and hemodynamics in achieving the maximum effect of the hepatic artery infusion chemotherapy (HAIC) in patients with primary or metastatic hepatic malignancies. The retrograde analysis of hepatic artery (HA) anatomy and of radionuclide flow data on 23 patients treated by HAIC was performed. The HA anatomy was analysed according to two classification systems: the first one proposed by Michels, which describes 10 variants, and the second one proposed by Suzuki, which describes 3 variants – single, double or multiple HA with 3 subtypes of each variant (celiac, mesenteric and mixed). Additionally, before starting HAIC, ^{99m}Tc human macroalbumin was injected through the catheter at a slow rate into the HA of 10 patients with abnormal variants of HA anatomy. Radionuclide testing was performed with the aim to evaluate the subsequent intrahepatic distribution of chemotherapy agents. The intra-arterial regimen of HAIC for all patients consisted of a 5-day infusion of 5-fluorouracil or floxuridine with addition of doxorubicin or cisplatin. Such treatment was repeated every 3–4 weeks 3–6 times for every patient. The typical anatomy of HA branching was seen in 12 (52.2%) patients. The double origin of HA (according to Suzuki's classification) was seen in 9 (39.1%). In 5 (21.7%) of them the right HA was coming out from the superior mesenteric artery. In the remaining 4 (17.4%) patients the left HA was coming out from the left gastric artery. In one patient, multiple HA were observed, and there was no possibility to perform HAIC at all. The preliminary embolization of one of HA was performed in 3 patients with double HA according to Suzuki's classification. Redistribution of hepatic flow through intrahepatic collaterals was achieved in all 3 patients and assessed by radionuclide examination. The aberrant left HA was not embolized in 4 patients, because the metastatic tumours were located in the right liver lobe in 3 patients. Reduction of tumour size was noted in all patients with the adequate distribution of hepatic blood flow assessed by angiography and radionuclide perfusion study. In conclusion, the assessment of variant anatomy of HA, based on Suzuki's classification, was more useful in planning and conducting the HAIC. Radionuclide examination was helpful in the evaluation of the intrahepatic distribution of arterial blood flow and may be used as a control measure of HAIC quality, especially for patients with abnormal variants of HA anatomy.

Key words: intraarterial infusion chemotherapy, hepatic arterial vascular anatomy and its variants, liver perfusion, radionuclide flow study

INTRODUCTION

Despite advances in diagnostic imaging, the hepatic neoplasms are often diagnosed when they are be-

yond surgical resectability. Surgical resection remains the best treatment, unfortunately, only a little part of patients is surgical candidates for such radical treatment. In such situations an aggressive therapeutic approach by using the hepatic artery infusion

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chemotherapy (HAIC) is justified. Non-resectable hepatic neoplasms associated with a dual or triple arterial supply cannot be effectively perfused by selective insertion of only one catheter. Placement of two or more catheters is not practical. In order to achieve the maximum effect of HAIC with one catheter, the vascular anatomy and hemodynamics of the liver and adjacent organs should be carefully evaluated before intraarterial treatment (1).

The aim of this study was to evaluate the impact of different variants of liver vascular anatomy and hemodynamics assessed by angiography and radionuclide flow data in achieving the maximum effect of HAIC in patients with primary or metastatic hepatic malignancies.

MATERIALS AND METHODS

The retrograde analysis of hepatic artery anatomy and radionuclide flow data of 23 patients directed to interventional radiologist for HAIC of liver tumours was performed. There were 3 patients with primary and 20 patients with metastatic liver tumours. Critical to the selection of patients for HAIC was that their tumours were confined to the liver. Exclusion criteria included the usual contraindications to angiography and chemotherapy. The initial selective hepatic arteriography was performed by injection of contrast material at a rate of 3 to 6 ml for a total of 8–10 seconds, depending on the size of the liver and the vascularization of the tumours. A typical filming period was 10–15 seconds. Radiological evaluation of the hepatic artery (HA) anatomy was performed before percutaneous placement of infusion catheter. The HA anatomy was analysed according to two classification systems: 1) the first one proposed by Michel (2), which describes 10 variants, 2) and the second one, proposed by Suzuki (3), which describes 3 variants – single, double or multiple HA with 3 subtypes of each variant (celiac, mesenteric and mixed). The preliminary embolization of one of HA in patients with a duplicated source of arterial blood flow according to Suzuki's classification was performed in 3 patients with double HA. The intra-arterial regimen of HAIC for all patients consisted of a 5-day infusion of 5-fluorouracil or floxuridine with addition of doxorubicin or cisplatin. Such treatment was repeated every 3–4 weeks 3–6 times. Because of the evidently higher injection rate of contrast material during angiography, it does not truly reflect the distribution of chemotherapy materials, which are usually infused more slowly. Additionally, before starting HAIC, ^{99m}Tc macroalbumin (70–74Bq of 0.5 to 1.0 ml solution) was injected through the catheter at a slow rate into the HA of 10 patients with abnormal variants of HA anatomy.

Scintigraphy (Dyna camera 4/15, Picker, USA, equipped with a low-energy high-resolution parallel-hole collimator) was performed at the anterior and lateral views with the aim to evaluate the possible subsequent intrahepatic distribution of chemotherapy agents.

The clinical results of HAIC were evaluated according to the effectiveness of liver perfusion through one catheter and according to the dynamic changes of tumour size during the period of HAIC. Also, we analysed the frequency of anatomic variants of hepatic artery (HA), which could influence the necessity of embolization of additional extrahepatic arteries for achieving more effective HAIC.

RESULTS

The anatomic and hemodynamic considerations were evidently helpful in achieving the effectiveness of liver perfusion.

Anatomic consideration. The typical anatomy of HA branching was seen in 12 (52.2%) patients. These patients had singled HA coming out of the celiac artery. In two of them the liver was supplied additionally by small branches from the right inferior phrenic artery and left gastric artery. The embolization of these branches was not performed, because there were no tumours in this region. The double origin of HA (according Suzuki's classification) was seen in 9 (39.1%). In 5 (21.7%) of them the right HA was coming out from the mesenteric superior artery (MSA). In the rest 4 (17.4%) patients the anomalous branches of the left HA were coming out from the left gastric artery (LGA). In one patient multiple origin HA were observed, there was no common HA at all. It was impossible to perform HAIC for this patient. The redistribution of hepatic flow was performed in 3 patients with the double outcome of HA by occlusion of one of them. The right HA coming of from the MSA was occluded for one patient and embolization of the left HA was performed for 2 patients. The aberrant left HA was not embolized in 4 patients, because the metastatic tumours were located in the right liver lobe of 3 patients.

Hemodynamic consideration. The hemodynamics of HAIC was evaluated according to two aspects: 1) peculiarity of extrahepatic circulation and 2) peculiarity of intrahepatic circulation, categorized by angiography and radionuclide flow data.

Extrahepatic circulation was defined as tributaries of the common HA, proper HA, left and right HA, which supply the organs adjacent to liver. These vessels include the gastroduodenal artery (GDA), right gastric (RGA), supraduodenal (SDA) and cystic artery (CA). The extrahepatic branches, with exclu-

sion of CA and RGA, came out only from common and proper HA in 20 patients. The catheter was in need to be placed below the mentioned branches, because the blood flow in these branches had the hepatofugal direction. The control scintigraphy was informative in avoiding of the unnecessary infusion of the stomach, duodenum and pancreas in all these patients. Severe celiac artery orifice stenosis was assessed for one patient with providing blood supply to the liver from the superior mesenteric artery (SMA) through the pancreatico-duodenal collaterals. The intraarterial infusion through the catheter inserted superselectively into the pancreatico-duodenal artery was optimal according to radionuclide perfusion scintigraphy, and a clinical effect of HAIC for this patients was obtained.

Intrahepatic circulation was characterized by patterns of lobar or segmental liver flow distribution and by uptake in the tumour. The distribution of liver flow in our patients was presumably uniform in each lobe or segment, with exception of 4 patients in whom HAIC was complicated by obstructive arteriitis after 3–4 sessions of HAIC. Occlusion of the proper HA occurred in 2 of these patients. The HAIC was interrupted for one of them and for the other one the HAIC was prolonged, because the bypassed collaterals were adequately developed and the perfusion of the liver (according to the radionuclide scintigraphy data) was sufficient. The distribution of tumour flow was different in 2 patients with arterio-venous shunting in tumour tissue and in patients with component of liver cirrhosis. The radionuclide hepatic flow study was very informative in assessing the intrahepatic and tumour flow distribution in such patients.

Redistribution of hepatic flow through intrahepatic collaterals after embolization of one of HA was achieved in all 3 patients and was assessed by a radionuclide flow study. The reduction of tumour size was noticed in all these patients at the time of treatment.

DISCUSSION

The prognosis of patients who have primary or secondary liver tumours is poor. The median survival period for patients with untreated liver metastases is 2–5 month. The rationale for transcatheter treatment is based on the principle to provide an access for delivery of chemotherapeutic agents selectively as close as possible to the tumours. However, the adjacent organs may also be infused as a result of catheter malposition. The distribution of chemotherapeutic agents may be insufficient as a result of decreased arterial flow related with various liver disease statuses. Besides, about of 27–28% of pa-

tients have a double HA and about 2–3% a triple HA. Such variants of HA anatomy are attributed to a high risk of misperfusion during HAIC (4). Embolization of one or both additional HA may led to improvement of liver perfusion (5). In spite of this, growth of parasitic small arteries from inferior phrenic arteries into the tumor of the right or left hepatic lobe creates the situation when occlusion of one of HA not prevents continue growth of the tumor (6). In conclusion, there is necessity to achieve arterial devascularization of the entire tumor tissue by help of embolization of all aberrant arterial branches (5, 7). Our and other experience confirms such statements, because a decrease in size of the tumor in one lobe with simultaneous increase in size in the noninfused lobe was observed repeatedly. According to our experience the radionuclide assessment of liver perfusion is of great informative value for the effectiveness of HAIC in all clinical situations (4). It is very important to emphasize that the distribution patterns of radionuclides may be significantly different from those obtained in contrast angiography (8, 9). Additionally, the different anatomic variants of HA braching may greatly influence the results of HAIC. Knowledge of anatomical variants of HA is fundamental in achieving the optimal HAIC effect (2, 3). The so-called typical variant of HA anatomy was seen in only 52% of cases. The two classification systems of liver vascular anatomy and hemodynamics were compared according to their suitability for assessing the necessity of preliminary embolization of parasitic arterial supply and for achieving a maximum effect of HAIC. Assessment of variant anatomy of HA, based on Suzuki's classification, was more useful in planning and conducting HAIC.

CONCLUSIONS

1. Aberrant hepatic arteries occur in approximately half of population. Their occlusion attempting to redistribute the entire hepatic flow is essential in achieving the maximal effect of intraarterial infusion chemotherapy for patients with liver tumours.
2. Radionuclide examination allows an easy evaluation of the intrahepatic distribution or arterial blood flow and may be used as a control measure of HAIC quality, especially for patients with abnormal variants of HA anatomy.

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**KEPENŲ ARTERINĖS KRAUJOTAKOS IR
RADIONUKLIDŲ PERFUZIJOS VARIANTŲ REIKŠMĖ
INTRAARTERINĖS INFUZINĖS CHEMOTERAPIJOS
ATLIKIMO TECHNIKAI IR REZULTATAMS GYDANT
LIGONIUS SU PIRMINIAIS IR METASTAZINIAIS
KEPENŲ AUGLIAIS**

S a n t r a u k a

Šio darbo tikslas buvo nustatyti kepenų arterinės kraujotakos (KAK) ir radionuklidais įvertintos kepenų perfuzijos (RKP) reikšmę siekiant maksimalaus kepenų infuzinės chemoterapijos (KICHT) efektyvumo sergantiems pirminiais ir metastaziniais kepenų augliais. Retrogradiškai buvo išanalizuoti 23 ligonių, gydytų KICHT metodu, KAK ir

RKP variantai. KAK variantams analizuoti buvo panaudotos 2 klasifikacinės sistemos: 1) Michels, kuri siūlo naudoti 10 variantų, bei 2) Suzuki, siūlanti 3 variantus, iš kurių kiekvienas dar turi po 3 tipus. Suzuki variantai skiriasi pagal skaičių magistralinių arterijų, iš kurių išeina 3 pagrindinės kepenų arterijų (KA) šakos (dešinioji, vidurinioji ir kairioji): 1) pirmasis, kai visos trys KA šakos atsišakoja nuo vieno arterinio kamieno (viengubos kraujotakos variantas); 2) antrasis – kai visos trys KA šakos atsišakoja nuo dviejų arterinių kamienų (dvigubos kepenų kraujotakos variantas); 3) trečiasis – kai visos trys pagrindinės KA šakos atsišakoja nuo 3 arterinių kamienų (trigubos kraujotakos variantas). Galimi trys kiekvieno iš šių variantų tipai: 1) visos KA šakos atsišakoja nuo truncus celiacus (“celiac” variantas), 2) visos KA šakos atsišakoja nuo a mesenterica superior (“mesenteric” variantas) ir 3) įvairios KA šakos atsišakoja nuo abiejų arterinių kamienų (mišrus tipas). Papildomai 10-čiai ligonių su anomaline kepenų kraujotaka buvo atliekamas kepenų perfuzijos tyrimas, kurio metu ^{99m}Tc radionuklidais buvo suleidžiamas labia lėtai, panašiai kaip ir chemoterapiniai preparatai. Visas KICHT kursas sudarė penkių parų infuzijas, kartojamas 3–6 kartus kas 3–4 savaites.

Normali KAK pasitaikė 12 (52,2%) ligonių. Dvigubos KAK variantas, pagal Suzuki, pasitaikė 9 (39,1%) ligoniams, penkiems iš jų (21,7%) dešinioji KA atsišakoja nuo a. mesenterica superior kamieno, o kairioji KA – nuo truncus celiacus. Likusiems keturiems (17,4%) ligoniams kairioji KA atsišakoja nuo a. gastrica sin. Vienam ligoniui KAK vyko per daugelį smulkių šakų, todėl jam nebuvo įmanoma atlikti KICHT. Trims ligoniams iš skirtingų kamienų išeinančios KA šakos buvo preliminariai embolizuotos. Per vieną kateterį infuzuojamo preparato gerą pasiskirstymą visose kepenyse šiems ligoniams patvirtino radionuklidinio tyrimo duomenys. Keturiems ligoniams papildomos KA šakos, išeinančios iš smulkesnių arterinių kamienų, nebuvo embolizuotos, nes trims iš jų augliai lokalizavosi kitoje skiltyje. Gydomo laikotarpiu augliai sumažėjo visiems ligoniams.

Manome, kad Suzuki klasifikacija yra praktiškai paranesnė planuojant KICHT ir siekiant maksimalaus jos efektyvumo. Radionuklinis kepenų perfuzijos tyrimas suteikia daug reikiamos informacijos apie KICHT efektyvumą, ypač ligonių, turinčių anomalinę KAK, atveju.

Raktažodžiai: intraarterinė infuzinė chemoterapija, kepenų arterinės kraujotakos anatomija ir jos variantai, kepenų perfuzija, radionuklidų tėkmės tyrimai