The in Vivo Distribution of ^{99m}Tc-Phytate IL-2 Complex on Selective Splenic Arterial Injection*

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=국문초록=

비장동맥에 선택적으로 투여한 Interleukin-2와 ^{99m}Tc-Phytate 혼합물의 생체내 분포

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Interleukin-2 (IL-2)는 많은 immunoenhancing lymphokine의 한 종류로서 lymphokine activiated killer (LAK) cell의 생성을 자극시켜 혹종의 종양세포를 죽인다고 알려져 있다. 최근 간종양에서 비장동맥 또는 간동맥으로 투여한 IL-2가 비장의 임파계를 자극하여 LAK cell을 생성하여 어느정도 효과가 있음이 밝혀지면서, 여러가지의 투여 방법이 시도되고 있다. 그러나 각종의 투여 방법에서 실제로 투여한 IL-2의 인체내 분포에 관한 연구는 없다. 저자들은 비정맥과 간문맥에 이상이 없는 증례의 비동맥에 IL-2와 ^{99m}Tc-phytate 혼합물을 투여하고, IL-2의 생체에서의 비장과 간에 어떻게 분포하는지 알아 보기 위하여 ^{99m}Tc의 radioactivity를 계측하여 보았다. 6예의 간세포암과 3예의 위암으로부터의 전이성간암에서 동맥조영술적방법을 이용하여 초선택적 비장동맥에 투여한 IL-2와 ^{99m}Tc-phytate 혼합물이 비장 27%, 간 73%의 분포를 보여 비장을 거쳐온 ^{99m}Tc의 방사능이 간에 많이 침착함을 확인하였고 간과 비장이외의 부위 즉 골수, 복수 또는 폐장이나 늑막에는 전혀 방사능 분포가 없음을 알 수 있었다.

따라서 비정맥이나 간문맥에 이상이 없는 증례에서 IL-2의 비장동맥 투여는 목적하는 바 IL-2의 생체내 분포를 이룩할 수 있을 것으로 사료된다.

INTRODUCTION

Interleukin-2 (IL-2) is an immunoenhancing lymphokine and stimulates lymhokine activated killer (LAK) cells to effect their cytotoxicity against tumor cells. IL-2 is applied to treatment of unresctable hepatoma and advanced stomach cancer, especially metastatic liver tumor. The route of administraton is variable. Systemic venous injection and intra-splenic arterial injection were attempted firstly, and nowadays intra-splenic arterial infusion therapy is introduced by some authors[1].

We studied the distribution of IL-2 on superselective intra-splenic arterial injection by ^{99m}Tc-phytate IL-2 complex.

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INDEX TERMS: Interleukin-2, distribution
Interleukin-2, splenic arterial injection

MATERIALS AND METHOD

Three cases of metastatic tumor of liver from advanced stomach cancer and six of primary hepatocelluar carcinoma of liver were randomly selected with a consent form. All were male patients and 54.6 years of average age.

The 7-F end-hole catheter was introduced into splenic artery, and the patency of splenic vein and portal vein was confirmed by the splenic arteriogram. IL-2 (doses being variable to the tumro size and body weight; usually 10,000 unit/kg of body weight: Y-1168, KAIST, Korea), diluted with 10 ml normal saline, was mixed with 1 mCi ^{99m}Tc-phytate, and injected into the splenic artery with 2 ml/sec by hand. In the primary hepatocelluar carcinoma, prior to IL-2 injection trans-hepatic arterial chemoembolization (TACE) was done with 40 mg Adriamycine and 8 mg Mitomycine C mixed with 10 ml Lipiodol. In the cases of metastatic tumors from stomach cancer, TACE was not performed prior to IL-2 injection.

The liver-spleen scan was done with Rota camera and Macro-11 computer system (Siemens Co. Germany) within 30~45 minutes after the injection. 35 frames were accumulated with 1 frame/second of posterior scan. The regions of interest (ROI) of the liver and the spleen were drawn on the posterior scan and average counts of their radioactivity were calculated (Fig. 1).

The distribution of IL-2 was measured as absolute radioactivity count of the liver and spleen, radioactivity of each matrix of them and by the relative radioactivity of ^{99m}Tc-phytate between liver and spleen, although a few photopenic space occupying lesions (less than one-fifth of the liver) were noted in liver.

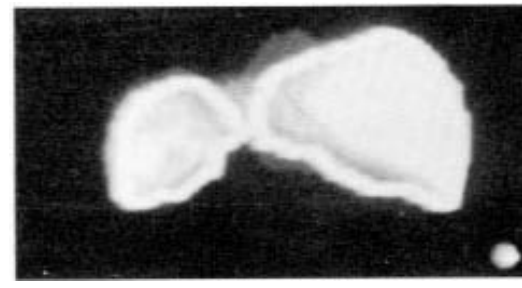

Fig. 1. ROIs of the liver and spleen on posterior scan. Results were as follows :
Total count : liver ; 70718 (cells ; 425)
spleen ; 21893 (cells ; 180)
Average count : liver ; 166
spleen ; 121

RESULT

Average count of the whole liver was 38918.6 (73%), and that of spleen was 14491.6 (27%). The liver to spleen ratio of each organ radioactivity was 2.7:1.

Average count per each matrix of the liver was 135.1 and that of the spleen was 96.4. Liver to spleen ratio was 1.5:1.

There was no definite extrahepatic and extrasplenic radioactivity such as bone marrow radioactivity, free peritoneal cavity or pleural space radioactivity, although all the patients had impaired liver function and further more some patients with ascites.

DISCUSSION

LAK cells, activated in vitro by IL-2, inhibit the growth of established melanoma pulmonary metastasis[2], and reduce the hepatic neoplasm[3,4]. By the way of splenic arterial transition, IL-2 administration is variable in the literatures, such as systemic venous injection, selective intra-splenic arterial injection, continuous intra-splenic arterial infusion with pump system[3], or selective hepatic arterial infusion of lymphokine-activated killer (LAK) cells[4] and combined method of them[3].

There is a report of in vivo distribution of cells grown in T cell growth factor (TCGF) after intravenous injection[5]. But no reports of the distribution of LAK cells with IL-2 after intra-splenic arterial administration have appeared. This study was therefore undertaken to determine the distribution of LAK cells with IL-2 by intra-splenic arterial administration in human. There showed much more splenic uptake of ^{99m}Tc-pytate IL-2 complex and much radioactivity in liver of patent splenic vein and portal vein. There was no definite bone marrow activity or pulmonary activity even though all most all of the cases had impaired liver function. The LAK could be generated by IL-2 in spleen and get into the liver through splenic vein and protal vein. By this way, those can have a LAK effect on hepatic neoplasm.

Even though a simple study of the distribution of ^{99m}Tc-phytate, this is thought of be an imaging of the reticuloendothelial systems of liver and spleen and can demonstrate the LAK cell distribution in liver in vivo.

As a conclusion, the direct administration of IL-2 into splenic artery by arterial injection or continuous infusion could fit the purpose of the in vivo distribution of Interleukin-2 to the liver.

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