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World J Gastroenterol 2006 August 28; 12(32): 5237-5239
World Journal of Gastroenterology ISSN 1007-9327

CASE REPORT

Pharmacokinetics of paclitaxel in a hemodialysis patient with advanced gastric cancer: A case report

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Received: 2006-03-07 Accepted: 2006-05-23

Abstract

We report for the first time the possibility of weekly paclitaxel chemotherapy for a patient with advanced, nonresectable gastric cancer undergoing hemodialysis. A 50-year-old man with chronic renal failure due to bilateral polycystic kidneys, who had undergone hemodialysis three times a week for 5 years, presented with hematemesis in December 2004. Based on the diagnosis of gastric cancer with lymph node metastases, surgery was performed. On the 15th postoperative day, the patient was treated with chemotherapy using paclitaxel. Paclitaxel was administered at a dose of 60 mg/m^2 as a 1 h iv infusion in 250 mL of saline. Hemodialysis was started 1 h after the completion of the paclitaxel infusion and was performed for 3 h. Paclitaxel was administered weekly on d 1, 8, and 15 on a 28-d cycle. The maximum plasma concentration of paclitaxel was 1390 μg/L. The area under the curve of paclitaxel was 4398.6 μg·h/L. Grade 2 leukopenia was encountered during the first cycle. The plasma concentrations of paclitaxel from 6 to over 24 h after the infusion were 0.01 to 0.1 μmol/L in our patient, and these concentrations have been shown to be effective on inhibiting the growth of gastric cancer cells without producing adverse side effects in the patient. The plasma concentration of paclitaxel was not influenced by hemodialysis. We conclude that the pharmacokinetics of paclitaxel is not altered in a patient with renal failure, and that weekly paclitaxel is a suitable treatment regimen for hemodialysis patients with advanced gastric cancer.

Key words: Paclitaxel; Gastric cancer; Hemodialysis

Kawate S, Takeyoshi I, Morishita Y. Pharmacokinetics of paclitaxel in a hemodialysis patient with advanced gastric cancer: A case report. *World J Gastroenterol* 2006; 12(32): 5237-5239

http://www.wjgnet.com/1007-9327/12/5237.asp

INTRODUCTION

The necessity of chemotherapy for hemodialysis patients with malignancies has increased as the life span of hemodialysis patients has grown longer because of improvements in hemodialysis. The median survival time of patients receiving the best supportive care for advanced, nonresectable gastric cancer (AGC) is only 3 to 4 mo. Some randomized studies have demonstrated the superiority of chemotherapy over best supportive care for improving patient prognosis, and the significance of performing chemotherapy for patients with AGC is now recognized[1,2]. Although TS-1 has frequently been used for patients with AGC as a first line chemotherapy in Japan, this drug is prohibited for use in patients with renal failure because adverse reactions, such as bone marrow depression, may be enhanced. In this case report, we describe for the first time the possibility of weekly paclitaxel chemotherapy for a hemodialysis patient with AGC.

CASE REPORT

A 50-year-old man with chronic renal failure due to bilateral polycystic kidneys, who had undergone hemodialysis 3 times a wk for 5 years, presented with hematemesis in December 2004. Endoscopic examination demonstrated a large tumor on the lesser curvature of the antrum. Biopsy specimens of the tumor revealed poorly differentiated adenocarcinoma. Computed tomography of the abdomen showed enlarged lymph nodes surrounding the stomach and displayed bilateral polycystic kidneys. Based on the diagnosis of gastric cancer with lymph node metastases, surgery was performed. On entering the peritoneal cavity, peritoneal disseminations were encountered. Although a curative intervention was not possible, distal gastrectomy was performed to prevent bleeding from the cancerous lesion. On the 15th postoperative d, the patient was treated with chemotherapy using paclitaxel.

Paclitaxel was administered at a dose of 60 mg/m^2 as a 1 h iv infusion in 250 mL of saline. The following premedication was administered as a 60 min pretreatment prior to paclitaxel: dexamethasone, 10 mg iv; chlorphenamine, 10 mg iv; and ranitidine, 50 mg iv. Hemodialysis was started 1 h after the completion of the paclitaxel infusion and was performed for 3 h. Paclitaxel was administered weekly on

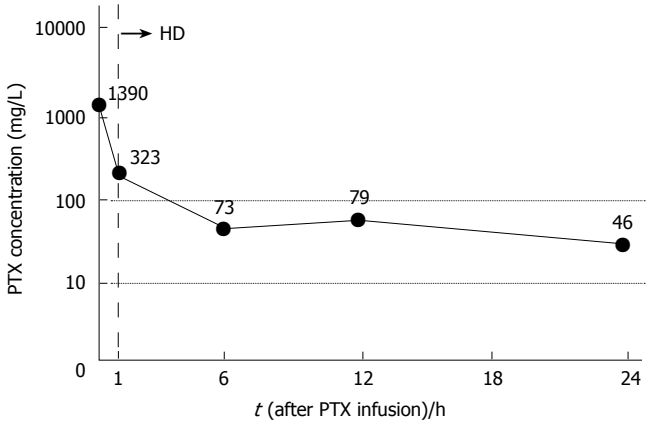

Figure 1 The plasma concentrations of paclitaxel following iv infusion. PTX: Paclitaxel; HD: Hemodialysis.

d 1, 8, and 15 on a 28-d cycle.

The plasma concentrations of paclitaxel following iv infusion are shown in Figure 1. The maximum plasma concentration (Cmax) of paclitaxel was 1390 μg/L. The area under the curve (AUC) of paclitaxel was 4398.6 μg·h/L. Grade 2 leukopenia occurred during the first cycle. Chemotherapy had to be stopped because bleeding from the jejunum near the anastomosis occurred, in spite of the fact that the platelet count was normal during the first cycle. Unfortunately, peritonitis carcinomatosa occurred, and the patient died in April 2005.

DISCUSSION

Anticancer drugs such as 5-FU, cisplatin, and irinotecan hydrochloride are effective for gastric cancer, but in a patient with hemodialysis-dependent renal failure, the dosages of these drugs must be carefully chosen because of potential side effects arising from the increased blood concentration of these drugs. Paclitaxel is the first drug from a group of drugs that inhibit microtubule disaggregation and is extensively metabolized by the liver and secreted in bile, with less than 10% extracted by the kidneys[3,4]. As a single agent, phase II study results on gastric cancer have demonstrated an overall response rate of approximately 15% to 20%[5,6]. Paclitaxel has a cytotoxic effect on human gastric cancer cell lines in a dose- and time-dependent manner. Chang *et al*[7] reported that exposure of gastric cancer cells to 0.01 μmol/L of paclitaxel for 24 h appeared to be cytotoxic. On the other hand, some investigators have reported that a paclitaxel threshold of 0.1 μmol/L was informative with respect to neutropenia, and that the total dose and AUC did not correspond with the incidence or severity of neutropenia[8,9]. In our phase I study of weekly paclitaxel and doxifluridine in AGC patients, the recommended dose of paclitaxel was 80 mg/m^2 plus doxifluridine at 533 mg/m^2. However, the effective rate was 33.3% with no adverse events at a paclitaxel dose of 60 mg/m^2[10,11]. Therefore, we decided to use a dose of 60 mg/m^2 of paclitaxel for the first cycle to ensure the safety of our patient. To our knowledge, there are a small number of reports in the literature on the treatment of advanced ovarian cancer with paclitaxel in patients with renal failure, but there are no reports of chemotherapy with paclitaxel in an AGC patient with renal failure[12,13]. The plasma concentrations of paclitaxel at 6 to over 24 h after the infusion were 0.01 to 0.1 μmol/L in our patient, and these concentrations have been shown to be effective on inhibiting the growth of gastric cancer cells without producing adverse effects for patients. Kim *et al*[14] reported the pharmacokinetic analysis in the treatment of relapsed breast cancer by weekly paclitaxel. In that report, the peak concentrations at 0 min (Cmax), 30 min, and 24 h in patients treated with a dose of 60 mg/m^2 of paclitaxel were 2.18 ± 0.68, 0.65 ± 0.20, and 0.017 ± 0.012 μmol/L, respectively. These findings are similar to our results and suggest that the plasma concentration of paclitaxel is not influenced by hemodialysis.

Chemotherapy has to be stopped because of bleeding from the postoperative peptic ulcer. Neither thrombocytopenia nor coagulopathy occurs as a result of chemotherapy. We conclude that the pharmacokinetics of paclitaxel is not altered in a patient with renal failure and that weekly paclitaxel is a suitable treatment regimen for patients with AGC on hemodialysis.

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S- Editor Pan BR **L- Editor** Zhu LH **E- Editor** Ma N