The Uptake of Anticancer Drugs by Tumor Tissues and Lymph Node and the Effectiveness of Postoperative Adjuvant Chemotherapy on Survival Time

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ABSTRACT: Forty-one patients with advanced gastric cancer underwent gastrectomy and the correlation between tissue uptake of the adjuvant drug and the prognosis were studied. The patients were preoperatively administered Tegafur (Futural, Taiho Pharmaceutical Co. Ltd, Japan) and samples of tissue were obtained intraoperatively. 5-FU levels in the tumor and lymph nodes were measured by gas chromato-massfragmentography (GCMF). The patients in whom the 5-FU uptake by the tissues was measured and who were given over 60 g of Tegafur as postoperative adjuvant chemotherapy, were divided into two groups; namely, one group in whom the 5-FU uptake by the tumor tissue and lymph nodes was over 0.05 μg/g and the other in whom the uptake was lower than 0.05 μg/g. There were no significant differences in the background factors of either group. Each survival rate was calculated by the Kaplan-Meier method, and the generalized Wilcoxon method was used for statistical analysis. There was no statistically significant correlation between the 5-FU uptake by the tumor and the prognosis, however the 5-year survival rate in the group whose 5-FU uptake of the lymph nodes was over 0.05 μg/g was statistically significant (p=0.018).

KEY WORDS: gastric cancer, Tegafur, 5-FU uptake by the tissue, prognosis

INTRODUCTION

In the past, most tumors have been treated by surgery alone and it is only now that combined treatment strategies, investigating the integration of surgery with better and more sophisticated radiotherapy, chemotherapy and perhaps immunotherapy, are being performed. Fresh approaches are very much needed. In discussing the antitumor effect of an anticancer drug, its concentration and accumulation for a certain period of time in the tumor tissue are important parameters in the case of solid carcinoma.

We studied the uptake of Tegafur by tumors and lymph nodes, and found considerable individual differences.\(^1\) The concentration of the chemotherapeutic agent in these tissues and the relationship between the use of Tegafur as a postoperative adjuvant chemotherapeutic agent and the patient's prognosis were evaluated in the present study.
MATERIALS AND METHODS

Materials
This study was conducted on 41 patients with stage III and IV gastric cancer, who underwent gastrectomy between March, 1978, and July, 1980. There were 36 men and five women, the male to female ratio being 36:5. Their ages ranged from 29 to 78 years, with an average of 61.4 ± 15.1 years.

Staging was done according to the General Rules for Gastric Cancer Study in Surgery and Pathology in Japan.

Methods

A. Drug administration
Prior to surgery, 750 mg of Tegafur (FT-207) was administered twice daily for three consecutive days either as a suppository or as an enteric coated tablet. Some of the excised tumor tissue and regional normal lymph nodes along the gastroepiploic artery were frozen for Tegafur and 5-FU concentration assays. As postoperative adjuvant chemotherapy, 600 to 800 mg/day of Tegafur in the form of enteric coated tablets was administered in two divided doses after the seventh postoperative day.

B. Measurement of drug levels in the tissues
Tegafur was measured using high pressure liquid chromatography (HPLC) and 5-FU was measured using gas chromatography-mass fragmentography (GCMF).

C. Analysis survival time
Tissue drug concentrations were measured in all the 41 patients following the preoperative medication and their clinical courses were followed after the commencement of postoperative adjuvant chemotherapy. Patients with a 5-FU tumor concentration of over 0.05 μg/g and those with levels of less than 0.05 μg/g could be distinguished. Each group was further divided into those patients who were treated with a total postoperative Tegafur dose of more than 60 g and those treated with less than 60 g. Patients with 5-FU tumor concentrations of over 0.05 μg/g, and a total dose of more than 60 g were designated as group T-1, and those with a 5-FU tumor concentration of more than 0.05 μg/g and a total Tegafur dose of less than 60 g were designated as group T-2. Those with a 5-FU tumor concentration of less than 0.05 μg/g, but a total dose of more than 60 g of Tegafur were designated as group T-3. Those with 5-FU tumor concentrations of less than 0.05 μg/g, and a total dose of less than 60 g of Tegafur were designated as group T-4 (Fig. 1). Drug concentrations in the lymph nodes were similarly classified into L-1, L-2, L-3 and L-4 groups (Fig. 2).