

Short Report

## The Effect of Oral Administration of Amphotericin B on the Incorporation of 5-Fluorouracil into Human Gastric Cancer Tissue

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NAKAZAWA, I., OUCHI, E., OUCHI, K. and WAGAI, K. *The Effect of Oral Administration of Amphotericin B on the Incorporation of 5-Fluorouracil into Human Gastric Cancer Tissue.* Tohoku J. exp. Med., 1981, 133 (3), 361-362 — Amphotericin B (AmB)-5-fluorouracil (5-FU) combination therapy against cancer was evaluated when both were given orally. Seven gastric cancer patients were treated in this manner, and 4 gastric cancer patients treated with 5-FU alone to serve as the control. AmB syrup and 5-FU syrup were administered orally for 3 days before surgical operation. Then, the drugs were given through a gastric tube into the stomach 4 hr before the start of the gastric surgery. Lesion tissues and healthy tissues were collected from each patient and the 5-FU titers were measured by bioassay. It was shown in the majority of the gastric cancer cases that the 5-FU levels in the lesion tissues were substantially higher than those in the surrounding normal tissues, whereas in the gastric cancer patients who received 5-FU alone, most of the lesion tissues showed lower 5-FU content as compared with that of the surrounding tissues. ——— Amphotericin B syrup; 5-FU syrup; gastric cancer chemotherapy

Amphotericin B (AmB) is a polyene antibiotic which increases cell membrane permeability. 5-Fluorouracil (5-FU) is an anticancer drug which belongs to pyrimidine antagonists. In this study, the combined effects of AmB syrup and 5-FU syrup were tested by measuring the concentration of 5-FU in the cancerous tissues of gastric cancer patients.

*Materials and methods.* Seven gastric cancer patients were given 24 ml of AmB syrup (2,400 mg of AmB) with 50 ml of water and 300 mg of 5-FU syrup for 3 days before surgical operation. In addition, the same amounts of AmB syrup and 500 mg of 5-FU syrup with 50 ml of water were given through a gastric tube into the stomach 4 hr before the start of gastric surgery. Four gastric cancer patients were also treated with 5-FU alone in this manner. Immediately after the stomach was taken out, the stomach was gently washed twice with physiological saline solution. Then, the cancer lesion and surrounding normal tissues from each patient were promptly collected and stored at -20°C. Bioassays using *Staphylococcus aureus* 209P (Cylinder cup bioassay method) were performed to measure the titer of 5-FU present in each tissue.

*Results and discussion.* As shown in Table 1, in 5 of the 7 cancer cases that received combination therapy, the ratio of the 5-FU content of the cancer tissue to that of the normal tissue surrounding the lesion was higher than the ratio obtained in 4 control cases.

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Presant et al. (1976) reported a combination therapy using AmB and BCNU. Nakazawa et al. (1978) reported that an intravenous drip of AmB had promoted the incorporation of neocarzinostatin (NCS) into human gastric tissues. Furthermore, Nakazawa et al. (1980) tried NCS and AmB syrup combination therapy, in order to reduce toxicity of AmB, and recognized the results that suggest the positive effect of AmB syrup on enhancing the efficiency of NCS therapy against gastric cancer. In this work, AmB syrup plus 5-FU syrup combination therapy was studied in order to make the cancer chemotherapy more effective. The results obtained in this work strongly suggest that AmB syrup may be an effective adjunct in the 5-FU syrup therapy against gastric cancer.

TABLE 1. *Contents of 5-FU in human gastric cancerous and normal tissues*

Case	Age	Sex	5-FU content ( $\mu\text{g/g}$ tissue)		
			Cancer tissue	Normal tissue	Ratio*
A. AmB+5-FU syrup combined therapy					
1 Y.K.	77	F	9.38	0.64	14.66
2 R.I.	51	F	0.52	0.07	7.43
3 S.N.	45	M	0.12	0.03	4.00
4 C.E.	66	F	0.78	0.24	3.25
5 K.K.	52	F	0.98	0.40	2.45
6 Y.H.	75	M	0.48	0.47	1.02
7 Y.C.	63	F	0.10	0.16	0.63
B. 5-FU syrup treatment alone					
1 T.S.	80	F	0.47	0.46	1.02
2 T.M.	58	M	0.12	0.24	0.50
3 Y.F.	71	M	0.07	0.14	0.50
4 T.K.	50	M	0.06	0.27	0.22

\* Ratio: 5-FU content of cancer tissue/5-FU content of normal tissue.

#### References

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