Absorption of 5-Fluorouracil through Gastric Epithelium

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MISHINA, T., WATANABE, H., MIYAKODA, K., ARAKI, H., FUJIWARA, T. and KOBAYASHI, T. Absorption of 5-Fluorouracil through Gastric Epithelium. Tohoku J. exp. Med., 1978, 125 (3), 303-304 — We examined the amount of 5-Fu absorbed through the gastric epithelium after oral administration in both dogs and patients with bladder tumors. The concentrations of 5-Fu in the serum, bladder wall, tumor mass and regional lymphnodes were sufficiently high to suppress the growth of tumor cells. —— 5-Fu; chemotherapy for bladder tumors

METHODS

Animal experiment. Five adult dogs weighing 5.0 to 12.0 kg were anesthetized with an intramuscular injection of Ketalar 2 mg/kg. Then, dry syrup of 5-Fluorouracil (5-Fu), 10 mg per kg of body weight, was orally administered to each dog. Samples of serum, bladder wall and regional lymphnodes were taken from these dogs before, and 1, 2, 3 and 4 hr after oral administration. The bioassay for 5-Fu was performed using 209-P strain of Staphylococcus aureus.

Clinical study. Ten patients with bladder cancer were examined. On commencement of surgery, 500 mg of 5-Fu were orally administered into the stomach of each patient. Neither antibiotics nor antimicrobial agents had been administered for at least 72 hr prior to surgery. Samples of serum, bladder wall, tumor mass and regional lymphnodes were taken 1 to 2 hr after oral administration. The bioassay was also performed on these samples using the same strain as in the animal experiment.

RESULTS

The results of the animal experiment are summarized in Fig. 1. The concentrations of 5-Fu in the serum, bladder wall and regional lymphnodes showed the highest values 1 hr after administration, and they gradually decreased as time went by. The mean values of 5-Fu concentration obtained from patients with bladder cancer are shown in Fig. 2.

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Fig. 1. 5-Fu concentrations in dogs. △—△, serum; ●—●, bladder wall; ○—○, regional lymphnode.

Fig. 2. 5-Fu concentrations in patients.

DISCUSSION

Since the introduction of 5-Fu by Heidelberger et al. (1957), it has become one of the antineoplastic agents most extensively used both for clinical purposes and for laboratory investigations. Hartmann and Heidelberger (1961) reported that 5-Fu inhibits thymidilate synthetase activity, with resulting inhibition of synthesis of DNA, and possibly RNA. Of various routes of its administration, e.g., intravenous, intra-arterial, topical, and oral, the oral route has been used less frequently.

In the experiment on the dogs, the highest concentration of 5-Fu was detected in the regional lymphnodes and the lowest in the serum at 1 hr after oral administration, while at 2 hr after administration, the highest concentration was detected in the bladder wall and the lowest in the regional lymphnodes.

In the clinical studies, the highest concentration of 5-Fu was discovered in the serum, the next in the tumor mass, and the lowest in the regional lymphnodes. The concentration of 5-Fu in the tumor mass was much higher than that in the bladder wall.

In both experimental and clinical examinations, the concentrations of 5-Fu were always sufficient to suppress the growth of tumor cells. The present study, therefore, suggests that the oral administration of 5-Fu is effective against infiltrative and metastatic bladder tumors.

References