6. Acute Gastric Ulceration Due to Excessive Reduction of Blood Pressure in Hypertensive Patients

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Influence of hypertensive therapy on gastrointestinal tracts has not been examined probably by following two reasons. One is that gastrointestinal arteries have so many anastomoses that they are thought to be hard to fall into embolism, apart from other organs such as brain, heart and kidneys. The other reason is that most patients with abdominal disorders generally show normo-or-hypotension, and so doctors did not measure blood pressure of these patients who required no hypertensive therapy, except for rare cases.

Our clinical observations have revealed that most patients with recurrent gastric ulceration have hypotensive tendency throughout all their life, in comparison with normal controls. And untreated hypertensive patients rarely suffer from gastric ulceration. These two clinical findings suggest that excessive reduction of blood pressure in hypertensive therapy can produce gastric ulceration.

Then we examined the relationship between reduction rate of blood pressure in hypertensive therapy and rate of gastric ulceration.

Next, animal experiments (Water Immersion and Restraint Stress on SHR) were done to demonstrate the reality of our hypothesis. Last, our observations were justified in epidemiological analysis of National Nutrition Research and National Health Research by the Japanese Ministry of Health and Welfare. And we proposed the safety range of hypertensive therapy, from gastroenterological point of view.

(I) Clinical statistics

(i) Blood pressures of 197 outpatients (19-83 yrs.) were measured within two months before endoscopic examination, all of whom complained of abdominal discomforts (such as nausea, epigastralgia, etc.). Blood pressures of gastric ulcer patients ($n = 76$) were statistically lower than that of normal controls ($n = 121$) in both sexes, and in each class of age

($P < 0.01$).

(ii) There was negative correlation between rate of gastric ulceration and the level of blood pressure. And there was no gastric ulcer patient, whose SBP showed beyond 170 mmHg, on the other hand, eighty percent of patients whose SBP showed below 100 mmHg had gastric ulceration. Fig. 1.

(iii) During antihypertensive therapy when measured just before endoscopy, SBP of gastric ulcer patients showed lower than that of patients who formed no ulcer in old age beyond 60 years. Fig. 2.

(II) Animal experiments

After per os injection of captopril (70 mg/kg/day) to nine spontaneously hypertensive rats successively for seven days, they were simultaneously given water immersion and restraint stress ($20 \pm 1^\circ\text{C}$, for 6 hours). Immediately after the stress loading, their

Fig. 1. Frequency distribution of patients with gastric ulceration, according to the level of SBP (mmHg) measured just before endoscopic examination.

Fig. 2. Reduction rate of SBP after administration of antihypertensive drugs and endoscopic diagnosis. (I: 60-69 yrs. II: 70-79 yrs. U: gastric ulcers, N: normal controls, A: SBP measured just before endoscopic examination, B: Maximum SBP measured in untreated hypertension).

Fig. 3. Relationship between SBP (mmHg) measured after per os injection of captopril (70mg/kg per os x 7 days) and Ulcer Index of SHRs after loading of WIRS (20 ± 1°C, 6 hrs.).

stomachs were removed under anesthetization of 1% ethylether, and linear ulcers on gastric mucosa were measured in length and expressed as ulcer index. The relationship between blood pressure of each rat after captopril administration and ulcer index was as follows,

$$Y = 179/X^{0.5} + 120 \quad (\gamma = -0.72, P < 0.01)$$

This formulation shows the more blood pressure reduced, the more easily gastric ulceration occurred if stress adds and when blood pressure reached down

to a certain level, which is about 140mmHg, ulcer index could abruptly increase. Fig. 3.

(III) Epidemiological analysis

In statistical study of National Nutrition Research and National Health Research, there was a strong negative correlation between rate of gastroduodenal patients and amount of Na-uptake (g/person/day), in recent ten years (1975-1984) ($\gamma = -0.90$, $P < 0.01$). And if 10.0g/person/day of Na-uptake could be actualized, rate of gastroduodenal ulcer patients in Japan may reach up to 8.0 o/oo, which is 60% increase of present patients. (Rate of gastroduodenal ulcer patients, in 10.0g/person/day of Na-uptake, is within 6.2-9.7 o/oo in probability of 0.95).

(IV) Our proposition

We make two propositions, based on clinical observations, animal experiments and epidemiological analysis of basic research by the Japanese Ministry of Health and Welfare.

(i) To prevent iatrogenic gastric ulceration, the reduction rate of blood pressure in hypertensive therapy is not to be beyond 30% in severe hypertension and 20% in moderate one.

(ii) In Japan, the national aiming amount of Na-uptake, which is under 10.0g/person/day, requires to be reexamined in gastroenterological point of view.

REFERENCES

- 1) T. Mizuno, et al: Influence of systolic blood pressure on ulceration of stomach and duodenum. Japanese Journal of Medicine **22-4**: 305, 1983.
 - 2) T. Mizuno, et al: Influence of cold stress on systolic blood pressure (SBP) of outpatients. Japanese Journal of Medicine **24-4**: 360, 1985.
 - 3) T. Mizuno, et al: Recent antihypertensive therapy and gastric ulceration in old age. Japanese Journal of Medicine **25-4**: 421, 1986.
 - 4) T. Mizuno: Easy ulcerative tendency of the stomach in hypotensive patients. Yokohama Medical Bulletin **38, 3-4**: 87, 1987.
 - 5) T. Mizuno, et al: Why the Hypotensive Ulceration Theory dropped out of the Etiological History of Gastric Ulceration? Yokohama Medical Bulletin 39, 1-2: 1, 1988.
 - 6) T. Mizuno, et al: Influence of aging on blood pressure and ulcer index of SHR and WKY. Japanese Journal of Medicine (in print).
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