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# The Studies on the Gastrin Levels in the Patients with Renal Failure

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*Fasting and postprandial gastrin levels were measured by radioimmunoassay in serum from 15 patients with renal failure and compared with those in 15 healthy controls. Pre- and posthemodialysis gastrin levels were also measured.*

*The fasting serum gastrin levels and serum gastrin response to a standard meal in the patients with renal failure were significantly higher than those in normal controls.*

*Fasting and meal stimulated gastrin levels were not significantly different in renal failure patients with peptic ulcer when compared with those in renal failure patients without peptic ulcer.*

*There were no statistically significant differences in the serum gastrin levels before and after hemodialysis in patients with renal failure.*

Key Words: *Hypergastrinemia, Renal failure, Peptic ulcer*

## INTRODUCTION

The kidney is thought to play an important role in the inactivation of endogenous gastrin. This is based on the facts that hypergastrinemia is frequently observed in patients with acute and chronic renal failure[1-3] and in experimental animals with bilateral nephrectomy,[4,5] and the fact that the enzyme which deamide the C-terminal tetrapeptide of gastrin can be extracted from mouse kidney homogenates.[6]

We conducted this study to investigate the changes of serum gastrin concentrations in patients with renal failure and to delineate the role of gastrin on the pathogenesis of peptic ulcer that frequently combines in patients with renal failure. We also investigated not only the changes of fasting serum gastrin concentrations, but also postprandial gastrin concentations in pre- and post dialysis state.

Until now, only a report dealing with renal failure appeared in Korean literature.[7]

## MATERIALS AND METHODS

Fifteen patients with renal failure who had been admitted to the Department of Internal Medicine of Kyung Hee University Hospital from June, 1983 to October, 1983, were studied. The control was 15 normal persons without renal disease, peptic ulcer or atrophic gastritis.

After a 10-hr fasting, venous blood samples were taken and then each subject ate a standard meal. The meal consisted of two hard boiled eggs, one piece of bread and a cup of milk.

Postprandial blood samples were taken at 30, 60 and 120 minutes after eating the standard meal. All blood samples were kept refrigerated under $-20°C$ after separation of serum. Fiberoptic gastroscopy with biopsy was performed in all patients with renal failure.

Serum gastrin concentrations were measured by radioimmunoassay using a kit made by Abbott Company.

## RESULTS

There was no difference in age and sex between controls and the patients with renal failure. Mean concentrations of serum creatinine and BUN were 10.6mg% and 70.8mg% respectively in patients with renal failure in contrast to normal values in controls. Serum Ca concentrations were in normal range

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in both groups (Table 1).

Of the patients with renal failure, 8 of 15 patients complained of dyspepsia and 4 of 15 had peptic ulcers (2 with gastric ulcer and 2 with duodenal ulcer). Thirteen of 15 patients had chronic renal failure and 2 had acute renal failure. Eight patients had been treated with hemodialysis (Table 2).

In patients with renal failure, the mean fasting serum gastrin concentration was 258.2pg/ml, a significantly higher value than that in the control (85pg/ml) ($P<0.001$) (Table 3).

Table 1. Clinical findings in the normal controls and patients with renal failure

| | Normal controls (n=15) | Renal failure (n=15) |
|---|---|---|
| Age (years) | 46.9±10.2 | 56.2±15.2 |
| Sex (M:F) | 6:9 | 8:7 |
| Creatinine (mg%) | 1.0±0.2 | 10.6±5.3* |
| BUN (mg%) | 10.2±2.5 | 70.8±33.4* |
| Creatinine clearance (ml/min) | — | 4.5±2.3 |
| Calcium (mEq/L) | 4.5±0.8 | 4.6±0.5 |
| | Mean±S.D. | *p<0.005 |

Table 2. Clinical characteristics in the patients with renal failure

| | | Number |
|---|---|---|
| Dyspepsia | (+) | 8 |
| | (−) | 7 |
| Peptic ulcer | (+) | 4 |
| | (−) | 11 |
| Hemodialysis | (+) | 8 |
| | (−) | 7 |
| Disease | CRF | 13 |
| | ARF | 2 |

Table 3. Serum gastrin response to a standard meal (pg/ml)

| | Normal controls (n=15) | Renal failure (n=15) |
|---|---|---|
| Fasting | 86±27.6 | 258.2±104.3* |
| 30 min | 157.8±67.5 | 399.8±137.5* |
| 60 min | 135.3±53.7 | 454.1±202.7* |
| 120 min | 117.8±46.2 | 467.4±197.9* |
| | Mean±S.D. | *p<0.001 |

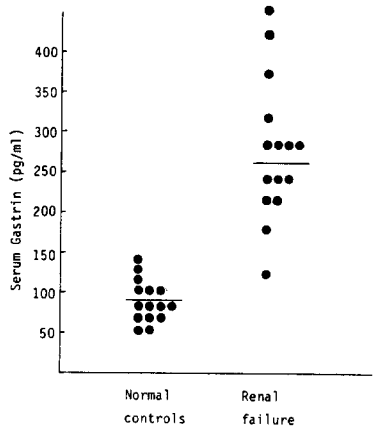


Fig. 1. *Comparison of serum gastrin concentration between normal controls and the patients with renal failure.*

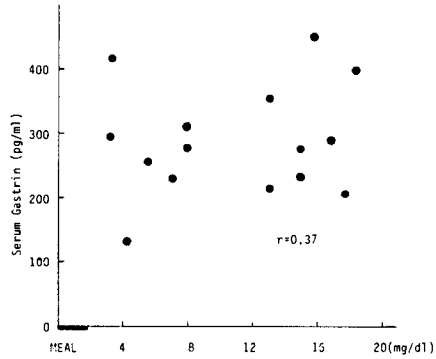


Fig. 2. *Relationship between fasting serum gastrin and creatinine in the patients with renal failure.*

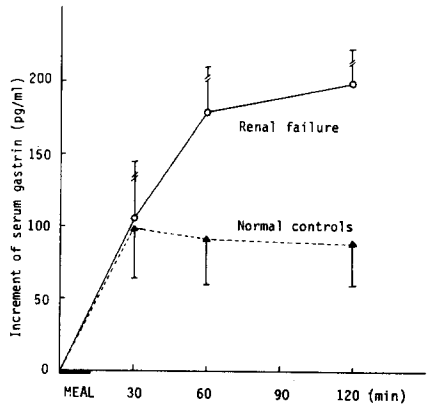


Fig. 3. *Increment of serum gastrin in response to a standard meal in normal and renal failure patients. Vertical bars indicate the standard deviation of the mean. *p<0.001*

The correlation coefficient between fasting serum gastrin concentrations and creatinine was 0.37, not significant statistically.

Meal stimulated serum gastrin concentrations were significantly higher in the renal failure group than those of control at 30, 60 and 120 minutes of postprandial samples (Table 3) ($P<0.001$).

The peak increment in gastrin concentrations was also significantly higher in the renal failure group than controls at postprandial 60 and 120 minutes samples (Fig. 3) ($P<0.001$).

There was no statistically significant difference in fasting and postprandial serum gastrin concentrations between the group of the patients with peptic ulcer and those without ulcer. And there was also no statistically significant difference in the peak increment (peak concentration- basal concentration) of gastrin between the ulcer and nonulcer group in patients with renal failure (Table 4, Fig. 4).

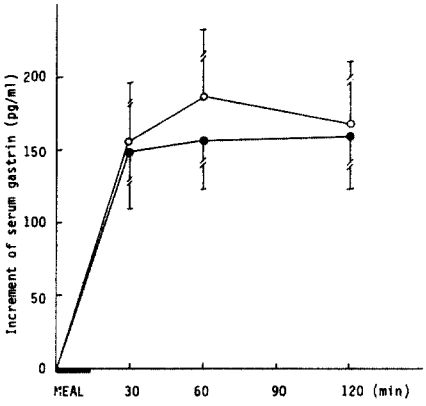


Fig. 4. *Increment of serum gastrin in response to a standard meal in renal failure patients with peptic ulcer (•—•) and without peptic ulcer (o—o). Vertical bars indicate the standard deviation of the mean.*

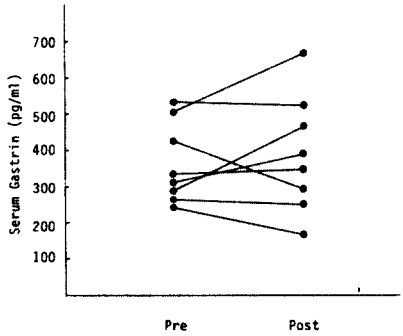


Fig. 5. *Serum gastrin levels before and after hemoidialysis in the patients with renal failure.*

Table 4. Serum gastrin response to a standard meal in renal failure patients with peptic ulcer and without peptic ulcer (pg/ml)

| | Renal failure (n=4) | Renal failure (n=11) |
|---|---|---|
| Fasting | 246.3±27.9 | 289.2±130.6 |
| 30 min | 397.0±144.2 | 363.3±187.5 |
| 60 min | 428.8±156.0 | 403.2±252.1 |
| 120 min | 465.0±181.9 | 381.8±182.1 |

Mean±S.D.

Table 5. Serum gastrin levels before and after hemodialysis in renal failure patients

| Case No. | Serum gastrin (pg/ml) | |
|---|---|---|
| | Predialysis | Postdialysis |
| 1 | 258 | 228 |
| 2 | 269 | 448 |
| 3 | 406 | 246 |
| 4 | 561 | 519 |
| 5 | 567 | 764 |
| 6 | 288 | 294 |
| 7 | 326 | 302 |
| 8 | 252 | 157 |
| Mean±S.D. | 365.9±123.4 | 369.8±198.1 |

In 8 patients treated by hemodialysis, when serum gastrin concentrations were measured before and after dialysis, there were no statistically significant changes due to hemodialysis with a mean predialysis value of 365.9pg/ml and a post-dialysis value of 369.8pg/ml (Table 5, Fig. 5).

## DISCUSSION

In the previous studies, it was accepted that pentagastrin was inactivated in the liver and gastrins such as G17 and G34 were inactivated in the organs other than liver.[9-14]

Hypergastrinemia observed both in acute and chronic renal failure suggests a certain role of the kidney in metabolism of endogensous gastrin.[1-3,7] And previous studies have shown that serum gastrin concentration parallels with glomerular function[1-3,7] and is reduced to a normal level after kidney transplantation. But there was no change in serum gastrin concentration after hemodialysis in spite of a reduction of serum BUN and creatinine.[2]

Newton et al.[15] reported that a certain amount of gastrin was degraded in the renal cortex after administration of radioactive labelled gastrin. Davidson et al.[16] reported that about 30% of endogenous gastrin was inactivated by the kidney in one blood perfusion by measuring the difference of serum gastrin concentrations separately from the renal artery and vein. But they couldn't detect any significant amount of gastrin excreted into urine, suggesting the possibility of a high rate of catabolism of gastrin in the kidney.

There are two possibilities in the mechanism of hypergastrinemia in patients with renal failure; excessive production and disturbance in catabolism of gastrin. It is accepted that renal failure per se does not induce hypergastrinemia and that accompanying atrophic gastritis or hypochlorohydria can not promote over-production of gastrin.[2,17]

As to the catabolism of gastrin, kidney seems to play a major role. Davidson et al.[18] tried to compare the changes of serum gastrin in bilateral nephrectomy and bilateral ureter ligation groups before and after development of uremia using rats as experimental animals. Serum gastrin was increased only in the bilateral nephrectomy group showing that loss of normal functioning renal mass was associated with hypergastrinemia regardless of development of uremia.

The present study has shown that fasting serum gastrin concentration (258.2pg/ml) was significantly higher than those of normal controls (86pg/ml) in the patients with renal failure but there was no correlation between serum creatinine and gastrin concentrations. The absence of correlation may be due to the fact that as about half of the patients had received regular hemodialysis, the serum creatinine couldn't accurately reflect the degree of renal failure.

The reasons why peptic ulceration occurs frequently in chronic renal failure is not valid. But the increment of acidity in gastric juice, excessive secretion of gastrin or secondary hyperparathyroidism has been proposed. In the present study, the serum Ca concentrations in the patients with renal failure were all within normal limits. However, most patients had taken phosphate binding gel for a long time and this probably made the serum Ca concentrations normal. We didn't try to measure the acidity of the gastric juice. But the increment of the gastric acidity was variable according to many investigators.[19,21]

Taylor et al.[22,23] investigated the gastrin response to meal stimulation and found that this was increased and prolonged in chronic renal failure especially in the subgroup of big gastrin but not in little gastrin. They measured the clearance rate of little gastrin in 4 patients with chronic renal failure in pre- and postprandial period and reported that there were no significant changes between the two periods, suggesting that the kidney played no role in the metabolism of little gastrin.

Although little gastrin is 6 times more potent than big gastrin in stimulation of gastric acid secretion, as little gastrin showed no response postprandially, they suggested that hypergastrinemia didn't relate directly with the increased frequency of peptic ulceration in renal failure.

In the present study, serum gastrin concentrations in patients with renal failure were significantly increased not only in fasting but also in postprandial period, more marked and prolonged in postprandial period (Table 3, Fig. 3). These findings are in accordance with the report of Taylor et al.[22,23] But there was no significant difference in fasting and postprandial gastrin response between the patients with renal failure with peptic ulcer and those without peptic ulcer and it is implicated that the increased incidence of peptic ulcer in renal failure couldn't be related to hypergastrinemia (Fig. 4).

Korman et al.[17] reported that there was a tendeny of reduction of serum gastrin concentrations in 8 patients with renal failure after treatment by hemodialysis, but not significant statistically. Reeder et al.[24] also reported that there was no significant change in serum gastrin concentrations in the patients with chronic renal failure after hemodialysis. In the present study there was no significant change in serum gastrin concentrations after hemodialysis. Gastrins are middle molecular weight substances and they are thought to be unable to pass through the dialysis membrane.

Strunz et al.[25] investigated changes in serum gastrin concentrations separately in the carotid artery, jugular vein, femoral vein, renal vein and mesenteric vein of dogs during continuous intravenous infusion of little gastrin and observed that there was no significant difference in the level of gastrin concentrations among them and suggested that degradation of little gastrin could occur in all capillary endothelium.

Conclusively, there still remains a lot of unsolved problem in the field of study of the relationship between gastrin and renal function.

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