Upsala J Med Sci 79: 155–160, 1974

Gastric Secretion in Hyperparathyroid Subjects Before and After Parathyroid Surgery

HENRY JOHANSSON, BENGT FURBERG, URBAN KRAUSE, GUDMAR LUNDQVIST and ÅKE RIMSTEN

From the Departments of Surgery, Clinical Research II, Clinical Physiology, and Clinical Chemistry, University Hospital, Uppsala, Sweden

ABSTRACT

In 61 patients with verified hyperparathyreoidism (HPT) the influence of parathyroidectomy on gastric acid and mucus secretion (sialic acid) as well as on serum gastrin concentration was studied. Patients with both normocalcemic (N-HPT) and hypercalcemic HPT (H-HPT) have been investigated. The pre-operative serum gastrin level was essentially similar in patients with N-HPT and H-HPT. The serum gastrin level was not influenced by the parathyroidectomy. The gastric acid secretion and the content of sialic acid in the gastric juice were unaffected by parathyroidectomy. Achylia or hypochylia after two different doses of submaximal histamine stimulation were found in 13 patients.

INTRODUCTION

The relationship between parathyroid hormone, hyperparathyroidism (HPT) and gastric acid secretion has been the subject of many investigations (Donegan & Spiro, 1960; Ward et al., 1964; Barreras & Donaldson Jr, 1967; Smallwood, 1967; Reeder et al., 1970). These studies have been encouraged by the suggestion that patients with HPT (see Dent et al., 1972) have an increased frequency of peptic ulcer.

Some clinical studies have indicated an increased gastric acid secretion in hyperparathyroid patients (Ward et al., 1964), which may be caused by an increased gastrin release due to hypercalcemia (Rosato et al., 1973). Studies in dogs, however, have shown no effect of hypercalcemia on the gastric acid secretion, calcium infusion did not alter the plasma gastrin concentration (Allen & Elliott, 1961; Ward et al., 1964; Reeder et al., 1970).

Other mechanisms have been discussed concerning the etiology of peptic ulcer in HPT. In the rat an ulcerogenic property of parathyroid hormone was found by Kelly (1970). Even in rats, however, there are findings which contradict such a proteolytic effect. Menguy & Masters (1965) found that parathyroid hormone seems to afford some protection against cortisone-induced ulceration.

In a previous study (Furberg et al., 1973) we reported our preliminary results on gastric secretion and plasma gastrin in patients with HPT after parathyroidectomy. The present study deals with our experience from a larger material. The results in this study do not differ essentially from our earlier findings: that gastric acidity and gastric mucus secretion as well as serum gastrin are unaffected by parathyroidectomy.

MATERIAL AND METHODS

Sixty-one patients with histologically verified HPT were included in the investigation, 41 subjects were preoperatively hypercalcemic (H-HPT) and in 29 of these adenomas were found at operation; 12 had hyperplasia. 20 patients belonged to the so-called normocalcemic group (N-HPT), i.e. these patients all had serum calcium values within the normal range (below 5.2 mEq/l) or had a mean serum calcium level of 5.1–5.2 mEq/l, but never values above 5.3 mEq/l. The histological diagnosis in the normocalcemic group was adenoma in 2 cases and hyperplasia in 18.

Details of the age (mean and range) of the patients and the pre- and post-operative serum calcium levels (mean values with S.D.) are presented in Table I.

Symptoms of gastritis and/or peptic ulcer disease were present in 11 patients (Table II). In 8 of these patients a duodenal ulcer had been radiologically diagnosed at some time. Of these 8 symptomatic patients, 2 suffered hemorrhage from an ulcer within 1 year before parathyroidectomy (Table II).

The neck explorations were performed according to the principles for goitre surgery. In the adenoma cases all 4 glands were identified, if possible, and the adenoma removed. In patients with hyperplasia, subtotal

Table I. *The age (mean and range) of 61 patients with HPT and their pre- and postoperative serum calcium levels. See text*

	N-HPT with adenoma or hyperplasia	H-HPT with adenoma	H-HPT with hyperplasia
No. of pats.	20	29	12
Age (yrs)			
Mean	48	60	50
Range	31–64	32–74	32–66
Ca/S (mEq/l) Mean±S.E.			
Preop.	5.0±0.04	5.9±0.11	5.5±0.06
Postop.	4.6±0.05	4.7±0.06	4.6±0.14

Table II. *Characteristics of 11 hyperparathyroid subjects with gastritis and/or peptic ulcer disease. See text*

	N-HPT	H-HPT adenoma	H-HPT hyperplasia
Gastritis and/or peptic ulcer disease	6	5	0
Duration of symptoms			
<5 years	6	2	0
>5 years	0	3	0
Proven peptic ulc. disease	4	4	0
without bleeding	4	2	0
with bleeding	0	2	0

parathyroidectomy was performed with the removal of 3 of 4 parathyroid glands.

The gastric secretion was studied after histamine stimulation before and 4 weeks after parathyroidectomy. The secretion rate and concentration of hydrogen ion and of sialic acid were determined. The histamine was administered intravenously by constant infusion in two doses: dose rate I, 2.5 μg histamine-dihydrochloride per kg body weight and hour; dose rate II, 13 μg per kg body weight and hour. The content of sialic acid was considered to represent the gastric mucus and was determined using the thiobarbituric acid method of Warren (1959) after hydrolysis in 0.1 M HCl for 1 hour. Calcium was determined in a Perkin-Elmer atomic absorption spectrophotometer. The gastrin was measured by a solid-phase radioimmunoassay (Lundqvist et al., 1974). The antigastrin serum (No. 2604) was obtained from Dr J Rehfeld, Copenhagen, Denmark, and its binding capacity and cross-reactivity against the different types of gastrins are presented in detail elsewhere (Rehfeld et al., 1972). Human Synthetic Gastrin I (ICI Chemicals, Cheshire, England) was used for iodination and standards.

RESULTS

All patients with hypercalcemic HPT became normocalcemic after parathyroid operation. In patients with normocalcemic HPT, the serum calcium level decreased to low-normal values in all instances after the parathyroidectomy (Table I).

Patients with radiologically proven peptic ulcer disease had pre- and post-operative serum calcium levels of the same magnitude as the whole group. The mean serum calcium level in patients with normocalcemic HPT and peptic ulcer disease was pre-operatively 5.0±0.15 (S.D.) in comparison with 5.0±0.17 (S.D.) in the whole group. Post-operatively, the values were 4.6±0.15 (S.D.) and 4.6±0.23 (S.D.), respectively. The mean serum calcium value in patients with hypercalcemic HPT

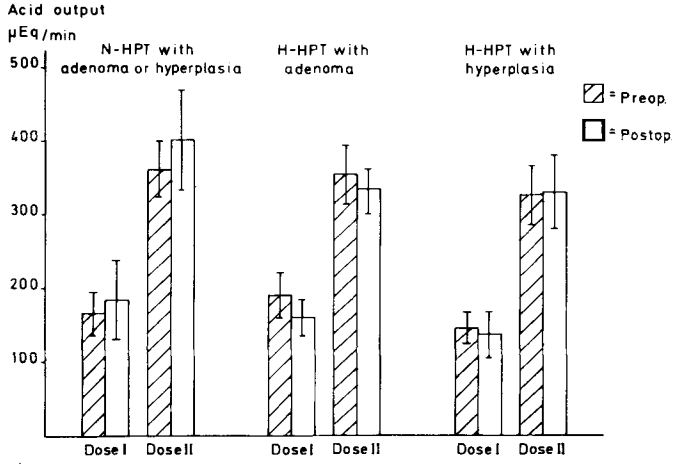

Fig. 1. Gastric acid secretion in subjects with HPT without hypochylia or achylia before and after parathyroid operation. Dose I=histamine dihydrochloride 2.5 μg per kg body weight and hour. Dose II=histamine dihydrochloride 13 μg per kg body weight and hour. See text.

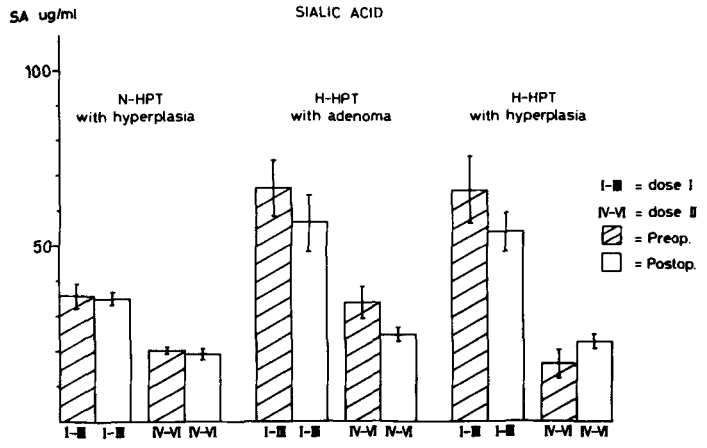

Fig. 2. Concentration of total sialic acid (SA) in gastric juice in subjects with HPT before and after parathyroid operation. Doses as in Fig. 1. See text.

in combination with peptic ulcer was pre-operatively 5.8±0.24 (S.D.) compared with 5.9±0.58 (S.D.) in the whole group. The post-operative values were 4.7±0.24 (S.D.) and 4.7±9.31 (S.D.), respectively.

Achylia after submaximal histamine stimulation (dose II) was found in one subject with normocalcemic HPT and in 6 cases with hypercalcemic HPT. Hypochylia (no free acid after the lower dosage of histamine) was found in 1 normocalcemic and in 6 hypercalcemic subjects. The gastric acid secretion during histamine stimulation in the rest of the material is illustrated in Fig. 1. The gastric acid output did not differ significantly pre- and post-operatively either in normocalcemic or hypercalcemic subjects. The pre-operative values were of the same magnitude both in patients with normocalcemic and hypercalcemic HPT.

The gastric content of sialic acid is demonstrated in Fig. 2. The content of sialic acid in gastric juice was unchanged before and after the operation in all groups, lower values, however, was found in all patients with normocalcemic HPT. (This part of the results has been presented earlier; Furberg et al., 1973.)

The serum gastrin level in patients without achylia or hypochylia is shown in Table III and Fig. 3 and in patients with hypochylia in Fig. 4 and in patients with no acid in Fig. 5. As shown in Fig. 3, the plasma gastrin in patients with normocalcemic HPT and "normal" gastric acid secretion was, before operation, 120±37 pg/ml and after operation 97±26 pg/ml. In patients with

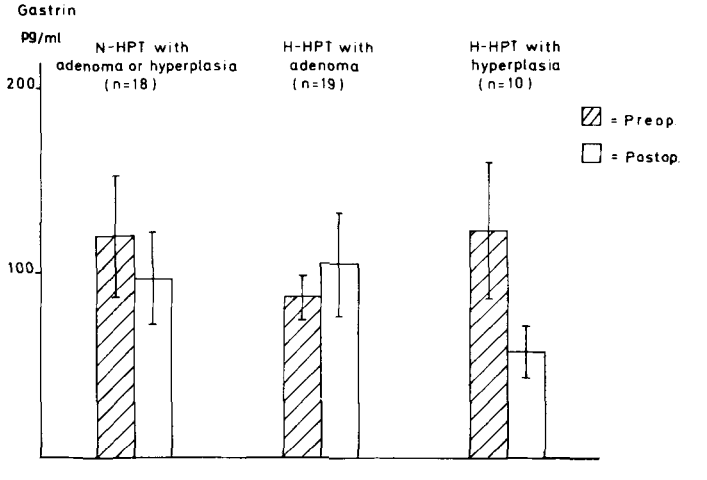

Fig. 3. Serum gastrin levels in the material presented in Table III.

Table III. *Serum gastrin level (mean and S.E.) in pg/ml in patients with HPT before and after parathyroid operation. Only patients without hypochylia or achylia are included. Diagramatic representation is given in Fig. 3*

	N-HPT with adenoma or hyperplasia $M \pm$S.E.	H-HPT with adenoma $M \pm$S.E.	H-HPT with hyperplasia $M \pm$S.E.
Gastrin (pg/ml)			
Preop.	120±33 (n=18)	87±12 (n=19)	123±37 (n=10)
Postop.	92±26 (n=18)	105±28 (n=19)	57±14 (n=10)

hypercalcemic HPT the corresponding values were: for the adenoma cases, 87±12 pg/ml and 105±28 pg/ml, and for patients with hyperplasia 123±37 pg/ml and 57±14 pg/ml, respectively. These differences are not significant ($p<0.05$).

The plasma gastrin showed, both in hypochylic and in achylic patients, high values with large variations (Figs. 4, 5). In some patients the pre-operative values were higher than the post-operative; in others the reverse was found.

DISCUSSION

An ulcer frequency of 14% in our material may indicate a relation between HPT and peptic ulcer disease. The figure 20% shown in the normocalcemic group may be misleading due to the fact that HPT is often looked for in patients with gastric symptoms. The material was, however, almost entirely collected from patients with urological symptoms.

The mechanism behind the relationship between HPT and peptic ulcer is unclear. Calcium certainly plays some rôle in the gastric secretion. The importance of the calcium ion in the secretory response to exogenous acetylcholine was demonstrated by Douglas & Rubin (1961) and Douglas & Poisner (1963). It has been suggested by Nordgren et al. (1973) that this mechanism is counteracted by thyrocalcitonin by reducing the available calcium necessary for the release or effect of acetylcholine in the secretory mechanism. According to the same authors this influence of thyrocalcitonin may guard against the development of gastric ulcers in subjects with HPT. Whether or not such an effect of thyrocalcitonin influenced our results is not certain.

There is evidence from our investigation that neither the gastric acid output nor serum gastrin was significantly changed after parathyroidectomy. Our results were uniform with regard to gastric secretion and were in agreement with those reported earlier in the literature (Dent et al., 1972; Christiansen, 1973). The results also showed that pre-operatively the acid output was of the same order in patients with normocalcemic and hypercalcemic HPT. Our study, however, gave divergent results with regard to gastrin. Thus, the gastrin level decreased post-operatively in patients with hyperplasia and hypercalcemia but remained unchanged in the other groups. Even the literature gives conflicting results concerning serum gastrin after parathyroid operation (Dent et al., 1972; Ingemansson et al., 1973). It seems that there is a threshold in the serum calcium values before the

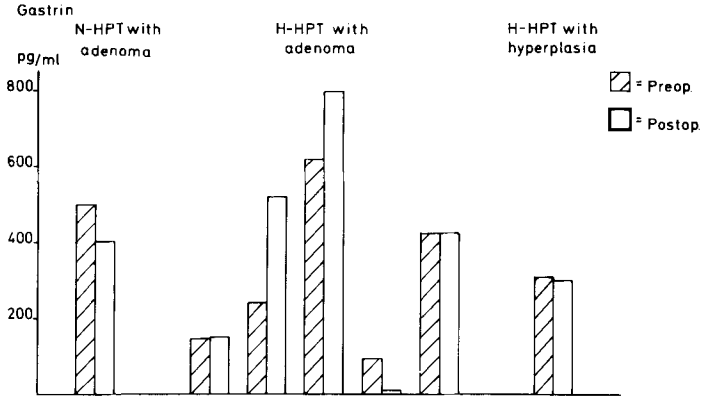

Fig. 4. Serum gastrin levels in 7 subjects with HPT and with hypochylia before and after parathyroid operation. See text.

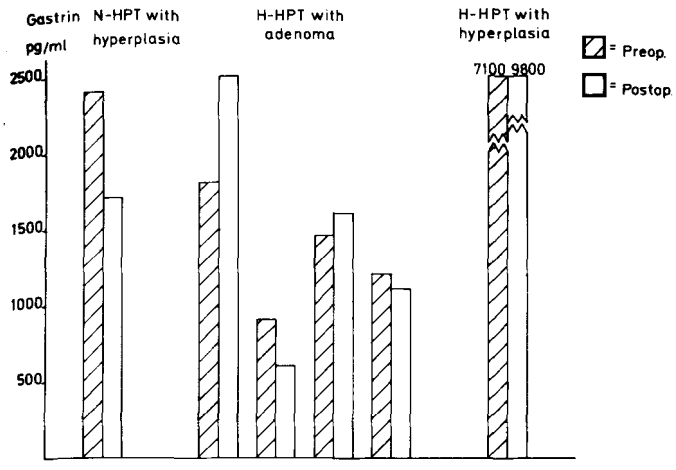

Fig. 5. Serum gastrin levels in 6 patients with HPT and with achylia before and after parathyroid operation. See text.

amount of circulating gastrin is increased (Dent et al., 1972). Similarly, the rôle of parathyroid hormone in the control of plasma gastrin is certainly essential, although very little is known of its mode of action. It has been suggested by Sizemore et al. (1973) that a possible interhormonal relationship exists between calcitonin and gastrin in man, calcitonin inhibiting gastric secretion and, conversely, gastrin stimulating calcitonin secretion. The findings of a marked elevation of the plasma gastrin in achlorhydric patients are in agreement with results reported earlier in the literature (McGuigan & Trudeau, 1970; Yalow & Berson, 1970; Stadil & Rehfeld, 1971; Dent et al., 1972). In our series the patients with pre-operatively elevated plasma gastrin did not show a fall post-operatively. In such cases, Dent et al. (1972) reported an initial decrease often followed by a gradually increase to pre-operative values.

Our results indicate that the gastric content of sialic acid was lower in patients with normocalcemic HPT than with hypercalcemic HPT. Whether this reflects a decreased protective activity of the gastric mucosa and contributes to the large number of subjects with peptic ulcer disease in the normocalcemic group is difficult to show. In the same way, it is not possible to explain whether the higher level of gastric content of sialic acid in the hypercalcemic HPT contributed to a defence mechanism of the gastric mucosa and the lower incidence of complications in relation to the normocalcemic group. Yet, it is evident from our results that the content of sialic acid is unchanged before and after operation in all hyperparathyroid groups. Therefore the protection against gastric ulceration in hyperparathyroidism still seems to be an open question. It has been shown in the rat by Öhrn et al. (1974) that after a 14-day period of treatment with parathyroid hormone the level of sialic acid in gastric juice did not change. From another experimental study in rats, Frenning et al. (1974) suggested that parathyroid hormone unspecifically damaged the gastric mucosa making it more vulnerable to peptic ulceration.

Our investigation could not demonstrate any differences in gastric output or in plasma gastrin between hyperparathyroid subjects with or those without peptic ulcer disease. On the other hand, our clinical impression concerning the ulcer disease in our material indicates the importance of performing parathyroid surgery before treating the ulcer disease surgically in hyperparathyroid patients with peptic ulcer.

ACKNOWLEDGEMENT

This investigation was supported by a grant from AB Leo Research Foundation.

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Received April 1, 1974

Address for reprints:

Urban Krause, M.D.
Department of Surgery
University Hospital
S-750 14 Uppsala 14
Sweden