REVISTA ESPAÑOLA DE FISIOLOGIA, 34, 187-190. 1978

Serotoninergic Stimulation of Gastrin Secretion

J. H.-Hierro, M.ª J. Sánchez y J. Peña

Departamento de Fisiología Humana
Facultad de Medicina
Universidad de Extremadura
Badajoz (Spain)

(Received on October 6, 1977)

J. H.-HIERRO, M.ª J. SANCHEZ and J. PEÑA. *Serotoninergic Stimulation of Gastrin Secretion.* Rev. esp. Fisiol., 34, 187-190. 1978.

The effect of serotonin (10 mg/kg weight) on the gastrin serum levels in rats has been studied. Serum concentrations of gastrin increase significantly from the 56.52 ± 6.68 pg/ml basal value to 116.87 ± 3.27 pg/ml at 105 minutes, whereas gastrin in control animals decreases progressively throughout that time.

Serum concentration of serotonin was also measured at different times after its administration. An increase to 3.31 ± 0.6 μg/ml, maximum value, at 90 minutes was observed anteceding the gastrin peak by 15 minutes.

Previous studies have shown that gastrin is synthetized in the G-cells which are present in the gastrointestinal tract (8, 13, 14, 16, 18, 20). Gastrin has also been shown to be present in granules in the cytoplasm of these cells (8, 14).

The release of gastrin, from the cytoplasmic gastrin-containing granules into the circulation is influenced by various stimulating agents (1, 2, 8, 10, 22) and inhibiting agents (7, 11, 19).

However, any influence that serotoninergic stimulation may have upon the gastrin secretion is unknown, although there is some convincing evidence that serotonin can influence the secretion of other hormones (3, 5, 6, 9, 12).

In the present work we investigated the effects of serotonin administration on serum gastrin levels.

Materials and Methods

Male Charles River rats weighing 200-250 g were used in this study. The rats housed at 22 ± 2° C on a 12 h light = 12 h dark cycle. The animals were divided into two lots: *experimental* and *control*.

The experimental lot was divided again into 7 smaller groups with five animals in each group and injected intraperitoneally with a dose of 10 mg/kg of serotonin-creatinine-sulfate (Sigma) dissolved in 2 ml of a 2 % carboxy-methyl-cellulose (Sigma) solution.

The control lot was equally divided into 7 smaller groups with five animals each one and injected intraperitoneally with 2 ml of a 2 % carboxy-methyl-cellulose solution.

Before the injection, animals were fas-

ted for 24 h; water was provided *ad libitum*.

At various time periods (30, 60, 90, 105, 120 and 150 min) after drug administration, rats were anesthetized with ether (Merck), the abdominal cavity was oppened and each animal was exsanguinated by withdrawing blood from the abdominal aorta. Serum samples were stored at —20° C until the assay.

Blood samples were collected from the abdominal aorta of animals anesthetized with ether (Merck). Serums were stored at —20° C until the assay.

Serum gastrin was measured by radioimmunoassay using the kit commercially supplied by Cea Ire Sorin. Serum serotonin was measured as previously described (21). All serum samples were assayed in duplicate.

Results

An increase in serum gastrin was evident 90 min after the intraperitoneal injection of serotonin (fig. 1 *A*). The mean peak gastrin response occurred at 105 minutes (116.87 ± 3.27 pg/ml). At 120 min the values began to fall, reaching basal levels at 150 min. The control groups showed a gradual decrease in serum gastrin levels during the 150 min studied.

Figure 1 *B* shows the serum serotonin levels, after exogenous administration. Ninety minutes after serotonin administration, serum serotonin concentration reached a peak (3.31 ± 0.6 μg/ml) while the serum serotonin levels remained at baseline in the control group during the same collection period.

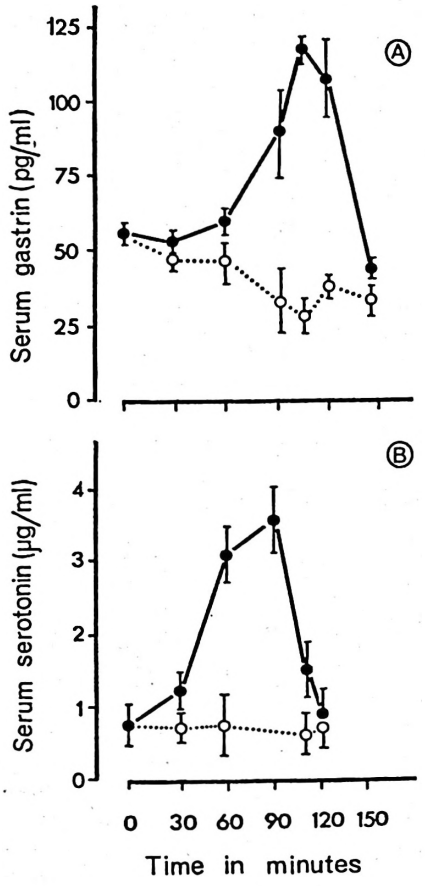

Fig. 1. *Mean levels in serum concentrations of gastrin (A) and serotonin (B), in rats after serotonin (●——●) and serotonin solvent administration (O— — —O).*
Each value is the mean ± S.E. from 5 rats.

Discussion

Comparing the gastrin serum levels in both the experimental group and the control group one sees that they are significantly different (fig. 1). In the serotonin injected animals the gastrin levels increased to a mean peak at 105 min, whilst in the control group the gastrin levels decreased gradually.

These results suggest that the determining cause of this increase is the exogenous serotonin administered. Comparing the gastrin and the serotonin serum levels one observes that the serum serotonin increase precedes the serum gastrin increase. The mean serotonin peak is reached at 90 min, while the mean gastrin peak is reached at 105 min.

The studies of OKABE *et al.* (15) support, indirectly, this stimulating effect of serotonin on gastrin secretion. These

authors observed a great number of gastric ulcerous lesions in rats after subcutaneous serotonin administration. These ulcers could be caused by an HCl hypersecretion, probably connected with a previous gastrin increase, as has often been demonstrated.

RATTAN and GOYAL (17) recently reported that venous administration of small serotonin doses stimulates lower oesophageal sphincter contractions in the opossum. CARTER *et al.* (4) demonstrated that this effect is also observed after pentagastrin intravenous administration. Possibly, serotonin caused the oesophageal sphincter contraction by increasing the serum gastrin level.

According of this, together with the topographic proximity of the enterochromaffin cells and G-cells in the intestinal tube, and considering the results of the present study, lead us to suppose that serotonin activates directly or indirectly the serum gastrin levels.

Acknowledgements

We gratefully acknowledge the technical assistance of Mrs. I. MOLLO-CRISTENSEN and to Mr. P. GARCÍA DE LA CASA, as well as to Mr. F. REQUENA for his assistance with statistics, and to the *Analytical Chemistry Department* for their collaboration.

Resumen

Se estudia en ratas el efecto de la administración intraperitoneal de serotonina sobre los niveles séricos de gastrina.

Las concentraciones séricas de gastrina se elevan significativamente pasando desde 56,52 ± 6,89 pg/ml de gastrina sérica basal a 116,87 ± 3,27 pg/ml a los 105 minutos. Por el contrario, en los animales controles los niveles séricos de gastrina descienden progresivamente durante los 150 minutos de estudio.

Simultáneamente, se han medido las concentraciones séricas de serotonina después de la administración de dicha amina, observándose un aumento hasta valores máximos a los 90 minutos. Este aumento antecede en 15 minutos al de gastrina.

References

1. BARRERAS, R. F. and DONALDSON, R. M.: *Gastroenterology*, **52**, 670-675, 1967.
2. BOLMAN, III, R. M., COOPER, G. W., GARNER, S. C., MUNSON, P. L. and WELLS, S. A., Jr.: *Endocrinology*, **100**, 1014-1021, 1977.
3. BRODIE, B. B. and SHORE, P. A.: *Ann. N.Y. Acad. Sci.*, **66**, 631-642, 1957.
4. CARTER, D. C., OSBORNE, D. H., LENNON, J. and HENDERSON, M.: In «Proc. 2nd. Internat. Symp. Histamine H_2 Receptor Antagonists» (Burland, W. and Simkins, M. A., eds.), *Excerpta Medica*, Amsterdam, 1977, pp. 135-144.
5. CLEMENS, J. A., SAWYER, B. D. and CERIMELE, B.: *Endocrinology*, **100**, 692-698, 1977.
6. CURZON, G. and GREEN, A. R.: *Life Sci.*, **7**, 657-663, 1968.
7. DALTON, M. D., EISENSTEIN, A. M., WALSH, J. H. and FORDTRAN, J. S.: *Gastroenterology*, **71**, 24-29, 1976.
8. FORSSMAN, W. G. and ORCI, L.: *Z. Zellforsch.*, **101**, 419-432, 1969.
9. GORDON, A. E. and MELDRUM, B. S.: *Biochem. Pharmacol.*, **19**, 3042-3044, 1970.
10. GREGORY, R. A. and IVY, A. C.: *Quart. J. Exp. Physiol.*, **31**, 111-128, 1941.
11. HANSKY, J., SOVENY, C. and KORMAN, M. G.: *Gastroenterology*, **61**, 62-68, 1971.
12. MARTING, J. E., ENGEL, J. N. and KLEIN, D. C.: *Endocrinology*, **100**, 675-680, 1977.
13. MCGUIGAN, J. E.: *Gastroenterology*, **53**, 697-705, 1967.
14. MCGUIGAN, J. E.: *Gastroenterology*, **55**, 315-327, 1968.
15. OKABE, S., TAKATA, Y., TAKEUCHI, K., NAGANUMA, T. and TAKAGI, K.: *Am. J. Dig. Dis.*, **21**, 618-625, 1976.
16. PEARSE, A. G. E.: *J. Histochem. Cytochem.*, **17**, 303-313, 1969.
17. RATTAN, S. and GOYAL, R. K.: *J. Clin. Invest.*, **59**, 125-133, 1977.
18. SOLCIA, E., VASSALLO, G. and SAMPIETRO, R.: *Z. Zellforsch*, **81**, 474-486, 1967.
19. SCHLEGEL, W., RAPTIS, S., DOLLINGER, H. C. and PFEIFFER, E. F.: In 1st Internat.

Symp. Hormonal Receptors in Digestive Tract Physiology, INSERM Symposium N. 3» (Bonfils, S., Fromageot, P. and Rosselin, G., eds.). Elsevier/North-Holland. Biomedical Press. Amsterdam, 1977, pp. 361-377.

20. TOBE, T., CHEN, S.-T., HENMI, K. and FUKUCHI, K.: *Am. J. Surg.*, **132**, 581-582, 1976.
21. UDENFRIEND, S., WEISSBACH, H. and CLARK, C. T.: *J. Biol. Chem.*, **215**, 337-344, 1955.
22. UVNÄS, B.: *Acta Physiol. Scand.*, **6**, 117-122, 1943.