EFFECT OF LUTEINIZING HORMONE-RELEASING HORMONE UPON INSULIN RELEASE FROM RAT ISLETS IN VITRO

M. KLIER, V. SCHUSDZIARRA and E. F. PFEIFFER
Department of Internal Medicine I, University of Ulm, Steinhövelstr. 9, 7900 Ulm/donau, FRG

Received 17 October 1980

1. Introduction

The demonstration of a luteinizing hormone-releasing hormone (LHRH) or LHRH-like material in the islets of Langerhans of the rat [1] adds another peptide to those common to the central nervous system and the gastrointestinal tract and endocrine pancreas. Since no biological effect of LHRH upon islet cell function has been reported this study was designed to determine the effect of synthetic LHRH upon insulin release from isolated rat islets. Low concentrations (10^{-8} M and 10^{-10} M) of LHRH significantly reduced insulin secretion at 100 mg/dl glucose while at 10^{-6} M LHRH there was no effect.

2. Materials and methods

Male Wistar rats (Thomae, Biberach) (180–200 g body wt) were killed by decapitation. The removed pancreases were subjected to collagenase (Serva, Heidelberg) digestion as in [2]. Batches of 10 isolated islets were incubated in 2 ml Krebs-Ringer-bicarbonate buffer containing glucose at 100 mg/dl with or without LHRH (Serva, Heidelberg) at 10^{-6} M, 10^{-8} M and 10^{-10} M final conc., respectively. For the determination of the viability of the incubated islets 2 control groups obtained from the same pancreases were incubated in parallel in all experiments in the presence of glucose at 50 mg/dl and 200 mg/dl, respectively, and only those experiments were considered to be valid where an insulin response to increasing concentrations of glucose was observed. The islets were incubated at 37°C in the presence of 95% O_2 and 5% CO_2 for 2 h. Aliquots of 50 μl incubation medium were taken at 0, 30, 60, 90 and 120 min for the radioimmunological determination of insulin [3,4]. Incremental insulin release from every 10 islets was calculated for the 2 h incubation period after subtraction of the basal concentrations. For statistical comparison Student's t-test for non-paired data was employed and values of $p < 0.05$ or less were considered to be significant.

Address correspondence to V. S.

3. Results and discussion

During the incubation of the islets with glucose at increasing concentrations, the insulin release was 274 ± 10 μU . 120 min^{-1} . 10 $islets^{-1}$ at 50 mg glucose/dl, 352 ± 8 μU . 120 min^{-1} . 10 $islets^{-1}$ at 100 mg glucose/dl and 583 ± 7 μU . 120 min^{-1} . 10 $islets^{-1}$ at 200 mg glucose/dl, respectively ($p < 0.001$).

The effect of LHRH upon insulin release during

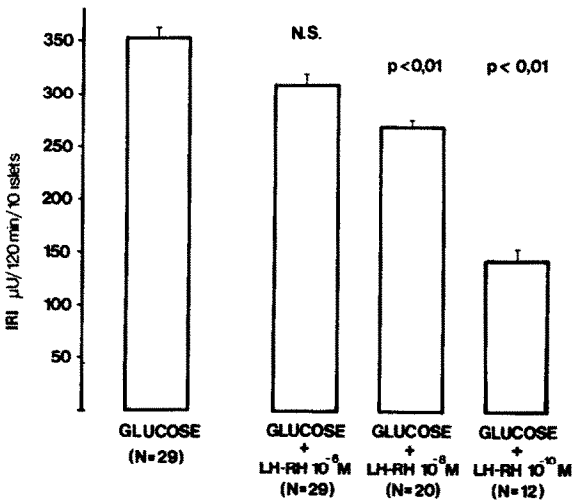

Fig.1. Effect of luteinizing hormone–releasing hormone (LHRH) upon insulin release from isolated rat islets during incubation with glucose at 100 mg/dl.

the incubation with glucose at 100 mg/dl was dose-dependent, as shown in fig.1. LHRH, at 10^{-6} M final conc., had no effect upon insulin secretion compared to the controls. However, LHRH at 10^{-8} M and 10^{-10} M elicited a significant reduction of insulin release to 272 ± 5 μU . 120 min^{-1} . 10 $islets^{-1}$ and 150 ± 17 μU . 120 min^{-1} . 10 $islets^{-1}$ ($p < 0.01$), respectively.

This study demonstrates that LHRH has an inhibitory effect upon insulin release from rat islets in vitro. The strongest effect was observed at the lowest concentration of LHRH employed. The presence of LHRH-like material in rat islets [1] may suggest that it is another candidate peptide which participates in the modulation of islet cell function together with other neuropeptides originally isolated from the hypothalamus such as TRH [5–7] and somatostatin [8–11].

Acknowledgements

The work was supported by DFG grant SFB 87 G 6. We thank W. Friedrich for excellent technical assistance in this study.

References

[1] Seppälä, M., Wahlström, T. and Leppäluoto, J. (1979) Life Sci. 25, 1489–1496.
[2] Lacy, P. E. and Kostianowsky, M. (1967) Diabetes 16, 35–39.
[3] Yalow, R. S. and Berson, S. A. (1960) J. Clin. Invest. 39, 1157–1175.
[4] Herbert, V., Lau, K. S., Gottlieb, C. W. and Bleicher, S. J. (1965) J. Clin. Endocrinol. Metab. 25, 1375–1384.
[5] Morley, J. E., Garvin, T. J., Pekary, A. E. and Hershman, J. M. (1977) Biochem. Biophys. Res. Commun. 79, 314–318.
[6] Martino, E., Lernmark, Å., Seo, H., Steiner, D. F. and Refetoff, S. (1978) Proc. Natl. Acad. Sci. USA 75, 4265–4267.
[7] Engler, D. and Jackson, I. M. D. (1980) Proc. Ann. Meet. Endocrine Society, p. 106.
[8] Orci, L. and Unger, R. H. (1975) Lancet ii, 1243–1244.
[9] Alberti, K. G. M. M., Christensen, N. J., Christensen, S. E., Hansen, A. P., Iversen, J., Lundbaek, K., Seyer-Hansen, K. and Orskov, H. (1973) Lancet ii, 1299–1301.
[10] Taniguchi, H., Utsumi, M., Hasegawa, M., Kobayashi, T., Watanabe, Y., Murakami, K., Seki, M., Tsutou, A., Makimura, H., Sakoda, M. and Baba, S. (1977) Diabetes 26, 700–702.
[11] Schusdziarra, V., Zyznar, E., Rouiller, D., Boden, G., Brown, J., Arimura, A. and Unger, R. H. (1980) Science 207, 530–532.