TRIGLYCERIDE LOWERING EFFECT OF SOMATOSTATIN AND ITS ANALOGS

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Received 26 April 1977

1. Introduction

Clinical interest in the possible use of somatostatin (SS) to inhibit glucagon secretion in diabetes mellitus has led to the search for analogs of SS with greater and/or more selective activities and with a prolonged biologic effectiveness. Several SS analogs with either a higher potency in suppressing insulin and glucagon secretion [D-Trp^8]-SS [1] or a greater effect for inhibition of glucagon than insulin [D-Cys^{14}]-SS [2] and [D-Trp^8–D-Cys^{14}]-SS [3,4] have now been developed. In the course of a study designed to compare the relative efficacies of the foregoing analogs as glucagon suppressants in alloxan diabetic dogs, it was noted that plasma samples were less turbid after a subcutaneous injection of the peptides than after a saline control. In order to test if there is an influence of SS and its analogs on postabsorptive triglyceride levels, we have measured plasma triglyceride levels in the plasma of insulin deprived fasted alloxan diabetic dogs after a single injection of SS, [D-Trp^8]-SS, [D-Trp^8–D-Cys^{14}]-SS, or saline, respectively.

2. Materials and methods

Seven chronic alloxan diabetic dogs weighing between 19 kg and 25 kg were used for the various experiments. Insulin treatment was discontinued 40 h before the start of an experiment, and food was withheld for 20 h. The dogs received, on four different experimental days separated by at least a seven day interval, a subcutaneous (s.c.) injection of either 1 mg [D-Trp^8]-SS (n = 5), 1 mg [D-Trp^8–D-Cys^{14}]-SS (n = 5), 1 mg SS (n = 7), all dissolved in 2 ml saline, or a 2 ml saline (n = 4) control injection. Blood samples were obtained at frequent intervals from a foreleg vein before and after an injection.

Triglyceride concentrations were measured by an enzymatic method of Eggstein and Kreutz [5] using a commercial kit (Boehringer Mannheim). For statistical analysis of the data, the Student t-test for two groups was used because not every dog was studied in every experimental protocol.

3. Results and discussion

The effects of SS and the SS analogs upon triglyceride levels are shown in fig.1. In the control group, mean triglyceride concentrations increased from a baseline level of 65.9 ± 4.3 mg% by about 20 mg% after 3 h. Following [D-Trp^8]-SS injection, triglycerides declined about 10 mg% from a baseline of 64.8 ± 3.9 mg% while after the injection of SS and [D-Trp^8–D-Cys^{14}]-SS, triglyceride levels declined, respectively, 15 mg% from a mean baseline of 53.3 ± 3.0 mg% and 24 mg% from a baseline level of 65.6 ± 4.3 mg%. The triglyceride-lowering effect of the agents was not related to their glucagon-reducing activity which was greatest for [D-Trp^8–D-Cys^{14}]-SS and [D-Trp^8]-SS [6].

Sakurai et al. [7] and, more recently, Pointer et al. [8] have reported that SS reduces postprandial

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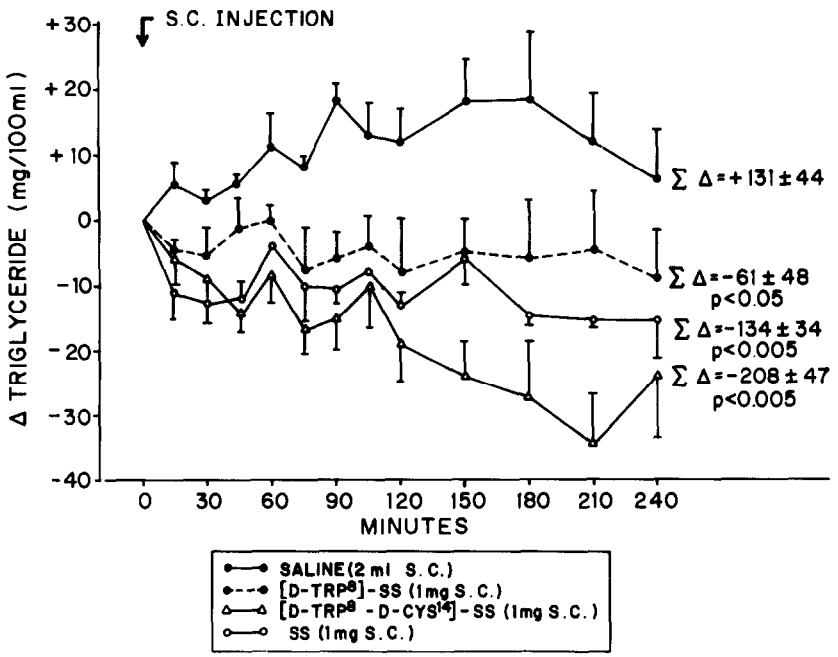

Fig.1. Changes in mean plasma triglyceride levels (± SEM) after a subcutaneous (s.c.) injection of 1 mg somatostatin (SS), 1 mg [D-Trp^8]-SS, 1 mg [D-Trp^8–D-Cys^{14}]-SS and 2 ml saline, respectively.

triglyceride levels. The present study is the first demonstration of an effect on triglyceride levels in the postabsorptive state, suggesting an influence of SS and its analogs on endogenous triglyceride turnover. The mechanism of the apparent triglyceride lowering action of these agents in insulin-deprived alloxan diabetic dogs remains to be determined.

Acknowledgements

This work was supported by VA Institutional Research Support grant 549-800-01, NIH Grants AM02700-16, I-ROI-AM18179-03, AM18811, and HD90690, National Foundation Grant 1-411, The American Diabetes Association, North Texas Affiliate and Karl Thomae Pharmaceuticals. The authors wish to thank Margaret Cason, Grace Chen, Ron Kaiser, and Bob Galyean for technical assistance and Billie Godfrey for secretarial assistance.

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