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The Effect of Cysteamine on the Somatostatin Content of Guinea-pig Islets

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ABSTRACT

Cysteamine is known to deplete the immunoreactive somatostatin content in different organs from rat and mouse. The aim of the present work was to test if cysteamine also affects the somatostatin content in guinea-pig islets, since guinea-pigs have a carbohydrate metabolism different from that of other laboratory animals. Cysteamine was injected to guinea-pigs and the pancreatic islets were isolated four hours later. Cysteamine was also incubated in vitro with isolated pancreatic islets from untreated guinea-pigs. Cysteamine depleted the somatostatin content in the pancreatic islets in both the in vivo and in vitro studies.

INTRODUCTION

It is well known that the ulcerogenic substance cysteamine (2-amino-ethanethiol), injected in vivo, causes a selective depletion of somatostatin in many organs in both the mouse and rat (7, 6, 3). Besides somatostatin, cysteamine also depletes prolactin (3). In addition, cysteamine is known to decrease the somatostatin content of pancreatic islets in vitro (4, 5).

The guinea-pig is associated with several biochemical peculiarities and both its insulin and glucagon amino acid sequences are different from those of other animals. The general amino acid sequence for somatostatin seems, however, to be conserved in guinea-pigs (1). In view of its biochemical peculiarities,it is of particular interest to follow the effect of cysteamine on somatostatin in the guinea-pig. In the present study we therefore measured somatostatin in isolated pancreatic islets of guinea-pigs after administration of cysteamine in vivo and after exposure of the islets to cysteamine in vitro.

MATERIALS AND METHODS

Each of six guinea-pigs received a subcutaneous injection of 60 mg/kg body weight of cysteamine (Aldrich, Beerse, Belgium) dissolved in distilled water. The animals were killed four hours after the injections. Three control animals remained untreated and were killed together with the injected animals. The pancreatic glands were rapidly removed and islets were isolated by means of a collagenase digestion technique (2). Groups of 25 islets from each animal were then sonicated and extracted in 250 µl of ice-cold acid alcohol (0.18 mol/l HCl in 70 % alcohol) at 4°C overnight. The somatostatin content was determined as described below.

Effects of cysteamine in vitro were studied in collagenase-isolated islets from nine normal guinea-pig pancreases. Groups of 25 islets were exposed for four hours at 37°C to cysteamine dissolved at a concentration of 10 or 100 µg/ml in tissue culture medium (Parker 199) containing 10 % (v/v) calf serum. The somatostatin content of the islets was determined after sonication and extraction in ice-cold acid alcohol as described above.

For determination of the somatostatin content, the acid alcohol extracts of the islet homogenates were centrifuged at 2000 rpm for 20 minutes and the somatostatin content of the supernatant was assayed by a radioimmunological method (Kit nr. 038192; Immuno Nuclear Corp.,Stillwater, Minnesota 5508, USA) using synthetic somatostatin-14 as standard. The sensitivity of the method was approximately 3 pg per tube.

Results are expressed as mean values $\pm$ standard errors of the means ($m \pm SEM$). Probabilities (P) of chance differences between groups were calculated by Student's t-test.

RESULTS

Four hours after the subcutaneous administration of cysteamine the somatostatin content of the pancreatic islets was significantly depleted compared with that in the control animals (176 $\pm$ 11 pg/islet versus 934 $\pm$ 47 pg/islet). In vitro incubation of islets with cysteamine for four hours at a concentration of 100 µg/ml resulted in a marked depletion of somatostatin, but at 10 µg/ml cysteamine did not have this effect. The somatostatin values were 331 $\pm$ 47 pg/islet with 100 µg/ml, 640 $\pm$ 116 with 10 µg/ml and 873 $\pm$ 139 in the controls (see figs. 1 and 2).

DISCUSSION

The present results show that not only treatment with cysteamine in vivo but also exposure to cysteamine in vitro causes a rapid and marked depletion of immunoreactive somatostatin in pancreatic islets from guinea-pigs. This is in accordance with previous observations in islets from mice and rats (4, 5).

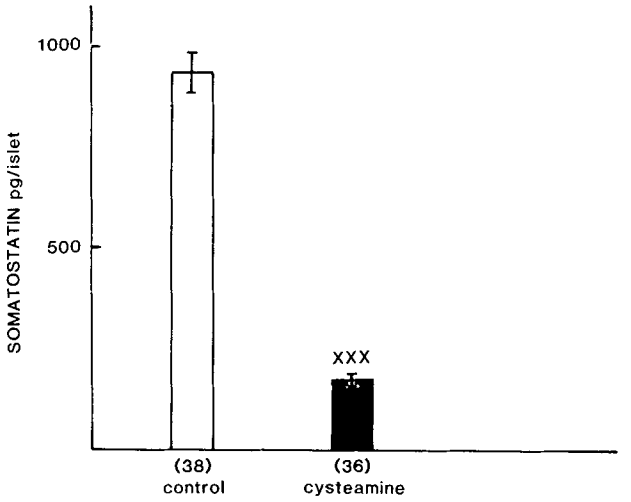

Fig. 1. The bars show the somatostatin content of pancreatic islets from control guinea-pigs and from guinea-pigs treated with cysteamine (60 mg/kg B.W.) four hours before the animals were killed. The numbers of batches are given within parentheses. Means $\pm$ S.E.M. are given. xxx: $P < 0.001$ in relation to the control group.

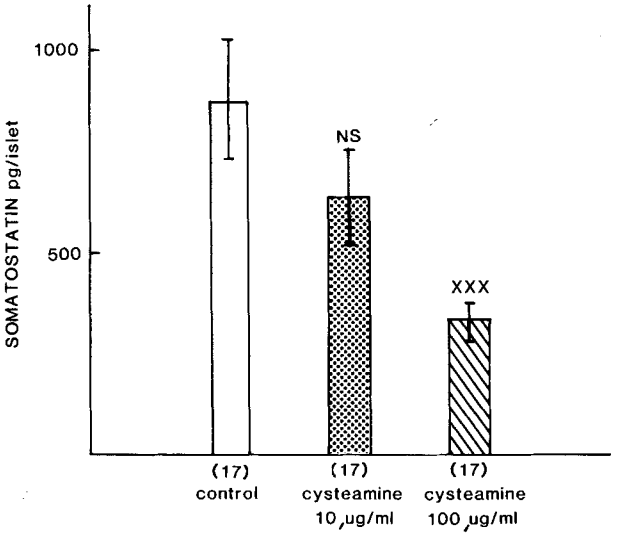

Fig. 2. The bars show the somatostatin content of pancreatic guinea-pig islets incubated for four hours with and without cysteamine in the medium. The numbers of batches are given within parentheses. Means $\pm$ S.E.M. are given.NS: $P > 0.05$; xxx: $P < 0.001$ in relation to the control group.

Other studies indicate that the loss of immunoreactive somatostatin occurs without changes in the pancreatic insulin or glucagon content (6). Although the mechanism for the cysteamine action is not known, there is support for the view that the action is intracellular (6). Since in many aspects the guinea-pig has a metabolism different from that of many other laboratory animals, it is of interest to note that the depletion of immunoreactive somatostatin by cysteamine is pronounced in this animal, also.

ACKNOWLEDGEMENTS

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