THE EFFECTS OF CAERULEIN ON EXOCRINE PANCREATIC SECRETION IN PIGS

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(Accepted 27 July 1982)

ABSTRACT


Caerulein administered to anaesthetized pigs by slow i.v. infusions at doses of 0.5, 1.0 and 2.0 ng kg⁻¹min⁻¹ for 30 min, stimulated pancreatic juice production, increased the protein content of the juice and enhanced its amylolytic, lipolytic and proteolytic activities. In a single experiment, an i.v. infusion of secretin (0.001 U kg⁻¹min⁻¹) lasting through the whole experimental time, provoked potentiation of the caerulein stimulatory effects on pancreatic juice production, protein content and amylolytic activity.

INTRODUCTION

The pharmacological actions of caerulein on systemic blood pressure, extracellular smooth muscles and secretions associated with the digestive tract were elucidated by Erspamer et al (1967).

Recently, this frog skin decapeptide (Erspamer et al 1966), strictly related to CCK-PZ and particularly to CCK-OP (Anastasi et al 1968), received renewed attention both for possible central effects on feeding behaviour (Della Fera et al 1980) and for peripheral effects as a pancreotropic agent in sheep (Beretta et al 1981). Besides observations on the responsiveness of this animal species to the exocrine pancreatic secretagogue effects of caerulein, these findings provided further interest in the biological properties of this peptide on ruminant digestive functions, and opened new perspectives on the physiological roles of a g.i. hormone such as CCK-PZ. To evaluate comparatively the exocrine pancreatic stimulatory properties of caerulein, we now report results obtained in pigs which were tested in order to: a) investigate the responsiveness to caerulein of a species which is known to be relatively insensitive to the activity of pancreozymin (Hickson 1970) and b) check the possible use of caerulein as a pancreotropic agent for improving pancreatic digestion in another important animal species.

MATERIAL AND METHODS

14 Large white x Landrace female pigs weighing 20-33 kg, fed with solid standard pig-diet and drinking water ad libitum were employed. Food but not water was
withdrawn 20 hours before the experiments. Anaesthesia was induced by sodium pentobarbitone (25 mg kg\(^{-1}\) i.v.) and maintained with small i.v. amounts of the same depressant. The trachea was cannulated and a polyethylene catheter was inserted into the right safenous vein. A right paracostal incision (15-18 cm) of the abdominal wall was made and after the opening of the duodenum, a polyethylene tube (1.0 mm bore) was inserted into the pancreatic duct. A continuous i.v. slow infusion (1 ml min\(^{-1}\)) of sterile, warmed (37°C), isotonic saline was administered to the animals during the whole experimental procedure except for the 30 min of caerulein administration. During this time synthetic caerulein (Ceruletide- Farmitalia SpA) dissolved in saline was administered at the same rate of infusion at doses of 0.5, 1.0 or 2.0 ng kg\(^{-1}\)min\(^{-1}\). Only a single dose of the peptide was tested on each animal. An additional experiment was performed in which a priming slow i.v. infusion of secretin (Sigma) in saline (0.001 U kg\(^{-1}\)min\(^{-1}\)) replaced that of saline alone. In this case the concurrent dose of caerulein selected was 1.0 ng kg\(^{-1}\)min\(^{-1}\).

The collection of the pancreatic juice and the analytical methods to determine its protein content as well as its amylolytic, lipolytic and proteolytic activities was carried out by procedures described previously (Beretta et al 1981). Activation of proteolytic enzyme was accomplished with freshly prepared porcine enterokinase.

RESULTS

The mean effects of the graded doses of caerulein employed in the different experiments are shown in FIG.1, in which sections A, B, C, D and E correspond respectively to pancreatic juice volume, protein content of the juice and amylolytic, lipolytic and proteolytic activities. The values have been expressed as % variations of the mean basal values (=100) recorded during the 1.5 hour period (3 samples) before caerulein infusion. This procedure was followed in order to reduce the variations between individual animals by comparing the effects of the drug against the initial values of each animal. Although the animals showed variations in sensitivity to caerulein, the overall effects confirm the stimulatory properties of this peptide in pigs. The responses are shown in FIG.1 and summarized in TABLE 1. They indicate that:

a) the effects of caerulein occur promptly and last for a relatively long period (2.0-2.5 hours)

b) the lower dose tested elicited too high stimulations to be considered the effect of a threshold dose

c) the dose response relationship considered at peak effects is proportional up to the dose of 1.0 ng kg\(^{-1}\)min\(^{-1}\) but at the higher dose of 2.0 ng kg\(^{-1}\)min\(^{-1}\) the response appeared to plateau, at least in two of the five parameters examined (e.g. lipolytic and proteolytic activities).