Exocrine pancreatic response to the venom of the scorpion, *Tityus trinitatis*

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SUMMARY This paper records for the first time the exocrine pancreatic response to scorpion venom, in this case that of *Tityus trinitatis*, a scorpion endemic in Trinidad. The crude venom injected intravenously into fasting anaesthetised dogs induced a secretion of the exocrine pancreas. The secretion evoked was rich in enzymes.

Acute pancreatitis has been described after the sting of the scorpion of Trinidad, *Tityus trinitatis* (Waterman, 1938; Poon-King, 1963; Bartholomew, 1970). Bartholomew (1970) in his series reported 30 cases of scorpion stings, 24 of whom had clinical features of acute pancreatitis with raised serum amylase. Waterman (1938) had reported finding at laparotomy two cases of acute oedematous pancreatitis, two of haemorrhagic pancreatitis, and 12 with pseudocysts of the pancreas after stings of *Tityus trinitatis*. Many workers have reported stimulation of secretion from salivary and lacrimal glands (Bücherl and Buckley, 1971) and of adrenal glands (Henriques *et al.*, 1968) after envenomation; however, there have been no reports of pancreatic secretion after envenomation by this or any other venom. This work was undertaken to examine the action of the venom of *Tityus trinitatis* on the exocrine secretion of the canine pancreas.

Methods

In fasting mongrel dogs, anaesthesia was induced with Epontal (Bayer), a non-barbiturate agent of very short duration of action and continued with chloralose intravenously, an anaesthetic agent known to have only minimal pancreatic action. Endotracheal intubation was maintained throughout the experiments and assisted respiration when necessary. Laparotomy was performed through a small upper mid-line incision. With careful technique to minimise handling of the pancreas, a cannula was inserted for a short distance into the pancreatic duct near its termination without opening the duodenum. The

cannula was then secured and the laparotomy incision closed. A venous catheter was introduced into the femoral vein and advanced into the inferior vena cava.

Crude venom of the scorpion *Tityus trinitatis* obtained by electrical milking was stored as a dry powder at -20°C . The dried venom was dissolved in normal saline immediately before use and was administered slowly through the venous catheter.

Pancreatic juice was collected under oil in weighed tubes. Amylase was measured by the Phadebas method (Ceska *et al.*, 1969), lipase activity was measured on an emulsified olive oil substrate and trypsin activity resulting from the canine enterokinase activation of the pancreatic juice was measured by the Bapna method of Erlanger *et al.* (1961). All measurements were made on 10 or 15 minute collections of pancreatic juice.

Results

A range of doses of venom was first given to three 10–11 kg dogs in order to establish a dose which produced an exocrine pancreatic response. Doses of 0.1 mg, 0.2 mg, 0.3 mg, 0.4 mg, and 1.0 mg produced no pancreatic response. In the 10 kg dog shown in Fig. 1, after an injection of 2.0 mg venom which evoked no pancreatic response, an injection of 4.0 mg (0.4 mg/kg) of venom evoked the following response: volume output 0.58 ml, amylase 1.1 KU, lipase 382 KU, and trypsin 8.9 mg.

In another animal with a basal unstimulated pancreatic output 0.42 ml, amylase 0.6 KU, lipase 47.7 KU, and trypsin 4.1 mg over a 10-minute period, the intravenous injection of 10 mg venom (1 mg/kg) increased the output in the following collection

Fig. 1 Pancreatic response to venom. Dog given 2.0 mg venom (0.2 mg/kg) at time 31 minutes followed by 4.0 mg venom (0.4 mg/kg) at time 46 minutes.

period to 0.92 ml volume, amylase 10.7 KU, lipase 198 KU, and trypsin 16.7 mg. In the following collection period the output fell to volume 0.09 ml, amylase 0.6 KU, lipase 43.7 KU, and trypsin 2.6 mg.

The pancreatic response in another dog to serial injections of 11 mg venom (1.0 mg/kg body weight) is shown in Figs. 2 and 3. The response in this animal is interesting in that it showed an increasing rate of enzyme secretion with repetition of the stimulus.

In the animal shown in Fig. 4, the pancreas was stimulated throughout the experiment by a continuous intravenous infusion secretin (Boots) 16 U/h. After an initial stabilisation period venom (1 mg/kg) was administered. A very slight increase in volume resulted but the enzyme output increased from 0.3 KU to 2.8 KU amylase. The concentration of the secreted enzyme increased from 0.15 KU to 1.1 KU/ml.

Discussion

The secretory effects of scorpion venoms on various

Fig. 2 Volume response to multiple injections of venom. Dog given 11 mg venom (1 mg/kg), at times indicated.

Fig. 3 Enzyme response to multiple injections of venom. Dog given venom, 11 mg (1 mg/kg) at times indicated

Fig. 4 Pancreatic response to venom during continuous infusion of secretin, 16 U/h. Venom, 10 mg (1 mg/kg), given at time 61 minutes.

glands have been reported. It is well known that scorpion venom causes increased salivary and lacrimal secretions (Bücherl and Buckley, 1971) and adrenal secretion (Henriques *et al.*, 1968) but no reports have ever been published on the effect of scorpion venom on pancreatic secretion.

The observation that acute pancreatitis frequently occurs in Trinidad after the sting of the scorpion *Tityus trinitatis* prompted the investigation of the effect of this venom on the exocrine pancreas. The results of this study on fasting anaesthetised dogs with cannulated ducts show that the crude venom is a pancreatic secretagogue evoking a juice that is rich in enzyme content. Against a background infusion of secretin 16 U/h the venom caused a very slight increase in flow but a significant increase of enzyme output and concentration.

Effects on other organs were observed during various stages of envenomation in this study—namely, salivation, lacrimation, and cardiac arrhythmias. Scorpion venoms are known to contain neurotoxins which result in the release of acetylcholine at the neuromuscular junction from post-

ganglionic parasympathetic neurons (Benoit and Mambrini, 1967; Diniz and Torres, 1968; Henriques *et al.*, 1968; Katz and Edwards, 1972; Gomez *et al.*, 1973) and the clinical syndrome resulting from scorpion poisoning and its rapidity of action reflect this.

The venom of *Tityus trinitatis* is shown in this study to evoke an exocrine pancreatic response slight in volume but rich in enzymes similar to that known to be evoked by acetylcholine. Accordingly, we suggest that the secretory action of the venom of *Tityus trinitatis* may also be caused by the release of acetylcholine from nerve endings to the pancreas.

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