Vasopressin in the Treatment of Acute Experimental Pancreatitis

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IT HAS BEEN established [5, 7, 12] that portal pressure falls after the administration of vasopressin. In 1960 we studied this effect and showed that after ligature of the portal trunk the sudden rise of pressure was counteracted by vasopressin while systemic arterial pressure was minimally affected.[18]

We then agreed with McMichael,[15] who in 1932 proposed that this effect was due to an increase in capillary (mesenteric) tone, which in turn decreased blood flow in the portal system.

Delaney and coworkers [6] attempted, by using radioisotopes, to measure in dogs changes in capillary or tissue blood flow in the stomach, esophagus, duodenum and pancreas during vasopressin administration (0.01 clinical units/Kg. body weight/minute). They found decreasing flow in the esophagus (−65%), stomach (−67%), duodenum (−43%) and pancreas (−83%). This considerable decrease in capillary flow in the pancreas together with the fact that vasopressin is used frequently in our department in cirrhosis of the liver with hemorrhage from esophageal varices etc. in which some affection of the pancreas might also be present aroused our curiosity as to the effect of vasopressin on pancreatitis.

We therefore investigated the effects of vasopressin infusion on experimentally induced acute pancreatitis.

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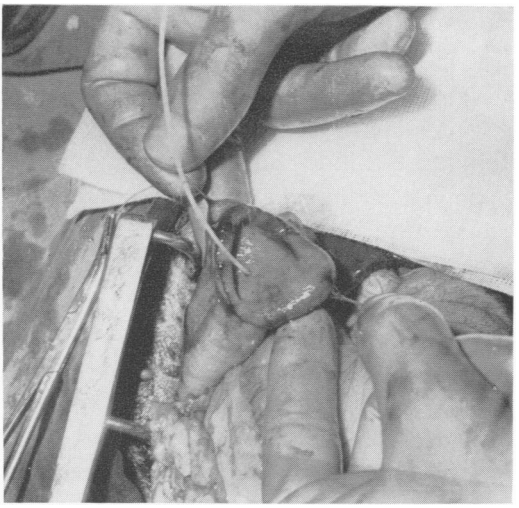

FIG. 1. Insertion of the catheter into the main pancreatic duct.

Material and Methods

Twenty mongrel dogs, weighing between 8 and 10 Kg. were used. After general anesthesia with thiopental sodium, a midline laparotomy was performed. Pancreatitis was produced by introduction into the main pancreatic duct of a mixture of 6 cc. of blood, 40,000 H.U.M. of trypsin * and 2 cc. of bile, under pressure of 200 mm. Hg (Fig. 1). This mixture was preserved for 24 hours before operation at a temperature of 30° C.[17]

At the same time, the femoral vein and artery were exposed and venous and ar-

* Trypsilin, Mochida Pharmaceutical Co. Ltd., Tokyo.

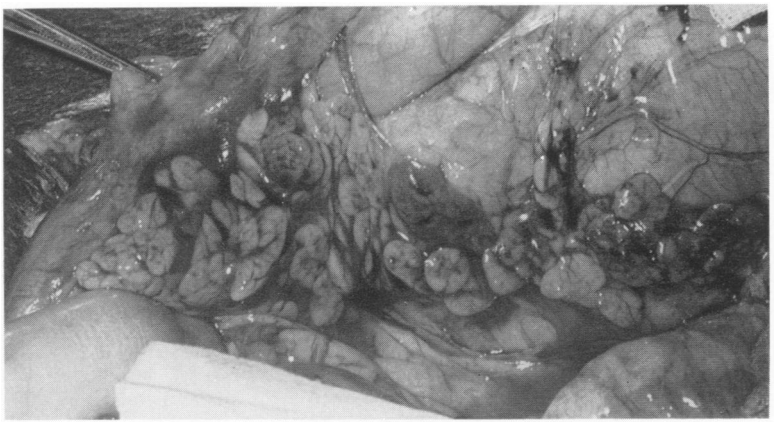

FIG. 2. Dog No. 11. Pancreas 15 minutes after infusion of the bile, blood and trypsin mixture.

terial pressures were recorded and electrolyte infusions and drugs were administered through the indwelling catheters.

Soon after infusion of the bile and trypsin mixture the pancreas showed extensive edema and within 15 to 30 minutes hemorrhagic areas also appeared (Fig. 2). Small biopsies from the tail of the pancreas (Fig. 3) showed edema and interlobular hemorrhagic infiltration.

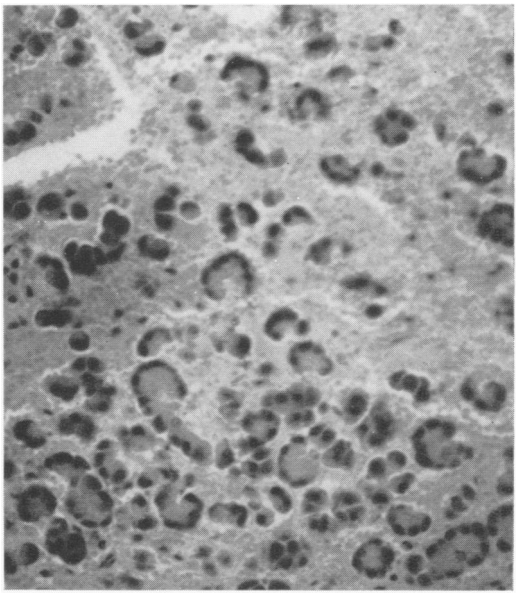

FIG. 3. Biopsy taken from the pancreas of dog No. 11 (Fig. 2), 20 minutes after the infusion. Diffuse inter and intralobular hemorrhagic infiltration (Hemat. and eosin H.P.).

The animals were divided in two groups. Group A were controls and dogs of group B were treated with vasopressin.

Group A, Controls was composed of 10 animals, to which after induction of pancreatitis and closure of the abdomen, dextrose and physiologic saline was given. All control animals died in severe shock, within 4 to 16 hours after the onset of the pancreatitis. The blood pressure began to fall progressively from the first minutes after operation while venous pressure remained at preoperative levels until shortly before death. Serum amylase levels fluctuated at elevated concentrations until death (Fig. 4). Postmortem examinations revealed large quantities of bloody fluid in the peritoneal cavity, and extensive congestion and edema of the abdominal organs and espe-

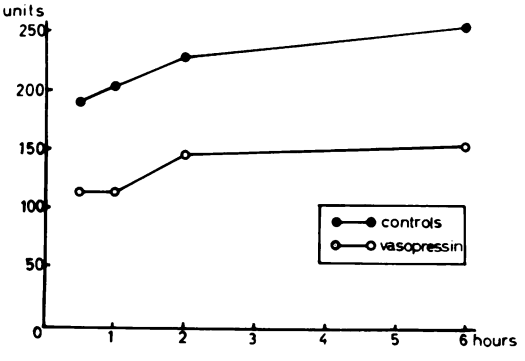

FIG. 4. Mean values of serum amylase (Wohlgemuth units) after induction of pancreatitis.

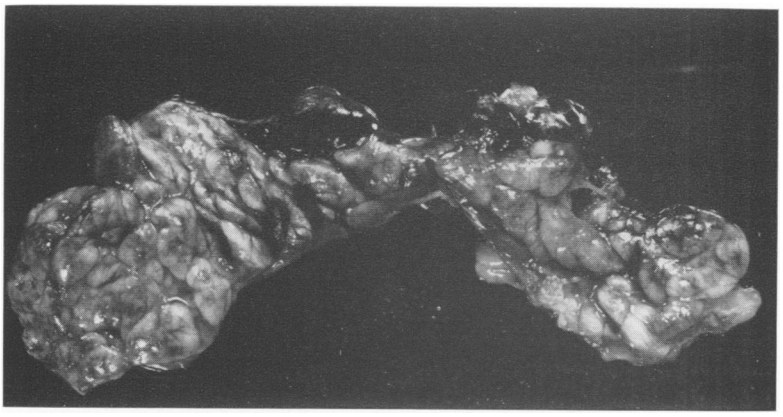

FIG. 5. Pancreas of dog No. 11 having died 11 hours after induction of pancreatitis.

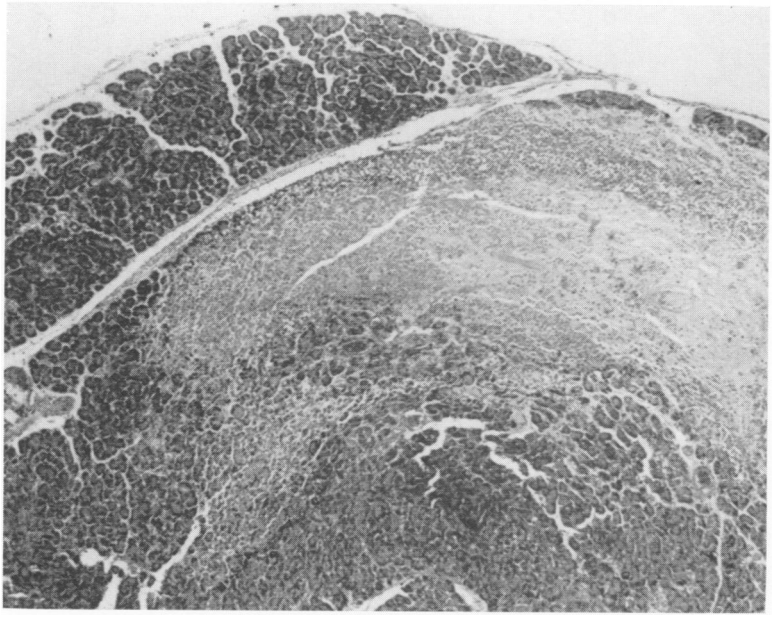

FIG. 6. Section of the pancreas shown in Fig. 5. Acute hemorrhagic and necrotic pancreatitis (Hemat. and eosin H.P.).

cially of the small intestine. The pancreas was usually dark red with necrotic areas of various sizes (Fig. 5). Microscopic sections showed severe hemorrhagic necrotic pancreatitis (Fig. 6).

Group B, parenteral administration of vasopressin.* These animals were given simultaneously with intraductal injection of the bile and trypsin mixture, 500 cc. of 5% Dextrose with 80 units of vasopressin intravenously. The solution was given over a period of 6 hours and was followed by intramuscular administration of 20 units of vasopressin every 4 hours, for the next 5 days. All the animals of this group awakened, stood up and walked about 8–12 hours after the operation and were able to take water or liquid nourishment 24 hours postoperatively.

Two dogs died 24 and 40 hours after operation. The postmortem examinations showed severe necrotic pancreatitis.

Four animals of this group were sacrificed every 3 days, while in excellent con-

* Pituitrin, Parke Davis & Company.

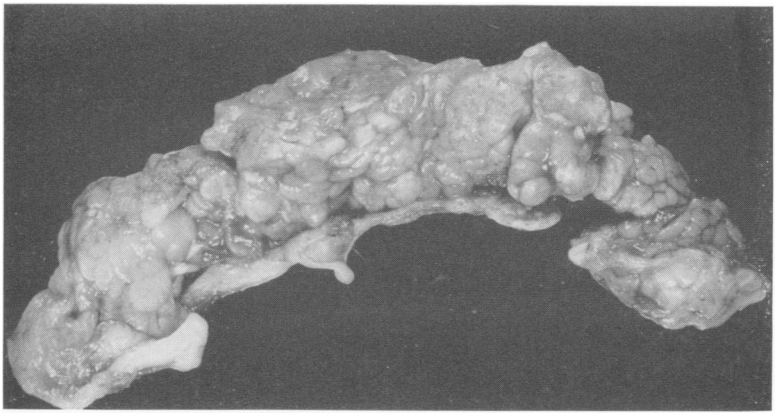

FIG. 7. Pancreas of dog No. 8, sacrificed on the 3rd day after induction of pancreatitis.

dition. Postmortem examinations revealed small quantities of turbid fluid in the peritoneal cavity and a relatively pale pancreas with scattered steatonecrotic areas (Fig. 7). Microscopic examination showed hemorrhagic pancreatitis entering the chronic stage (Fig. 8).

The four remaining dogs were sacrificed 10 days after operation while in excellent health and with normal serum amylase values. A transient elevation in serum amylase in the first 24 hours, was followed by a progressive fall. At postmortem the pancreas was pale and appeared almost normal (Fig. 9). Microscopic sections showed satisfactory preservation of the parenchyma and some increase of interstitial tissue and inflammatory infiltration with lymphocytes and some histiocytes (Fig. 10).

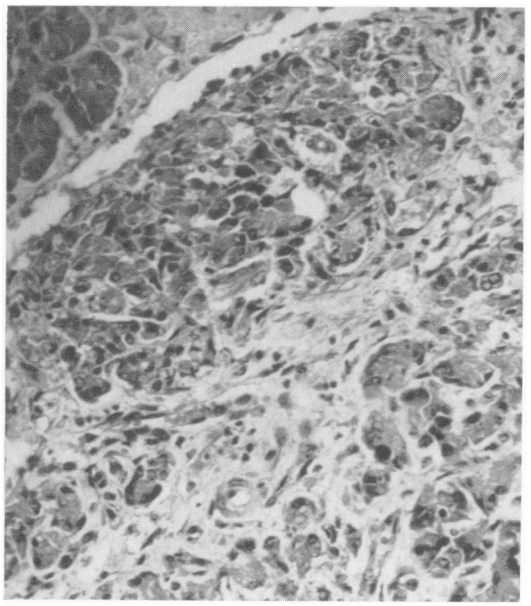

FIG. 8. Section of the pancreas shown in Fig. 7. Hemorrhagic pancreatitis entering a chronic phase (Hemat. and eosin, H.P.).

Mean amylase values, in the first 6 hours in all animals that were treated with vasopressin, were lower than those in controls (Fig. 4). Arterial blood pressures, during the first 6 hours when it was measured showed no significant fluctuations.

Discussion

Delaney *et al.*[6] observed that capillary blood flow in the pancreas decreases by 83% after administration of vasopressin. Our experiment was undertaken to study the effect of this hormone on the course of acute pancreatitis and with the belief that administration of vasopressin would have an adverse effect on the pancreas, because of decreased capillary blood flow. However the results showed the contrary. The course of the pancreatitis is more benign and survival is clearly much longer than in controls. We propose three probable explanations.

1. Vasopressin, by decreasing pancreatic blood flow, decreases secretion of activated enzymes into the systemic circulation and

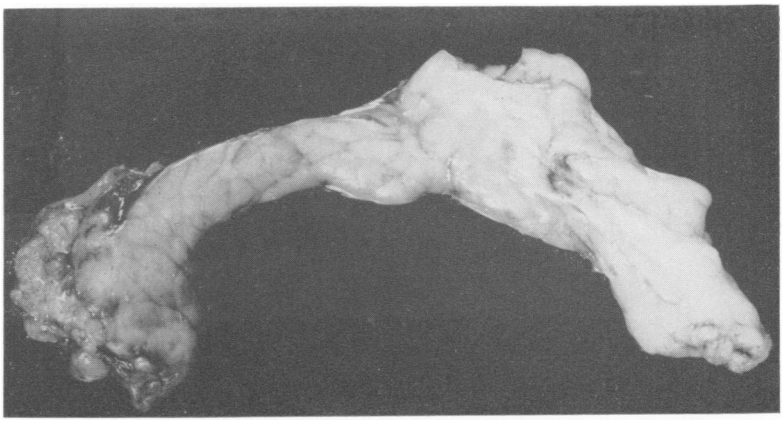

FIG. 9. Dog No. 12. Pancreas of dog sacrificed on the 10th day after induction of pancreatitis.

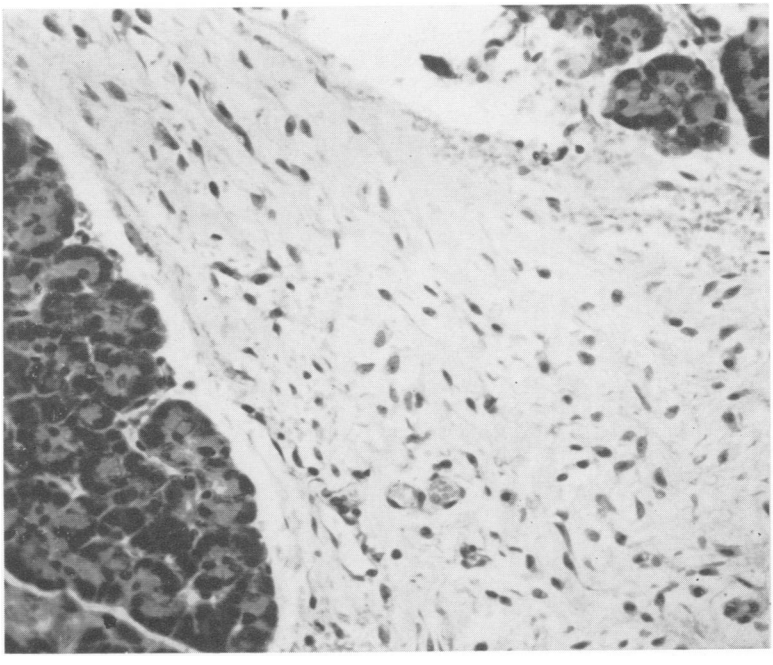

FIG. 10. Section of the pancreas shown in Fig. 9. Well preserved lobules and cellular infiltration of the interstitial connective tissue (Hemat. and eosin, H.P.).

thus the toxic reaction of shock is minimized. Enzyme values in control animals, in the first postoperative hours are higher than those of the treated animals.

2. Vasopressin probably possesses antishock properties. By its action on blood vessels it prevents both visceral stagnation of blood and the development of hypovolemia.

3. Vasopressin protects the animals from stasis in the portal system which occurs with acute pancreatitis. In the dog this is a frequent fatal complication and is probably due to metabolic acidosis and the production of toxic materials in the hypoxic gut.[1-4, 8-11, 13, 16]

We do not, as yet, have data to support any one explanation over another. Studies will continue in order to provide a more satisfactory explanation of the mode of action of vasopressin on acute experimental pancreatitis.

Summary

We have shown that vasopressin may be a useful substance in the treatment of the acute experimental pancreatitis in dogs. Survival of treated animals was longer than that of control animals. The probable mode of action of vasopressin is discussed.

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