Effect of Phenylbutazone on Acute Hemorrhagic Pancreatitis in Dogs

S N MATHUR, N ARORA, INDU CHOUHAN, R VANJANI
Departments of Surgery and Pathology, J L N Medical College and Hospital, Ajmer 305 001

Abstract
Experiments were conducted on 24 mongrel dogs to study the effect of phenylbutazone on acute experimental pancreatitis. Necrotic—hemorrhagic pancreatitis was produced by local infiltration of autologous bile. The severity of pancreatitis was assessed by biochemical estimation and histopathological examination. Pretreatment with phenylbutazone reduced the severity of pancreatitis, both biochemically and histologically (total score 6.0 ± 1.52 in the test group vs 8.33 ± 1.80 in the control group; p < 0.01).

Key Words: Pancreatitis, phenylbutazone.

Introduction
The pathologic spectrum in acute pancreatitis ranges from minimal oedema to severe necrotic—hemorrhagic pancreatitis. While drugs like glucagon, apritin and corticosteroids have failed to produce a consistent beneficial effect in acute pancreatitis, a non-steroidal anti-inflammatory drug, oxphenbutazone, has been reported to protect dogs from pancreatitis produced by the closed duodenal loop technique.1 Similarly, increased survival in rats has been reported with the use of indomethacin.2

Recently, Loughie et al3 studied the effect of phenylbutazone on severe necrotic—hemorrhagic pancreatitis produced in the rat by intraductal injection of trypsin and reported that phenylbutazone pretreatment did not alter the mortality rate but reduced the severity of pancreatitis. They suggested that the effect of the drug seemed to be related to its anti-inflammatory properties independent of prostaglandin synthesis. The present study was undertaken to evaluate the role of phenylbutazone, if any, in reducing the severity of pancreatitis, and also to evaluate if the drug produced any changes in the levels of serum calcium, bilirubin and amylase.

Material and Methods
Twenty-four mongrel dogs of either sex, weighing approximately 14-24 kg, were used. The animals were divided into two groups of twelve animals each. Control animals were not given the test drug. Test animals were given phenylbutazone in a dose of 50 mg/kg body weight, eight hours and one hour before induction of pancreatitis.

Induction of Pancreatitis
The animals underwent midline laparotomy under general anaesthesia and full asepsis. The gall bladder was exposed and, after applying purse-string suture, about 5-7 ml of bile was aspirated. To induce pancreatitis 0.5 ml of autologous bile was injected locally at four points at equal distances. The abdomen was closed in layers. After 48 hours, both the control and test animals were re-explored and underwent pancreatic-duodenectomy. The tissue specimens were examined histopathologically.

Biochemical Estimations
Blood samples were collected and analysed for serum amylase, bilirubin and calcium levels at the time of induction of pancreatitis and at reexploration.

Histological Quantitation
Grading of various histological types of pancreatitis was done as follows, with scores ranging from 1 to 3 in each type.

Grade I: No pancreatitis; normal acinar pattern, no inflammatory changes in peripancreatic region.

Grade II: Peripancreatitis; inflammatory exudate in the peripancreatic area.

Grade III: Interstitial pancreatitis; interstitial oedema with mononuclear interstitial infiltration.

Grade IV: Septal pancreatitis; intra and interlobular septal acute and chronic inflammatory exudate with necrosis of parenchymal cells.

Grade V: Hemorrhagic pancreatitis; areas of inter and intralobular hemorrhages.

The score for each histopathological pattern was calculated, the highest possible score for an individual dog being twelve. All histological sections were examined thoroughly and independently without prior knowledge of pretreatment.

Results

Biochemical Estimations
Hyperamylasemia was observed in all the animals. In the control animals serum amylase levels rose from 73 ± 11·06 Somogyi units before induction to 1,040 ± 152 after 48 hours. In test animals corresponding levels
were $71 \pm 0.69$ and $803 \pm 281$. The rise in amylase levels in the test group was less marked, but the difference from the control group was not significant ($p > 0.05$; NS).

Serum bilirubin levels rose in both the groups: from $0.48 \pm 0.17$ mg/dl before induction to $2.00 \pm 0.85$ mg/dl after 48 hours after in control animals, and from $0.32 \pm 0.20$ to $1.63 \pm 0.44$ in test animals. This rise in the control animals was insignificantly higher ($p > 0.10$; NS).

Control animals showed serum calcium levels of $10.00 \pm 0.56$ mg/dl before induction and $9.68 \pm 0.30$ after 48 hours. Test animals showed corresponding levels of $10.03 \pm 0.88$ and $9.53 \pm 0.56$. The fall in calcium levels in test animals was not significantly different ($p > 0.10$; NS).

**Histopathology**

An average histological score of $8.33 \pm 1.80$ was observed in control animals and $6.0 \pm 1.72$ in test animals ($p < 0.01$).

**Discussion**

Experimental acute pancreatitis can be produced in animals either by creating a closed duodenal loop or by injecting various substances into the pancreatic duct under pressure. The closed loop technique produces interstitial pancreatitis, which is consistent in its development and varies in its severity. Local infiltration of autologous bile produces necrotic-hemorrhagic pancreatitis of mild to moderate severity. The method is inexpensive and simple, the complications of surgery are minimal and pancreatitis of required severity can be achieved by varying the amount of bile injected.

The severity of pancreatic damage in experimental pancreatitis has been graded histologically in various experimental studies by the use of histological scoring systems. In the present study, phenylbutazone pre-treatment reduced the histological severity of pancreatitis.

Serum amylase levels rise within two to twelve hours of the onset of symptoms of pancreatitis, reaching a peak within 24 to 48 hours and returning to normal within three or four days. Mild jaundice occurs in 20%—30% of patients and usually appears on the second day. Hypocalcemia is also a feature of acute pancreatitis. Phenylbutazone pretreatment caused a less marked and nonsignificant alteration of all the above parameters in our study.

Among non steroidal anti-inflammatory drugs, oxyphenbutazone and indomethacin have earlier been shown to be beneficial in acute pancreatitis. Phenylbutazone pretreatment resulted in reduced severity of acute hemorrhagic pancreatitis in our study and an earlier one.

**References**