EFFECT OF DIBUTYLTIN DICHLORIDE ON LIPASE AND AMYLASE ACTIVITY IN SERUM AND PANCREAS OF RATS

S. Kümmel, H.-G. Haufe, J. Merkord and G. Hennighausen*

Institute of Pharmacology and Toxicology, University of Rostock, Schillingallee 70,
D - 18055 Rostock

Abstract

Dibutyltin dichloride (DBTC) induces a pancreatitis in rats after single administration of 4 mg/kg i.v. or 30 mg/kg DBTC p.o. The pathohistological characterization of the toxic effects of DBTC on the pancreas was completed by pathobiochemical parameters. 24 hours after administration of DBTC the activities of amylase and lipase were increased in serum but not in pancreas tissue of male rats. Together with the pathohistological findings this data indicate that DBTC induces an interstitial pancreatitis, which may be of interest as a simple experimental model of pancreatitis.

Introduction

A pancreatitis induced by chemical compounds is of increasing toxicological and experimental interest. In studies of toxic effects of DBTC on bile ducts and on the biliary excretion of organotin in mice and rats (Barnes and Magee 1958, Hennighausen et al. 1980, Merkord et al. 1982 and 1991) signs of acute pancreatitis were observed (Merkord et al. 1989 and 1991). Electron microscopically the first ultrastructural changes were visible 6 hours after administration of a single dose of DBTC (6 mg/kg body weight), consisting in an enlargement of Golgi cisterns, numerous electron dense autophagosomes, residual bodies and myelin figures in the mitochondrial matrix. One day after treatment acute interstitial pancreatitis has been developed. In the present paper the enzyme activities of amylase and lipase in serum and pancreas in male rats after single administration of DBTC are described. In addition we examined the effect of DBTC after oral administration. Beside pathobiochemical characterization of interstitial pancreatitis induced by DBTC these data are of interest to the development of an experimental model of pancreatitis.

Material and Methods

Male rats (Rozt: Wistar) weighing 80 - 120 g have been used in this study. For intravenous administration (4 mg/kg body weight) DBTC (Schering AG, Berlin) was first dissolved in 100 % ethanol (2 parts) and then mixed with glycerol (3 parts). The control group of animals have got the solvent. The animals were starved 24 hours prior to the experiments and were killed 4, 8, 12, 16, 20 and 24 hours after the treatment. For oral administration (30 mg/kg body weight) DBTC was dissolved in vegetable oil. The animals were killed 24, 48 and 96 hours after treatment. The pancreatic tissue was fixed in calcium-formalin and processed for haematoxylin and eosin. Blood samples were collected and the activities of amylase and lipase in serum and in pancreas tissue were estimated with test kits of Boehringer/Mannheim GmbH (4, 5). The significance was calculated by Student's t-Test.

Results

After intravenous treatment of rats with DBTC an significant increase of amylase activity was observed (Fig. 1).

Fig. 1 Activity of serum amylase in rats after administration of solvent and of DBTC (i.v., 4 mg/kg) ■ DBTC, ▨ control; $\bar{x} \pm s_x$, $n = 7 - 13$, * $p < 0,05$

The maximum was reached after 20 hours (Fig. 1). The level of lipase activity in serum showed an increase after 8 hours with a maximum after 20 hours (Fig. 2). Both enzyme activities decreased 24 hours after application of DBTC.

The estimation of enzyme activity in rat pancreas tissue after intravenous DBTC-administration showed no significant difference of amylase level between control group and DBTC treated rats. The level of lipase activity was increased only 8 hours after DBTC treatment.

In the histopathological examination of pancreas tissue by light microscopy 12 and 16 hours after intravenous DBTC administration a oedema of pancreas and an enlargement of the acinar ducts were observed. After 24 hours an inflammatory infiltration was developed with eosinophilic granulocytes, histiocytes, lymphocytes and plasma cells (Fig. 3).

24 hours after oral administration of DBTC an increase of amylase activity in rat serum was observed. After 48 and 96 hours we found normal amylase activities. The lipase activity showed after 24 hours a significant elevation and decreased to control level until 96 hours after treatment.

Fig. 2 Activity of serum lipase in rat after administration of solvent and of DBTC (i.v., 4 mg/kg) [DBTC, control; $\bar{x} \pm s_x$, $n = 7 - 13$, $*p < 0,05$]

Fig. 3 Pancreas of rat with bilio-pancreatic duct 24 hours after DBTC administration (i.v., 4 mg/kg)

Discussion

In several studies about the effects of DBTC injuries of rat pancreas has been observed (1, 2, 3). Merkord et al. described an acute interstitial pancreatitis after intravenous DBTC administration (2, 3). The present paper characterize some pathobiochemical parameters of this pancreatitis. The increase of amylase and lipase activity in rat serum is an important sign of the DBTC induced pancreatitis during the first 24 hours. The lipase activity in serum seems to be more sensitive to indicate the start of interstitial pancreatitis. There were no changes of amylase and lipase activities in pancreas tissue after treatment of rats with 4 mg/kg of DBTC i.v. The interstitial pancreatitis is considered as initial step of pancreatitis. The use of the DBTC induced pancreatitis as a simple experimental model of pancreatitis is under further investigation.

Acknowledgement: The authors wish to thank Mrs. Dipl.-Pharm. Hausmann for the good cooperation at the examination in the pancreatic tissue and Mrs. Neumann for her expert technical assistance.

References

1. Barnes, J.M. and Magee, P.N. (1958) The biliary and hepatic lesions produced experimentally by dibutyltin salts, *J. Pathol. & Bacteriol.* 75, 267 - 279
2. Merkord, J. and Hennighausen, G. (1989) Acute pancreatitis and bile duct lesions in rat induced by dibutyltin dichloride, *Exp. Pathol.* 36, 59 - 62
3. Merkord, J., Jonas, L. and Hennighausen, G. (1991) Morphological lesions of pancreas and bile duct in rats induced by dibutyltin dichloride (DBTC), *Arch. Toxicol., Suppl.* 14, 75 - 79
4. Neumann, U. and Ziegenhorn, J. (1978) in: *Organisation des Laboratoires-Biologie Prospektive, IV^e Colloque du Pont-a-Mousson*, S. 627
5. Rauscher, E., Neumann, U., Schaich, E., v. Bülow, S. and Wahlefeld, A.W. (1985), *Clin. Chem.* 31, 14 - 19

**Received: August 13, 1993 - Accepted: September 20, 1993 -
Accepted in revised camera-ready format: December 12, 1993**