

Acute pancreatitis complicating excessive intake of phenolphthalein

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Summary

A case is described in which a patient presented with acute pancreatitis following inadvertent ingestion of large quantities of phenolphthalein for the treatment of his chronic constipation. There was complete recovery and no sequelae from the acute attack of pancreatitis.

KEY WORDS: pancreatitis, phenolphthalein.

Introduction

The cathartic effect of phenolphthalein was discovered in 1902 by Vamossy, during a study undertaken by the Hungarian government to determine its safety as an additive for identification of artificial wines. His observations were published after he had been unsuccessful in attempting to produce toxic effects in himself, his associates and a variety of animals. Since that time, phenolphthalein has been widely employed as a cathartic. A number of side effects have been reported, including encephalitis (Kendal, 1954), vomiting with intestinal colic (Knox, 1958), epidermal necrolysis (Potter, 1960) and erythema multiforme (Baer and Harris, 1967). The complication of acute pancreatitis has not previously been reported.

Case report

A 34-year-old scaffolder was admitted in October 1982 with a 24-hr history of severe epigastric pain radiating to the back, nausea, vomiting and urine discolouration. There was no history of alcoholism, biliary disease or infection, and his only medication was phenolphthalein, which he had been taking for the past 2 years for the treatment of chronic constipation. Forty-eight hours before admission he inadvertently took 2 g of phenolphthalein in the purified form.

On examination he looked unwell, pyrexial and jaundiced. There was generalized abdominal tenderness and guarding with reduced bowel sounds. Investigations on admission showed a raised serum

bilirubin; (120 $\mu\text{mol/l}$), negative Australian antigen and an amylase of 4,000 iu/l. There was a leucocytosis of $14 \times 10^9/\text{l}$, 89% of which were neutrophils. His serum calcium and gamma glutamyl transpeptidase, fasting blood lipids and viral screening were all normal. Radiological investigations including plain X-rays, oral cholecystogram and hepato-biliary scintigraphy with HIDA were normal. An ultrasound examination of the liver and gallbladder failed to show any abnormality. His urine was red in colour and had an alkaline pH. Haemoglobin pigment testing was negative and acid/alkali titration confirmed the presence of phenolphthalein. Treatment of the patient was conservative with bed rest, chest physiotherapy, analgesia, nasogastric intubation and intravenous fluids. His serum amylase returned to normal in 48 hr and his serum bilirubin in 72 hr.

Endoscopic retrograde cholangiopancreatography examination carried out during the convalescent period was reported as normal. The patient remains well to date and has not used phenolphthalein again.

Discussion

Dihydrocycphthalophenone, α -di(p-hydroxyphenyl)phthalide, $\text{C}_{20}\text{H}_{14}\text{O}_4=318.3$, is a diphenylmethane cathartic. It is practically insoluble in water and is available in the purified white or faintly yellow impurified preparation. Up to 15% of the therapeutic dose of phenolphthalein is absorbed. The remainder is excreted in the faeces. The absorbed portion is largely eliminated by the kidney, most of it in conjugated form. Some of the drug absorbed from the intestine may be excreted in the bile and the resulting enterohepatic circulation may contribute to prolongation of the cathartic effect of the drug.

The mechanism of pancreatitis itself has never been fully elucidated. There are a number of suggested explanations including (Bockus, 1969) blockage of the ampulla of Vater, leading to reflux of bile into the pancreatic duct causing an increase in the ductal pressure, which in turn leads to rupture of acini. Another theory is that the pancreatic duct

becomes blocked by epithelial metaplasia. A virus (because of the association of mumps with acute pancreatitis), reflux of the duodenal contents of the pancreatic duct, and thrombosis in the pancreatic vessels leading to infarction of the pancreas with resulting release of the pancreatic juices (Hueper, 1927), have all been postulated as possible causes.

In addition to cases in which ingestion of phenolphthalein has been followed by toxic effects, many cases have been reported in which large amounts of the drug have been taken with no untoward effects. While it is clear, therefore, that phenolphthalein does not exert a direct toxic action, the well-documented reports of skin reactions indicate that it is capable of producing a hypersensitivity reaction. Post-mortem examination of a fatal case of encephalitis after phenolphthalein ingestion (Kendal, 1954) showed haemorrhagic areas throughout the length of the intestine, in the kidneys, the liver and the brain. If hypersensitivity is to be dismissed, then the possibility of a direct toxic effect on the acini must be

considered, as some of the drug finds its way into the bile by means of the enterohepatic circulation and can enter the pancreatic duct system.

The relationship of the ingestion of phenolphthalein to the subsequent pancreatitis in this case may have been coincidental, but the possibility of it being the cause cannot be denied.

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