Effect of cysteamine on bile secretion in the rat

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Abstract:
The effect of cysteamine, a specific somatostatin depletor, on biliary secretion was studied in urethane-anesthetized rats. Different groups of rats received ip cysteamine at 25, 100 or 340 mg/kg just before bile collection commenced. Other groups of rats were pretreated with cysteamine (340 mg/kg ip) at 4 or 24 h prior to bile duct cannulation and bile collection. Bile secretions were collected at 30-min intervals for 4 h after bile duct cannulation. Total proteins, cholesterol, total lipids, glucose and several hepatic enzymes were assessed in bile. Results indicated that basal bile secretion was only slightly reduced and tended to decrease after drug administration (~13% decrease after 340 mg/kg). Cysteamine induced dose-dependent decrease in protein secretion, and the maximum effect was reached at a dose of 340 mg/kg. The effect of cysteamine on protein secretion was prolonged, since it was still observed 24 h after the treatment with cysteamine. Cholesterol and lipid secretion was inhibited by 52.5 and 42.5%, respectively, by the drug, with the latter effect being evident 24 h after drug administration. In addition, the drug inhibited biliary glucose and aspartate aminotransferase concentrations, but increased that of alkaline phosphatase. The results suggest that acute administration of cysteamine inhibits protein, cholesterol and lipid secretion into bile.

Key words:
cysteamine, bile secretion, somatostatin, rat

Introduction

Cysteamine (2-aminoethanethiol) is a natural product of mammalian cells forming the terminal region of the acetyl-coenzyme A molecule, where it is linked to the pantothenic acid moiety by a peptide bond. Cysteamine arises by enzymatic degradation of acetyl-coenzyme A via the action of the enzyme pantetheinase [28]. Cysteamine has many clinical applications, namely it has been used as a radioprotective agent [31], in the management of acetaminophen hepatotoxicity [19] and currently is the only available treatment for nephropathic cystinosis, a lysosomal storage disease leading to renal insufficiency in many cases early in childhood [11].

One important property of cysteamine is that its systemic or local administration causes a rapid and selective depletion of neuropeptide somatostatin from the brain, peripheral tissues and endocrine cells [17, 26, 27]. The drug most likely modifies chemically the disulfide group of the somatostatin molecule in tissue granules rendering it biologically and immunologically unreactive [17]. Somatostatin is widely distributed throughout the central and peripheral nervous systems, the gastrointestinal tract as well as in various peripheral organs. The gastrointestinal tract contains about 70% of the total body somatostatin, which is found in neurons and fibers of both the submucosal and the myenteric plexus and the pancreas as well as in the D cells of the stomach, gut and pancreatic islets [13]. Somatostatin might act as a putative neurotrans-