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Octreotide inhibits hepatic cystogenesis in a rodent model of polycystic liver disease by reducing cholangiocyte adenosine 3',5'-cyclic monophosphate.

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BACKGROUND AND AIMS: In polycystic liver diseases (PCLDs), increased cholangiocyte proliferation and fluid secretion are key features and cholangiocyte adenosine 3',5'-cyclic monophosphate (cAMP) is an important regulator of these processes. Thus, we assessed cAMP levels and evaluated octreotide (an analogue of somatostatin known to inhibit cAMP) in hepatic cyst growth using an in vitro model of cystogenesis and an in vivo animal model of autosomal recessive polycystic kidney disease (ARPKD), one of the PCLDs. METHODS: Expression of somatostatin receptors (SSTRs) was assessed by reverse-transcription polymerase chain reaction and confocal microscopy in cholangiocytes from normal and polycystic kidney (PCK) rats, the ARPKD model of autosomal recessive polycystic kidney disease. Effects of octreotide on cAMP levels and cyst expansion were studied in vitro using PCK bile ducts grown in 3-dimensional culture. The effects of octreotide on hepatic and renal cystogenesis were investigated in PCK rats in vivo. RESULTS: In cholangiocytes and serum of PCK rats, cAMP concentrations were approximately 2 times higher than in normal rats. SSTR subtypes that bind octreotide (ie, SSTR2, SSTR3, and SSTR5) were expressed in both normal and PCK cholangiocytes. In vitro, octreotide inhibited cAMP levels by 35% and reduced cyst growth by 44%. In vivo, octreotide lowered cAMP content in cholangiocytes and serum by 32%-39% and inhibited hepatic disease progression, leading to 22%-60% reductions in liver weight, cyst volume, hepatic fibrosis, and mitotic indices. Similar effects were observed in kidneys of PCK rats. CONCLUSIONS: This preclinical study provides a strong rationale for assessing the potential value of octreotide in the treatment of PCLDs.

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