Increased polyamine (PA) catabolism has been shown to induce acute pancreatitis (AP) in animals, and this effect can be prevented by blocking hyper-catabolism. We hypothesized that SBP-101 (diethyl-dihydroxyhomospermine), a synthetic analog of spermine that reduces intracellular PA pools, could attenuate AP. This study sought to characterize effects of SBP-101 in AP utilizing the biphasic effects of cerulein-uniformity. SBP-101 has two distinct potencies, acting as a PA catabolizer (at 3 mg/kg) or as a PA antagonist (at 10 mg/kg), as determined by polyamine analysis. SBP-101 was found to be effective in reducing polyamine pools, reducing acute pancreatitis in two animal models. SBP-101 administration to cerulein-induced AP mice reduced serum enzymes, amylase, and lipase, tissue injury, and overall histologic severity as compared to the Cer control. Histological analysis showed that SBP-101 (10 mg/kg) was effective in both the pancreas and the other AP-injured tissues. These data suggest that SBP-101 may be a novel therapeutic agent for the treatment of acute pancreatitis.

Methods

Acute Pancreatitis was induced in C57BL/6 mice with 100 nmol intraperitoneal injection of cerulein (Cer). Mice were then randomized into four groups (SBP-101 0.1 mg/kg, 1 mg/kg, Cer alone, or saline control). Six hours post-Cer injection, mice were euthanized and their sera were collected. Pancreatic tissue was collected and stained with hematoxylin and eosin for histological analysis. The severity of pancreatitis was scored using a modified scoring system.

Results

SBP-101 (10 mg/kg) significantly reduced serum amylase and lipase levels, pancreatic tissue injury, and overall histologic severity as compared to the Cer control. Histological analysis showed that SBP-101 (10 mg/kg) was effective in both the pancreas and the other AP-injured tissues. These data suggest that SBP-101 may be a novel therapeutic agent for the treatment of acute pancreatitis.