Pancreat Disord Ther 2017, 7:3 (Suppl) DOI: 10.4172/2165-7092-C1-006

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2nd Intenational Conference on

PANCREATIC DISORDERS & TREATMENT

September 13-14, 2017 Dallas, USA

Role of melatonin and its metabolite AFMK in the pancreatic protection and pancreatic exocrine function

Jaworek J Szklarczyk J, Kot M, Nawrot-Porabka K, Bonior J, Góralska M, Leja-Szpak A and Pierzchalski P Jagiellonian University Medical College, Poland

elatonin is well known as pancreatic protector, and pancreatic secretagogue but the effects of melatonin metabolite: ▲N1-acetyl-N2-formyl-5methoxykynuramine (AFMK) on acute pancreatitis and on pancreatic amylase secretion was not known. The aim of this study was to compare the effects of melatonin and its metabolite: AFMK on caerulein-induced pancreatitis (AP) and amylase secretion in the wistar rats. AP was induced by subcutaneous caerulein infusion (25 microgram/ kg). Melatonin or AFMK were given intraperitoneally to the rats prior to the induction of AP. For in vitro study pancreatic acinar cell line AR42J were used. Secretory studies were conducted on Wistar rats equipped with pancreatic cannulas pancreatic secretion was stimulated with diversion of pancreato-biliary juice (DPBJ). In this part of the study the lorglumide, the CCK1 receptor antagonist was administered to assess the involvement of CCK in the secretory effect of investigated substances. Both melatonin and AFMK significantly diminished histological manifestations of AP, decreased amylase and TNF alpha blood levels, reduced lipid peroxidation and augmented antioxidant enzyme in the pancreas of AP rats. In AR42J cells melatonin and AFMK alone or combined with caerulein markedly increased protein signals for heat shock protein (HSP60), and reduced that for TNF alpha. Administration of melatonin or AFMK resulted in dose-dependent increases of pancreatic amylase secretion. These changes in amylase outputs were accompanied by significant increase of CCK plasma levels. Pretreatment with CCK1 receptor blocker completely abolished above secretory effects of AFMK and melatonin on pancreatic exocrine function. From this we can conclude that AFMK and melatonin attenuated acute pancreatitis working as the neutralizers of free radicals, and activators of antioxidant enzyme. AFMK is probably involved in considerable part of beneficial effect of melatonin on the pancreas as part of its scavenging cascade. Administration of both AFMK and melatonin significantly stimulated pancreatic amylase secretion and this stimulation is probably dependent on the release of CCK by these substances.

mpjawore@cyf-kr.edu.pl