Summary of the work

Dariel Thereska
Dr.med

The effects of incretin mimetic Exenatide and DPP-4 inhibitor Sitagliptine in mild acute experimental pancreatitis

Promotionsfach: Chirurgie
Doktorvater: Prof. Dr. med. Jens Werner

Incretins are a new class of pharmacological agents with antihyperglycemic actions that mimic effects of endogenous incretin hormones, including glucose-dependent enhancement of insulin secretion, used for DMTII treatment. Dipeptidyl peptidase-4 (DPP-4) inhibitors, increase blood concentration of the incretin GLP-1. The two best known representatives of these two subgroups are Exenatide and Sitagliptine respectively. Over the last years, there have been several reports associating acute pancreatitis (AP) with the use of Exenatide and Sitagliptine, but this association is still controversial.

Our aim was to investigate whether exenatide and sitagliptine influence the course of mild acute pancreatitis by evaluating the histological and biochemical effects of these two drugs in a rat experimental model of mild AP.

Our pilot study also evaluated potential adverse effect of these two drugs in healthy animals. In this study, 18 rats were divided into 3 groups (control, control + exenatide, control + sitagliptine) and were observed for 24 hours.Our pilot study shows that there is no adverse effect of these two drugs on healthy control animals. In this pilot study, we evaluated histological, biochemical and enzymatic parameters of local and systemic injury and we did not note any negative effect of exenatide and sitagliptine in healthy subjects. Especially, no animal developed any sign of acute pancreatitis or any form of pancreatic injury.

The goal of the present study was to evaluate the consequences of the administration of Exenatide and Sitagliptine during AP. We selected the cerulein pancreatitis model to induce mild acute pancreatitis in rats. For this study, 21 rats were divided into 3 groups (mild pancreatitis, mild pancreatitis + exenatide, mild pancreatitis + sitagliptine) and were observed over 24 hours. The effects of these drugs were evaluated by histomorphological and biochemical parameters in pancreatic-tissue, lung-tissue and in serum. Enzymes which were

measured included: amylase, lipase, SGOT, SGPT, LDH, creatinine, urea, and MPO activity. For none of the parameters measured, neither the histologic scoring of pancreas or lungs, nor any laboratory value, a significant difference of the two treatment groups compared to control group was found. Thus the two drugs do not negatively influence the course of pancreatitis

Taking all these results together, we can conclude that exenatide and sitagliptine, generally do not induce A.P and do not affect the course of mild experimental pancreatitis.