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Use Of Intra-pancreatic Injection Of Penicillin G As An Attractive Strategy Against POPF: A Porcine Experiment

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Background : Postoperative pancreatic fistula (POPF) is one of the most fatal complications following pancreatic surgery. Soft pancreatic texture is constantly mentioned as one of the most contributory predictors of POPF. Soft pancreas has poor SHC and higher incidence of parenchymal tearing, frequently leading to POPF. We previously validated that intrapancreatic injection of penicillin G can enhance hardness and suture holding capacity (SHC) of the pancreas through prompting the fibrosis process in the mouse model. We were herein intended to validate whether intrapancreatic injection of penicillin G has the potential of significantly decreasing the incidence and severity of POPF in the porcine model.

Methods : After general anesthesia, pancreaticojejunostomy was performed in the pig model. Jackson-Pratt (JP) drains were inserted to the site of pancreaticojejunostomy and were fixed extraperitoneally. Serial amylase level from JP drain was determined on the daily basis. On the determined day, the pigs were euthanized and the histologic characteritics of pancreas specimens were determined using Massion-trichrome and special immunohistochemical stains.

Results : Penicillin-G injected pig groups exhibited the significantly decreased levels of amylase measured in the JP drains ($P < 0.05$). It was found that the intrapancreatic injection of penicillin G activated human pancreatic stellate cells (HPSCs) to produce various fibrotic materials such as transforming growth factor-β1 (TGF-β1) and metalloproteinases-2. The pancreatic hardness and SHC were increased to the maximum at the second day after injection and then it gradually subsided demonstrating its reversibility.

Conclusions : Intra-parenchymal injection of penicillin G promoted pancreatic hardness and SHC. Moreover, intra-parenchymal injection of penicillin G exhibited the potential of decreasing POPF in the pig model. The causing mechanism could be attributed to the enhanced fibrogenic potential by activating TGF-β1 signaling pathway. Therefore, intra-parenchymal injection of penicillin G could be could be utilized to prevent and minimize POPF during pancreatic surgery after safety profiles were fulfilled in the further studies.

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