Dipeptidyl peptidase-4 (DPP-4) is an enzyme responsible for the degradation and inactivation of incretins such as GLP-1 and GIP. Vildagliptin (VG), a new inhibitor of DPP-4, increases glucose depended insulin secretion by increasing GLP1 and regulates plasma glucose levels (1,2). We aimed to observe the effects of long and short term VG treatment on possible beta cell regeneration, apoptosis and regulation of islet morphology in neonatal streptozotocin (STZ) diabetic rats.

In this study three groups including control group, diabetic (n2STZ) group and treatment (n2STZ+VG) group were recruited for 36 neonatal rats. STZ (100 mg/kg,ip) were injected to n2STZ and n2STZ+VG group in the second day after birth. VG (60 mg/kg/day,orally) was administered to n2STZ+VG group during 8 and 28 days. The pancreatic tissue sections were immunostained using insulin, glucagon, somatostatin and PCNA antibodies. TUNEL method was performed for apoptosis. Body weights and blood glucose levels were measured at 10th and 30th days. All data were analyzed with statistical methods.

Blood glucose levels in n2STZ groups were significantly increased compared to control in 10 (p<0.001), n2STZ+VG group were significantly lower (p<0.01) compared to n2STZ groups in 30 days old rats. Islet size and number in n2STZ groups were detected decreasing compared to control and n2STZ+VG groups in both term groups. Immunopositive insulin cells and beta cell clusters were scattered in exocrine tissues and duct epithelia, and area of insulin (+) cells and islets size increased in n2STZ+VG groups compared to n2STZ groups in both 10 and 30 days old rats (respectively p<0.001, p<0.05). In n2STZ groups, glucagon and somatostatin immunopositive cells were significantly increased within the islets compared to n2STZ+ VG and control groups in both short and long term groups (p<0.001). In 10 and 30 days old rats, number of PCNA immunopositive cells within the islets in n2STZ+ VG group was significantly higher than n2STZ and control groups (p<0.001). In 10 days old rats, apoptotic cells number of islets in n2-STZ+ VG and control groups was lower than n2-STZ group (p<0.001). Apoptotic cells were observed within exocrine tissue cells and duct epithelium, but there was no significant difference in 30 days old rats for all groups.

The results show that vildagliptin as a DPP4 inhibitor promotes beta cell neogenesis from duct epithelium or acinar cells by inducing some of the endocrine progenitor cells, induces islet cells proliferation by increasing the expression of PCNA, and reduces apoptosis in the islets, also regulates morphological reorganization of the islets in the STZ diabetic neonatal rats.


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Fig. 1: Immunolocalization of insulin in the pancreas of all groups. A, D Control Group. B, E n2STZ Group. C, F n2STZ+VG Group. Upper: 10 days old rats, bottom: 30 days old rats. Scale bar = 20 µm.