The distribution of the islets of Langerhans in pancreas of euglycemic spontaneously hypertensive rats

Key words: Hypertension, Islets of Langerhans, Insulin.

Considering the fact, that pancreatic beta cells are responsible for production of all insulin needed to maintain the glucose homeostasis, the problem of beta cells pull control in patients with hypertension is rather topical. It cannot be ruled, that genetical defects of congenital hypertension formation can affect the mechanisms of maintaining of the cell mass of pancreatic endocrinocytes and lead to violation of glucose metabolism and diabetes mellitus development. Moreover, the violation of cytoarchitectonic of pancreatic islets of Langerhans may lead to impairment of the insulin secretion, which can be due to local impairment of the blood circulation in patients with hypertension.

The aim was to study the features of SHR islets’ distribution in pancreas.

Materials and methods. The glucose blood level and the insulin concentration were measured from tail vein. The immunofluorescence analysis was made and data were processed with statistical application kit with evaluation of reliability of differences in experimental groups with Student’s t-criterion.

Results. The object of current study was the animals with fasting normoglycemia and Wistar rats with 3.94 mmol/l fasting glucose level. The morphometrical assay showed 78.8% of pancreatic islets in SHR are small islets, while in Wistar rats their share is 44.3%. Noteworthy is the great amount of solely beta-cells in SHR and total absence of large islets.

Conclusions. The violation of pancreas’ cytoarchitectonic and changes of islets’ distribution with prevailing of small islets with area less than 1500 μm² were observed.

Beta-cells in normoglycemic SHR were characterized with 2-fold increased concentration of immunoreactive insulin compared with normotensive Wistar rats.
Hypertension and diabetes mellitus are the diseases with steadily increasing morbidity in population of many countries. [8,12]. It had long been considered, that arterial hypertension and diabetes mellitus are not mutually generated diseases, however their comorbidity is proved [8,11,12]. Considering the fact, that pancreatic beta cells are responsible for production of all insulin needed to maintain glucose homeostasis, the problem of beta cells pull control in patients with hypertension is rather topical. It cannot be ruled, that genetical defects of congenital hypertension formation can affect the mechanisms of maintaining of the cell mass of pancreatic endocrinocytes and lead to violation of glucose metabolism and diabetes mellitus development [5,9]. Moreover, the violation of cytoarchitectonics of pancreatic islets of Langerhans may lead to impairment of the insulin secretion [7,10], which can be due to local impairment of the blood circulation in patients with hypertension. 

The aim was to study the features of SHR islets’ distribution in pancreas.

Materials and methods

The study was carried out in 10 normotensive male Wistar rats (systolic blood pressure is 105.0±1.1 mm Hg) and 15 hypertensive male rats (systolic blood pressure is 155.7±0.9 mm Hg) in age of 5–6 months. The glucose blood level from tail vein was measured with glucometer (GlucoCard-II, Japan), the insulin concentration was measured with ELISA kit (DRG, USA). In histological slices of 5-micrometer taken from different parts of pancreas the insulin was detected with immunoﬂuorescence assay after 20-hour incubation with insulin antibodies and 1-hour incubation with IgG conjugated with FITC (Peninsula Lab. Inc., Great Britain). The immunoﬂuorescence analysis was made with the fluorescence microscope AxioImager-A2 (Carl Zeiss, Germany) and the system of digital image analysis AxioVision (Carl Zeiss, Germany). Data were processed with statistical application kit with evaluation of reliability of differences in experimental groups with Student’s t-criterion.

Results

We have previously shown [6], that spontaneously hypertensive rats can be divided into 3 groups according to the fasting glycemia level: animals with normoglycemia (n=15, 32%), with impaired glucose tolerance (n=18, 38%) and with hyperglycemia (n=14, 30%). The object of current study was the animals with fasting normoglycemia (4.73±0.10 mmol/l) and Wistar rats with 3.94±0.09 mmol/l fasting glucose level.

The morphometrical assay showed 78.8±7.7% of pancreatic islets in SHR are small islets with area less than 1500 μm², while in Wistar rats their share is 44.3±5.8% (Table 1).

Table 1

| Islets’ type                  | Wistar rats | SHR rats | Reliability |
|------------------------------|-------------|----------|-------------|
| Single beta cells            | 4.1±0.6     | 11.9±1.3 | p < 0.001   |
| Small, area <1500 μm²        | 102.5±13.5  | 95.9±9.4 | p > 0.05    |
| Medium, area 1500 – 3500 μm² | 70.7±4.5    | 11.0±1.4 | p < 0.001   |
| Large, area 3500 – 7500 μm²  | 30.7±4.7    | 3.2±1.2  | p < 0.001   |
| Giant, area >7500 μm²        | 23.1±4.3    | 0±0      | p < 0.001   |

Noteworthy is the great amount of solely beta-cells in SHR (9.7±1.1% compared with 0.04±0.006% in Wistar rats) and total absence of islets with area above 7500 μm². It should be noted, that the distribution of pancreatic islets of adult SHR rats largely corresponds to the distribution of Wistar rats in age of one month after the change of embryonal beta-cells type to adult type, and in young Wistar rats underwent chronic prenatal stress [1].

It has been noted earlier the hypertension formation in SHR was accompanied by age-related changes on insular apparatus of pancreas with decrease of beta-cells pull [2], which significantly differs from age-related evolution of...
The distribution of the islets of Langerhans in pancreas of euglycemic spontaneously hypertensive rats. [4]. At the same time the decrease of beta-cells amount in SHR was largely compensated by higher concentration of immunoreactive insulin in endocrinocytes (2.54±0.14 conventional milliUnits (mU) compared with 1.17±0.06 mU in Wistar rats). This is likely to provide the maintenance of a sufficient level of immunoreactive insulin in peripheral blood flow (10.99±0.37 μME/ml compared with 8.61±0.41 μME/ml in Wistar rats) and maintain of fasting euglycemia. However, taking into account the higher levels of blood concentration of lipids, triglycerides and cholesterol in SHR compared with Wistar rats [3,6]. It should be assumed, that normoglycemic status of hypertensive rats should not be considered as index of physiological state of carbohydrate homeostasis in these rodents, since a presence of lipid metabolic violations subsequently could contribute to the impairment of glucose tolerance and metabolic syndrome formation.

Conclusions
1. It has been observed the violation of pancreas’ cytoarchitectonic and changes of islets’ distribution with prevailing of small islets with area less than 1500 μm².
2. Beta-cells in normoglycemic SHR were characterized with 2-fold increased concentration of immunoreactive insulin compared with normotensive Wistar rats.

Prospects for the future research is related to the study of pancreatic islets’ remodeling due to arterial hypertension.

Conflicts of Interest: authors have no conflict of interest to declare.

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