PHYSIOLOGY

Blood Glucose, Gas Exchange, and Hematological Parameters in Rats with Experimental Diabetes Mellitus After Carotid Glomectomy

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In glomectomized rats with denervated sinus carotid reflexogenic zones as compared with sham-operated controls, the diabetogenic action of streptozotocin was manifested by more pronounced changes in several hematological parameters, including marked elevation of blood glucose and reductions of oxygen consumption, the respiratory quotient, blood hemoglobin concentration, the hematocrit, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. These findings attest that the carotid sinus receptors play an important functional role in producing the symptom complex of diabetes mellitus.

Key Words: *carotid receptors; diabetes mellitus; blood; hyperglycemia; gas exchange*

Considering that one function of reflexogenic zones in the carotid sinus is to act as receptors for glucose [3], the purpose of our study described here was to compare blood glucose levels and the major indexes of red blood cells and gas exchange in animals with experimentally induced diabetes mellitus before and after bilateral carotid glomectomy [2].

MATERIALS AND METHODS

A total of 38 random-bred female rats weighing 180-200 g were used. Their blood samples were assayed for red cell count, hemoglobin, hematocrit, glucose, and the following red cell indexes: mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and mean corpuscular volume (MCV). Gas exchange was measured in rats in a closed system using oxygen and carbon dioxide analyzers. Oxygen consumption (absorption) and carbon dioxide evolution were expressed in ml/min, and the respiratory quotient (RQ) was calculated as the ratio of the volume of carbon dioxide given off to the volume of oxygen absorbed.

Of the 38 rats, 19 were glomectomized, while the remaining 19 were sham-operated and served as controls. Diabetes mellitus was induced in all rats by a single intraperitoneal injection of streptozotocin (Serva) in a dose of 80 mg/kg 14 days after surgery. This compound, which is a highly specific beta-cell poison, reliably produces a form of disease closely resembling the clinical presentation of type 1 diabetes. In both groups, blood glucose and hemoglobin concentrations, the hematocrit, and the red cell and gas exchange indexes were determined 14 days after surgery and 2 days after streptozotocin administration. All tests were carried out in daytime (from 10:00 h to 15:00 h) in the fall.

RESULTS

The results summarized in Table 1 indicate that glomectomy substantially elevated blood glucose;

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TABLE 1. Blood Levels of Glucose and Hemoglobin, and Red Cell and Gas Exchange Indexes in Sham-Operated and Glomectomized Rats before and after Streptozotocin Injection ($M \pm m$)

Parameter	Sham-operated rats	Glomectomized rats	Diabetic sham-operated rats	Diabetic glomectomized rats
Glucose, mmol/liter	5.111±0.194	7.093±0.231	16.16±0.820	21.58±1.820
RBC, cells×10^6/μl	8.089±0.132	7.703±0.116	7.647±0.091	7.141±0.149
Hemoglobin, g%	14.32±0.289	14.22±0.203	13.85±0.255	12.18±0.264
Hematocrit, %	44.50±0.717	43.10±0.540	41.80±0.743	39.30±0.653
MCH, pg	17.70±0.381	18.46±0.220	18.11±0.369	17.06±0.433
MCHC, %	32.18±0.606	32.99±0.420	33.13±0.688	30.99±0.617
MCV, μ^3	55.01±0.731	55.95±0.880	54.66±0.769	55.87±0.748
O_2 consumption, ml/min	5.650±0.260	5.244±0.190	5.485±0.272	5.184±0.212
CO_2 release, ml/min	4.863±0.278	4.004±0.166	4.209±0.336	3.833±0.307
RQ	0.858±0.014	0.762±0.020	0.765±0.018	0.740±0.015

reduced the red cell count, carbon dioxide release, and the RQ; tended to decrease oxygen consumption, blood hemoglobin concentration, and the hematocrit; and had little effect on the red cell indexes MCH, MCHC, and MCV. The reduced red cell numbers and the tendency toward lowered hemoglobin and hematocrit levels in the glomectomized animals are signs of an anemic process not accompanied by impaired hemoglobin synthesis, since the MCH and MCHC values remained essentially unchanged. These findings confirmed our results obtained earlier by measuring diurnal variations in hematological parameters in rats following carotid glomectomy [6]. The occurrence of anemia after denervation of the carotid sinus reflexogenic zones is associated with enhanced hemolysis [5]. Carotid receptors have been shown to play an important role in the elicitation of reflexes from the pancreatic insular apparatus in response to alterations in the blood concentration of glucose [3,4]. Glucose should therefore be expected to rise in the blood of glomectomized animals as a result of inactivation of the mechanism triggering the reflex-mediated regulation of its blood level. On the other hand, the insular apparatus has been shown capable of responding directly to alterations in the level of glycemia [8]. Of the two mechanisms - neural and humoral - by which blood glucose is maintained at a relatively constant level, the neural (central) mechanism appears to be more sensitive. Thus, the nondiabetic glomectomized rats mainly differed from the nondiabetic sham-operated controls in having much higher blood glucose levels and lower erythrocyte counts, blood hemoglobin and hematocrit values, and gas exchange indexes.

When diabetes developed in both groups after streptozotocin administration, these differences between the two groups remained, but the trend toward lowered hemoglobin and hematocrit values in the glomectomized rats became more pronounced. While elevations in blood glucose in both groups were similar (about 3-fold), the signs of anemia and inhibited gas exchange were more pronounced in the glomectomized rats, and these rats, unlike the sham-operated animals, had lower MCH and MCHC values than before the induction of diabetes, which is an indication of abnormal hemoglobin synthesis. It is noteworthy that the decreases in the red cell count and RQ in the glomectomized rats before streptozotocin injection were similar to those in the sham-operated animals after its injection. Reflexes from carotid receptors are directed at preserving energy resources and at restoring them when they are deficient [1], and this can evidently be confirmed by comparing the red cell and gas exchange indexes recorded in this study for sham-operated and glomectomized animals with diabetes mellitus. The impaired glucose absorption by body tissues in diabetes results not only in carbohydrate deficiency but also in oxygen deficit, especially in the brain tissue. The physiological significance of hyperglycemia in diabetes mellitus appears to consist in providing the central nervous system with an adequate supply of glucose as the permeability of the blood-brain barrier to glucose is greatly reduced so that the latter can enter the brain only when its blood concentration is elevated [7].

The alterations recorded in the red cell and gas exchange parameters (including marked reductions in the red cell count and RQ and a tendency toward lowered hemoglobin and hematocrit values) along with a marked elevation of blood glucose in the glomectomized rats before the injection of streptozotocin, as well as in the sham-operated animals after its injection, are indicative of pronounced disturbances in gas exchange and energy metabolism.

It follows, then, that inactivation of carotid receptors leads to functional manifestations of prediabetes, and that the diabetogenic action of streptozotocin in glomectomized animals is accompanied by greater alterations in blood levels of glucose and hemoglobin and in red cell and gas exchange indexes than in sham-operated animals. This study has thus demonstrated an important physiological role of the carotid sinus reflexogenic zones in the development of adaptive responses in health and in diabetes mellitus.

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Comparative Analysis of Effects from Prolonged Peripheral and Intracerebral Exposure to β-Endorphin

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During a long-term (7-day) continuous exposure of rats to β-endorphin from an implanted minipump by the subcutaneous route, changes in their motor activity (stereotypy) and pain sensitivity (hypoalgesia) were similar, though less marked, than those observed during such exposure by the intracerebral route, whereas the change in feeding behavior with the subcutaneous (peripheral) route of β-endorphin administration (hyperphagia) was opposite to that seen with intracerebral administration (hypophagia).

Key Words: β-*endorphin; osmotic minipumps; feeding behavior; pain sensitivity*

It has been demonstrated in numerous experimental studies that most endogenous regulatory peptides (RPs) are formed through specific proteolytic processing from high-molecular precursor proteins. The precursor protein for β-endorphin (En), β-lipotropin, and adrenocorticotropic hormone is proopiomelanocortin [3,6].

There is biochemical evidence that mammals possess enzyme systems responsible for the biotransformation, inactivation, and elimination of peptides [6,13]. As has frequently been pointed out [1,13], this explains why it is difficult, in experiments using exogenously administered RPs, to evaluate the real role of peptides in the regulation of physiological functions, especially since the experimentally used doses of RPs far exceed their concentrations in tissues and biological fluids. The levels of En and many other RPs in the body are regulated by highly complex feedback mechanisms. The major components of the regulatory system concerned are the hypothalamus, pituitary, and adrenals [3,6]. It has been shown that the level of En in the anterior pituitary correlates most closely with its plasma level [3,7], that the main source of En contained in the

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