Cardiomyopathy and angiogenesis defects of Wistar rat fetuses of diabetic and hypercholesterolemic mothers

Objective: We aimed to illustrate the histogenesis, lactic dehydrogenase isoenzymes electrophoresis, and DNA damage of cardiac muscles and blood vessels during prenatal life of maternal diabetic or hypercholesterolemic mother.

Methods: Eighty fertile male and virgin female Wistar rats (1 male/3 females), weighing approximately 130 g, were mated and zero date of gestation was determined. Diabetes was induced at the fifth day of gestation by intraperitoneal injection of a single dose of 60 mg streptozotocin/kg body weight in citrate buffer, pH 4.6. At the same time, hypercholesterolemia was carried out by feeding virgin rats a diet containing 3% cholesterol for 6 wk before the onset of conception. Pregnant rats were arranged into three groups: control, diabetic, and hypercholesterolemic (n = 20). The animals were sacrificed and embryos were separated at 7-, 13-, 15-, 17-, and 19 d old, respectively, and subjected to light and transmission electron microscopy, lactic dehydrogenases isoenzymes electrophoresis, DNA fragmentation, and comet assay. The sera of the mothers were examined for fasting glucose level, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, and creatine phosphokinase levels.

Results: Diabetic and hypercholesterolemic mothers exhibited a significant increase of sera cholesterol level, low-density lipoprotein, and creatine phosphokinase activity. Histologic findings of embryos of diabetic and hypercholesterolemic mothers revealed cardiomyopathy and malformation of blood vessels with an apparent degeneration of their endothelium. Transmission electron microscopy possessed massive necrosis of muscle fibers, disorganization of Z and I bands, and mitochondrial damage. Lactic dehydrogenase isoenzyme electrophoresis was altered and genomic DNA fragmentation was markedly increased.

Conclusion: Maternal diabetes or hypercholesterolemia led to marked alterations in blood vessel differentiation as well as to cardiomyopathy during prenatal growth as assessed by the disruption of fine structures, abnormal lactic dehydrogenase isoenzymes electrophoresis, and an increase of...
DNA damage. These may be attributed to the marked oxidative stress and liberation of free oxygen radicals, which interrupted the myocardium structure and function during organogenesis.