Hypothesis

Is There a Link Between Stress, Beta-Endorphin and Diabetes Mellitus ?

Milan M. Terzic MD, PhD.

Department of Obstetrics and Gynaecology, School of Medicine, University of Belgrade, Yugoslavia

Beta-endorphin (beta-EP), neuropeptide cleaved from precursor pro-opiomelanocortin (POMC) under the control of Corticotropin Releasing Hormone (CRH), is generated in the CNS, hypothalamus and anterior pituitary, ovarian, testicular, thymic, pancreatic and placental tissues[1,2,3]. Production of beta-EP is extremely increased in stressful situations.

In the endocrine pancreas beta-EP containing cells are in close proximity to insulin containing ones. It has been confirmed that infusion of beta-EP caused a significant rise in plasma glucose concentration preceded by a significant increase in peripheral glucagon levels. Insulin responses to intravenous pulses of different glucose amounts were significantly reduced by beta-EP infusion. So, beta-EP stimulates glucagon inhibits basal and glucose-stimulated insulin secretion. Intravenous administration of small doses of beta-EP caused an immediate suppression of basal and glucose-stimulated insulin secretion. This effect was associated with a significant reduction of the glucose disappearance rates suggesting that the inhibition of insulin was of biological relevance.[4]

Beta-EPs are components of the intrapancreatic regulatory system which means beta-EP of pancreatic origin may function as paracrine or autocrine regulator of pancreatic islet cells[5]. The study performed in type-2 diabetes mellitus patients showed that infusion of human beta-EP produced significant and simultaneous increments in both insulin and glucagon concentration and decreased plasma glucose levels[6]. But, when the same diabetics were rendered euglycemic by an insulin infusion, beta-EP did not produce the expected decrease in plasma glucose concentration nor raise plasma insulin levels; only the response of glucagon was preserved. It is very important to stress on the fact that beta-EP at low dose levels inhibited and at high dose concentration augmented stimulated insulin secretion in experimental conditions, which supports the idea that a naloxone

Thai J Obstet Gynaecol 1994; 6: 17-18

sensitive beta-endorphin-binding component is present in pancreatic islets[7].

Having in mind that pregnancy is a diabetogenic factor in the very recent investigation, we confirmed that immunoreactive beta-EP in peripheral blood of pregnant women was found to increase with the progression of gestation, reaching maximal at term. This finding is particularly expressed in insulin dependent pregnant women. The cited study also confirmed that insulin caused a significant rise of beta-EP blood levels 1 hour after administration. Peripheral blood beta-EP levels did not significantly differ in insulin independent patients, in comparison with the healthy controls, while insulindependent one presented significantly higher levels. Inhibiting insulin secretion, beta-EPs are incorporated in the complex mechanism of gestational diabetes development[8].

In conclusion, there is a strong relationship between beta-EP rise caused by stress and diabetes mellitus.

References

1. Akil H, Vatson SJ. Endogenous opioids: biology and function. Ann Rev Neuroscience 1984;7:223-6.
2. Jevremovic M, Terzic M, Kartaljevic G, Popovic V, Rosic B, Filipovic S. The determination of immunoreactive Beta-endorphin concentration in the human fetal and neonatal thymus. Horm Metab Res 1991;23:623-4.
3. Terzic M, Jevemovic M, Kartaljevic G, Popovic V, Rosic B, Filipovic B. Identification of beta-endorphin activity in human fetal and neonatal pancreas. J Endocrinol Invest 1991;14:194.
4. Giugliano D, Cozzolino D, Salvatore T, Torella R, D'Onofrio F. Beta-endorphin-induced inhibition and stimulation of insulin secretion in normal humans is glucose dependent. Diabetes 1988;37: 1265-70.
5. Terzic M, Stimec B, Jevremovic M, Plecas D, Zizic V, Jovanovic M. Beta-endorphin level elevation in the human fetal and neonatal pancreas: a consequence of intrapartal stress or the possible existence of pancreatic islet cells autocrine control ? Thai J Obstet Gynaecol 1993;5:19-24.
6. Giugliano D, cozzolino D, Salvatore T, Ceriello A, Giunta R, Torella R, D'Onofrio F. Beta-endorphin and islet hormone release in type-2 diabetes mellitus; the effects of normoglycemia, enkephalin, naloxone and somatostatin. Diabetes Metab 1987;13:618-24.
7. Schleicher RL. Beta-endorphin inhibits insulin secretion from isolated pancreatic islets. Endocrinol 1989;124:1254-8.
8. Terzic M, Stimec B, Jevremovic M, Petronijevic A. The influence of beta-endorphins on gestational diabetes development. Thai J Obstet Gynaecol 1993;5:15-8.