Bangladesh J Obstet Gynaecol, 2014; Vol. 29(2) : 63-64

Editorial

Insulin Resistance in PCOS

Insulin resistance, recently recognized as a strong predictor of disease in adults, has become the leading element of the metabolic syndrome and renewed as a focus of research. The condition exists when insulin levels are higher than expected relative to the level of glucose. Thus, insulin resistance is by definition tethered to hyperinsulinemia. There is a well established association between PCOS, insulin resistance and hyperinsulinemia. Insulin resistance is a pivotal defect in PCOS probably counts as one of the most important advances in the battle to control the disorder. This metabolic abnormality leads to a compensatory increase in circulating insulin and this elevated insulin level directly stimulates the ovary and adrenal gland to produce excess androgens[1,2]. It also decreases hepatic sex hormone binding globulin (SHBG)[3], so increasing biologically available free testosterone concentration in the circulation[4,5] causing hyperandrogenemia. This excess androgen is responsible for anovulation, oligomenorrhea, hirsutism and infertility.

Possible mechanism of hyperinsulinemia:

There are some postulated theories, which suggested responsible factors for hyperinsulinemia.

a) Functional problems in the insulin receptor could be a consequence of insulin receptor gene mutations. There are three categories of peripheral target tissue insulin resistance.

   i) Decreased insulin receptor numbers

   ii) Decreased insulin bindings

   iii) Post receptor failure

b) Defective post receptor signal transduction: The phosphorylation of serine and threonine residues on the insulin receptor reduces signal transmission and excessive serine phosphorylation by a mechanism extrinsic to the insulin receptor has been demonstrated as a possible post-receptor defect in patients with PCOS, changing signal transduction[6]. Serine phosphorylation of beta chain of insulin receptor and at the same time of adrenal and ovarian P450c17 enzyme would explain both hyperinsulinemia and hyperandrogenism.

Due to this receptor defect insulin can't work to utilize blood glucose. As a result blood glucose level increased and which stimulates pancreatic beta cells to secrete insulin. This positive vicious cycle causes more and more insulin secretion resulting hyperinsulinemia and hyperandrogenism. Hyperinsulinemia, reflecting peripheral insulin resistance, is linked to hypertension, obesity, hyperlipidemia and glucose[7,8] Hyperinsulinemia, insulin resistance, and impairment of glucose-stimulated insulin release are intertwined biologically. A single process (hyperinsulinemia) could generate all three simultaneously. Understanding the pathophysiology of the basal hyperinsulinemia may provide guidance in the development of effective and specific therapies.

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Editor

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