Libyan International Medical University
Faculty of Basic Medical Science

Polycystic ovarian syndrome & insulin resistance

Submitted by: Bushra Moftah Rashid

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Abstract :

reported that women with PCOS had increased insulin responses during oral glucose tolerance testing that were not accounted for by obesity. Furthermore, women with typical PCOS had raising the possibility insulin resistant, These observations launched a new field of study on the mechanisms for the association between insulin resistance and PCOS A new field. High levels of insulin Insulin resistance is when the body's cells do not respond normally to insulin. As a result, insulin blood levels become higher than normal. Many women with PCOS have insulin resistance, especially those who are overweight or obese, have unhealthy eating , do not get enough physical activity, and have a family history of diabetes (usually type 2 diabetes). Over time, insulin resistance can lead to type 2 diabetes.

Introduction:

Polycystic ovary syndrome (PCOS), also known as polycystic ovarian disease , is a common health problem caused by an imbalance of reproductive hormones. The hormonal imbalance creates problems in the ovaries. The ovaries make the ovum that is released each month as part of a healthy menstrual cycle. With PCOS, the ovum may not develop as it should or it may not be released during ovulation as it should be.

PCOS can cause missed or irregular menstrual periods. Irregular periods can lead to:
Infertility In fact, PCOS is one of the most common causes of female infertility.
Development of cysts (small fluid-filled sacs) in the ovaries .[1]

Discussion:

-First study: investigated the cellular mechanisms of the disorder of insulin action found in the polycystic ovary syndrome (PCOS). Approximately 50% of PCOS women (PCOS-Ser) had a significant increase in insulin-independent beta-subunit phosphate incorporation in skin fibroblast insulin receptors that was present in serine residues while insulin-induced tyrosine phosphorylation was decreased. PCOS skeletal muscle insulin receptors had the same abnormal phosphorylation pattern. The remaining PCOS women (PCOS-n1) had basal and insulin-stimulated receptor autophosphorylation similar to control. Phosphorylation of the artificial substrate poly GLU4:TYR1 by the PCOS-Ser insulin receptors was significantly decreased ($P < 0.05$) compared to control and PCOS-n1 receptors. The factor responsible for excessive serine phosphorylation appeared to be extrinsic to the receptor since no insulin receptor gene mutations were identified, immunoprecipitation before autophosphorylation corrected the phosphorylation defect and control insulin receptors mixed with lectin eluates from affected PCOS fibroblasts displayed increased serine phosphorylation. Our findings suggest that increased insulin receptor serine phosphorylation decreases its protein tyrosine kinase activity and is one mechanism for the post-binding defect in insulin action characteristic of PCOS .[2]

-Second study: PCOS is often associated with insulin resistance as well as with defects in insulin secretion. These abnormalities, together with obesity, explain the substantially increased prevalence of glucose intolerance in PCOS, PCOS-related insulin resistance is an important cause of NIDDM in women. The insulin resistance in at least 50% of PCOS women appears to be related to excessive serine phosphorylation of the insulin receptor. A factor extrinsic to the insulin receptor, presumably a serine/threonine kinase, causes this abnormality and is an example

of an important new mechanism for human insulin resistance related to factors controlling insulin receptor signaling. Serine phosphorylation appears to modulate the activity of the key regulatory enzyme of androgen biosynthesis, P450c17. It is thus possible that a single defect produces both the insulin resistance and the hyperandrogenism in some PCOS women . Recent studies strongly suggest that insulin is acting through its own receptor (rather than the IGF-I receptor) in PCOS to augment not only ovarian and adrenal steroidogenesis but also pituitary LH release. Indeed, the defect in insulin action appears to be selective, affecting glucose metabolism but not cell growth. Since PCOS usually has a menarchal age of onset, this makes it a particularly appropriate disorder in which to examine the ontogeny of defects in carbohydrate metabolism and for ascertaining large three-generation kindreds for positional cloning studies to identify NIDDM genes. Although the presence of lipid abnormalities, dysfibrinolysis, and insulin resistance would be predicted to place PCOS women at high risk for cardiovascular disease, appropriate prospective studies are necessary to directly assess thi .[3]

-Third study : The cells in ovaries produce some of essential hormones, including oestrogen and progesterone. These cells also secrete a small amount of testosterone. Testosterone is actually essential for many bodily functions, including libido and bone formation. if have really high insulin levels all the time then it causes ovaries to overproduce testosterone. bodies usually have a system in place which prevents hormone levels from getting too high. Unfortunately this isn't the case with testosterone and bodies also don't anticipate insulin making testosterone levels higher. As a result, there's nothing to prevent testosterone levels spiraling out of control. It doesn't just end there though. When it comes to hormones, 80% should be bound to cells and 20% should be free in the body. The 'free' hormones are generally the ones which cause problems. Excess levels of 'free' testosterone can:

Get into hair follicles and make hair fall out.

Settle in hair follicles in our face and make it produce thick dark hair.

–Get into skin glands and cause acne. In most people, Sex Hormone Binding Globulin (SHBG) acts as a testosterone 'sponge', binding to excess testosterone and preventing it from causing these problems. However, insulin resistance reduces the amount of SHBG, thereby increasing testosterone levels.[4]

Conclusions:

We found that obese PCOS women had significantly increased glucose levels during an oral glucose tolerance test compared with age- and weight-matched ovulatory hyperandrogenic (*i.e.*, elevated plasma androgen levels). The insulin resistance in at least 50% of PCOS women appears to be related to excessive serine phosphorylation of the insulin receptor

References:

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