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Endometriosis and Progesterone Resistance

New insight reveals the role endometriosis plays in the disruption of progesterone activity - a potential factor impacting reproductive health.

Endometriosis Linked to Multiple Health-Related Issues

Endometriosis is a gynecologic disease characterized by the growth of endometrial-like tissue outside of its natural location within the uterus.

For example, endometriosis lesions have been located in the ovaries; pelvic organs including the bowel and bladder; and have even been discovered in the lung, nasal cavity, and brain.

This disease affects 5-10% of reproductive-age women and is characterized by cyclical pelvic pain; infertility; and mood disorders making endometriosis a major health problem - significantly impacting the quality of life of so many.

Endometriosis has also been clearly linked to multiple fertility and reproductive-related concerns including endometrial inflammation, fallopian tube dysfunction, ovulatory disorders, and miscarriage.

In fact, a recent study revealed women with a history of infertility and endometriosis have nearly a 53% chance of miscarriage versus approximately 12% for fertile women without endometriosis.

In the same study, women with endometriosis who had previously undergone artificial reproductive technology procedures were found to have a remarkably-high miscarriage rate of 58.1%.

Importance of Progesterone Receptors

Progesterone is a steroid hormone largely produced by the ovaries, the adrenal glands, and the placenta during pregnancy. Progesterone, also known as the pregnancy hormone - or "*progestational hormone*" - plays a vital role in pregnancy support, and its hormonal impact is mediated by the activation of progesterone receptors located within certain tissues of the body, including the endometrium - the functional lining of the uterus responsible for pregnancy implantation following conception.

In order to exert its action, progesterone binds to two forms of receptors known as PGR-A and PGR-B - each with its own unique function.

PGR-B receptors are largely responsible for progesterone action, while PGR-A receptors oppose PGR-B receptors resulting in diminished progesterone activity.

Both progesterone receptors are expressed during the proliferative phase (pre-ovulatory portion) of a woman's cycle and increase with rising estrogen levels during this time. Throughout the secretory (or post-ovulatory) phase of the cycle PGR-B receptors remain relatively constant, while PGR-A receptors decline in number.

Importantly, a specific balance between these two receptors appears essential to a properly functioning endometrium in preparation for early implantation and pregnancy. Accordingly, abnormal PGR-A and PGR-B receptor expression in endometrial cells has been associated with infertility and early pregnancy loss.

Endometriosis a Progesterone Disruptor

Progesterone receptor resistance at the level of the endometrium has been identified in women with infertility. In a subset of women, normal progesterone levels did not result in healthy maturation of the endometrium during the postovulatory phase of the menstrual cycle due to a markedly reduced number of progesterone receptors in the target cells of the endometrium.

This condition, known as "*pseudocorpus luteal insufficiency*", occurred as a result of progesterone resistance as the endometrium failed to develop following the administration of progesterone supplementation.

Thus, despite healthy progesterone levels, or additional progesterone support, some women fail to sustain a healthy endometrium secondary to an abnormal reduction in progesterone receptor function.

In addition, a recent 2023 study by Gomaa et al. revealed that women suffering from recurrent miscarriage had a significantly lower number of both estrogen and progesterone receptors within the endometrial tissue compared to controls. Interestingly, there was no difference in the progesterone and estrogen levels noted between the two groups, but there was a significant difference in these levels within the endometrial environment - indicating both diminished progesterone and estrogen receptors within the endometrium could be linked to recurrent miscarriages.

While progesterone receptor dysfunction has been associated with reproductive issues, the exact mechanism for this defect is still unknown. But one new promising area of interest lies with the association between endometriosis and progesterone resistance.

In terms of endometriosis, substantial evidence reveals endometriosis lesions display suppressed progesterone expression. Specifically, endometriosis lesions are deficient in both PGR-A and PGR-B receptors. This resistance results in progestin treatment failure in women undergoing hormonal treatment for endometriosis.

Given endometriosis lesions show an inherent resistance to progesterone, further investigation has attempted to evaluate whether or not the normal endometrium in women with endometriosis may also exhibit diminished progesterone activity.

Although still not entirely clear, several studies reveal a decrease in the PGR-B to PGR-A ratio along with relatively high PGR-A expression (the receptor responsible for diminishing progesterone action) in the endometrium of women with endometriosis - seemingly indicating a potential for progesterone disruption within the uterine environment. Such a finding certainly sheds light on one potential mechanism for infertility and miscarriage - increased progesterone resistance within the endometrial tissue of women impacted by endometriosis.

True Health Matters Summary

Progesterone is a fundamental hormone critical to human reproduction and a healthy pregnancy. Progesterone resistance is the inability of specific target tissues - including the endometrium - to respond appropriately to progesterone. Recent scientific insight suggests endometriosis lesions exhibit diminished progesterone activity via progesterone resistance resulting in treatment failure. This endometriosis-related resistance may also impact a healthy endometrial environment sparking critical consequences for reproduction and other aspects of female health. Thus, there is an immediate need for further research to examine the potential association between endometriosis and endometrium-related progesterone resistance to better guide treatment approaches.

References:

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