

Mood Symptoms During Fertility Treatment: The Role of Hormones

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Fertility treatment often involves invasive, time-consuming tests and procedures, and complicated medication schedules-all of which add to the stress of the diagnosis. There have been many studies investigating the effects of infertility and its treatments that suggest an increase in distress as well as symptoms of depression and anxiety in infertile women. The psychological effect of the hormones women take during infertility treatment has not been adequately studied, despite the fact that mood swings and depression are known side effects of ovulation induction medications and that women undergoing ovulation induction often complain of psychological problems.

Ovulation induction is an important part of many fertility treatments. It is utilized to stimulate egg maturity and cause ovulation in women for whom ovulation is an underlying cause of infertility. Non-hormone medications and/or hormone medications that have similar actions as natural hormones are used to stimulate the ovaries to produce mature oocytes. They can be taken orally or through injections.

In a natural menstrual cycle, ovulation requires the presence of several hormones with specific actions. Between menses and ovulation, follicles within the ovary are maturing. Estrogen levels in this phase are rising and peak around the time of ovulation. Progesterone levels at this time are much lower than those of estrogen. After ovulation, estrogen levels decline and progesterone levels increase.

It has long been known that depression is twice as common in women than men and that women are most at risk of developing depression during their reproductive years. Studies have been conducted that support the role of hormonal changes in the onset of mood and anxiety symptoms during premenstrual, post-partum, and perimenopausal periods in a woman's life. The interaction of the gonadal steroids estrogen and progesterone and brain systems implicated in mood disorders is very complex. Based on studies of women with premenstrual dysphoric disorder, post-partum depression, and perimenopausal depression, it appears that it is the normal fluctuation in hormone levels during these periods that trigger mood symptoms in some women. Studies have shown that the absolute levels of estrogen and progesterone measured at various points during reproductive events do not correlate with mood symptoms. It is not always clear which women will be vulnerable and the exact fluctuations triggering mood symptoms have not been clearly defined.

The root cause of the mood problems a woman experiences during infertility treatment is unclear. Since we know there is some connection between mood symptoms and hormone fluctuation, it is plausible that some of the distress women experience during an ovulation induction/insemination or embryo transfer cycle is related to the hormones they are being given. We also know that women are coping with feelings of grief, uncertainty, failure, and guilt, all of which are often associated with sadness, anxiety and irritability. These are the same symptoms that women with hormonally influenced mood symptoms describe. Further confounding the effort to determine the cause of mood problems during fertility treatment is that the timing of the

highest levels of psychological distress and anxiety during a cycle correlates with the periods when there is the greatest hormonal fluctuation. Women undergoing their first year of fertility treatment and those with fertility that has lasted greater than 5 years often have more distress than those within years 2-5 of fertility treatment. Another factor that might implicate psychological stress rather than hormones is the observation of some clinicians that mood problems are not seen nearly as frequently in oocyte donors, even though they are taking the same hormone medications as women undergoing ovulation induction procedures using their own gametes.

While there have been numerous studies documenting the psychological burden of fertility treatment, there have only been a few studies specifically investigating the role of hormones during ovulation induction. Gonadotropin releasing hormone agonists suppress a woman's menstrual cycle, effectively causing menopause. GnRH agonists have been associated with depression in women who are taking it to treat endometriosis. A more recent study of the effect of GnRH agonists on mood during its use for ovulation induction did not show an increase in depression. In a study of clomiphene citrate and human menopausal gonadotropin (stimulates follicle growth), both have been shown to be associated with significant mood symptoms.

One recent study did look specifically at mood and anxiety symptoms in women undergoing IVF/ET (embryo transfer) procedures. Modest elevations in depression and anxiety measures were seen throughout the treatment cycle. The highest levels of depression occurred in response to declining levels of estrogen. The role of progesterone was also investigated. Generally, progesterone is thought to contribute to depression. In this study, higher levels of progesterone were associated with lower levels of depression.

There is no doubt that women experience mood and anxiety symptoms during hormone therapy for fertility treatment. The causes of these symptoms are multiple, including the psychological issues involved in having to undergo fertility treatment. In addition, there are specific points during a treatment cycle that are associated with increased anxiety and distress. The length of time one has been pursuing fertility treatment also affects how vulnerable a woman might be to symptoms of depression and anxiety. There is now some evidence to suggest that, among women given hormone therapy for fertility treatment, fluctuating levels of hormones, especially declining levels of estrogen, will have a negative effect on mood beyond that attributable to psychological distress.