Leuprorelin as a Treatment for Endometriosis

By: Santora, Emily Guerrero, Anna Keywords: Endometriosis, endometrium, endometriotic lesions, pelvic pain, leuprorelin, leuprolide acetate, Lupron, Uterus, disease

Leuprorelin, or leuprorelin acetate, is a manufactured drug that has been prescribed as a treatment for endometriosis, a medical condition in which body tissue that typically lines the uterus grows outside of the uterus, since 1989. Leuprorelin is a modified version of a gonadotropin-releasing hormone, a type of hormone that helps regulate the female menstrual cycle. The drug inhibits the production of estrogen, a female sex hormone, that enables endometrial gland growth. After two weeks of injections, leuprorelin stops the production of estrogen, and without estrogen, endometrial glands become inactive. That decreases the growth of uterine tissue outside of the uterus, which helps decrease the pain associated with endometriosis. Although physicians commonly prescribe leuprorelin as of 2019, women with endometriosis have reported adverse side effects and health complications.

Healthcare professionals diagnose endometriosis by finding endometriotic lesions in a woman’s pelvic region, or the lower part of the trunk of the body, beneath the abdomen and above the thighs. Women with endometriosis often experience pelvic pain. Specific pain symptoms of women with endometriosis are dysmenorrhea, or painful menstrual cramps, and dyspareunia, or painful sexual intercourse. Healthcare professionals diagnose a woman with endometriosis by monitoring the woman’s symptoms and taking medical images or tissue samples of the uterus. As of 2019, healthcare professionals do not know the cause of endometriosis and no cure for the disease exists. Instead, healthcare professionals are able to treat symptoms, like pelvic pain, by prescribing medications like leuprorelin.

During the 1970s, researchers Andrew Schally and Roger Guillemin extracted and classified chemicals that signaled the pituitary gland, or the part of the brain responsible for releasing certain hormones, to activate what they called releasing factors. Schally and Guillemin worked in separate laboratories and studied how the brain interacts with glands that produce hormones. The researchers extracted substances from the hypothalamus of the brains of sheep and pigs. The hypothalamus helps regulate hormone production by sending signals to the pituitary gland, thyroid gland, and gonad glands. The pituitary, thyroid, and gonad glands produce hormones that travel through the bloodstream to start or stop different metabolic processes in the body. In 1969, Schally and Guillemin had independently isolated and purified a protein from the hypothalamus called thyroid releasing factor. Then, in 1971, Schally had discovered the structure of one particular hormone produced in the hypothalamus, which he called gonadotropin-releasing hormone. Gonadotropin-releasing hormone triggers the release of gonadotropins, or hormones that the pituitary gland releases, which participate in growth, sexual development, and reproductive function of mammals.

During the 1970s and 1980s, researchers learned more about gonadotropin-releasing hormone and eventually developed the chemical leuprorelin. In 1971, Schally described gonadotropin-releasing hormone in relation to the secretion of two gonadotropins: follicle stimulating hormones, or FSH, and luteinizing hormones, or LH. The pituitary gland releases both, FSH and LH. In women, FSH and LH trigger ovulation, or the release of an egg, during the middle of the menstrual cycle. A year later, in 1972, Schally began to develop a modified gonadotropin-releasing hormone to create new methods of birth control. He created a chemical that caused an initial increase in FSH and LH production, but after continued use, the chemical suppressed FSH and LH production. That modified gonadotropin-releasing hormone suppresses estrogen generation and thereby prevents the ovulation, the release of eggs, during a woman’s menstrual cycle. In 1980, he began to apply this chemical to treat various disorders. In 1985, the US Food and Drug Administration, or FDA, approved the gonadotropin-releasing hormone leuprorelin to treat prostate cancer in males. Healthcare professionals started administering leuprorelin to patients with endometriosis in 1989.

Leuprorelin can reduce the pain women experience with endometriosis. The FDA approved leuprorelin to treat endometriosis in females in 1989 after researchers found that the drug reduced symptoms of endometriosis and the size of endometriotic lesions, or inflamed sores visible in the uterus that are a common symptom of endometriosis. At a molecular level, leuprorelin suppresses signals sent from the pituitary gland to the ovaries, which are responsible for estrogen production. The US National Institutes of Health, or NIH, headquartered in Bethesda, Maryland, identifies leuprorelin as a hazardous drug, which means that only healthcare professionals with personal protective gear such as gloves and laboratory coats can handle the drug. The NIH expresses that women who plan to become pregnant should not receive leuprorelin injections due to potential risks to the fetus. According to healthcare professionals, leuprorelin injections are not a reliable method.

A healthcare professional administers a leuprorelin injection to decrease a patient’s endometrial gland growth, which helps to decrease symptoms of pain that women with endometriosis often experience. There are two different types of leuprorelin...
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Despite the negative side effects, as of 2019, physicians commonly prescribe leuprorelin injections to patients experiencing pain or infertility associated with endometriosis. Leuprorelin injections are also used during fertility treatments like in vitro fertilization. As of 2019, an oral leuprorelin drug has entered phase II clinical trials for patients with endometriosis, which means researchers are testing the drug’s short-term side effects and its effectiveness compared to other treatments.

There are several studies on the negative side effects of leuprorelin injections for women with endometriosis. During clinical trials of the drug, researchers found that most women experienced bone-thinning while receiving injections. Most women in the clinical trials also reported hot flashes, or sudden sweating, and headaches. Furthermore, the Endometriosis Research Center in Delray Beach, Florida, found that half of women surveyed experienced negative side effects that persisted for more than six months, and a fourth of women surveyed experienced side effects that persisted for more than five years. In another study conducted by the Endometriosis Research Center, half of the women surveyed stated that leuprorelin injections did not help subside painful symptoms of endometriosis. In several studies with women who did not have endometriosis but did receive leuprorelin injections, researchers noted that most women experienced difficulties with memory and coordination.

Dosages that a patient may receive, including an 11.25 mg injection every three months, or a 3.75 mg injection every month. Leuprorelin is usually administered over six months. During the first week of injections, estrogen levels temporarily increase, which may worsen painful symptoms. After estrogen levels begin to decrease, painful symptoms subside. After about two months of injections, menstruation usually stops. Leuprorelin may cause menopause-like symptoms, such as bone-thinning and hot flashes due to the decreased production of estrogen. Patients who experience those side effects may also concurrently participate in add-back therapy. During add-back therapy, a patient also takes a daily pill that contains small doses of estrogen or progesterone, which are female reproductive hormones. Low levels of those hormones help control some of the negative side effects of leuprorelin like hot flashes and bone-thinning.

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