



LETROZOLE - NOVEL DRUG FOR MEDICAL MANAGEMENT FOR TUBAL ECTOPIC PREGNANCY

Obstetrics & Gynaecology

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ABSTRACT

Ectopic pregnancy is one of the most common life-threatening conditions leading to increased maternal morbidity and mortality in the first trimester. With advances in diagnostic modalities, one can now diagnose most ectopic pregnancies before their rupture and other catastrophic events. Methotrexate is the most common drug used for medical management but has adverse effects and needs strict monitoring. We report a case of tubal ectopic pregnancy which was successfully managed with letrozole. We were able to prevent maternal morbidity, reduce cost of therapy and preserve future fertility in our patient.

KEYWORDS

ectopic, medical management, fertility, letrozole, methotrexate

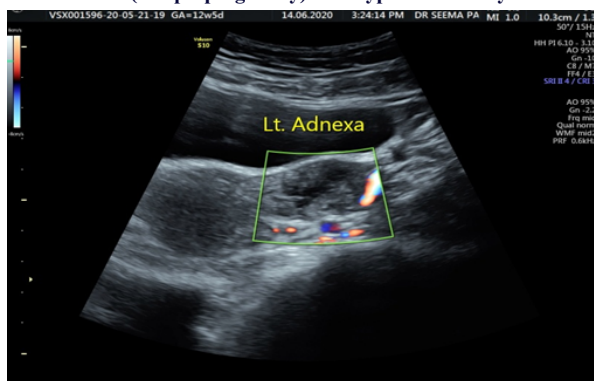
INTRODUCTION:

Around 1-2% of all pregnancies and 2-5% of those conceived by assisted reproductive techniques (ART) may end up in ectopic pregnancy.^[1] These can be managed expectantly, medically or surgically. Methotrexate (1982) remains the drug of choice for medical management of unruptured ectopic pregnancies. However it requires intramuscular administration, has adverse effects and requires monitoring.^[2] Hence, the need for a new drug. Letrozole (third-generation aromatase inhibitors) acts by reducing estrogen, disrupting the physiological functions of progesterone needed to maintain pregnancy and has a luteolytic effect on corpus luteum.^[3]

Case:

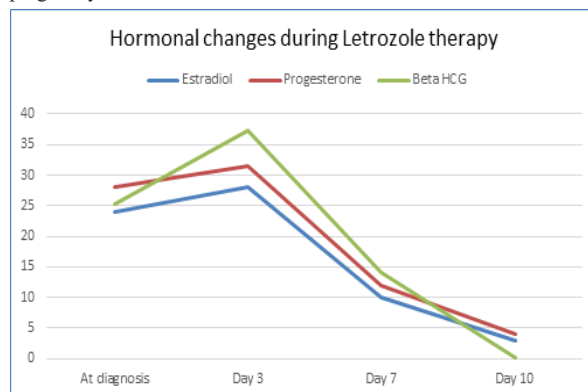
A 23 years old woman with history of primary sub fertility came to us with amenorrhea of 20 days and positive urine pregnancy test. On ultrasonography (USG), intrauterine gestational sac was not seen. There were some hyperechoic shadows in the endometrial cavity with bilateral clear adnexae. Her serum β hCG was 1065 mIU/ml. On repeat USG after 1 week, the uterine cavity still did not show a gestational sac (Fig 1). However the left adnexa revealed a hypervascular mass separate from the ovary, with sac like structure within it, as seen in fig 1. There was no free fluid in pelvis and serum β hCG was 2529 mIU/ml. These findings were suggestive of left sided unruptured ectopic pregnancy.

Fig 1: USG Doppler showing an empty uterine cavity with left adnexal mass (ectopic pregnancy) with hypervascularity.



Her baseline investigations like complete blood count, liver and renal function tests were normal. As the patient was clinically stable, she and her husband were counselled and given the option of medical termination of ectopic pregnancy using letrozole. She was given letrozole 2.5mg twice a day. Her serum β hCG, Estradiol (E2) and progesterone were done at the start of therapy and repeated after 72 hours, 7 days and 10 days as seen in graph 1. She was continued on letrozole for 10 days. Her blood reports showed a gradual fall in the

hormonal levels as seen in graph 1. She did not have any complaints other than spotting. After 10 days the serum β hCG was below pregnancy level and the USG was normal.



Graph 1: Hormonal changes in serum estradiol, progesterone and β HCG levels during the course of therapy with letrozole.

We successfully managed an early unruptured ectopic pregnancy with letrozole and avoided the morbidity of taking an injectable preparation (methotrexate), its side effects as well as any surgical intervention.

DISCUSSION:

During early pregnancy there is interplay of various hormones like human chorionic gonadotrophins (HCG), progesterone and estrogens. When progesterone is given as an additional support for pregnancy, some of it may get converted to estrogen.^[7] There are different types of estrogen receptors (nonclassical membrane-bound receptor, alpha and beta protein receptors in human placenta) which support the possible role of estrogen in maintaining early pregnancy.^[4,7] Studies on early pregnancy loss have shown association with estrogen function disruption.^[5,6,7]

Letrozole acts by inhibiting aromatase enzyme leading to reduction in serum estrogen as seen in fig 2.^[3,7,8] This suppresses the progesterone receptors leading to disruption of its physiological functions which is essential for maintenance and development of early pregnancy. It also has a luteolytic effect on the corpus luteum.^[3,7,8] This leads to resorption of the growing ectopic pregnancy.^[7,8]

Letrozole was effective with better safety profile, acceptability and lesser cost than methotrexate.^[7] It can be a promising drug for medical treatment of early unruptured ectopic pregnancy.^[7] Using the same hypothesis, letrozole may have a role in early intrauterine pregnancy termination. More definitive studies and adequately powered randomized clinical trials are needed to test this hypothesis.

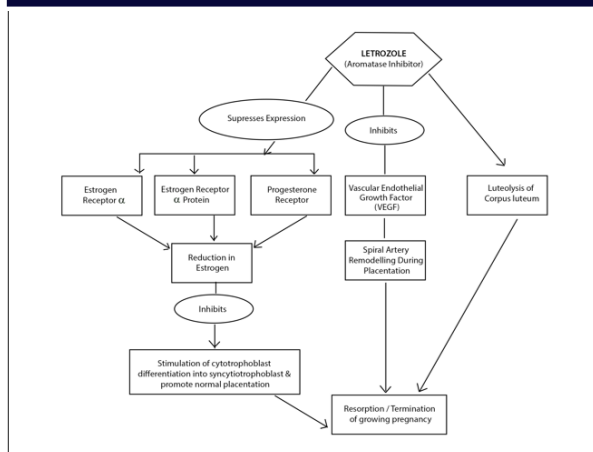


Fig 2: Mechanism of action of letrozole in reducing serum estrogen and termination of ectopic pregnancy

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