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Studying the effect of Metformin and Enzyme inhibitor drags on the level of aromatase Enzyme in the women have hormone disorder the Kirkuk city.

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Abstract

This study included (100) samples of women used drugs Metformin, enzyme inhibitor in (Azadi General Hospital) (20) blood samples aspirated from healthy women as control sample. The samples were divided into three groups; the first group (40) women used Metformin (have primary infertilits), the second group (40) women used Letrazole (have Secondary infertilits). The third group was the healthy women(control). The results of the study indicated a significant decrease ($p<0.05$) in the Activity of Aromatase level in Primary infertile women age groups (18-25), (26-35) and (36-45). the results of this study reveal that three is significant decrease in the Activity of Aromatase ($p<0.05$) in women who have Secondary infertility with age groups (18-25), (26-35) and (36-45). This Drugs causes decreasing the level of the Estrogen by inhibiting the Aromatase Enzyme . The Drugs also called as (Enzyme inhibitor) because they inhibit Aromatase enzyme, This proves that the Letrazole Drugs has an effective role in stimulating ovulation in women who have primary and secondary infertility.

Keywords: Metformin, enzyme inhibitor, Aromatase Enzyme, Hormones disorder.

Introduction

Metformin

Metformin is used to treat high blood sugar levels that are caused by a type of diabetes mellitus or sugar diabetes called type 2 diabetes. With this type of

diabetes, insulin produced by the pancreas is not able to get sugar into the cells of the body where it can work properly. It is also used in the treatment of polycystic ovary syndrome [1]. Metformin is generally well tolerated. Common side effects include diarrhea, nausea and abdominal pain. It has a low risk of causing low blood sugar. High blood lactic acid level is a concern if the medication is prescribed inappropriately[2, 3].

Letrozole

Is being used commonly as an infertility treatment. Letrozole is a recent addition to the drugs being used for fertility treatment. Fertility drugs are used often in infertility treatments[4]. There are two situations in which fertility drugs may be useful. First, these drugs can be used to induce an egg to develop and be released in women who are not ovulating. This is known as ovulation induction. Fertility drugs can also be used to increase the chances of pregnancy in women who are already ovulating [5].

Aromatase Enzyme

Aromatase, also called estrogen synthesis , is an enzyme responsible for a key step in the biosynthesis of estrogens. Aromatase is an enzyme found in the liver, responsible for the conversion of the androgens androstenedione and testosterone into the estrogens estrone and estradiol. The aromatase enzyme can be found in many tissues including gonads, brain, adipose tissue, placenta, blood vessels, skin, and bone[6, 7]. In the human, aromatase is expressed in a number of cells, including the ovarian granulosa cell, the placental, the testicular Leydig cell [8].

Location &Period Of The Study

The steady has carried out in Azadi General Hospital in Kirkuk governorate from(September 2017) to (February 2018). The steady included(100)patients have hormones disorder ,their ages (18-45) years old. After checking their conditions throughout medical &clinical tests by specialist doctors in this aspect. As well as choosing random group included (20)Sample of healthy women of age (18-45) years old. Their conditions were checked by specialist doctors in this hospital . The samples divided into three groups :-

*- Group No.1: - included (40) women used Metformin .

*- Group No.2: - included (40) women used Letrazole .

*- Group No.3: - included (20) healthy women.

Method of Collection the Sample

100 blood sample Collected from women who have hormones disorder And from healthy women of age (18-45) years old. The blood samples were taken from the vein .10 mL from each patient ,the blood was put in disposable test tubes . The tubes are empty of (EDTA) , After that , The blood was left in room temperature for 20 minutes , The blood was separated by using centrifuge at speed of (3000) rpm for 10 minutes. The serum was extracted by using micropipette ,put 1mL of blood serum in disposable tube in order to make(ARO) test

Assay Of Aromatase(ARO) Enzyme

Aromatase (ARO) enzyme was assay in blood serum depending On (IRMA) (Immunity Radiation Measurement) by Using Kit from Izotop Company , following the instructions of the kit and according to the instruction of the Company who made Elisa machine.

Results and Discussion

The figures (1),(2),(3) shows the Activity of Aromatase in the women infected with primary infertility treated with " Metformin "(G1) ,and infertile women treated with "Letrozole" (G2) compare with control group (142.6±13.9pg/ml) ,(130.8±11.46pg/ml) and(200.1±140.6pg/ml).(140.5±11.7pg/ml),(129.1±10.3pg/ml)and(203.0±141.5pg/ml).(139.4±10.6 pg/ml), (131.9±12.5 pg/ml) and(201.2±140.6 pg/ml) respectively. Result revealed a significant decrease($p<0.05$) in the Activity of this enzyme in G1and G2 as compared with the control in the third age group. The results of the study agree with results of [٩,١٠ ,1١].

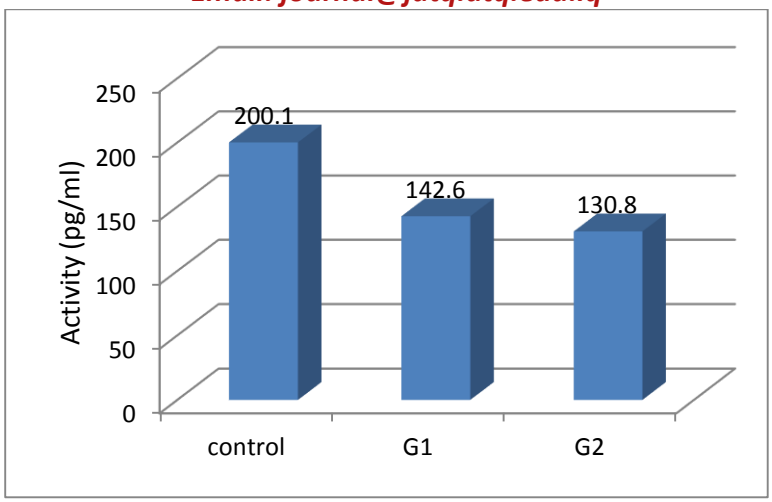

Figure 1: Activity of Aromatase level in Primary infertile women age group (18-25)

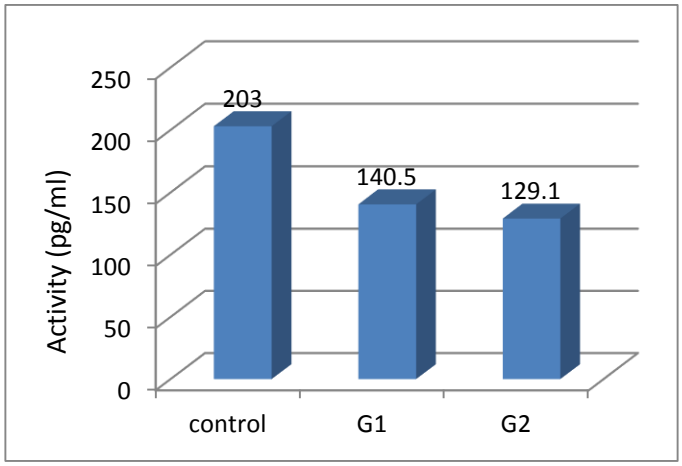

Figure 2: Activity of Aromatase level in Primary infertile women age group (26-35)

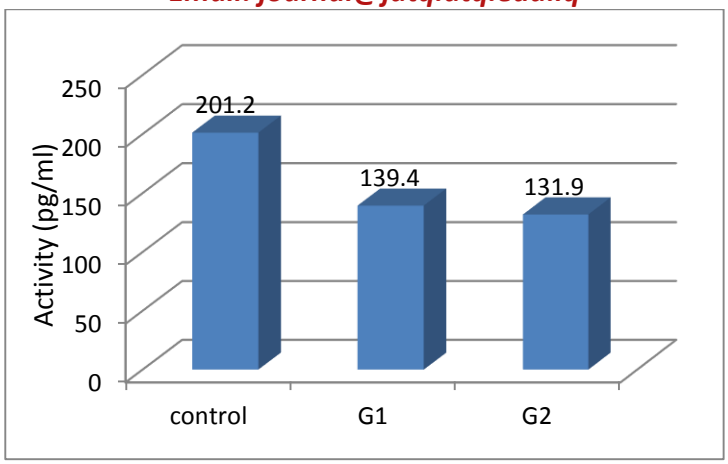

Figure 3: Activity of Aromatase level in Primary infertile women age group (36-45)

The figures (4),(5),(6) shows the activity of aromatase in G1and G2 in compare with the(control) group . Results showed a significant decrease in the activity of this Enzyme at level ($p<0.05$) in G1and G2 as compared with the (control) group in the third age group. The figure (4) included the age group (18-25),which revealed a significant decrease in the activity of this enzyme between G1(222.4±134.6pg/ml), in comparison with control group (238.4±150.7 pg/ml),and also significant decrease in G2(123.9±112.36pg/ml)in comparison with control group, but there is significant rising between G1, in compare with women group G2. The results of the study agree with results of [7,8].

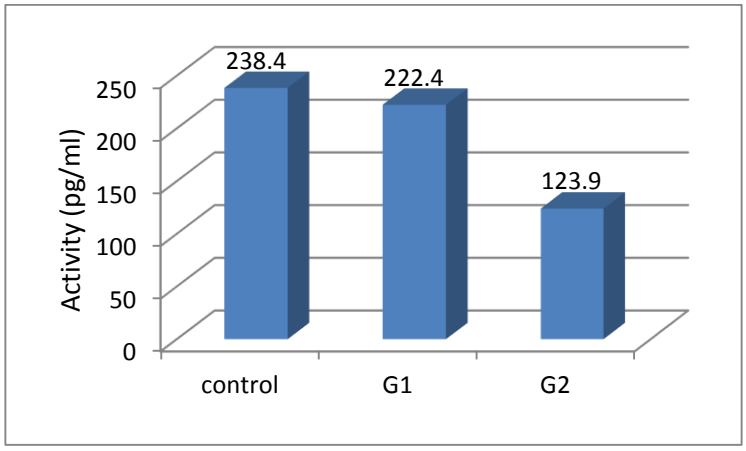

Figure 4: Activity of Aromatase level in Secondary infertility women age group (18-25)

The figure (5) included the age group (26-35),,which revealed a significant decrease in the activity of this enzyme between G1(221.1±133.5pg/ml), in comparison with control group (230.1±144.3 pg/ml),and also significant decrease in G2(122.8±111.31pg/ml) in comparison with control group, but there is significant rising between G1, in comparison with women group G2. The results of the study agrees with results of [11].

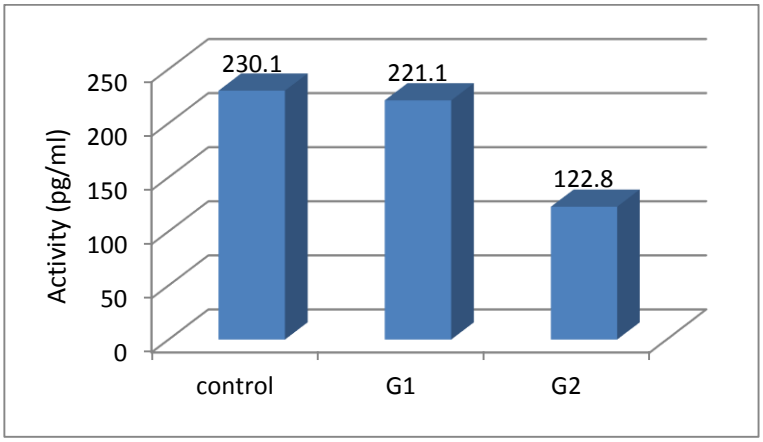

Figure 5: Activity of Aromatase level in Secondary infertile women age group (26-35)

The figure (6) included the age group (36-45),,which revealed a significant decrease in the activity of this enzyme between G1(123.8±112.1pg/ml), in comparison with control group (222.2±134.4 pg/ml),and also significant decrease in G2(120.6±110.42 pg/ml) in comparison with control group, but there is significant rising between G1, in comparison with women group G2. The results of the study agrees with results of [6,7].

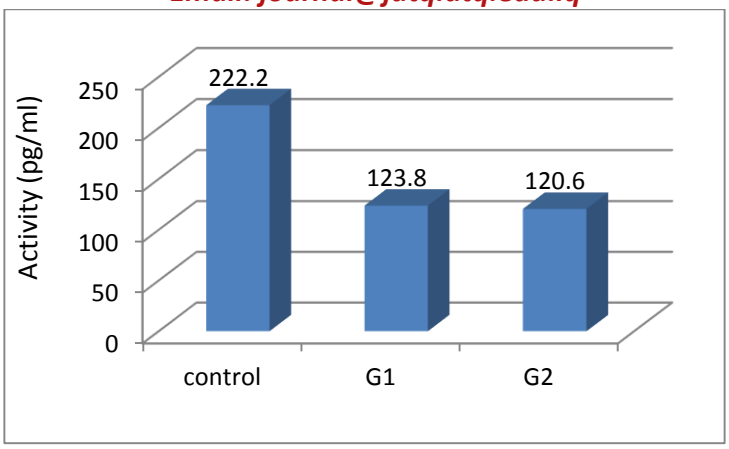

Figure 6: Activity of Aromatase level in Secondary infertile women age group (36-45)

Form these results it was revealed that the changes in Activity of Aromatase is caused by treatment with (Letrozole) medication which it is considered one of the fertility stimulating medication. The medication also called as (Aromatase enzyme inhibitor) because it inhibits aromatase enzyme, The enzyme stimulating FSH ,LH and then activates the ovulation. This medication has higher average of success than the (Metformin) in the women who want to get Pregnant. The success average expectations more than 80% [11] .This medication causes decreasing the high averages of the estrogen by inhibiting the Aromatase enzyme .This agrees with the results of the researcher [12].and also agrees with [13] and his group from their study the Letrozole medication for group of women infected with breast cancer, the study revealed decreased levels of the estrogen in the women infected who treated with the Letrozole medication. and this agrees with [14]from his study for the women had Breast Cancer which had decreased levels of the estrogen and the decreased levels of the(aromatase enzyme). The aromatase enzyme action on changing the androgen to estrogen in the tissues .This happens mainly in the dipose tissues [15].Also the aromatase enzyme is considered the main source to provide the women by estrogen hormone after the amenorrhea .The medication is used in helping to decrease the estrogen which it is produced by the body ,and then stops the cancer cells from proliferation growing [16].From those results , it was revealed that the decrease concentration of this enzyme plays important role in fertility. This agrees with the results of researcher [8].The decrease concentration of this enzyme leads to women fertility, producing ovum ready for

fertilization .The current study showed a high pregnancy average in the women who are unable to ovulate when they treated this medicines .It acts by decreasing Estrogen concentration inhibiting the aromatase enzyme. This agrees with the results of the researcher [17].

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دراسة تأثير عقار Metformin و مثبط الإنزيم على مستويات إنزيم Aromatase Enzyme في النساء المصابات باضطرابات هرمونية في مدينة كركوك.

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الملخص:

شملت هذه الدراسة (١٠٠) عينة من النساء يستخدمن عقاري Metformin ومثبط الإنزيم في (مستشفى أزادي العام) في مدينة كركوك.(٢٠) عينة دم سحبت من نساء غير مصابات كعينة ضابطة.العينات قسمت إلى ثلاثة مجاميع'المجموعة الأولى(٤٠)من نساء يستخدمن عقار Metformin (مصابات بالعقم الأولي),المجموعة الثانية:(٤٠)من نساء يستخدمن عقار مثبط الإنزيم(مصابات بالعقم الثانوي), والمجموعة الثالثة (٢٠) من نساء غير مصابات كعينة(ضابطة) .لقد بينت نتائج البحث بوجود انخفاض معنوي في مستوى فعالية إنزيم الارومتيزعند مستوى($p<0.05$) في مجموعة النساء المصابات بالعقم الأولي للفئات العمرية (25-18),-36) (45'(35-26) . و أظهرت نتائج البحث أيضا انخفاضاً معنوياً ($p <0.05$) في مستويات فعالية إنزيم الأرومتايز في مجموعة النساء المصابات بالعقم الثانوي للفئات العمرية (25-18), (45-36)'(35-26) . هذا العقار يسبب انخفاض عالي في معدلات الاستروجين بواسطة تثبيط فعالية إنزيم الأرومتايز,وكذالك يدعى هذا العقار (Enzyme inhibitor) لأنه يثبط إنزيم الأرومتايز .وهذا يبرهن إن عقار Letrazole له دور فعال في تحفيز الاباضة في النساء المصابات بالعقم الأولي والنساء المصابات بالعقم الثانوي .