

The Efficacy of Metformin in Treatment of Ovarian Cysts

*Jawed F. H. Al-Mossawe

ABSTRACT :

This study reflects the effectiveness of metformin (hypoglycemic agent) in medical treatment of ovarian cysts; compared with hormonal therapies (medroxyprogesteron acetate and \or conjugated estrogens vaginal cream) .Or treatment by both metformin together with medroxyprogesteron and\or conjugated estrogen vaginal cream .And it shows that the use of both drugs (medroxyprogesteron 5mg\day for 20 days for two courses with interval of 8 days in between ,and\or conjugated estrogen vaginal cream 0.625mg twice daily together with metformin 500mg) was more effective(89.48%) than the uses of metformin alone(76.47), and medroxyprogesteron and\or conjugated estrogens vaginal cream(68.75%), in the treatment of the ovarian cysts.

Key words: Metformin, Medroxyprogesteron Acetate, Conjugated estrogens vaginal cream, ovarian cyst(s)

* Department of pharmacology of The-Qur Medical Collage

INTRODUCTION:

There are many different forms of ovarian cysts, there is also large number of causes for them. Understanding the factors which induce ovarian cysts are critical. Without information ,it isn't always possible to get the correct treatment(1) .The most common type of ovarian cysts is definitely the functional cyst ,which will happen when the typical sequence of the menstruation cycle go wrong in some ways(2) .It is not uncommon for women to develop ovarian cysts during pregnancy and most cysts are found to be benign .If the cyst is small and harmless ,then it can shrink on its own and no treatment is needed(1,6).Ovarian cysts during pregnancy can be a stressful time but the sooner during staring treatment of the cysts from the root cause, it can cure them safely avoiding surgery and focus on planning for the new arrival rather than worrying about the patient

safety(3).Ovarian cysts are quite in women who are within; the age when they can have a baby. Through normally ovarian cysts do not cause much of problem , but malignant cysts lead to serious issues. Therefore, even if the cyst seems a miner issue and is non-malignant, it is still better to stop further complication(2,5).Natural cure is a very vast term; it covers many forms of treatment which are very different from each other. Unlike conventional method in natural cure, there are no single treatment .It should be very careful while deciding which natural cure practitioner to approach. There are many practitioner who call their mode of treatment natural cure , just because they do not have any scientific data to support their treatment. The expertise, knowledge and skill of practitioner play a big role in dealing with ovarian cysts. However, you have to keep in mind that natural cure alone is not effective enough to completely cure ovarian

The Efficacy of Metformin in Treatment of Ovarian Cysts

cysts. They might take many herbs and supplement, but natural cure can not cure cysts right from the root. Natural cure addresses only the symptoms. So; holistic approach is the best solution while treating ovarian cysts(4,5,6). Halfway through the menstrual cycle, the pituitary gland usually signals the follicle to break open and discharge the egg. After release the egg, two hormones, progesterone and estrogen are released by ruptured follicle. There are two cysts the follicle fails to release progesterone, resulting in a hormonal imbalance, this imbalance stimulate growth of more cysts(7,8).

Insulin resistance-leads to excessive insulin level in the blood. This stimulates the ovaries to over-produce androgen, which can cause the development of polycystic ovarian syndrome(4,8). Metformin is the only available biguanide, which is the first choice in over-weight patients. It does not exert a hypoglycemic action in non-diabetic subjects unless given in over-dose. It is used for the symptomatic management of polycystic ovary syndrome(licensed indication); it improves insulin sensitivity; may aid weight reduction, helps to normalize menstrual cycle(increasing the rate of spontaneous ovulation); and may improve hirsutism(9,10,11).

PATIENTS AND METHOD:

All the patients with ovarian cysts, were investigated and managed in Bent Al-Huda Teaching Hospital in Thi-Qar government. The majority of those patients had a history of single cyst, and the other patients has history of multiple ovarian cysts, as confirmed by their history, clinical examinations as well as ultrasonic study, which reflect either single or multiple ovarian cyst(s), unilateral or bilateral cyst(s), as

well as the size and any other criteria of the cyst(s). Hormonal analysis mainly for estrogen. progesterone were also done for some patients. Other investigations involved spiral CT-scan and/or MRI if available with some patients, were also studied. Other routine examinations such as complete blood picture and E.S.R., also done for most of the patients. The total number 52 patient had been investigated and managed, with age ranged between 25-45 years old as shown in(table 3).

DOSAGES AND DURATION OF TREATMENT:

17 patient were treated either by metformin in a dose of 500mg/day for 2 months; other 16 patient were treated by medroxyprogesteron acetate in a dose of 5mg/day for 21 day and then repeated this course after 8 days with same dose, either alone /or together with conjugated estrogens vaginal cream(0.625mg-2 times per a day). And the third group are 19 patient were treated by both metformin(50mg\day) for 60 day, and medroxyprogesteron acetate 5mg/day with or\ without conjugated estrogens vaginal cream(0.625mg twice daily) for two courses with 8 free drug days in between(3,8,12). The every new results of these investigations, mainly ultrasonic results were compared during each visit. And according to these results; the terms good improvements, or good responses were used in this study.

RESULTS:

In this study the number of the patients which were treated by metformin were 13(76.47%) out of 17 patient were completely respond to the treatment and had good improvements, as they compared with 11patient (68.75%) , who were treated by medroxyprogesteron acetate with/or

without conjugated estrogens vaginal cream out of 16 patient had good improvements. While the third group 19 patient were treated by both (metformin and medroxyprogesteron acetate with or\ without conjugated estrogens vaginal cream) by a doses and duration of treatment which were also previously mentioned (reported), were 17(89.48%) out of 19 patient, had good responses for both or the three drugs, as shown in table (1). And the distribution of the ovarian cysts in this study; showing that the single ovarian cyst was 46(88.47%), more than the multiple cysts: 6(11.54%); in which the single cyst(s) were more in the right ovary: 31(67.40%) than that in the left ovary: 15(32.60%). And the multiple cyst(s) were also more in the right ovary: 4(66.67%), than that in left ovary: 2(33.34%) –(table 2).

DISCUSSION :

Ovarian cysts are very common pathological condition for female. An ovarian cyst is a fluid sac on an ovary in female reproductive system which can be cured by chemotherapeutic drugs(14). So, in the present study: it was found that metformin 13(76.47%) was more effective than medroxyprogesteron with\ or without conjugated estrogens vaginal cream 11(68.75%) in the treatment of ovarian cyst(s). While 17(89.48%) of the patients respond well to both metformin together with medroxyprogesteron with\ or without conjugated estrogens vaginal cream as a combination therapy for treatment of ovarian cyst(s), that in chemotherapeutic treatments of ovarian cyst(s); depend on factors related to the age of the female, size ,number, and type of the cyst(s), if the cyst(s) were unilateral or bilateral situation (Table 2), also depend on the chemotherapeutic agent(s) and their pharmacokinetic criteria ,and duration

of treatment(3). In this paper it was found that the usages of hormonal therapy (medroxyprogesteron with\ or without conjugated estrogens vaginal cream) together with metformin, had good percentage of response, that in some studies reflect: that insulin resistance; a high level of insulin can stimulate ovarian androgen production, which lead to the production of male hormones. This reduces the sex – hormone binding globulin or (S.H.G.B.). The S.H.G.B. can in turn aggravate the ovarian cyst(s) condition to quite an extent(8). Metformin is for the symptomatic management of polycystic ovary syndrome (unlicensed indication); it improves insulin sensitivity; may aid weight reduction; help to normalize menstrual cycle (increasing the rate of spontaneous ovulation), and may improve hirsutism (11). In other studies they found that women who tend to form frequent functional cysts may be put on birth control pills, that birth control pills stop the ovaries from function and, therefore, prevent further cyst from developing(15). In recent time, quite a few medication alternatives have arrived that can cure ovarian cysts. But most of them are successful completely. The fact is, it is only through holistic remedies that cyst in the ovary can be successfully treated. Besides, the holistic system causes no side effects. And thus is 100% safe, sound and dependable methods of treatment for undesirable ovarian cysts. The holistic approach runs on the principle of forewarned is forearmed, believes that cysts in the ovary need to be eradicated by removing the causes. Treating the body as a whole and identifying all the contributing factors of the problem, this approach target the spiritual, mental and physical level; the person and educates her not to runaway from it with courage and confidence. Once all the contributing

The Efficacy of Metformin in Treatment of Ovarian Cysts

factors are identified, they can be treated separately-and this is why the holistic approach is so successful in treating ovarian cysts(2,16).It was also found that the distribution of ovarian cyst(s) in this study; were high percentages as a single cyst than the multiple cysts.We concluded from this study: that the combination of both

metformin together with medroxyprogesteron with\ or without conjugated estrogens vaginal cream is more effective for treatment of ovarian cysts in a correct doses and duration.

Table (1) The state (results) of the treatments of ovarian cysts by either medroxyprogesteron with\or without conjugated estrogens vaginal cream, Metformen or both drugs.

| State of responses(improvements) | Treatment by medroxyprogesteron with\ or without conjugated estrogens vaginal cream | Treatment by only metformin | Treatment by all or both drugs |
|--|---|-----------------------------|--------------------------------|
| Patients with good improvements(results) | 11(68.75%) | 13(76.47%) | 17(89.48%) |
| Patients without improvements(results) | 5(31.25%) | 4(23.53%) | 2(10.53%) |
| Total | 16 | 17 | 19 |

Table (2) Distributions of the ovarian cysts according to their site and their number(multiplicity)

| Site of the cyst(s) | Single cyst(s) | Multiple cyst(s) |
|---------------------|----------------|------------------|
| Right cyst | 31(67.40%) | 4(66.67%) |
| Left cyst | 15(32.60%) | 2(33.34%) |
| Total | 46(88.47%) | 6(11.54%) |

REFERENCES:

- 1- Marc Sundfor, Lyn Tylor, 'Ovarian cysts symptoms, causes and treatment', JANSSEN LIBRARY, Gynecology 2000:19(4):32-35.
- 2- [http:// www.artidedashashboard.com](http://www.artidedashashboard.com), By Mary Park,Oct.1009.
- 3- G.Glyton, T.L .Lewis and G.D. Prinker, Gynecology by Ten Teacher, 'Treatment of ovarian cysts' , 14th Ed. 1985:193-219.
- 4- Sills E.S., Perioe M., Palermo G.D., 'Correction of hyperinsulinemia in oligoovulatory women with clomiphen-resistant Polycystic Ovary Syndrome, Eur. J. Obstet. Gynecol. Reprod. Biol. 2002:93(4),135-141.

- 5- Zervon M., Martines F.J., Amsden G.W. 'Management of ovarian cyst in married females in 25-45 years old' Amer. J. of gynecology and obstetric, Vol. 20 N1(January and February), 1999; 7-11.
- 6- Pukender J., Rautianen M., 'Emergency treatment of ovarian cysts', British J.of Gynecology. And obstetric, 1996, 37suppl. C., 53-61.
- 7- Pepine C. J. et al, 'Hormonal analysis in early pregnancy' ,Am. J. Gynecol. 1998, (82):21-24.
- 8- Patery N.L. , Jenarf F.M. et al, Medicine and surgery, 'A study of serum progesterone and estrogen hormones in female patients in relation to Diabetes Mellitus with ovarian cysts', 1998(xxv)4,9.
- 9- Osterion I., Brut V.L., et al,'Safty of Metformin' B.M.J. 1993, 306, 893-911.
- 10- Baily C.J. and Turner R.C., 'Metformin', N. Engl. J. Med., 1996, 334(9): 574-579.
- 11- B.N.F. (British National Formulary), 55th Ed, March, 2008, Page368.
- 12- Dunn C.J. and Peters D.H. 'Metformin: A Review of its Pharmacologic Properties and Therapeutic Use in Diabetes Mellitus', 'Drugs', 1995, 49(5):721-749.
- 13- Hassan S.S., Romero R., et al, 'Patients with an ultrasonographic ovarian cysts, have 50% risk of early spontaneous preterm delivery', Am. J. of gynecology and obstetric, 2000:182(6). 1458-1467.
- 14- Brown M.J., Hydock S. Hormonal analysis in early pregnancy', 'Drugs', 2000:5, (Supple2): 201-212.
- 15-<http://www.X.Plain.com>, The Patient Education Institute, Inc. 2005.
- 16- Kolhapure S.A., Mitra S.K.' Uses of Metformin', 'Medicine Update' 2007:12(2), 25-32.

فعالية عقار المتفورمين في علاج مرض المبايض المتكيسة

*د.جواد الموسوي

الخلاصة

إن هذه الدراسة تعكس لنا الاختلاف بين عقارين (Metformin) و medroxyprogesterone acetate with or without conjugated estrogens vaginal cream) في فعاليتها الدوائية في علاج المبايض المتكيسة. والتي تبين أن ٨٩,٨٤% فعال في ما إذا استعمل العقارين أو (العقاقير) المذكورة أعلاه سوية. بينما توضح الدراسة بأن ٧٦,٧٥% فعال في دوائية لعقار (Metformin) فيما إذا استعمل لوحده في علاج المبايض المتكيسيه وان ٦٨,٧٥% نسبه فعاليه عقار Medroxyprogesterone acetate with or without conjugated estrogens vaginal cream) إذا استعمل لوحده .

*كلية الطب – جامعة ذبقار – قسم الأدوية/السموم