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TUXUMDON ZAHIRASI PAST BO'LGAN KECH REPRODUKTIV YOSHDAGI AYOLLARDA OVULYASYONNI RAG'BATLANTIRISHDA KLOMIFEN SİTRAT BO'LGAN MADDALARNING SAMARALI BAHOLANISH

Axmedjanova X.Z., Olimova K.J., Shukurov F.I.

Toshkent tibbiyot akademiyasi, O'zbekiston

✓ *Rezume*

Maqsad: past tuxumdon zaxirali kech reproduktiv yoshdagi ayollarда ovulyatsiyasini rag'batlantirishda kломифен sitrat saqlovchi preparat samaradorligini baholash.

Material va tadqiqot usullari. Tadqiqotga 60 nafar past tuxumdon zaxirali ayollar kiritildi, ulardan, I-gruxni 30 nafar past tuxumdon zaxirali ayollar, II-guruxga 30 nafar tuxumdon zaxirasi o'ta past ayollar tashkil etdi. Nazorat guruxini - 20 nafar yosh reproduktiv yoshdagi ayollar tashkil etdi. Barcha ayollarga ovulyatsiyani rag'batlantirish maqsadida kломифен sitrat saqlovchi preparat berildi. Tuxumdonlar zaxirasini baholash uning biokimoyiy va exografik markerlarini o'lchash orqali amalaga oshirildi.

Natijalar va ularning muxokamasi. I-guruxda 23 (76,7%) nafar ayollarda ovulyatsiya sodir bo'lishiga erishildi. Ulardan 2 (11,7%) nafarida ovulyatsiya kломифен sitrat saqlovchi dorining dozasi 100mg.gacha oshirilganda, 5(29,4%) nafarida esa 150mg miqdorda berilganda sodir bo'ldi. Ushbu guruxning 15 (73,0%) nafar ayolida homiladorlik sodir bo'ldi. II- guruxda 21 (76,7%) nafar ayollarda ovulyatsiya sodir bo'lishiga erishildi. Ulardan 3 (10%) nafarida ovulyatsiya kломифен sitrat saqlovchi dorining dozasi 100mg.gacha oshirilganda, 2(29,4%) nafarida esa 150mg miqdorda berilganda sodir bo'ldi. Ushbu guruxning 15 (66,7%) nafar ayolida homiladorlik sodir bo'ldi.

Xulosa. Past tuxumdon zaxirali kech reproduktiv yoshdagi ayollarda ovulyatsiyani rag'batlantirishda kломифен sitrat saqlovchi preparatini qo'llash guruxlarda mos ravishda 76,7% va 70,0%da ovulyatsini sodir bo'lishiga va guruxlarga mos ravishda 73,0% va 66,7% ayollarda homiladorlik bo'lishiga olib keldi.

Kalit so'zlar: kech reproduktiv yosh, tuxumdonlar zaxirasi, ovulyatsiyani rag'batlantirish, kломифен sitrat o'z ichiga olgan moddalar.

ОЦЕНКА ЭФФЕКТИВНОСТИ КЛОМИФЕН ЦИТРАТ СОДЕРЖАЩЕГО ВЕЩЕСТВ В СТИМУЛЯЦИИ ОВУЛЯЦИИ У ЖЕНЩИН ПОЗДНЕГО РЕПРОДУКТИВНОГО ВОЗРАСТА С НИЗКИМ ОВАРИАЛЬНЫМ РЕЗЕРВОМ

Aхмеджанова X.З., Олимова К.Ж., Шукуров Ф.И.

Ташкентская медицинская академия, Узбекистан

✓ *Резюме*

Цель: оценка эффективности применения кломифен цитрат содержащего вещества в стимуляции овуляции у женщин позднего репродуктивного возраста с низким овариальным резервом.

Материалы и методы. В исследование были включены 60 женщин с пониженным овариальным резервом, из них: I- основную группу вошли - 30 женщин с низким овариальным резервом и во II - 30 женщин с крайне низким овариальным резервом получавших кломифен цитрат содержащий препарат для стимуляции яичников, группу сравнения составили- 20 женщин аналогичной патологией, но отказавшихся от приема кломифен



цитратом содержащего препарата. Всем пациенткам для стимуляции овуляции была назначена кломифен цитратом содержащего вещества. Оценка овариального резерва у женщин был проведены с помощью оценке его биохимического и эхографического маркеров.

Результаты. В I группе больных овуляция была достигнута у 23 (76,7%) пациенток. Из них у 2-х (11,7%) овуляция наступила после второго цикла на дозе в 100мг и у 5 (29,4%) после третьего месяца овуляции на дозе в 150мг кломифен цитратом содержащего препарата в день. Беременность наступила у 15 (73,0%) больных этой группы: у одной больной в первом же цикле лечения при приеме 50мг кломифен цитратом содержащего препарата, у второй на третьем цикле стимуляции овуляции при дозе 100мг данного препарата. Во 2-й группе больных овуляция была достигнута у 21 (70,0%) больных. У трех (10%) и у двух (6,7%) из них овуляция произошла после второго и третьего месяца стимуляции с применением 100-150мг кломифен цитратом содержащего препарата в день, Беременность наступила у 15 (66,7%) больных этой группы. Беременность в группе сравнения наступила у 3 (15,0%) пациенток.

Заключение. Применение кломифен цитратом содержащего препарата у женщин с позднего репродуктивного возраста с низким и крайне низким овариальным резервом приводит индукцию овуляции у 76,7% и 70,0% женщин соответственно, и наступлению беременности у 73,0% и 66,7% женщин соответственно.

Ключевые слова: поздней репродуктивный возраст, овариальный резерв, стимуляция овуляции, кломифен цитратом содержащий вещества.

EVALUATION OF THE EFFECTIVENESS OF CLOMIPHENE CITRATE CONTAINING SUBSTANCES IN STIMULATION OF OVULATION IN WOMEN OF LATE REPRODUCTIVE AGE WITH LOW OVARIAN RESERVE

Akhmedhanova Kh.Z., Olimova K.Zh., Shukurov F.I.

Ташкентская медицинская академия, Узбекистан

✓ *Resume*

Objective: to evaluate the effectiveness of the use of clomiphene citrate-containing drug in ovulation stimulation in women of late reproductive age with low ovarian reserve.

Materials and methods. The study included 60 women with reduced ovarian reserve, of which: I - the main group included - 30 women with low ovarian reserve and II - 30 women with extremely low ovarian reserve treated with clomiphene citrate containing a drug for ovarian stimulation, the comparison group consisted of - 20 women with a similar pathology, but refused to take a clomiphene-containing drug. All patients were prescribed clomiphene citrate containing substances to stimulate ovulation. The assessment of the ovarian reserve in women was carried out by assessing its biochemical and echographic markers.

Results. In group I patients, ovulation was achieved in 23 (76.7%) patients. Of these, 2 (11.7%) ovulated after the second cycle at a dose of 100 mg and in 5 (29.4%) after the third month of ovulation at a dose of 150 mg of clomiphene citrate-containing drug per day. Pregnancy occurred in 15 (73.0%) patients of this group: in one patient in the first cycle of treatment when taking 50 mg of clomiphene citrate-containing preparation, in the second in the third cycle of ovulation stimulation at a dose of 100 mg of this drug. In the 2nd group of patients, ovulation was achieved in 21 (70.0%) patients. Three (10%) and two (6.7%) of them ovulated after the second and third months of stimulation using 100-150 mg of clomiphene-containing drug per day. Pregnancy occurred in 15 (66.7%) patients of this group. Pregnancy in the comparison group occurred in 3 (15.0%) patients.

Conclusion. The use of clomiphene citrate-containing drug in women from late reproductive age with low and extremely low ovarian reserve leads to the induction of ovulation in 76.7% and 70.0% of women, and the onset of pregnancy in 73.0% and 66.7% of women, respectively.

Key words: late reproductive age, ovarian reserve, ovulation stimulation, clomiphene citrate containing substances.

Dolzarbligi

Ayloning yoshi tuxumdonlar zahirasini belgilovchi eng muhim fiziologik omildir [1,2]. Yoshga bog'liq follikulalar sonining fiziologik kamayishi tug'ilish uchun juda muhimdir. Ayollarda bu muammo sababli bepushtlik bilan davolanishshga murojaat qilishlarining tobora keng tarqalgan sababiga aylanib bormoqda [3,4]. Ayollarda reproduktiv qarish tuxumdonlardagi ootsitlarning soni va sifati yoshga qarab kamayib borishi haqidagi umumiy qabul qilingan nazariyaga amal qiladigan jarayondir [5,6]. Tuxumdonlarning qarishi follikulalar guruxi saqlanadigan ootsitlar soni va sifatining pasayishi bilan bog'liq fiziologik jarayondir [7,8]. Tuxumdonlar zahirasi kamaygan kech reproduktiv yoshdagi ayollarda ovulyatsiyani rag'batlantirishda klomifen sitratni o'z ichiga olgan Duinum® preparatini samaradorligini baholash bo'yicha nashr etilgan tadqiqotlar hozirgacha mavjud emas [9,10].

Past tuxumdon zaxirali kech reproduktiv yoshdagi ayollarda klomifen sitratni o'z ichiga olgan preparatlarning follikulogenez va endometriy qalinligiga qay darajada ta'sir qilishi haqidagi savolga hanuzgacha aniq javob topilmagan. Yuqorida aytilganlarning barchasi past tuxumdon zaxirali kech reproduktiv yoshdagi ayollarda tuxumdonlarni rag'batlantirish va fertillikni tiklash uchun klomifen sitratni saqlovchi preparatning samaradorligini baholashga bag'ishlangan ushbu izlanish tadqiqotning dolzarbligini ta'kidlaydi.

Tadqiqotning maqsadi past tuxumdon zaxirali kech reproduktiv yoshdagi ayollarda ovulyatsiyani rag'batlantirishda klomifen sitrat saqlovchi preparat samaradorligini baholash.

Material va usullari

Tadqiqotga 60 nafar past tuxumdon zaxirali ayollar kiritildi, ulardan, 1- gruxni 30 nafar past tuxumdon zaxirali ayollar, II -guruxga 30 nafar o'ta tuxumdon zaxirasi o'ta past ayollar tashkil etdi. Nazorat guruxini - 20 nafar yosh reproduktiv yoshdagi ayollar tashkil etdi. Barcha ayollarga ovulyatsiyani rag'batlantirish maqsadida klomifen sitrat saqlovchi dori berildi. Tuxumdonlar zaxirasini baholash uning biokimyoviy va exografik markerlarini o'lhash orqali amalaga oshirildi. Tadqiqotga kiritilgan ayollarning o'rtacha yoshi $35,5 \pm 0,2$ yoshni tashkil etdi. Tadqiqotda klinik, gormonal, ultratovush va statistik tadqiqot usullaridan foydalanildi. Chanoq a'zolarining ultratovush tekshiruvi SAMSUNG (Koreya) apparatida mos ravishda 3,5-4,5 va 6-7 MGts chastotali transabdominal va transvaginal datchiklar yordamida amalga oshirildi.

Mazkur tadqiqotda biz tuxumdonlarni rag'batlantirish maqsadida ilk bor klomifen sitrat saqlovchi Duinum® preparatidan foydalandik. Ushbu preparatni ayollarga berishda biz ularda aniqlangan tuxumdonlar zaxirasini qay darajada ekanligini hisobga olgan holda berdik.

Olingen natijalarni statistik qayta ishlash Statistica for Windows 7.0 dasturi yordamida amalga oshirildi. Ma'lumotlar $M \pm m$ sifatida taqdim etiladi. $p < 0,05$ ga to'g'ri keladigan farqlar statistik ahamiyatga ega deb hisoblandi.

Natijalar va tahlillar

Barcha ayollarda tuxumdonlar zahirasining darajasiga qarab, quyidagi sxema bo'yicha klomifen sitratini o'z ichiga olgan preparat yordamida ovulyatsiya rag'batlantirildi: 1- guruxga kiruvchi past tuxumdon zaxirali ayollarda ovulyatsiyani rag'batlantirish 1-oyda, hayz siklining 3-7-kunlari orasida 1 tabletkadan 1 marta 5 kun davomida (50 mg) ichish tavsiya qilindi. Xayz siklini 2-oyida xayzni 3-7 kunlari, tuxumdonlar ovulyatsiyani rag'batlantirishni 1 tabletkadan 2 marta 5 kun davomida (100 mg), xayz siklini 3-oyida xayzni 3-7 kunlari esa 1 tabletkadan 3 maxaldan (150 mg) 5 kun davomida ichish buyurildi.

2-guruxga kiruvchi o'ta past tuxumdon zaxirali ayollarda ovulyatsiyani rag'batlantirish 1-oyda, hayz siklining 2-6-kunlari orasida 1 tabletkadan 1 marta 5 kun davomida (50 mg) ichish tavsiya qilindi. Xayz siklini 2-oyida xayzni 3-7 kunlari, tuxumdonlar ovulyatsiyani rag'batlantirishni 1 tabletkadan 2 marta 5 kun davomida (100 mg), xayz siklini 3-oyida xayzni 3-7 kunlari esa 1 tabletkadan 3 maxaldan (150 mg) 5 kun davomida ichish buyurildi.

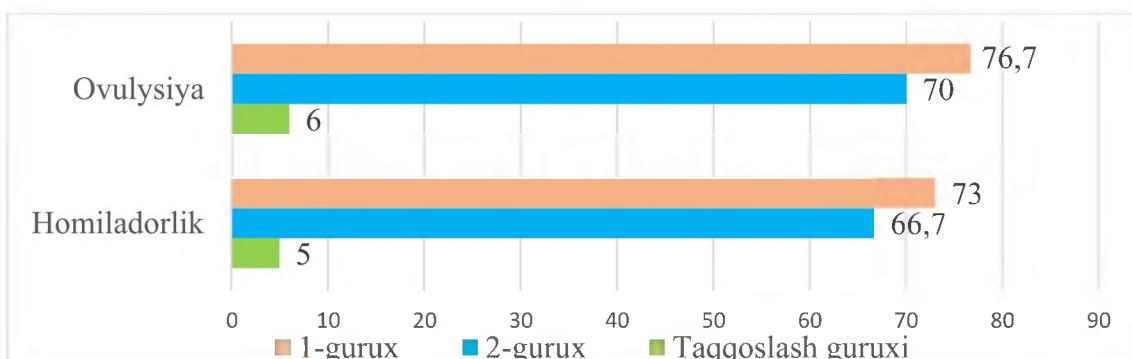
Xayz sikli dinamikasida va davolanish vaqtida tuxumdonlar funksiyasini rag'batlantirish samaradorligini baholash maqsadida ultratovush yordamida follikulometriya o'tkazildi va endometriyning qalinligi o'lchandi. Ultratovush tekshiruvida endometriyning qalinligi va exogenligi, hayz davrining 8, 12 va 14-kunlarida etakchi follikullarning soni va hajmini shuningdek xayzning ikkinchi yarmida sariq tana hosil bo'lishi baholandi.



Ovulyatsiyani rag‘batlantirish uchun klonifien sitrat preparatini o‘z ichiga olgan olgan bemorlarning 1-guruhida maksimal follikulaning diametri sezilarli darajada ($p<0,05$) o‘sdi va o‘rtacha $2,2 \pm 0,4$ sm.ni tashkil etdi, II- guruhda ushbu ko‘rsatkich $2,0 \pm 0,3$ sm.ni tashkil etdi. Ushbu ikkala guruh ayollarida endometriyning qalinligi ham sezilarli darajada oshdi ($p<0,05$) va I-guruhda o‘rtacha $0,9 \pm 0,03$ sm va II-guruhda $1,0 \pm 0,2$ sm.ni tashkil etdi. Shu bilan birga, ushbu ko‘rsatkichlar bo‘yicha ikki guruhni taqqoslash shuni ko‘rsatdiki, 1-guruhdagi bemorlarda maksimal follikulaning diametri va endometriyning qalinligi 2-guruh mos ko‘rsatkichlaridan sezilarli darajada oshib ketgan ($p<0,05$).

I-guruhdagi ayollarda ovulyatsiya 23 (76,7%) naferida sodir bo‘ldi. Ulardan 2 tasida (6,6%) ovulyatsiya ikkinchi xayz sikkida rag‘batlantiruvchi preparatni kuniga 100 mg ichgach sodir bo‘ldi. Bir (3,3%) nafer bemorda esa uchinchi davolash sikkida rag‘batlantiruvchi preparatni kuniga 150 mg etkazganda sodir bo‘ldi. Homiladorlik ushbu guruhdagi 17 (73%) nafer bemorlarida yuz berdi. bir nafer bemorda ovulyatsini rag‘batlantirishning birinchi sikkida klonifien sitrat saqlovchi preparatni miqdori 50 mg miqdorda qabul qilganda, ikki naferida esa ovulyatsiyani rag‘batdantirishning uchinchi sikkida klonifien sitrat saqlovchi preparatni 100 mg dozada qabul qilganida sodir bo‘ldi.

II-guruh bemorlarida ovulyatsiya 21 (70,0%) nafer bemorlarda sodir bo‘ldi. Ulardan 3 (10,0%) naferida ovulyatsiya klonifensitrat saqlovchi preparatni kuniga 100-150 mg qo‘llash orqali ikkinchi va uchinchi rag‘batlantirish oylarida sodir bo‘lgan. Taqqoslash guruhidagi ayollarda homiladorlik 3 (10,0%) naferida sodir bo‘lgan (rasmga qarang).



Rasm. Klonifien sitrat saqlovchi preparatini qabul qilgan ayollarda ovulyatsiya va homiladorlikni salmog‘i, %.

Shunday qilib, klonifien sitrat saqlovchi preparat bilan ovulyatsiyani rag‘batlantirish samarali usul bo‘lib, tuxumdonlar zaxirasi past bo‘lgan kech reproduktiv yoshdagagi ayollarning 73,3%da ovulyatsiyaga erishishni ta‘minlaydi. Ovulyatsiyani rag‘batlantirish fonida, klonifien sitrat saqlovchi preparatni muddatidan oldin to‘xtatishni talab qiladigan jiddiy nojo‘ya ta‘sirlarga olib kelmadidi.

Olingan ma‘lumotlarga ko‘ra, klonifien sitrat saqlovchi preparatni qo‘llash bilan 60 ovulyatsiya sikkida xayz sikkining o‘rtalarida diametri 18 mm.dan ortiq bo‘lgan follikullarning o‘rtacha soni 44 ta (73,3%)ni tashkil qilib, ulardan barcha follikulalar etilgan va follikulogenetni rag‘batlantirishga erishilgan, 6 xayz sikkida ikkitadan follikula etilishiga erishilgan. Follikula rivojlanishining preovulyator bosqichiga bo‘lgan davr o‘rtacha $13,5 \pm 0,2$ kunni tashkil etdi. Ovulyatsiya sodir bo‘lganligi tasdiqlangan ayollarda hayz davrining 12-14-kunlarida dominant follikulning o‘rtacha diametri $18 \pm 1,3$ mm.ni tashkil etdi. Ikkala asosiy guruxga kiruvchi ayollardagi etakchi follikulaning o‘lchamlari klonifien sitrat saqlovchi preparatini turli dozalarini qabul qilganda solishtirishni ushbu jadvalda ko‘rish mumkin (1-jadvalga qarang).

1 –Jadval

Tadqiqotga kiritilgan ayollarda etilgan follikulalarning o‘lchami, ($M \pm m$)

KS saqlovchi preparat dozasi,mg	1-gurux, n=30			2-gurux, n=30		
	XSning 8- kuni	XSning 12-kuni	XSning 14-kuni	XSning 8- kuni	XSning 12-kuni	XSning 14- kuni
50	$9,1 \pm 0,2$	$16,0 \pm 0,2$	$19,1 \pm 1,2$	$9,0 \pm 0,1$	$16,0 \pm 0,2$	$19,0 \pm 1,2$
100	$9,0 \pm 0,1$	$15,8 \pm 0,1$	$19,0 \pm 1,3$	$8,8 \pm 0,3$	$15,8 \pm 0,3$	$18,8 \pm 1,4$
150	$8,9 \pm 0,3$	$15,0 \pm 0,3$	$18,9 \pm 1,2$	$8,7 \pm 0,4$	$15,6 \pm 0,1$	$18,7 \pm 1,21$
P	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05

Klonifien sitrat saqlovchi preparatning dozasiga qarab, xayz sikli davomida endometriy qalinligida ham sezilarli farqlar aniqlanmadidi (2-jadvalga qarang).



2-Jadval

Tadqiqotga kiritilgan klomifen sitrat saqlovchi qabul qilgan ayollarda endometriyning qalinligi, (M ±m)

KS saqlovchi preparat dozasi,mg	1-gurux, n=30			2-gurux, n=30		
	XSning 8-kuni	XSning 12-kuni	XSning 14-kuni	XSning 8-kuni	XSning 12-kuni	XSning 14-kuni
50	7,0±0,1	7,8±0,1	9,2±1,3	6,8±0,2	9,0±0,1	9,2±1,3
100	6,9±0,2	7,7±0,2	9,0±1,1	6,7±0,3	8,8±0,2	8,7±1,2
150	6,7±0,3	7,0±0,3	8,9±1,0	6,5±0,4	7,6±0,3	7,7±1,1
P	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05

Tadqiqotga kiritilgan jami ayollardan 44 (73,3%) nafarida ovulyasiya sodir bo‘lishiga erishildi. Kech reproduktiv yoshdagi 16 (8,3%) nafar ayolda klomifen sitrat saqlovchi preparati bilan uch oyda rag‘batlantirilishiga qaramasdan anovulyasiya holati saqlanib qoldi. Xayz siklining o‘rtasida endometriyning o‘rtacha qalinligi $9,2 \pm 0,3$ mm.ni tashkil etdi, bu urug‘langan tuxum xujayrani implantatsiyasi uchun qulay o‘lchamdir. Homiladorlik tadqiqotga kiritilgan ayollardan 42 (70,0%) nafarida sodir bo‘lgan. Klomifen sitrat saqlovchi preparatni qo‘llashda tuxumdonlarning javob berish reaksiyasini va homiladorlar salmog‘ini tahlil qilish, qo‘llanilayotgan klomifen sitrat saqlovchi preparatning dozasiga qarab, ya’ni, preparat dozasini kuniga 100mg.ga oshirish homiladorlik tezligini ikki baravar oshishiga olib kelishini ko‘rsatdi ($p<0,05$).

Shunday qilib, klomifen saqlovchi preparatni ovulyasiyani rag‘batlantirish maqsadida qo‘llash natijasida tadqiqotga kiritilgan ayollarning 42(70%) nafarida homilador bo‘lishiga erishildi va u guruxlarda mos ravishda 23(76,7%)nafar va 21(70,0%) nafarni tashkil etdi.

Xulosa

Past tuxumdon zaxirali kech reproduktiv yoshdagi ayollarda klomifen sitrat saqlovchi preparatini qo‘llash guruxlarda mos ravishda 76,7% va 70,0% ayollarda ovulyasini sodir bo‘lishiga, hamda guruxlarda mos ravishda 73,0% va 66,7% ayollarda homilador bo‘lishlikga olib keldi.

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