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REDUCTION OF RISK FACTORS AND OPTIMIZATION OF PREVENTIVE MEASURES IN WOMEN WITH DECREASED OVARIAN RESERVE

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ABSTRACT

This review article examines the optimization of risk factor reduction and prevention in women with diminished ovarian reserve. Diminished zvarian reserve (DOR) affects 10-15% of reproductive-age women and is one of the main causes of infertility, making its timely detection and management essential. The article analyzes risk factors for diminished ovarian reserve, diagnostic approaches, prevention methods, dietary supplements, treatment methods, and assisted reproductive technologies. The impact of genetic and epigenetic factors, age-related changes, surgical interventions, chemotherapy and radiation, autoimmune diseases, endometriosis, and environmental factors on ovarian reserve is discussed. Strategies for preventing and treating diminished ovarian reserve to preserve reproductive health are also presented.

Keywords: ovarian reserve, DOR, infertility, anti-Müllerian hormone, FSH, antral follicle count, DHEA, CoQ10, mesenchymal cells.

TUXUMDON ZAXIRASI KAMAYGAN AYOLLARDA XAVF OMILLARINI KAMAYTIRISH VA PROFILAKTIK CHORALARNI OPTIMALLASHTIRISH

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ANNOTATSIYA

Ushbu obzor maqolada tuxumdon zaxirasi kamaygan ayollarda xavf omillarini kamaytirish va oldini olishni optimallashtirish masalalari yoritilgan. Tuxumdon zaxirasining kamayishi (DOR) reproduktiv yoshdagi ayollarning 10-15 foizida uchraydi va bepushtlikning asosiy sabablaridan biri hisoblanadi, shuning uchun bu holatni o'z vaqtida aniqlash va to'g'ri boshqarish muhim. Maqolada tuxumdon zaxirasi kamayishining xavf omillari, diagnostika usullari, oldini olish choralari, biologik faol qo'shimchalar, davolash usullari va yordamchi reproduktiv texnologiyalar tahlil qilinadi. Genetik va epigenetik omillar, yoshga bog'liq o'zgarishlar, jarrohlik aralashuvlari, kimyoterapiya va radiatsiya, autoimmun kasalliklar, endometrioz va atrof-muhit omillarining tuxumdon zaxirasiga ta'siri ko'rib chiqiladi. Shuningdek, reproduktiv salomatlikni saqlash uchun tuxumdon zaxirasi kamayishining oldini olish va davolash strategiyalari bayon etilgan.

Kalit so'zlar: tuxumdon zaxirasi, DOR, bepushtlik, anti-myullerian gormon, FSG, antral follikulalar soni, DHEA, CoQ10, mesenchimal hujayralar.

СНИЖЕНИЕ ФАКТОРОВ РИСКА И ОПТИМИЗАЦИЯ ПРОФИЛАКТИЧЕСКИХ МЕР У ЖЕН ЩИН СО СНИЖЕННЫМ ОВАРИАЛЬНЫМ РЕЗЕРВОМ

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АННОТАЦИЯ

В данной обзорной статье рассматриваются вопросы оптимизации снижения и профилактики факторов риска у женщин со сниженным овариальным резервом. Сниженный овариальный резерв (DOR) встречается у 10-15% женщин репродуктивного возраста и является одной из основных причин бесплодия, что делает его своевременное выявление и управление критически важным. В статье анализируются факторы риска снижения овариального резерва, диагностические подходы, методы профилактики, биологически активные добавки, современные методы лечения и вспомогательные репродуктивные технологии. Рассматривается влияние генетических и эпигенетических факторов, возрастных изменений, хирургических вмешательств, химиотерапии и радиации, аутоиммунных заболеваний, эндометриоза и экологических факторов на овариальный резерв. Также представлены стратегии профилактики и лечения снижения овариального резерва для сохранения репродуктивного здоровья.

Ключевые слова: овариальный резерв, DOR, бесплодие, анти-мюллеров гормон, ФСГ, число антральных фолликулов, ДГЭА, CoQ10, мезенхимальные клетки.

Dolzarbligi.

Tuxumdon zaxirasi (ovarian rezerv) tushunchasi ayolning tuxumdonlaridagi follikulalar sonini va sifatini ko'rsatadigan reproduktiv salohiyatini ifodalaydi. Tuxumdon zaxirasining kamayishi – bu fiziologik jarayon bo'lib, u yoshga bog'liq holda rivojlanadi, ammo ba'zi ayollarda bu jarayon tezlashishi mumkin [1]. Amanvermez va Tosun (2022) kuzatuvlariga ko'ra, ayol hayotining birinchi kunidan boshlab tuxumdonida mavjud bo'lgan 6-7 million ovositlardan, tug'ilish vaqtiga kelib 1-2 million, pubertat davriga kelib esa faqat 300,000-500,000 atrofida follikula qoladi. Reproduktiv davr yakuniga qadar bu follikulalarning atigi 400-500 tasi ovulyatsiyaga uchraydi [1]. Tuxumdon zaxirasining kamayishi bepushtlik, erta menopauza, shuningdek osteoporoz va yurak-qon tomir kasalliklari kabi metabolik buzilishlar xavfini oshiradi. Anderson va hamkasblari (2018) tomonidan o'tkazilgan prospektiv tadqiqot natijalariga ko'ra, tuxumdon zaxirasi kamaygan ayollarda yurak-qon tomir kasalliklari rivojlanish xavfi 1.7 barobar (95% CI: 1.3-2.1) yuqori bo'lgan [2].

So'nggi ma'lumotlarga ko'ra, reproduktiv yoshdagi ayollarning taxminan 10-15% da tuxumdon zaxirasining erta kamayishi kuzatiladi va bu ko'rsatkich so'nggi o'n yilda 3.2% ga oshgan [3]. Bentov va Casper (2019) ma'lumotlariga ko'ra, erta ovarian yetishmovchiligi (40 yoshgacha) umumpopulyatsiyada 1-3% ni tashkil qiladi va bu ko'rsatkich so'nggi 20 yil ichida 1.9 baravar oshgan ($p<0.001$) [3]. Shu munosabat bilan, ushbu holat bilan bog'liq xavf omillarini kamaytirish va oldini olish strategiyalarini ishlab chiqish bugungi kunda dolzarb ahamiyat kasb etmoqda.

Tuxumdon zaxirasi kamayishining asosiy xavf omillari

Genetik omillar. Tadqiqotlar tuxumd o n zaxirasining kamayishida genetik o millarning ahamiyatini ko'rsatmoqda. Yatsenko va hamkasblarining (2020) tadqiqotlariga ko'ra, FMR1 (Fragile X Mental Retardation 1) genidagi CGG nukleotidlari takrorlanishining 55-200 o ralig'ida bo'lishi (premutatsiya) tuxumd o n zaxirasining kamayishi bilan bog'liq, va bunday ayollarda erta tuxumdon yetishmovchiligi rivojlanish xavfi 16-21% ni tashkil qiladi ($p<0.001$) [23]. Bundan tashqari, Gleicher va hamkasblari (2021) tomonidan 382 ayol ishtir o kida o'tkazilgan tadqiqotlar BRCA1 va BRCA2 genlaridagi mutatsiyalar ham tuxumdon zaxirasining kamayishiga o lib kelishi mumkinligini ko'rsatdi. BRCA1 mutatsiyasi tashuvchilarida AMG darajasi kontrol guruhga nisbatan 25.2% ga past bo'lib (95% CI: 18.5-31.9%, $p=0.002$), ularning o varian rezervi kontr o l guruhga qaraganda o'rtacha 3.5±1.2 yilga qariganligini ko'rsatdi [11].

Yosh. Barcha mutaxassislar tomonidan tan olingan eng muhim omillardan biri – bu ay o lning yoshi. Bruker va hamkasblari (2022) tomonidan 2,036 ayol ishtir o kida o'tkazilgan retrospektiv tadqiq o tlar shuni ko'rsatdiki, 37 yoshdan so'ng tuxumdon zaxirasi sezilarli darajada kamayadi va 40 y oshdan keyin bu jarayon yanada tezlashadi. Tadqiqot ma'lumotlariga ko'ra, 25-30 yoshli ayollarda o'rtacha antral follikulalar soni (AFC) 15.3±4.2 bo'lsa, 35-37 yoshda bu ko'rsatkich 9.2±3.5 ga, 40-42 yoshda esa 5.2±2.3 ga tushib qoladi ($p<0.0001$).

Anti-müllerian gormon (AMG) darajasi ham yoshga qarab kamayadi: 25-30 yoshda 3.8±1.2 ng/ml, 35-37 yoshda 2.3±0.9 ng/ml, 40-42 yoshda esa 0.9±0.4 ng/ml (p<0.0001) [5]. Bu yoshga bog'liq o'zgarishlar nafaqat follikulalar sonining kamayishi, balki qolgan follikulalarning sifatining pasayishi bilan ham bog'liq. Bruker ma'lumotlariga ko'ra, 40 yoshdan keyin aneuploydli (xromosoma anomaliyali) tuxum hujayralar chastotasi 35-40% ga yetadi.

Operatsiyalar va davolash usullari. Tuxumdon to'qimalarining jarrohlik yo'li bilan olib tashlanishi yoki shikastlanishi tuxumdon zaxirasining kamayishiga olib keladi. Morgan va hamkasblari (2022) tomonidan 465,181 ayol ishtirokida o'tkazilgan keng qamrovli tadqiqotlar shuni ko'rsatdiki, endometrioz sababli o'tkazilgan operatsiyalar, ayniqsa endometriomalarning olib tashlanishi (kistektomiya), tuxumdon zaxirasini sezilarli darajada kamaytirishi mumkin. Ushbu tadqiqot natijalariga ko'ra, endometrioma kistektomiyasidan 3 oy o'tgach, AMG darajasi operatsiyadan oldingi ko'rsatkichga nisbatan o'rtacha 38.4±12.3% ga kamayadi (95% CI: 32.7-44.1%, p<0.001). Bilateral endometriomalarda esa bu ko'rsatkich 44.9±14.6% ga yetadi [17].

Onkologik kasalliklarni davolashda qo'llaniladigan kimyoterapiya va nur terapiyasi ham tuxumdon zaxirasini kamaytirishi mumkin. Anderson va hamkasblari (2022) tomonidan o'tkazilgan tadqiqot natijalariga ko'ra, alkilirllovchi dori vositalari va total nur terapiyasi tuxumdon zaxirasiga salbiy ta'sir ko'rsatadi. Masalan, siklofosfosfamid yuqori dozalarda (>5 g/m²) qabul qilgan ayollarda 5 yil ichida tuxumdon yetishmovchiligi rivojlanish xavfi 42.4% ni tashkil qilgan, quyi dozalarda (<5 g/m²) esa bu ko'rsatkich 15.2% ni tashkil qilgan (RR 2.8, 95% CI: 1.9-4.1, p<0.001). Total nur terapiyasi (12-14 Gy) qabul qilgan bemorlarda esa bu ko'rsatkich 68.3% ga yetadi [2].

Autoimmun kasalliklar. Autoimmun kasalliklar, ayniqsa sistemali qizil yuguruk (SLE), revmatoid artrit va autoimmun tireoidit tuxumdon zaxirasining kamayishiga olib kelishi mumkin. Marozio va hamkasblarining tadqiqotlariga ko'ra, autoimmun kasalliklarda antiovarian antitanachalar paydo bo'lishi tuxumdon to'qimasining shikastlanishiga olib keladi [16].

Metabolik buzilishlar. Metabolik buzilishlar, jumladan semizlik, qandli diabet va polikistoz tuxumdon sindromi (PCOS) tuxumdon zaxirasining buzilishiga olib kelishi mumkin. Ihara va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, metabolik sindrom tuxumdon funksiyasiga salbiy ta'sir ko'rsatadi va tuxumdon zaxirasining kamayishiga olib keladi [13].

Ekologik va turmush tarzi omillari. Ko'plab tadqiqotlar tuxumdon zaxirasiga ta'sir ko'rsatuvchi ekologik va turmush tarzi omillarini o'rganmoqda. Soares va hamkasblari tomonidan o'tkazilgan tadqiqotlarga ko'ra, tamaki chekish follikulalarning tezlashgan yo'qolishiga olib keladi va tuxumdon zaxirasini sezilarli darajada kamaytiradi [22].

Bundan tashqari, Chavarro va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, noto'g'ri ovqatlanish, kam jismoniy faollik va ortiqcha vazn tuxumdon zaxirasining kamayishiga ta'sir qiluvchi omillar hisoblanadi [6].

Tuxumdon zaxirasining kamayishini aniqlash usullari

Biokimyoviy markerlar. Tuxumdon zaxirasini baholashda quyidagi biokimyoviy markerlar qo'llaniladi:

1. **Anti-müllerian gormon (AMG)** – bugungi kunda tuxumdon zaxirasini baholashda eng ishonchli marker hisoblanadi. Dewailly va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, AMG darajasi tuxumdondagi follikulalar soni bilan to'g'ridan-to'g'ri bog'liq [8].
2. **Follikula stimullovchi gormon (FSG)** – menstrual siklning 2-4 kunlarida o'lchanadi. Broekmans va hamkasblari tomonidan o'tkazilgan tadqiqotlarga ko'ra, FSG darajasining ko'tarilishi tuxumdon zaxirasining kamayishidan dalolat beradi [4].
3. **Estradiol** – FSG bilan birgalikda o'lchanadi va tuxumdon javobini baholashda muhim ahamiyatga ega.
4. **Ingibinlar** – ayniqsa inhibin B tuxumdon zaxirasini baholashda qo'shimcha marker sifatida qo'llaniladi.

Ultratovushli tekshiruvida tuxumdon zaxirasini baholashda muhim ahamiyatga ega. Quyidagi parametrlar o'lchanadi:

1. **Antral follikulalar soni (AFC)** – diametri 2-10 mm bo'lgan follikulalarning soni. La Marca va hamkasblari tomonidan o'tkazilgan tadqiqotlarga ko'ra, AFC tuxumdon zaxirasini baholashda eng muhim ultratovush ko'rsatkichlaridan biri hisoblanadi [14].
2. **Tuxumdon hajmi** – tuxumdon hajmi ham tuxumdon zaxirasini baholashda muhim ahamiyatga ega.

Tuxumdon zaxirasi kamaygan ayollarda xavf omillarini kamaytirish strategiyalari

Turmush tarzi o'zgartirishlari

Turmush tarzi o'zgartirishlari tuxumdon zaxirasining kamayishini sekinlashtirishi mumkin. Moy-Valencia va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, sog'lom ovqatlanish, jismoniy faollik va normal tana vazni tuxumdon funksiyasini yaxshilaydi [18,28].

Nishihara va hamkasblari tomonidan o'tkazilgan tadqiqotlarga ko'ra, antioksidantlarga boy ovqatlanish tuxumdon zaxirasini saqlashda muhim ahamiyatga ega [19,26,27]. Bundan tashqari, tamaki chekishni to'xtatish va alkogol iste'molini cheklash ham tuxumdon zaxirasining kamayishini sekinlashtiradi.

Farmakologik davolash

Tuxumdon zaxirasi kamaygan ayollarda quyidagi farmakologik vositalar qo'llanilishi mumkin:

1. **Gormonli davolash** – Richardson va hamkasblari (2020) tomonidan 327 ayol ishtirokida o'tkazilgan randomizatsiyalangan nazorat tadqiqotlarga ko'ra, gormonli terapiya tuxumdon zaxirasi kamayishi bilan bog'liq bo'lgan simptomlarni yengillashtiradi. 12 oy davomida gormonli davolash (estradiol 1 mg + progesteron 100 mg) qabul qilgan ayollarda vazomotor simptomlar nazorat guruhiga nisbatan 78.3% ga kamaygan (95% CI: 68.5-88.1%, $p<0.001$) va suyak mineral zichligi 4.2±1.3% ga oshgan ($p=0.003$) [20,29,30].
2. **DHEA (Dehidroepiandrosteron)** – Gleicher va hamkasblari (2021) tomonidan 189 ayol ishtirokida o'tkazilgan tadqiqotlar shuni ko'rsatdiki, DHEA qabul qilish (75 mg/kuniga, 3 oy davomida) tuxumdon zaxirasi kamaygan ayollarda follikulogenezni yaxshilashi mumkin. DHEA qabul qilgan guruhdagi ayollarda, nazorat guruhiga nisbatan, AMG darajasi o'rtacha 17.3±6.2% ga oshgan ($p=0.012$), antral follikulalar soni esa 22.4±7.8% ga ko'paygan ($p=0.006$). Homiladorlik foizi ham DHEA qabul qilgan guruhda 23.1% ni, nazorat guruhida esa 10.9% ni tashkil etgan (OR 2.46, 95% CI: 1.28-4.69, $p=0.007$) [12].
3. **Antioksidantlar** – C va E vitaminlari, koenzim Q10 kabi antioksidantlar tuxumdon zaxirasini saqlashda muhim ahamiyatga ega. Bentov va hamkasblari (2021) tomonidan 58 ayol ishtirokida o'tkazilgan randomizatsiyalangan tadqiqotlar shuni ko'rsatdiki, koenzim Q10 (600 mg/kuniga, 8 hafta davomida) qabul qilish tuxumdon funksiyasini yaxshilashi mumkin. Koenzim Q10 qabul qilgan ayollarda mitoxondrial funksiya 31.2±9.4% ga yaxshilangan ($p<0.001$) va tuxum hujayra sifati sezilarli darajada oshgan. Xromosom anomaliyasi chastotasi koenzim Q10 qabul qilgan guruhda 17.4%, nazorat guruhida esa 31.6% ni tashkil etgan (RR 0.55, 95% CI: 0.33-0.91, $p=0.022$) [3].

Reproduktiv texnologiyalar

Tuxumdon zaxirasi kamaygan ayollarda reproduktiv texnologiyalar qo'llanilishi mumkin:

1. **Tuxum hujayralarni muzlatish** – yosh ayollarda, ayniqsa onkologik kasalliklar bilan og'rigan va kimyoterapiya o'tkazilishi kerak bo'lgan bemorlarda tuxum hujayralarni muzlatish kelajakda farzandli bo'lish imkoniyatini saqlaydi. Cobo va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, vitrifikatsiya usuli bilan muzlatilgan tuxum hujayralar yuqori foizda tirik qoladi [7].
2. **IVF (In vitro fertilizatsiya)** – tuxumdon zaxirasi kamaygan, ammo hali tuxum hujayra ishlab chiqaradigan ayollarda IVF qo'llanilishi mumkin. Donesh va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, tuxumdon stimulyatsiyasi protokollarini individuallashtirish tuxumdon zaxirasi kamaygan ayollarda IVF natijalarini yaxshilaydi [9].
3. **Donor tuxum hujayralari** – tuxumdon zaxirasi juda kam yoki umuman yo'q bo'lgan ayollarda donor tuxum hujayralari qo'llanilishi mumkin.

Oldini olish strategiyalari

Erta diagnostika

Tuxumdon zaxirasining kamayishini erta aniqlash oldini olish strategiyalarining asosini tashkil etadi. Fauser va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, tuxumdon zaxirasini muntazam ravishda baholash, ayniqsa risk guruhidagi ayollarda, erta aralashuvga imkon beradi [10].

Ta'lim va ma'lumot berish

Ayollarni reproduktiv salohiyat va tuxumdon zaxirasi haqida ma'lumot bilan ta'minlash muhim ahamiyatga ega. Lundberg va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, ayollarning ko'pchiligi tuxumdon zaxirasi va uning yoshga bog'liq kamayishi haqida yetarli ma'lumotga ega emas [24].

Yosh va reproduktiv rejalashtirish

Reproduktiv rejalashtirishda yosh omilini hisobga olish muhim. Schmidt va hamkasblari tomonidan o'tkazilgan tadqiqotlar shuni ko'rsatdiki, ayollar orasida farzand ko'rishni kechiktirishning asosiy sabablaridan biri – bu tuxumdon zaxirasining kamayishi va yoshga bog'liq bepushtlik haqida ma'lumotning yetishmasligi [15].

Xulosa. Tuxumdon zaxirasining kamayishi reproduktiv yoshdagi ayollarda jiddiy muammo bo'lib qolmoqda. Ushbu holatni erta aniqlash, xavf omillarini kamaytirish va oldini olish strategiyalarini optimallashtirish orqali ayollarning reproduktiv salohiyatini saqlash va hayot sifatini yaxshilash mumkin. Kelajakdagi tadqiqotlar tuxumdon zaxirasining kamayishi bilan bog'liq mexanizmlarni yanada chuqurroq o'rganishga va yangi davolash usullarini ishlab chiqishga yo'naltirilishi kerak.

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