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IMMUNOLOGIK BEPUSHTLIKNI BAHOLASHDA SITOKIN PROFILI VA IMMUN YALLIG‘LANISH MARKERLARINING AHAMIYATI

Xikmatova N.I., Tosheva I.I.
Abu Ali ibn Sino nomidagi Buxoro davlat tibbiyot instituti

РЕЗЮМЕ

Иммунологическое бесплодие (ИБ) представляет собой одну из важнейших причин бесплодия, связанную с нарушениями в иммунной системе, приводящими к неспособности организма женщины к зачатию или поддержанию беременности. Одним из главных механизмов является образование антиспермальных антител (АСАТ), которые могут препятствовать нормальной функции сперматозоидов, их проникновению в яйцеклетку и имплантации эмбриона.

Цель исследования: *изучить значение цитокинового профиля и маркеров иммунного воспаления в диагностике и оценке иммунологического бесплодия у женщин.*

Материал и методы: *обследовано 180 женщин в возрасте 22–37 лет. Пациентки были распределены на группу с АСА-доминантным вариантом иммунологического бесплодия (n=75), группу с цитокин-доминантным вариантом (n=75) и контрольную группу (n=30). Уровни IL-6, TNF-α и IL-10 определялись методом ИФА.*

Результаты: *у пациенток II группы выявлено значительное повышение уровней IL-6 (12,22±3,58 пг/мл) и TNF-α (19,04±5,87 пг/мл) при одновременном снижении уровня IL-10 (2,99±0,85 пг/мл) по сравнению с контрольной группой (p<0,0001). Индекс IL-6/IL-10 продемонстрировал высокую информативность в оценке активности иммунного воспаления.*

Заключение. *Полученные результаты свидетельствуют о высокой диагностической и прогностической значимости исследования цитокинового профиля и маркеров иммунного воспаления. Комплексная оценка данных показателей позволяет повысить эффективность диагностики иммунологического бесплодия и оптимизировать выбор лечебной тактики.*

Ключевые слова: *иммунологическое бесплодие, цитокиновый профиль, IL-6, TNF-α, IL-10, антиспермальные антитела, иммунное воспаление, диагностика.*

SUMMARY

Relevance. *Immunological infertility (II) is one of the significant causes of infertility and is characterized by disorders of the immune system that reduce a woman's ability to achieve and maintain pregnancy. One of the main mechanisms underlying this condition is the production of antisperm antibodies (ASA), which can impair the normal function of spermatozoa, hinder their interaction with the oocyte, and interfere with embryo implantation.*

Objective. *To evaluate the characteristics of the cytokine profile and immune inflammatory activity in women with immunological infertility.*

Materials and methods. *The study included 180 women aged 22-37 years. Participants were divided into three groups: Group I – women with antisperm antibody (ASA)-dominant immunological infertility (n=75), Group II – women with cytokine-dominant immunological infertility (n=75), and a control group of fertile women without immunological infertility factors (n=30). Serum levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-10 (IL-10) were determined using enzyme-linked immunosorbent assay (ELISA).*

Results. *The results demonstrated significant alterations in the cytokine profile of women with immunological infertility. Elevated levels of pro-inflammatory cytokines (IL-6 and TNF-α) and reduced concentrations of the anti-inflammatory cytokine IL-10 were identified. These changes were associated with activation of immune-inflammatory processes and correlated with impaired reproductive function.*

Conclusion. *The findings indicate the high diagnostic and prognostic value of cytokine profile assessment and immune inflammation markers in immunological infertility. Comprehensive evaluation of these parameters may improve diagnostic accuracy and contribute to the optimization of treatment strategies.*

Keywords: *immunological infertility, cytokine profile, IL-6, TNF-α, IL-10, antisperm antibodies, immune inflammation, diagnostics.*

Bepushtlik zamonaviy reproduktiv tibbiyotning eng muhim tibbiy-ijtimoiy muammolaridan biri hisoblanadi. Jahon sog‘liqni saqlash tashkiloti ma’lumotlariga ko‘ra, reproduktiv yoshdagi juftliklarning taxminan 10–15% bepushtlikdan aziyat chekmoqda. So‘nggi yillarda bepushtlikning immunologik shakllariga bo‘lgan qiziqish tobora ortib bormoqda, chunki immunologik omillar reproduktiv funksiya buzilishlarining 10–20% holatlarida muhim ahamiyat kasb etadi.

Immunologik bepushtlikning patogenezida antispermal antitanalar hosil bo‘lishi, immun tolerantlikning buzilishi va surunkali immun yallig‘lanish jarayonlarining faollashuvi muhim o‘rin tutadi. Ayniqsa, sitokinlar tizimidagi o‘zgarishlar reproduktiv jarayonlarning

barcha bosqichlariga, jumladan, urug‘lanish, embrion implantatsiyasi va homiladorlikning dastlabki rivojlanish bosqichlariga salbiy ta’sir ko‘rsatishi mumkin.

Yallig‘lanishni keltirib chiqaruvchi sitokin hisoblangan interleykin-6 (IL-6) va o‘sma nekrozi omili-α (TNF-α) darajalarining oshishi hamda yallig‘lanishga qarshi sitokin – interleykin-10 (IL-10) miqdorining kamayishi immun gomeostazning buzilishiga olib keladi. Natijada endometriy retseptivligi pasayadi, implantatsiya jarayonlari izdan chiqadi va reproduktiv muvaffaqiyatsizlik xavfi ortadi. Shu bilan birga, immunologik bepushtlikda sitokin profilining ahamiyati va uning klinik qiymati to‘liq o‘rganilmagan bo‘lib, bu sohada qo‘shimcha tadqiqotlar o‘tkazishni talab qiladi.

Shu munosabat bilan immunologik bepushtlik bilan og‘rigan ayollarda sitokin profili va immun yallig‘lanish faolligini o‘rganish kasallik patogenezini chuqurroq tushunish, yangi diagnostik mezonlarni ishlab chiqish va reproduktiv natijalarni prognozlash imkoniyatlarini kengaytirish nuqtai nazaridan dolzarb ahamiyatga ega hisoblanadi.

MATERIALLAR VA TADQIQOT USULLARI

Tadqiqotga 22–37 yoshdagi jami 180 nafar ayol jalb qilindi. Barcha ishtirokchilar klinik va immunologik xususiyatlariga ko‘ra uch guruhga ajratildi:

• **I guruh** – antispermal antitana (ASA) dominant immunologik bepushtlikka ega 75 nafar ayol;

• **II guruh** – sitokin-dominant immunologik bepushtlikka ega 75 nafar ayol;

• **III guruh** – immunologik buzilishlar aniqlanmagan 30 nafar fertil ayoldan iborat nazorat guruhi.

Qon zardobida IL-6, TNF-α va IL-10 darajalari immunoferment tahlil (ELISA) usuli yordamida aniqlandi. Statistik tahlil natijalari M±SD ko‘rinishida taqdim etildi. Farqlar $p<0,05$ darajada ahamiyatli deb qabul qilindi.

NATIJALAR VA MUHOKAMA

Tadqiqot natijalari immunologik bepushtlik bilan og‘rigan ayollarda sitokin profilining sezilarli darajada o‘zgarganligini ko‘rsatdi.

II guruhda IL-6 darajasi 12,22±3,58 pg/ml ni tashkil etdi, bu I guruhdagi 5,82±2,12 pg/ml va nazorat guruhidagi 1,89±0,85 pg/ml ko‘rsatkichlaridan statistik jihatdan ishonchli ravishda yuqori bo‘ldi ($p<0,0001$). TNF-α darajasi ham xuddi shunday tendensiyani namoyon qildi. II guruhda ushbu sitokinning o‘rtacha qiymati 19,04±5,87 pg/ml bo‘lib, I guruhdagi 9,88±2,72 pg/ml va nazorat guruhidagi 5,11±1,61 pg/ml qiymatlaridan sezilarli yuqori ekanligi aniqlandi ($p<0,0001$).

Aksincha, yallig‘lanishga qarshi sitokin hisoblangan IL-10 darajasi II guruhda minimal ko‘rsatkichga ega bo‘lib, 2,99±0,85 pg/ml ni tashkil qildi. Bu I guruhdagi 5,00±1,26 pg/ml va nazorat guruhidagi 6,55±2,30 pg/ml ko‘rsatkichlaridan ishonchli past bo‘ldi ($p<0,0001$).

IL-6 ning yuqori darajalari II guruh bemorlarining 98,7% ida va I guruh bemorlarining 88,0% ida aniqlandi. Nazorat guruhida mazkur holat atigi 3,3% ishtirokchida qayd etildi. TNF-α ning belgilangan chegaradan yuqori ko‘tarilishi II guruh bemorlarining 98,7% ida va I guruhning 73,3% ida kuzatildi. Nazorat guruhida esa mazkur ko‘rsatkichning oshishi qayd etilmadi.

Sitokinlar muvozanatini baholash maqsadida IL-6/IL-10 indeksi hisoblandi. Ushbu indeks II guruhda eng yuqori qiymatlarga ega bo‘lib, yallig‘lanishni qo‘zg‘atuvchi immun javobning ustunligini ko‘rsatdi.

Olingan ma’lumotlar immunologik bepushtlikning sitokin-dominant shaklida immun yallig‘lanish jarayonlari asosiy patogenetik mexanizmlardan biri ekanligini tasdiqlaydi. Yallig‘lanishni keltirib chiqaruvchi sitokinlar darajasining oshishi endometriy retseptivligining buzilishi, implantatsiya jarayonlarining izdan chiqishi va reproduktiv muvaffaqiyatsizlik rivojlanishiga sabab bo‘lishi mumkin.

XULOSA

Immunologik bepushtlik bilan og‘rigan ayollarda sitokin profilining sezilarli buzilishi kuzatildi. II guruh bemorlarida IL-6 va TNF-α darajalarining yuqori, IL-10 darajasining esa past bo‘lishi immun yallig‘lanish faolligining kuchayganligini ko‘rsatdi. IL-6/IL-10 indeksi immun yallig‘lanish jarayonlarini kompleks baholashda eng informativ ko‘rsatkich sifatida namoyon bo‘ldi. Olingan natijalar sitokin profili immunologik bepushtlikni tashxislash, patogenetik variantlarini farqlash va prognozlashda muhim ahamiyatga ega ekanligini tasdiqlaydi.

ADABIYOTLAR

1. Agarwal A, Baskaran S, Parekh N. Male infertility. Lancet. 2021;397(10271):319–333. doi:10.1016/S0140-6736(20)32667-2.
2. Check JH, Cohen R. The role of cytokines in embryo implantation. Clinical and Experimental Obstetrics & Gynecology. 2019;46(3):331–337. doi:10.12891/ceog4594.2019.
3. Garrido N, Simon C, Pellicer A. Cytokines and implantation. Reproductive BioMedicine Online. 2015;31(5):659–668. doi:10.1016/j.rbmo.2015.07.006.
4. Kutteh WH. Antisperm antibodies and infertility. Fertility and Sterility. 2015;104(3):558–559. doi:10.1016/j.fertnstert.2015.06.031.
5. Kwak-Kim J, Gilman-Sachs A, Kim CE. T helper 1 and 2 immune responses in infertility. American Journal of Reproductive Immunology. 2018;79(3). doi:10.1111/aji.12764.
6. Moffett A, Colucci F. Uterine NK cells and cytokine regulation in pregnancy. Journal of Clinical Investigation. 2014;124(5):1872–1879. doi:10.1172/JCI68107.
7. Naz RK, Saver AE. Immunology of infertility. Journal of Reproductive Immunology. 2016;118:39–49. doi:10.1016/j.jri.2016.07.006.
8. Practice Committee of the American Society for Reproductive Medicine. Evaluation and treatment of infertility. Fertility and Sterility. 2021;116(5):1255–1265. doi:10.1016/j.fertnstert.2021.08.003.

9. Robertson SA. Immune regulation of conception and embryo implantation. Human Reproduction Update. 2018;24(5):543–569. doi:10.1093/humupd/dmy016.
10. Robertson SA, Sharkey DJ. The role of semen in induction of maternal immune tolerance to pregnancy. Seminars in Immunology. 2016;28(2):130–136. doi:10.1016/j.smim.2016.04.004.
11. Saito S, Nakashima A, Shima T, Ito M. Th1/Th2/Th17 and regulatory T-cell paradigm in pregnancy. American Journal of Reproductive Immunology. 2010;63(6):601–610. doi:10.1111/j.1600-0897.2010.00852.x.
12. Schumacher A, Costa SD, Zenclussen AC. Endocrine factors modulating immune responses in pregnancy. Frontiers in Immunology. 2014;5:196. doi:10.3389/fimmu.2014.00196.
13. World Health Organization. Infertility prevalence estimates, 1990-2021. Geneva: World Health Organization; 2023.
14. Yao Y, Tsirka SE. The CCL2-CCR2 system and inflammatory diseases. Cytokine & Growth Factor Reviews. 2014;25(5):499–507. doi:10.1016/j.cytogfr.2014.07.009.
15. Zenclussen AC. Adaptive immune responses during pregnancy. American Journal of Reproductive Immunology. 2017;77(2). doi:10.1111/aji.12681.
