EPIDURALNA PORODNA ANALGEZIJA V SPLOŠNI BOLNIŠNICI IZOLA

EPIDURAL LABOUR ANALGESIA IN IZOLA GENERAL HOSPITAL

Sabina Verem, Boštjan Lovšin, Zdenka Guzej, Janja Zver Skomina, Janislav Ravnikar, Dušan Deisinger, Andreja Smajila

Oddelek za ginekologijo in porodništvo, Splošna bolnišnica Izola, Polje 35, 6310 Izola

Izvleček

Izhodišča *V prispevku želimo predstaviti izkušnje lajšanja porodne bolečine z epiduralno analgezijo v SB Izola za triinpolletno obdobje (2003–2006), razliko v porodu z epiduralno analgezijo in brez nje ter zadovoljstvo porodnic.*

Metode *Retrospektivno smo analizirali 428 porodov: 214 porodnic, ki so rodile z epiduralno porodno analgezijo (EPA), in 214, ki so rodile brez EPA. Kontrolna porodnica je bila prva enakorodnica, ki je rodila pred porodnico iz raziskovalne skupine. Primerjali smo splošne značilnosti porodnic, trajanje in potek poroda, število izhodnih posegov, carskih rezov ter stanje novorojenčkov. V drugem delu smo z anketo ugotavljali oceno bolečine in zadovoljstvo 62 porodnic.*

Rezultati *V izolski porodnišnici je v obdobju od julija 2003 do decembra 2006 214 (10 %) porodnic rodilo s pomočjo EPA. V skupini porodnic z EPA v primerjavi s kontrolno skupino je bila statistično značilno večja povprečna starost porodnic (30,5 proti 28,7 let; p <0,0005), podaljšano trajanje poroda (278 proti 222 minut; p <0,0005), večje število porodov, pospešenih z infuzijo oksitocina (93,4 % proti 72,9 %; p <0,0001) ter večje število dokončanja poroda z izhodnim posegom (vakuumsko ekstrakcijo 14 % proti 1,9 %; p <0,0001). Izid poroda s carskim rezom je bil primerljiv v obeh skupinah. Uporaba EPA kljub večjemu številu izhodnih posegov in daljšim porodom ni vplivala na perinatalne izide in ni pomembnih razlik v oceni vitalnosti novorojenčka po Apgarjevi. Povprečna bolečina, ocenjena po lestvici VAS, je bila največja pred uporabo EPA (VAS 7), najmanjša med porodom (VAS 1,5) in nekoliko večja med iztisom (VAS 2,7). Večina porodnic je bila z uporabo EPA zadovoljnih, 92 % porodnic je analgezijo dan po porodu ocenilo kot dobro ali zelo dobro.*

Zaključki *Uporaba EPA je primerna in učinkovita metoda za lajšanje porodne bolečine. Zadovoljstvo porodnic s tem načinom lajšanja porodne bolečine je veliko. Uporaba EPA kljub večjem številu izhodnih posegov in daljšim porodom ni vplivala na morebitne slabše perinatalne izide.*

Ključne besede *porod; epiduralna analgezija; bolečina*

Abstract

Background *The study presents the experience with epidural analgesia (EPA) for pain relief in Izola General Hospital from 2003 to 2006, the differences of labour between epidural analgesia and without it and the parturients' satisfaction.*

Methods *A retrospective observational study was performed. Data were compared between 214 parturients with EPA matched by 214 parturients without. The control parturient was the equiipara with a term birth and the cephalic presentation of fetus that delivered just before the parturient of the EPA group. Maternal age, labor length, rate of oxitocin use, instrumental deliveries and cesarean sections, Apgar scores and birthweights were compared. The questionnaire was used to estimate the pain in 62 parturients.*

Results *In GH Izola in 214 parturients (10 %) EPA was applied for labour pain relief in the period from July 2003 till December 2006. In the EPA group there was a statistically significance*

compared with the control group: higher parturients' mean age (30.5 vs 28.7 y.o.; p < 0.0005), longer labour length (278 vs 222 min; p <0.0005), higher oxitocin use rate (93.4 % vs 72.9 %; p <0.0001) and higher instrumental delivery rate (vacuum extraction 14 % vs 1.9 %; p <0.0001). The cesarean section rates were equal in both groups. Despite the higher instrumental delivery rate and the longer labour length in the EPA group there were no worse perinatal outcomes, neither was statisticaly significant difference in Apgar scores compared with the control group. The mean intensity of pain was highest before the EPA application (VAS 7), lowest during the transition stage (VAS 1.5) and some higher during the second phase (VAS 2.7). Most of parturients in the EPA group were satisfied; 92 % of them evaluated the EPA as good or very good.

Conclusions *EPA is a very effective method for pain control during labor. The parturients' satisfaction with this pain control method is appropriate. Despite the higher instrumental delivery rate and the longer labour length EPA didn't worsen the perinatal outcome.*

Key words *labour; epidural analgesia; pain*

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PRIMERJAVA KONCENTRACIJ HORMONOV V SERUMU IN FOLIKLOVI TEKOČINI V MODIFICIRANIH NARAVNIH CIKLUSIH IN STIMULIRANIH CIKLUSIH

SERUM AND FOLLICULAR ENDOCRINE PROFILE DIFFERENCES BETWEEN MODIFIED NATURAL CYCLES AND STIMULATED CYCLES

Nina Jančar, Irma Virant-Klun, Eda Vrtačnik-Bokal

Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Ugotovili so, da je višja koncentracija antimüllerjevega hormona (AMH) povezana z boljšim uspehom oploditve in vitro (IVF).[1, 2] Ugotovili so tudi, da je višja serumska koncentracija luteinizirajočega hormona (LH) lahko povezana s slabšo kakovostjo jajčne celice.[3] V naši raziskavi smo primerjali koncentracije AMH, LH, folikel stimulirajočega hormona (FSH), estradiola (E_2) in progesterona (P) v serumu in foliklovi tekočini v modificiranih naravnih ciklusih (MNC) in ciklusih kontrolirane hiperstimulacije jajčnikov (KHJ).*

Metode *Vključenih je bilo 29 žensk, ki so bile v programu oploditve z biomedicinsko pomočjo v MNC, in 30 žensk, ki so imele IVF v ciklusih KHJ z gonadotropinom in antagonistom GnRH. Vzorce seruma in foliklove tekočine smo pridobili na dan vsrkanja jajčnih celic.*

Rezultati *Koncentracija AMH v foliklovi tekočini je bila približno 2-krat višja v MNC kot v ciklusih KHJ, medtem ko je bila serumska koncentracija AMH v obeh skupinah primerljiva. Serumska koncentracija LH je bila skoraj 50-krat višja, koncentracija LH v foliklovi tekočini pa skoraj 8-krat višja v ciklusih MNC kot v ciklusih KHJ. Koncentracija LH je bila skoraj 4-krat nižja v foliklih, kjer je prišlo do vstavitve zarodka, kot v foliklih, kjer do vstavitve ni prišlo. Našli smo pozitivno povezavo med serumskimi in folikularnimi koncentracijami AMH in LH v obeh skupinah. V ciklusih KHJ se je serumska koncentracija AMH višala z večanjem števila pridobljenih jajčnih celic in nižala s starostjo ženske. V MNC smo našli negativno povezavo med koncentracijo AMH v foliklovi tekočini in prostornine vsrkane foliklove tekočine ter med serumsko koncentracijo LH in prostornine vsrkane foliklove tekočine. Serumska koncentracija FSH je bila v ciklusih MNC 2-krat višja kot v ciklusih KHJ, folikularna koncentracija FSH pa je bila v obeh skupinah primerljiva. Serumska koncentracija E_2 je bila v ciklusih MNC 8-krat nižja, folikularna koncentracija pa 2-krat višja kot v ciklusih KHJ. Tudi serumska koncentracija P je bila v ciklusih MNC 8-krat nižja kot v ciklusih KHJ. Folikularna koncentracija P je bila v obeh skupinah primerljiva.*

Zaključki *Ugotovili smo, da se koncentracije hormonov v serumu in foliklovi tekočini močno razlikujejo med ciklusi MNC in ciklusi KHJ. Močno povišane koncentracije LH v serumu in foliklovi tekočini bi lahko vplivale na endometrijsko receptivnost in bi bile zato lahko odgovorne za slabši uspeh IVF v MNC. V ciklusih KHJ višja serumska koncentracija AMH napoveduje večje število pridobljenih jajčnih celic.*

Ključne besede *koncentracije hormonov; foliklova tekočina; modificiran naravni ciklus; kontrolirana hiperstimulacija jajčnikov*

Abstract

Background *It has been found that higher follicular anti-müllerian hormone (AMH) concentrations predict higher fertilization, implantation and pregnancy rates in women undergoing controlled ovarian hyperstimulation (COH).[1, 2] Higher serum luteinizing hormone (LH) concentration may negatively affect oocyte quality.[3] The aim of our study was to compare follicular and serum AMH, LH, follicle-stimulating hormone (FSH), estradiol (E_2) and progesterone (P) concentrations in modified natural cycles (MNC) and COH cycles*

Methods *Women undergoing in vitro fertilization (IVF) were included; 29 in MNC and 30 in COH cycles with gonadotropin and GnRH antagonist. Serum and follicular fluid samples were obtained on the day of oocyte retrieval.*

Results *Follicular AMH concentration was 2 times higher in MNC than in COH group, while serum AMH concentrations were comparable in both groups. Serum LH concentration was almost 50 times higher and follicular LH concentration almost 8 times higher in MNC than in COH group. Follicular LH concentration was almost 4 times lower in follicles with consequent implantation than in follicles without implantation. Serum and follicular concentrations of AMH and LH correlated with each other in both cycle groups. In COH group, serum AMH concentration was significantly higher with increasing number of retrieved oocytes and significantly lower with women's advancing age. In MNC group, there was a negative correlation between follicular AMH concentration and volume of follicular aspirate as well as between serum LH concentration and volume of follicular aspirate. Serum FSH concentration was 2 times higher in MNC than in COH group, while follicular FSH concentrations were comparable in both groups. Serum E_2 concentration was in MNC 8 times lower and follicular E_2 concentration 2 times higher than in COH group. Serum P concentration was 8 times lower in MNC than in COH group, while follicular P concentrations were comparable in both groups.*

Conclusions *The results of our study indicate that serum and follicular endocrine profile is different in MNC and in COH cycles. Extremely high follicular and serum LH concentration in MNC might affect endometrial receptivity and thus have negative effect on IVF success. Higher serum AMH concentration can predict higher number of retrieved oocytes in COH group.*

Key words *hormone concentrations; follicular fluid; modified natural cycle; controlled ovarian hyperstimulation.*

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RAZPOREDITEV GENOTIPOV HUMANIH VIRUSOV PAPILOMA PRI SLOVENSKIH BOLNICAH Z RAKOM MATERNIČNEGA VRATU IN PODTIPSKE RAZLIČICE HPV 16, HPV 18 IN HPV 33

DISTRIBUTION OF HUMAN PAPILLOMA VIRUS GENOTYPES IN WOMEN WITH CERVICAL CANCER IN SLOVENIA AND GENOMIC VARIANTS OF HPV 16, HPV 18 AND HPV 33

Nina Jančar,[1] Boštjan J. Kocjan,[2] Maja M. Lunar,[2] Željka Bogovac,[2] Mario Poljak,[2] Jasna Šinkovec,[1] Eda Vrtačnik-Bokal[1]

[1] Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana
[2] Inštitut za mikrobiologijo in imunologijo, Medicinska fakulteta, Univerza v Ljubljani, Zaloška cesta 4, 1000 Ljubljana

Izvleček

Izhodišča *Opredeliti razporeditev genotipov humanih virusov papiloma (HPV) pri bolnicah z rakom maternicnega vratu (RMV) v Sloveniji in ugotoviti, kolikšen delež RMV bi bilo mogoče preprečiti s cepljenjem proti HPV. Želeli smo določiti tudi podtipske različice treh najpogosteje zastopanih genotipov HPV.*

Metode *Pri vseh 278 vzorcih RMV smo najprej uporabili metodo verižne reakcije s polimerazo (PCR) z začetnikoma GP5+/GP6+. Pri negativnih vzorcih smo uporabili še PCR z začetnikoma CPI/CPIIg oziroma komercialno dostopni HPV genotipizacijski test INNO LiPA. Podtipske različice smo določili z metodo določanja nukleotidnega zaporedja genetskih regij LCR, E6 in E7.*

Rezultati *HPV-pozitivnih je bilo 262/278 (94,2 %) vzorcev RMV. Genotipi HPV so si sledili v naslednjem vrstnem redu po padajoči pogostnosti: 16, 18, 33, 45, 31, 51, 58, 59, 35, 52, 73 in 82. Podtipske različice smo opredelili pri 40/178 izolatih HPV 16, pri 20/34 izolatih HPV 18 in pri 11/13 izolatih HPV 33. Izolate HPV 16 smo razdelili v 26 genomskih različic. Osemintrideset izolatov (95 %) je spadalo v evropsko vejo, en izolat (2,5 %) v azijsko-ameriško vejo in en (2,5 %) v afriško vejo.[1, 2] Izolate HPV 18 smo razdelili v 18 genomskih različic. Devetnajst izolatov (95 %) je spadalo v evropsko vejo, en izolat (5 %) pa v afriško vejo.[2, 3] Izolate HPV 33 smo razdelili v 7 genomskih različic. Pet izolatov (45,5 %) je pripadalo prototipskim, 6 (54,5 %) pa neprototipskim različicam.[4]*

Zaključki *Prvič v Sloveniji smo na reprezentativnem vzorcu bolnic z RMV opredelili zastopanost vseh genotipov HPV neposredno pred uvedbo cepljenja proti HPV. Profilaktično cepljenje proti HPV bi lahko preprečilo do 77,1 % primerov RMV v Sloveniji, povzročenih s HPV 16 in HPV 18. Skoraj vsi izolati HPV 16 in HPV 18 so spadali v evropske veje, prototipske in neprototipske različice HPV 33 pa so bile skoraj enakomerno razporejene pri slovenskih bolnicah z RMV.*

Ključne besede *humani virusi papiloma; genotip; rak maternicnega vratu; podtipska različica*

Abstract

Background *To establish the distribution of human papillomavirus (HPV) genotypes in representative population of women with cervical cancer (CC) in Slovenia in order to contribute the lacking data on HPV in CC and to assess the potential local benefit of future prophylactic HPV vaccination. Furthermore, we wanted to determine genomic variants of the most common HPV genotypes.*

Methods *Polymerase chain reaction with GP5+/GP6+ primers was performed in all 278 CC samples for HPV DNA detection and genotyping. Negative samples were additionally tested using*

CPI/CPIIg primers and INNO-LiPA HPV genotyping assay. Genomic variants of HPV 16, HPV 18 and HPV 33 were determined by sequencing of LCR, E6 and E7 genetic regions.

Results *A total of 262/278 CC samples (94.2 %) were HPV DNA positive. HPV genotypes in Slovenian women with CC, in decreasing order of frequency, were: 16, 18, 33, 45, 31, 51, 58, 59, 35, 52, 73 and 82. Detailed genomic analysis was carried out on 40/178 isolates of HPV 16, 20/34 isolates of HPV 18 and 11/13 isolates of HPV 33. A total of 26 genomic variants of HPV 16 were identified. Thirty-eight isolates (95 %) belonged to the European branch; one isolate (2.5 %) belonged to the Asian-American branch and one (2.5 %) to African branch.[1,2] A total of 18 genomic variants of HPV 18 were identified. Nineteen isolates (95 %) belonged to the European branch and one isolate (5 %) belonged to the African branch.[2,3] Seven genomic variants of HPV 33 were identified. Five isolates (45.5 %) belonged to prototypic variants and 6 (54.5 %) belonged to non-prototypic variants.[4]*

Conclusions *Distribution of all HPV genotypes in Slovenian women with CC was in the present study established for the first time and represents baseline distribution before mandatory HPV vaccination. Prophylactic HPV vaccination with currently available vaccines could prevent up to 77.1 % of CC in Slovenia caused by HPV 16 or HPV 18. Almost all isolates of HPV 16 and HPV 18 belonged to European branches; prototypic and non-prototypic HPV 33 variants were almost equally distributed among Slovenian patients with CC.*

Key words *human papillomavirus; genotype; cervical cancer; genomic variant*

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ELEKTRONSKO MIKROSKOPSKA PRIMERJAVA SLUZNICE ODVZETE S PREGRADE V MATERNICI TER S STRANSKE STENE

ELECTRON MICROSCOPE COMPARISON OF ENDOMETRIUM FROM UTERINE SEPTUM AND ENDOMETRIUM FROM THE LATERAL WALL

Helena Ban-Frangež, Tomaž Tomaževič

Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Pregrada v maternici je znan dejavnik tveganja za spontani splav in prezgodnji porod, glede vpliva na sposobnost zanositve pa so mnenja še deljena. Mehanizem, kako pregrada povzroči omenjene zaplete, ni znan. Najverjetnejša se zdi teorija, ki pravi, da pregrada s sluznico, ki jo prekriva, nudi manj ugodno okolje za ugnezditev in nadaljnji razvoj zarodka. V raziskavi smo želeli ugotoviti, ali se sluznica, ki prekriva pregrado v maternici, morfološko razlikuje od sluznice s stranske stene maternice.*

Preiskovanke in metode dela *V prospektivno študijo smo vključili 30 zaporednih žensk s pregrado v maternici, ki smo jim med operacijo pregrade, načrtovane v času ugnezditvenega okna, odvzeli vzorca sluznice s površine pregrade in s stranske stene maternice ter ju primerjali pod elektronskim mikroskopom. Ocenjevali smo razvojno stopnjo pinopodijev ter primerjali število žleznih izvodil.*

Rezultati *Pinopodiji na sluznici s pregrade v maternici so bili v povprečju na razvojni stopnji 17,7. dne, na stranski steni pa na stopnji 18,1. dne (ns). Na pregradi sta bili v povprečju 2 žlezni izvodili na vidno polje pri 250-kratni povečavi, na stranski steni pa 2,5 izvodili (ns).*

Zaključki *Rezultati naše raziskave kažejo, da se sluznica s pregrade v maternici po številu žleznih izvodil ter razvojni stopnji pinopodijev ne razlikuje od sluznice s stranske stene maternice. Ostale tri raziskave, narejene v svetu, zasnovane na enak način, so potrdile razliko med vzorcema sluznice v opazovanih parametrih. Za jasnejši odgovor so potrebne dodatne študije na večjem številu vzorcev.*

Ključne besede *pregrada maternice; biopsija endometrija; ugnezditev*

Abstract

Background *Septate uterus is an important risk factor for spontaneous abortion and preterm delivery. The role of septate uterus in infertility is still questionable. The mechanism of the adverse effects of a septate uterus is not yet understood. The basic theory proposes that the septum represents a less suitable environment for a developing embryo when compared to the unaffected uterine wall. The aim of our study was to compare the endometrial surface morphology in women with septate uterus.*

Material and methods. *This prospective observational study includes endometrial biopsies that were taken from women with uterine septum. We have included 30 consecutive women who came for the hysteroscopic resection of the septum. The operation was scheduled at the time of the implantation window; an endometrial biopsy was performed and samples were taken from the septum and from the lateral wall and compared under electron microscope. Pinopode development stage and the number of endometrial glands were the main outcome measures.*

Results *Comparison of the endometrium from the septum with that of the lateral wall showed no difference in the number of endometrial glands (2.0 endometrial glands seen at 250 × magnification vs. 2.5; ns), not even in the pinopode stage (17.7 day vs. 18.1 day, ns).*

Conclusions *To our knowledge, there are three researches that have compared endometrium from the septum to the endometrium from the lateral wall in infertile women and all have differences in observed parameters. Our results cannot support earlier findings. The question of mechanism, how septum influences on pregnancy should be further investigated in the larger sample.*

Key words *uterine septum; endometrial biopsy; implantation*

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UPORABA HIALURONANA V POSTOPKU ZUNAJTELESNE OPLODITVE S PRENOSOM ENE BLASTOCISTE

USE OF HYALURONAN-RICH TRANSFER MEDIUM FOR A SINGLE BLASTOCYST TRANSFER IN VITRO FERTILIZATION PROCEDURE

Sara Korošec, Irma Virant-Klun, Tomaž Tomaževič, Helena Meden-Vrtovec

Klinični oddelek za reprodukcijo, Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Najbolj sprejemljivi način zmanjševanja deležev mnogoplodnih nosečnosti v postopku zunajtelesne oploditve (IVF) je prenos enega samega zarodka v maternico, a ob tem obstaja verjetnost, da se dosedanji delež nosečnosti zmanjša. Namen raziskave je bil ugotoviti, ali prenos ene same blastociste v maternico z uporabo s hialuronanom obogatenega gojišča omogoča večji delež nosečnosti kot prenos v gojišču, ki se rutinsko uporablja.*

Material in metode *V prospektivno randomizirano raziskavo smo zajeli 107 preiskovank, vključenih v 1., 2. ali 3. postopek klasičnega postopka IVF ali postopka z neposrednim vnosom semenčice v citoplazmo jajčne celice (ICSI), starih do 37 let in z vsaj eno razvito blastocisto. V študijski skupini 47 preiskovank smo blastociste prenesli v gojišču, obogatenem s hialuronanom, za kontrolno skupino 60 preiskovank pa smo uporabili običajno gojišče za gojenje in prenos blastocist. Primerjali smo delež nosečnosti v študijski in kontrolni skupini.*

Rezultati *Pri prenosu ene same blastociste v maternico smo ugotovili delež nosečnosti 30 %, dvoplodnih nosečnosti pa ni bilo. Po prenosu ene blastociste v gojišču, bogatem s hialuronanom, smo ugotovili za 11 % večji delež nosečnosti, kar pa ni statistično značilno. Razlike med študijsko in kontrolno skupino so bile značilne v podskupini preiskovank, ki so imele 2 ali več razvitih blastocist in so bile v 2. ali 3. postopku zdravljenja (p = 0,045).*

Zaključki *V postopku s prenosom ene same blastociste lahko dosežemo visoke deleže ugnezditve. Hialuronan pomembno izboljša delež ugnezditve le v izbrani podskupini preiskovank po pred tem neuspelem postopku IVF in z več razvitimi blastocistami.*

Ključne besede *blastocista; hialuronan; implantacija; zunajtelesna oploditev*

Abstract

Background *The best way to avoid undesirable multiple pregnancies following in vitro fertilization procedure (IVF) is to perform elective single embryo transfer, but the procedure might result in a reduction of the pregnancy rates. Aim of our study was to establish whether a single blastocyst transfer using a hyaluronan rich transfer medium results in higher pregnancy rates in comparison to the transfer using a conventional transfer medium.*

Material and methods *Our prospective randomized study included 107 patients enrolled in the 1st, 2nd and 3rd classical IVF or intracytoplasmic sperm injection (ICSI) treatment attempt. Patients included were under 37 years of age with at least one blastocyst developed in the procedure. In the study group (47 patients) blastocyst transfers using the hyaluronan rich transfer medium were performed and in the control group (60 patients) the conventional medium was used. The pregnancy rates in the study and in the control group were compared.*

Results *The average pregnancy rate per single blastocyst transfer was 30 %; there were no twin pregnancies. The single blastocyst transfer using hyaluronan resulted in a non-significantly higher pregnancy rate (11 %). A significantly higher pregnancy rate with the use of hyaluronan was found in the subgroup of patients with two or more blastocysts developed in their 2nd and 3rd IVF attempt (p = 0.045).*

Conslusions *The single blastocyst transfer results in high implantation rates. Hyaluronan significantly contributes to higher implantation rates in a selected subgroup of patients following previous implantation failure and with multiple blastocysts developed.*

Key words *blastocyst; hyaluronan; implantation; in vitro fertilization*

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DIAGNOSTIKA IN ZDRAVLJENJE BOLNIC S SINDROMOM POLICISTIČNIH OVARIJEV

DIAGNOSTICS AND TREATMENT OF PATIENTS WITH POLYCYSTIC OVARY SYNDROME

Nataša Vrhkar, Borut Kobal, Helena Meden-Vrtovec
Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Sindrom policističnih ovarijev (PCOS) je najpogostejša endokrinopatija v reproduktivnem obdobju, ki po evropskih merilih prizadene 15–22 % žensk. Je multisistemska reprodukcijsko-metabolna nepravilnost, zato se o njeni diagnostiki in zdravljenju še razpravlja. Ženske s PCOS so bolj ogrožene za razvoj diabetesa tipa 2, metabolnega sindroma, srčno-žilnih bolezni, depresije, nealkoholne maščobne okvare jeter, hiperplazije in raka endometrija ter nekaterih drugih oblik rakavih bolezni. Zato so pomembni zgodnja pravilna diagnoza ter zdravljenje in trajni nadzor PCOS. Do nedavnega je bila pri diagnozi PCOS težava pomanjkanje jasnih meril, leta 2003 pa sta Evropsko združenje za reprodukcijo in embriologijo in Ameriško združenje za reproduktivno medicino objavila definicijo PCOS. Za potrditev diagnoze morata biti prisotna vsaj dva od naslednjih meril: oligo- ali kronična anovulacija (manj kot 8 menstruacij letno oziroma pojavljanje na več kot 35 dni), klinični ali biokemični znaki hiperandrogenizma (alopecija, hirzutizem, seboreja, akne, virilizacija), vidni policistični jajčniki na vaginalnem ultrazvoku (VUZ) (prisotnih 12 ali več foliklov premera 2–9 mm v enem jajčniku ali obeh in/ali prostornina enega ali obeh jajčnikov, ki je večja od 10 cm^3). Potrebno pa je izključiti druge vzroke, ki imajo lahko podobno klinično sliko. Zdravljenje je odvisno od starosti bolnice, bolezenskih znakov, ki prevladujejo, in cilja, ki ga želimo doseči. Vsem bolnicam v prvi vrsti svetujemo zdrav način življenja, debelim bolnicam pa zmanjšanje telesne mase. Zdravljenje bolnic v adolescenci je usmerjeno na odpravljanje motenj menstruacijskega ciklusa (zaščita endometrija in neredne krvavitve), zdravljenje androgenizma, debelosti ter inzulinske rezistence (IR). V prvi vrsti svetujemo še hormonsko kontracepcijo (HK) z neandrogenimi gestageni (NG) z antiandrogeni (AA) ali brez ter po potrebi topično dermatološko zdravljenje (TDZ). V drugi vrsti svetujemo zdravljenje z gestageni v kombinaciji z AA in zdravili, ki povečujejo občutljivost na inzulin (ZPOI). Pri bolnicah v reproduktivni dobi, ki ne želijo zanositi, je zdravljenje usmerjeno v zaščito endometrija in zmanjšanje znakov androgenizma, debelosti, IR in presnovnih tveganj. V prvi vrsti svetujemo še HK z NG najbolje v kombinaciji z AA. Antiandrogeni učinek je možno okrepiti z dodatkom ZPOI, ki zmanjšajo tudi tveganje za razvoj sladkorne in srčno-žilnih bolezni. Pri zelo izraženi androgenizaciji pride v poštev tudi TDZ. Za zaščito endometrija in preprečevanje zanositve je primerna oblika zdravljenja vstavitev maternične vložka z levonorgestrelom. V obmenopavznem obdobju predpišemo nadomestno hormonsko zdravljenje v nizkih odmerkih. Bolnicam v reproduktivnem obdobju, ki želijo zanositi, skušamo sprožiti ovulacijo z zdravili ali kirurškim posegom. Za sprožitev ovulacije z zdravili je najprimernejše zdravilo klomifen citrat (CC). Priporočeni čas zdravljenja s CC je do šest mesecev. Vsaj v prvem ciklusu zdravljenja je priporočljivo nadzorovati odgovor jajčnikov in endometrija z VUZ. Če je odziv ugoden in ženska po šestih ciklusih zdravljenja ni zanosila, je smiselna odločitev intrauterina inseminacija. Pri neuspešnem zdravljenju s CC pri debelih bolnicah dodamo ZPOI. Če tudi na ta način ne uspemo sprožiti ovulacije, postopamo kot pri ostalih, pri katerih je naslednji korak zdravljenje z gonadotropini po metodi postopnega zviševanja odmerkov ali elektrokoagulacija jajčnikov (EKJ), če ta še ni bila napravljena med obravnavo neplodnosti. Slednje je priporočljivo predvsem pri bolnicah, odpornih na CC, ki imajo visoke koncentracije LH v plazmi. Po šestih neuspešnih ciklusih zdravljenja z gonadotropini in EKJ je priporočljivo zdravljenje s postopki oploditve z biomedicinsko pomočjo.*

Zaključki *PCOS zaradi svoje zapletene narave ostaja izziv za klinično prakso. Po najnovejših smernicah morata biti za potrditev diagnoze PCOS prisotna vsaj dva od naslednjih meril:*

oligo- ali kronična anovulacija, klinični ali biokemični znaki hiperandrogenizma, na VUZ vidni policistični jajčniki. Ženske s PCOS so bolj ogrožene za razvoj sladkorne, srčno-žilnih bolezni in nekaterih rakavih bolezni, zato je pomembno dolgoročno zdravljenje sistemskih učinkov PCOS. Slednje igra pomembno vlogo tudi pri zdravljenju ginekoloških težav, saj se poleg že uveljavljenih oblik zdravljenja s kombiniranim zdravljenjem odpirajo nove možnosti še uspešnejše obravnave bolnic s PCOS. V prvi vrsti še vedno svetujemo spremembo življenjskega sloga in zmanjšanje telesne teže, nadaljnja obravnava pa je odvisna od starosti bolnic, prevladujočih kliničnih znakov in reproduktivnih želja.

Ključne besede *sindrom policističnih ovarijev; diagnostika; terapevtski postopki*

Abstract

Background *Polycystic ovary syndrome (PCOS) is the most common female endocrinopathy of reproductive age affecting 15–22 % of women according to European standards. It is a multisystem reproductive-metabolic disorder and its diagnostics and treatment remain controversial. Women with PCOS are at increased risk of developing type II diabetes, metabolic syndrome, cardiovascular disease, depression, non-alcoholic fatty liver disease, endometrial hyperplasia and cancer and few other types of carcinoma. Due to all above, early correct diagnosis, treatment and permanent surveillance of PCOS are of great importance. The main difficulty with diagnosis of PCOS was until recently lack of clear diagnostic criteria. In 2003 the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine published a definition of PCOS. For a diagnosis of PCOS two of three criteria have to be met: oligo- or chronic anovulation (less than 8 menses per year or menses that occur at intervals greater than 35 days), clinical or biochemical signs of hyperandrogenism (alopecia, hirsutism, seborrhoea, acne, virilism), polycystyc ovaries seen on vaginal ultrasound (VUS) (presence of 12 or more follicles in both ovaries measuring 2–9 mm in diameter and/or ovarian volume larger than 10 cm^3 of either or both ovaries). Exclusion of other diseases with similar clinical presentation is necessary. Treatment depends on the age of the patient, predominating clinical signs and aim we try to achieve. First-line treatment for all patients includes life-style changes and weight reduction in obese patients. Management of adolescent patients is aimed at abolishment of menses irregularity and endometrial protection, treatment of hyperandrogenism, obesity, and insulin resistance (IR). In the first-line treatment we also recommend oral hormonal contraceptives (OHC) with non-androgenic gestagens (NG) with or without antiandrogens (AA) and topical dermatological treatment (TDT) if necessary. In the second-line treatment we recommend gestagens combined with AA an insulin sensitizing agents (ISA). Management of patients in reproductive age, who do not want to conceive, is aimed at endometrial protection and treatment of hyperandrogenism, obesity, IR and metabolic risks. In the first-line treatment we also recommend OHC with NG preferably combined with AA. Antiandrogenic effect could be strengthened by adding ISA, which also reduce risks of developing diabetes and cardiovascular disease. In cases of very distinctive hyperandrogenism TDT is possible. To protect endometrium and prevent conception insertion of intrauterine device with levonorgestrel is appropriate. In perimenopause we prescribe low-dosage hormonal replacement therapy. First-line treatment of patients of reproductive age, who want to conceive, is medicamental or surgical induction of ovulation. Clomiphene citrate (CC) is most suitable for medicamental induction of ovulation. Recommended duration of treatment with CC is up to six months. At least in the first cycle of treatment response of ovaries and endometrium with VUS is advisable. If response is satisfactory and a patient did not conceive after six months of treatment an intrauterine insemination is recommendable. In obese women, if treatment with CC is unsuccessful, addition of ISA is recommended. In case of failure of induction of ovulation we proceed as in other patients with whom the next step is treatment with gonadotrophines given by a step-up protocol or ovary electrocoagulation (OEC), if it has not been performed during management of infertility. The latter is advisable first of all for CC resistant women with high LH serum levels. After six unsuccessful months of treatment with gonadotrophines and OEC assisted reproduction techniques are recommended.*

Conclusions *Because of its complicated nature management of PCOS remains a challenge. According to most recent guidelines diagnosis of PCOS requires two of three criteria to be met: oligo- or chronic anovulation, clinical or biochemical signs of hyperandrogenism and polycystyc ovaries seen on VUS. Women with PCOS are at increased risk of developing diabetes, cardiovascular disease and certain types of carcinoma. Thus long-term treatment of systemic*

effects of PCOS is of great importance. The latter also has an important role in treating gynaecological problems because combined treatment together with traditional methods offers even more successful management of patients with PCOS. In the first-line treatment we still recommend life-style changes and weight reduction in obese patients. Further treatment depends on the age, predominating clinical signs and reproductive desires of the patient.

Key words *polycistic ovary syndrom; diagnostic procedures; therapeutic strategies*

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VPLIV MORFOLOGIJE IN RAZVOJA BLASTOCISTE NA IZID NOSEČNOSTI PRI PRENOSU ENE BLASTOCISTE V POSTOPKIH ZUNAJTELESNE OPLODITVE

EFFECT OF MORPHOLOGY AND BLASTOCYST DEVELOPMENT ON THE OUTCOME OF SINGLE-BLASTOCYST TRANSFER IN THE IN VITRO FERTILIZATION PROGRAMME

Brigita Valentinčič-Gruden, Irma Virant-Klun, Lili Bačer-Kermavner, Jerneja Kmecl, Jožica Mivšek, Tomaž Tomaževič, Eda Vrtačnik-Bokal

Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Večplodno nosečnost lahko preprečimo s prenosom enega samega zarodka. Namen raziskave je bil prospektivno oceniti vpliv razvitosti in morfologije blastociste na izid nosečnosti pri prenosu ene blastociste.*

Metode *V raziskavo je bilo vključenih 157 žensk, pri katerih smo prenesli eno samo blastocisto. Povprečna starost žensk je bila 33.6 let, (min. 20, maks. 42). Zarodki so bili razviti do blastociste in ocenjeni po kategorijah po Gardnerju. Pri 83 ženskah smo naredili elektivni prenos ene blastociste, čeprav sta se razvili dve ali več blastocist (Skupina 1), pri 74 pa prenos edine blastociste, ki se je razvila (Skupina 2).*

Rezultati *V Skupini 1 (2 ali več blastocist) je zanosilo 39,8 % žensk, v drugi skupini (ena sama blastocista) pa 23,0 % žensk; razlika je bila statistično značilna (P < 0,05). V primeru prenosa povsem razvite blastociste je bila stopnja zanositve v obeh skupinah žensk približno enaka (45,5 % vs. 44,6 %). Pri ženskah z elektivnim prenosom ene povsem razvite blastociste z dobro morfologijo embrioblasta in trofoblasta je bila stopnja zanositve statistično značilno višja kot pri ženskah s prenosom ene zgodnje blastociste s pričetkom tvorbe blastocela. V obeh skupinah je zanosilo več žensk s povsem razvito blastocisto, in sicer 45,6 %, z blastocisto z začetkom razvoja blastocela pa 7,1 %.*

Zaključki *Po prenosu ene blastociste je večja verjetnost zanositve pri ženskah z dvema ali več razvitimi blastocistami. Prav tako je verjetnost zanositve večja pri prenosu ene povsem razvite blastociste z dobro morfologijo embrioblasta in trofoblasta. Razvitost blastociste je ključni dejavnik elektivnega prenosa ene blastociste, ki morda zrcali genetski status zarodka.*

Ključne besede *blastocista; elektivni prenos enega zarodka; morfologija; razvitost blastociste; nosečnost*

Abstract

Background *Multiple pregnancy can be prevented by an elective single blastocyst transfer. The aim of this prospective study was to evaluate the effect of blastocyst development and morphology on the outcome of single blastocyst transfer.*

Methods *In this study 157 women with single blastocyst transfer were included; their mean age was 33.6 years, range 20–42. Embryos were cultured to the blastocyst stage and evaluated using the Gardner's classification. An elective single blastocyst transfer was performed in 83 women although 2 or more blastocysts developed (Group 1) and in 74 with only one developed blastocyst (Group 2).*

Results *In Group 1 (2 or more blastocysts) the pregnancy rate was a significantly higher than in Group 2 (1 blastocyst only) (39.8 % vs. 23.0 %; P < 0.05). After the transfer of a single expanded blastocyst no statistical difference in the pregnancy rate between the two groups*

was observed (45.5 % vs. 44.6 %). A significantly higher pregnancy rate was found after the transfer of one expanded blastocyst with a good embryoblast and trophoblast morphology compared to the transfer of a single early blastocyst (45.6 % vs. 7.1 %, P < 0.05).

Conclusions *After single blastocyst transfer, the likelihood of achieving a pregnancy is higher in women with 2 or more blastocysts developed. And also the likelihood of achieving a pregnancy is higher with an expanded blastocyst transferred with good embryoblast and trophoblast morphology. The blastocyst development is the main predictor of pregnancy, which may reflect the embryonic genetic status.*

Key words *blastocyst; elective single embryo transfer; morphology; development of blastocyst; pregnancy*

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