NOVA KLASIFIKACIJA MORFOLOGIJE SPERMIJEV PRED ICSI POD 6000-KRATNO POVEČAVO

NEW CLASSIFICATION OF SPERM MORPHOLOGY BEFORE ICSI AT MAGNIFICATION OF X6000

Katja Knez, Irma Virant-Klun, Branko Zorn, Tomaž Tomaževič, Eda Vrtačnik-Bokal
Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Pri ICSI se za vnos v jajčno celico običajno pod 400-kratno povečavo izbere na izgled normalen spermij, pri čemer ni možno opaziti okvar finih struktur spermija. Z novo metodo IMSI (angl. intracytoplasmic morphologically selected injection) pa se lahko pod 6000-kratno povečavo izbere gibljivi spermij z normalno glavo in bazo ter brez vakuol v glavi, ki lahko odslikavajo poškodbe jedra oziroma DNA (fragmentirana ali enoverižna). Takšni spermiji imajo zmanjšano oploditveno sposobnost ali pa vodijo v nenormalen razvoj zarodkov, neuspešno ugnezditev ali spontani splav.*

Metode *Namen te raziskave je bil ugotoviti, pri kakšnem deležu moških z nenormalno morfologijo spermijev (teratozoospermijo), vključenih v program ICSI, je pod 6000-kratno povečavo možno najti normalne spermije brez vakuol v glavi. S sistemom IMSI smo pri spermijih ocenjevali morfologijo glave (normalna = 2 točki), morfologijo baze (normalna = 1 točka) in odsotnost vakuol v glavi (ena majhna vakuola ali brez = 3 točke). Popolnoma normalen spermij (ali z eno majhno vakuolo) smo ocenili s 6 točkami. Spermije smo razdelili v tri razrede: I (6–4 točk), II (3–1 točka) in III (0 točk). Spermiji I. in II. razreda so bili primerni za injiciranje v jajčne celice, spermiji III. razreda pa ne.*

Rezultati *Pripravljeno seme smo pred postopkom ICSI pregledali s sistemom IMSI pri 13 moških, ki so imeli teratozoospermijo (samo ali v kombinaciji z drugimi nepravilnostmi semena). Spermije I. razreda smo lahko našli pri petih moških (38 %), pri ostalih (62 %) pa smo lahko našli samo spermije II. razreda. Spermije III. razreda smo našli pri vseh moških. Našli smo povprečno 0,7 spermija I. razreda in 6,1 spermijev II. razreda na moškega.*

Zaključki *Morfološko normalne spermije brez vakuol v glavi je možno najti pri manj kot polovici moških, vključenih v program ICSI. Nadaljnja raziskava bo pokazala, ali lahko s selekcijo spermijev s sistemom IMSI izboljšamo klinične rezultate metode ICSI pri parih z najtežjimi oblikami moške neplodnosti.*

Ključne besede *IMSI; morfologija spermijev; spermij I. in II. razreda; vakuola*

Abstract

Background *At conventional ICSI, sperm to be injected into the oocyte is chosen at magnification of 400 times which does not permit abnormalities of fine sperm structures to be seen. By using a new method, intracytoplasmic morphologically selected injection (IMSI), motile sperm with a normal head, base and no vacuoles present in the head can be selected at magnification of 6000 times. Vacuoles in the sperm head reflect the damage of nucleus and/or DNA (fragmented or single-stranded DNA). Spermatozoa with vacuoles in the head have lower fertilization capacity and lead to abnormal embryo development, unsuccessful implantation, or spontaneous abortion.*

Methods *The aim of this study was to evaluate the percentage of men with abnormal sperm morphology (teratozoospermia) included in the ICSI programme, in which it is possible to find a morphologically normal sperm without vacuoles in the head using IMSI method. In each selected sperm we evaluated the morphology of head (normal = 2 points), base (normal =*

1 point) and presence of vacuoles in the head (one small or no vacuoles = 3 points). Totally normal sperm (or with one small vacuole in the head) was allotted 6 points. According to this evaluation, sperm were divided into three classes: class I (6–4 points), class II (3–1 points) and class III (0 points). Sperm of class I and II were suitable for injection into the oocyte, whereas sperm of class III were not.

Results *Before ICSI, the prepared semen of 13 patients which had teratozoospermia (alone or in combination with other semen abnormalities) was evaluated by the IMSI method. Sperm of class I was found in 5 men (38 %), and sperm of class II in the remaining men (62 %). Sperm of class III was found in all men. On average, 0.7 sperm of class I and 6.1 sperm of class II per man with teratozoospermia were found.*

Conclusions *Morphologically normal sperm without vacuoles in the head can be found in less than half of men undergoing the ICSI programme. Further research will show, whether it is possible to improve the clinical results of the ICSI method by the sperm selection with the IMSI method.*

Key words *IMSI; morphology; sperm; class I and II; vacuole*

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USPEŠNOST LAPAROSKOPSKEGA ZDRAVLJENJA ENDOMETRIOZE PRI NEPLODNIH BOLNICAH

THE OUTCOME OF LAPAROSCOPIC TREATMENT OF ENDOMETRIOSIS-ASSOCIATED INFERTILITY

Vesna Šalamun, Martina Ribič-Pucelj, Tomaž Tomaževič, Andrej Vogler, Eda Vrtačnik-Bokal

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

Izvleček

Izhodišča *Številne raziskave ugotavljajo statistično značilno zmanjšano stopnjo zanositve pri bolnicah z endometriozo. Mehanizmi niso povsem pojasnjeni. Namen dela je ugotoviti uspešnost operativnega zdravljenja različnih stopenj endometrioze pri neplodnih bolnicah.*

Bolnice in metode *Uspešnost operativnega zdravljenja neplodnosti pri endometriozi smo ugotavljali s pomočjo anketnega vprašalnika, poslanega 281 bolnicam, ki so bile operirane na Ginekološki kliniki v Ljubljani v obdobju 1999 do 2006 zaradi endometrioze, ki je bila edini vzrok za neplodnost. Sto pedeset (53,4 %) anketirank, ki so odgovorile na vprašalnik, smo razdelili v skupino I (minimalna in blaga endometrioza) in v skupino II (zmerna in huda endometrioza) ter ugotavljali stopnjo zanositve (skupno, spontano in po postopkih zunajtelesne oploditve) in jo primerjali med skupinama. Sorazmerno majhen odstotek odgovorjenih anketirank je najverjetneje posledica dejstva, da smo anketirali tudi tiste, ki smo jih operirali že pred večimi leti in na vprašalnik niso odgovorile ali so spremenile naslov bivanja. Prikazali bomo delne rezultate, ker je raziskava še vedno v teku.*

Rezultati *Od 132 bolnic, ki so želele zanositi po operaciji endometrioze, je zanosilo 76,5 % (101/132) bolnic. V skupini I jih je zanosilo 86,8 % (79/91), od tega spontano 58,2 % (46/79), v postopkih zunajtelesne oploditve 41,8 % (33/79). V skupini II jih je zanosilo 53,6 % (22/41), od tega spontano 68,2 % (15/22) in v postopkih zunajtelesne oploditve 31,8 % (7/22). Razlika v stopnji zanositve med skupinama je statistično značilna ($\chi^2(1) = 0,00$; $p > 0,05$).*

Zaključki *Naši rezultati so primerljivi glede na pregled literature. Laparoskopsko zdravljenje neplodnosti je učinkovito zdravljenje v primeru minimalne, blage, zmerne in hude endometrioze in ima po naših rezultatih primarno mesto v zdravljenju neplodnosti pri endometriozi.*

Ključne besede *endometrioza; neplodnost; laparoskopsko zdravljenje*

Abstract

Background *Many studies have shown significant reduction of fertility in endometriosis. Mechanisms of infertility are still not completely clear. The aim of our study is to obtain the effectiveness of laparoscopic treatment of infertility for different stages of endometriosis.*

Methods *The effectiveness of laparoscopic treatment of infertility in endometriosis was observed through a questionnaire that was sent to 281 patients (pts), who had laparoscopic treatment at the Department of Obstetrics and Gynecology Ljubljana during the period from 1999 to 2006 due to endometriosis as the only cause of infertility. 53.4 % (150/281) pts, who answered the questionnaire, were divided into group I (minimal and mild endometriosis) and group II (moderate and severe endometriosis). We established the rate of pregnancy (in total, spontaneous and ART) and compared the results between two groups. Relatively small percentage of answered questionnaires was most likely due to the fact that the questionnaires were sent to pts who were operated several years ago and did not respond or have changed their address. Because the study is still ongoing, we present partial results.*

Results *For 132 pts wanting to get pregnant the overall pregnancy rate was 76.5 % (101/132). The rate of pregnant pts depended on the stage of endometriosis. In group I 86.8 % (79/91) pts became pregnant – 58. 2 % (46/79) spontaneously, 41.8 % (33/79) with ART. In group II 53.6 % (22/41) pts became pregnant – 68.2 % (15/22) spontaneously, 31.8 % (7/22) with ART. The difference between groups was statistically significant ($p < 0.05$).*

Conclusions *Our results are comparable to the results found in the literature. Laparoscopic treatment of infertility is effective in all four stages of endometriosis. According to our results laparoscopic treatment has the primary role in the treatment of endometriosis-associated infertility.*

Key words *endometriosis; infertility; laparoscopic treatment*

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SELEKCIJA SEMENČIC S HIALURONANOM IN RAZVOJ BLASTOCIST PO ICSI

SPERM SELECTION WITH HYALURONAN AND BLASTOCYST DEVELOPMENT AFTER ICSI

Lili Bačer Kermavner, Irma Virant-Klun, Eda Vrtačnik-Bokal, Tomaž Tomaževič, Helena Meden-Vrtovec

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

Izvleček

Izhodišča *S hialuronanom, ki je naravna substanca v kumulusu jajčne celice, je možno selekcionirati semenčice za postopek vnosa semenčice v citoplazmo jajčne celice (ICSI) na osnovi njihove zrelosti. Samo dovolj zrele semenčice imajo na glavi receptorje za vezavo na kumulus jajčne celice oziroma na hialuronan. Namen raziskave je bil ugotoviti oploditev in razvoj zarodkov do blastociste po oploditvi z ICSI glede na izbor semenčice s hialuronanom ali po standardnem morfološkem izgledu semenčice.*

Metode *V retrospektivno raziskavo smo vključili 17 parov, predvidenih za postopek ICSI. Polovico jajčnih celic vsake ženske smo oplodili s semenčicami po selekciji s hialuronanom (84 jajčnih celic), drugo polovico pa po morfološkem izgledu (89 jajčnih celic). Med skupinama smo primerjali stopnjo oploditve jajčnih celic in odstotek razvojno zaustavljenih zarodkov, morul in blastocist. Blastociste smo delili na zgodnje, razvite in povsem razvite.*

Rezultati *V skupini s semenčicami, selekcioniranimi s hialuronanom, je bilo oplojenih 65 %, v skupini s semenčicami selekcioniranimi po morfološkem izgledu, pa 70 % jajčnih celic. Med skupinama ni bilo statistično pomembne razlike. Prav tako ni bilo statistično pomembne razlike med deležem razvojno zaustavljenih zarodkov (47 % vs. 62 %), morul (11 % vs. 11 %) in blastocist (42 % vs. 26 %). V skupini po selekciji semenčic s hialuronanom je bilo statistično pomembno več povsem razvitih ($P \leq 0.04$) in zgodnjih ($P \leq 0{,}002$) blastocist.*

Zaključki *Uporaba hialuronana za selekcijo semenčic za metodo ICSI ne vpliva na stopnjo oploditve. Nadaljnji razvoj zarodkov je boljši v skupini po selekciji samenčic s hialuronanom. Za ocenitev vloge hialuronana pri zanositvi bo potrebno vključiti večje število parov.*

Ključne besede *selekcija semenčic; blastocista; vnos semenčice v citoplazmo jajčne celice; hialuronan; oploditev*

Abstract

Background *Selection of mature sperm for intracytoplasmic sperm injection (ICSI) has recently been made possible by hyaluronan, a naturally occurring substance found in the cumulus cells. Only fully mature sperm have the receptors on the head that effectively bind to the oocyte cumulus, or, to be more precise, to hyaluronan. The aim of this study was to evaluate the differences in fertilization rates and in embryo development to the blastocyst stage after ICSI performed either with sperm selected by hyaluronan or by standard morphological sperm appearance.*

Methods *This retrospective study involved 17 couples undergoing ICSI. One half of sibling oocytes were fertilized with sperm selected by hyaluronan (84 oocytes), and the other half with sperm selected on the basis of morphological appearance (89 oocytes). The comparison between the two groups involved fertilization rates and the percentages of arrested embryos, and delayed (morulae) and advanced blastocysts. Blastocysts were classified as early, developed and expanded.*

Results *In the group with hyaluronan-selected sperm 65 % of oocytes fertilized, and in the group with sperm selected by morphological appearance 70 % of oocytes. The fertilization rates did not statistically differ between the two groups, and neither did the percentages of arrested embryos (47 % vs. 62 %), morulae (11 % vs. 11 %), and blastocysts (42 % vs. 26 %). In the group with hyaluronan-selected sperm the shares of expanded and early blastocysts were significantly greater (P ≤ 0.04 and P ≤ 0.002, respectively) than in the group with sperm selected according to morphological appearance.*

Conclusions *The use of hyaluronan for sperm selection in ICSI does not affect fertilization rates. Hyaluronan-selected sperm improves subsequent development of embryos. A larger study sample is required for the assessment of hyaluronan-selected sperm on the achievement of pregnancies.*

Key words *sperm selection; blastocyst; intracytoplasmic sperm injection; hyaluronan; fertilization*

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MORFOLOŠKE NEPRAVILNOSTI SEMENA KOT NAPOVEDNIKI FRAGMENTACIJE DNK IN USPEŠNOSTI OPLODITVE PRI OPLODITVI Z BIOMEDICINSKO POMOČJO

SPERM MORPHOLOGICAL ABNORMALITIES AS INDICATORS OF DNA FRAGMENTATION AND FERTILIZATION IN ASSISTED REPRODUCTION

Barbara Dariš,[1] Veljko Vlaisavljević[2]

[1] Inštitut za biomedicinske vede, Medicinska fakulteta, Univerza v Mariboru, Slomškov trg, 2000 Maribor

[2] Oddelek za reproduktivno medicino in ginekološko endokrinologijo, Klinika za ginekologijo in perinatologijo, Univerzitetni klinični center Maribor, Ljubljanska 5, 2000 Maribor

Izvleček

Izhodišča *Ugotavljali smo povezanost med morfološkimi nepravilnostmi semena, deležem semenčic s fragmentirano DNK in stopnjo oploditve pri postopkih zunajtelesne oploditve.*

Metode *Analizirali smo semenske vzorce neplodnih parov iz postopkov IVF (n =10) in ICSI (n = 20). Morfologijo semenčic smo določali po strogih merilih po Tygerbergu. Za ugotavljanje deleža semenčic s fragmentirano DNK pri vzorcih semena smo uporabili tehniko TUNEL (terminal deoxynucleotidyl transferase (TdT)-mediated fluorescein-dUTP nick end labelling). Semenske vzorce smo analizirali s pretočnim citometrom.*

Rezultati *Pri vzorcih z večjim deležem semenčic s fragmentirano DNK (≥20 %) smo opazili povečano vsebnost morfološko spremenjenih semenčic v primerjavi z vzorci, ki so vsebovali nižji delež semenčic s fragmentirano DNK (< 20 %). Deleži semenčic amorfne oblike (10 proti 4 %) in deleži semenčic z nepravilnostmi glave (42 proti 30 %) so bili značilno večji pri vzorcih z ≥20 % semenčic s fragmentirano DNK. Pri preiskovancih iz postopkov IVF in ICSI ni bilo statistično značilne povezanosti med stopnjo oploditve in deležem semenčic s fragmentirano DNK. Ko smo določili prevladujočo morfološko nepravilnost pri semenskih vzorcih, smo ugotovili, da je delež semenčic z elongirano glavo negativno povezan s stopnjo oploditve pri postopkih ICSI (r = –0.45, P <0.05). Stopnja oploditve pri postopkih IVF je bila značilno manjša (35.3 %) v tistih primerih, kadar je bila prevladujoča morfološka oblika uporabljenega vzorca nepravilnost akrosoma.*

Zaključki *Količina semenčic z nepravilnostmi glave in semenčic amorfne oblike v vzorcih semena je povezana z deležem semenčic s fragmentirano DNK. Prevladujoče morfološke oblike v vzorcih semena, kot so semenčice z elongirano glavo in z nepravilnostmi akrosoma, lahko vplivajo na uspešnost oploditve pri OBMP.*

Ključne besede *morfologija semenčic; fragmentacija DNK; IVF; ICSI; oploditev*

Abstract

Background *To determine the relationship between sperm morphological abnormalities, DNA fragmentation and fertilization rate in IVF and ICSI.*

Methods *Sperm samples from 10 IVF and 20 ICSI cycles were analyzed. Morphology was assessed according to strict criteria, and DNA fragmentation was measured by terminal deoxynucleotidyl transferase (TdT)-mediated fluorescein-dUTP nick end labelling (TUNEL) using a flow cytometry.*

Results *There was a significant difference in the amount of morphological abnormalities between sperm samples with low (< 20 %) and high (≥ 20 %) degree of DNA fragmentation. The*

percentages of amorphous heads (10 vs. 4 %) and overall head abnormalities (42 vs. 30 %) were significantly higher in sperm samples with elevated degree of DNA fragmentation. No correlation was found between sperm DNA fragmentation and fertilization rate after IVF and ICSI. When the predominant morphological abnormality in sperm samples was determined, a negative correlation was found between the percentage of spermatozoa with elongated heads and fertilization rate in ICSI ($r = -0.45$, $P < 0.05$). The fertilization rate after IVF was lower in the case of acrosomal abnormalities (35.3 %), compared to the cases of other predominant morphological abnormalities.

Conclusions *Head abnormalities, especially amorphous heads, are related to elevated degree of DNA fragmentation. Predominant abnormal form in sperm samples, such as elongated heads and acrosomal abnormalities, may affect fertilization in ART.*

Key words *sperm morphology; DNA fragmentation; IVF; ICSI; fertilization*

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SPODBUJANJE OVULACIJE PRI POSTOPKIH OPLODITVE Z BIOMEDICINSKO POMOČJO

OVARIAN STIMULATION IN ASSISTED REPRODUCTION

Marija Gačić,[1] Helena Meden-Vrtovec,[2] Veljko Vlaisavljević[3]

[1] Medicinska fakulteta, Univerza v Ljubljani, Korytkova 2, 1000 Ljubljana
[2] Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana.
[3] Oddelek za reproduktivno in ginekološko endokrinologijo, Klinika za ginekologijo in perinatologijo, UKC Maribor, Ljubljanska 5, 2000 Maribor

Izvleček

Izhodišča *Od prve faze razvoja zdravil za indukcijo ovulacije je minilo že več kot 50 let. V tem času so se razvili novi pripravki, uporabljeni v različnih protokolih in različnih odmerkih, toda doslej še ni bil oblikovan protokol, ki bi ustrezal za vse ženske.*

Vsebina *Uspešnost indukcije ovulacije v postopkih oploditve z biomedicinsko pomočjo namreč ni odvisna le od pripravkov, temveč tudi od ključnih dejavnikov, kot so: starost ženske, značilnosti menstruacijskega ciklusa, indeks telesne mase, rezerva jajčnikov in pridružene bolezni. Prva uspešna nosečnost v postopku oploditve z biomedicinsko pomočjo je bila rezultat zunajtelesne oploditve v naravnem ciklusu brez uporabe zdravil. Zaradi sorazmerno majhne stopnje uspešnosti so pri teh postopkih naravni ciklus že v 70. letih nadomestili protokoli z uporabo klomifen citrata ali gonadotropinov. Največji napredek na tem področju je bilo uvajanje agonistov gonadoliberilina. Uporaba humanih menopavznih gonadotropinov in rekombinantnih oblik: rekombinantni FSH, rekombinantni LH, rekombinantni HCG v kombinaciji z agonisti GnRH je privedla do večje stopnje nosečnosti (20–60 %) pa tudi do večjega odstotka večplodnih nosečnosti in ovarijske hiperstimulacije. Zato so se pričela zopet uveljavljati načela, po katerih se uvajajo cenejši, manj zapleteni in bolj prijazni protokoli, ki ob naravnem ciklusu, minimalni in blagi ovarijski stimulaciji (uporaba klomifen citrata in letrozola ter majhnih odmerkov HMG ali rFSH) omogočajo uspešno indukcijo ovulacije in nosečnost pri približno 30 % zdravljenih žensk.*

Za tem, ko so se pol stoletja razvijali sofisticirani protokoli ovarijske stimulacije, so sodobna evropska priporočila usmerjena v manj agresivne, cenejše, dovolj učinkovite in bolj prijazne metode spodbujanja ovulacije v postopkih OBMP.

Poznamo tudi protokole pri slabo odzivnih jajčnikih. Da je odziv jajčnikov na stimulacijo z gonadotropini slab, označujemo, kadar se ob ustrezni stimulaciji jajčnikov razvijejo le trije folikli ali manj premera 16 mm, le en dominantni folikel ali pa so bili v preteklosti ciklusi stimulacije prekinjeni zaradi manj kot treh razvijajočih se foliklov.

Za nadaljevanje postopkov stimulacije pri teh bolnicah v literaturi zasledimo več predlogov:

- *dolgi protokol z večjimi dnevnimi odmerki gonadotropinov;*
- *zmanjševanje odmerkov GnRH agonistov ali prekinitev dajanja le-teh takoj ali kmalu po začetku stimulacije z gonadotropini;*
- *kratkotrajna uporaba agonistov GnRH v folikularni fazi;*
- *sekvencijska uporaba CC in eksogenih gonadotropinov.*

Odziv na stimulacijo jajčnikov spremljamo z merjenjem serumskega estradiola in uporabo transvaginalnega ultrazvoka za merjenje premera jajčnih foliklov in oceno dinamike razvoja ehografskega videza in debeline endometrija.

Postopek nadzora mora biti prilagojen posameznici, upoštevati pa mora prilagoditev protokolov časovnim obveznostim bolnice, redno preverjanje, ali je odmerek gonadotropinov ustrezen, časovno optimiziranje dajanja HCG, izogibanje razvoju hiperstimuliranja jajčnikov, zmanjšanje možnosti za nastanek večplodnih nosečnosti, ekonomičnost pri uporabi zdravil ter napredek na področju laboratorijskih tehnik reproduktivne biologije.

Zaključki *Zatem, ko so se pol stoletja razvijali sofisticirani protokoli ovarijske stimulacije, so sodobna evropska priporočila usmerjena v manj agresivne, cenejše, dovolj učinkovite in bolj prijazne metode spodbujanja ovulacije v postopkih OBMP.*

Ključne besede *ovarijska stimulacija; slaba odzivnost; nadzor*

Abstract

Background *It has passed more than 50 years from the developmental phase of ovulation induction. During this period new medications have been introduced, new protocols and dosage established, but the regimen, that would suit all women, has not been designed yet.*

Methods *The success of ovulation induction in assisted reproduction technologies (ART) does not depend only on medications used, but is influenced by contributing key factors, such as woman's age, characteristics of the menstrual cycle, body mass index, ovarian reserve and concomitant diseases. The first successful pregnancy followed ART in natural cycle without medications. Because of a relatively low success rate natural cycle was replaced in 70's by protocols that included clomiphene-citrate or gonadotropins. The introduction of gonadoliberin agonists represented the greatest advantage in this field. The use of human menopausal gonadotropins and recombinants: recombinant FSH, recombinant LH and recombinant HCG in combination with GnRH agonists resulted in significantly higher pregnancy rate (cumulative up to 65 %), but also higher multiple pregnancy rate and ovarian hyperstimulation rate. That is why cheaper, less complicated and patient friendly principles have been renewed, including natural cycle, minimal and mild ovarian stimulation (the use of clomiphene-citrate, letrozole and small doses of HMG or rFSH) that enable ovulation induction and pregnancy in about 30 % of treated women.*

For a half of the century sophisticated protocols of ovarian stimulation have been developed, but recent European recommendations favour the use of less aggressive, cheaper, effective and patient friendly methods of ovulation induction in ART.

There are also protocols for low responding ovaries, which we classify as development of three or less follicles 16 mm in size, only one dominant follicle, or if in past there had been previous cancellations of the cycle because of less than three follicles developed in spite of correct stimulation with gonadotropins.

In the literature there are some suggestions how to treat such patients:

– long protocol with higher daily doses of gonadotropins,
– lowering doses of GnRH agonists or stopping the application soon or immediately after stimulation with gonadotropins has started,
– short term use of GnRH agonists in follicular phase,
– sequential use of CC and exogene gonadotropins.

Ovarian response is monitored by serum estradiol determinations and vaginal ultrasound measurement of follicular size together with echographic estimation of endometrial development.

The procedure must comply with each individual and consider her obligations. There should be regular controls, if the dose of gonadotropins is suiting. The application of HCG should be optimized, the hyperstimulation of ovaries should be avoided and the possibility of multiple pregnancies should be lowered. We should also consider the economical side of the use of drugs and the development of the laboratory techniques in reproductive biology.

Conclusions *For a half of the century sophisticated protocols of ovarian stimulation have been developed, but recent European recommendations favour the use of less aggressive, effective and patient friendly methods of ovulation induction in ART.*

Key words *ovarian stimulation; low responders; monitoring*

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ZNAČILNOSTI ANAMNEZE PRI BOLNICAH Z ENDOMETRIOZO

CHARACTERISTICS OF HISTORY IN PATIENTS WITH ENDOMETRIOSIS

Renata Košir,[1] Nina Slabe,[1] Helena Meden-Vrtovec,[2] Martina Ribič-Pucelj,[2] Špela Smrkolj[2]

[1] Medicinska fakulteta Ljubljana, Vrazov trg 2, 1000 Ljubljana
[2] Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Endometrioza je estrogensko odvisna bolezen, ki prizadene od 5 do 20 % žensk v rodni dobi. Bolezen poteka progresivno in povzroča zelo raznolike klinične znake in simptome, od bolečin in vse do neplodnosti. Nekateri simptomi so odvisni od tega, na katerem mestu se bolezen pojavi. Najpogostejši simptomi so dismenoreja, disparevnija, kronična pelvična bolečina (KPB) in neplodnost. Endometrioza se pojavlja tudi pri ženskah brez kliničnih simptomov. Pri zunajmedenični endometriozi so lahko opazni tudi drugi simptomi in znaki, ki so odvisni od organskega sistema, v katerem se bolezen pojavi.*
Dismenoreja ali boleča menstruacija se lahko pojavi pred začetkom menstruacije, se med menstruacijo stopnjuje ali postane kronična in je prisotna ves menstruacijski ciklus. Boleče menstruacije se pojavijo pri 60–80 % bolnic z endometriozo. Disparevnija ali bolečine, ki nastanejo pri spolnem občevanju, se pojavljajo pri 25–50 % bolnic z endometriozo. Pogosteje je povezana z boleznijo, ki se pojavlja rektovaginalno ali na uterosakralnem ligamentu. Ugotovljeno je bilo tudi, da je napredovala endometrioza v primerjavi z začetnimi oblikami pogosteje povezana z dismenorejo in disparevnijo. KPB je pelvična bolečina, ki traja šest mesecev in se ne pojavlja ciklično. V 40–60 % je prav endometrioza vzrok KPB, še posebej kadar gre za globoko infiltrativno endometriozo. Pogosto je lahko edini znak endometrioze neplodnost. Incidenco neplodnosti pri ženskah z endometriozo težko ugotovimo, saj brez težav lahko zanosijo ženske z blago obliko endometrioze, prav tako pa je lahko ta blaga oblika bolezni vzrok za neplodnost. Vendar pa se ocenjuje, da ima 20–30 % neplodnih žensk endometriozo.

Zaključki *Anamnestični podatki so zelo pomembni pri prepoznavanju bolezni. Endometrioza sicer ne ogroža življenja, vendar predstavlja pomemben vzrok obolevnosti pri ženskah. Resno prizadene zdravje in kakovost življenja, s tem pa predstavlja velik javno-zdravstveni problem. Zaradi kompleksnosti kliničnih znakov, katerih intenzivnost ni vedno sorazmerna s stadijem bolezni, se bolezen včasih diagnosticira pozno. Zato je toliko bolj pomembno, da namenimo dovolj časa jemanju anamnestičnih podatkov.*

Ključne besede *endometrioza; dismenoreja; disparevnija; kronična pelvična bolečina; neplodnost*

Abstract

Background *Endometriosis is an estrogen dependent disease that affects 5 20 % of women of reproductive age. Course of the disease is progressive and leads to a variety of symptoms that range from pain complaints to infertility. Some symptoms depend on the location of the break out. The most frequent symptoms are dysmenorrhea, dyspareunia, chronic pelvic pain and infertility. Endometriosis is also found in asymptomatic women.*
Clinical signs and symptoms with extrapelvic endometriosis are based on the involved organ system.
Dysmenorhea may progress and begin prior to the onset of menses or become chronic and be noted throughout most of the menstrual cycle. Pain during menstrual cycle is estimated on 60–80 % of women with endometriosis. Dyspareunia is estimated on 25–50 % of women with endometriosis. It is frequently associated with rectovaginal and uterosacral ligament disease. It was established that advanced endometriosis is more frequently related to dysmenorrhea and deep dyspareunia in comparison with early disease. Chronic pelvic pain is defined as the pain that lasts 6 months and is not cyclic. In women being evaluated for

pelvic pain, the diagnosis of endometriosis is made in 40–60 %, especially when it comes to deep infiltrative endometriosis. Infertility can be the only presenting symptom. The incidence of infertility in women with endometriosis is hard to establish. Some women with mild endometriosis are able to conceive, however this mild endometriosis can cause infertility. There is estimation that 20–30 % of women with endometriosis are infertile.

Conclusions *Medical history is very important in recognizing the disease. Endometriosis does not threaten life but is associated with significant morbidity of women. It has a major impact on women's health and life quality and represents a significant public health issue. Because the clinical signs and symptoms are complex and there is sometimes lack of the association between the stage of the disease and intensivity of symptoms, the disease can be diagnosed too late.*

Key words *endometriosis; dysmenorhea; dyspareunia; chronic pelvic pain; infertility*

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POJAVLJANJE AVTOIMUNSKIH BOLEZNI PRI BOLNICAH Z ENDOMETRIOZO

APPEARANCE OF AUTOIMMUNE DISEASES IN PATIENTS WITH ENDOMETRIOSIS

Nina Slabe,[1] Renata Košir,[1] Helena Meden-Vrtovec,[2] Martina Ribič-Pucelj,[2] Špela Smrkolj[2]

[1] Medicinska fakulteta Ljubljana, Vrazov trg 2, 1000 Ljubljana
[2] Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Endometrioza je pogost, kompleksen ginekološki sindrom, pri katerem se zunaj maternične votline pojavi endometriju podobno tkivo, ki vsebuje stromo in žlezne strukture. Prizadene 5 do 20 % žensk v rodni dobi.[1] Današnje prevladujoče mnenje o etiopatogenezi temelji na predpostavki, da je endometrioza posledica spremenjenega imunskega odziva, kar opisuje avtoimunska teorija.[2, 3] Značilnosti avtoimnuskih bolezni, ki jih najdemo pri endometriozi, so pogostejše pojavljanje pri ženskah, vpletenost več organov, družinsko pojavljanje, genetska osnova, odziv na hormonsko zdravljenje, poškodba tkiva, aktiviranje poliklonskih limfocitov B, imunološke abnormnosti v funkciji limfocitov T in B ter pridružena avtoimunska bolezen. Ženske z endometriozo pogosteje obolevajo za astmo, revmatoidnim artritisom, sistemskim lupusom eritematozusom, Sjögrenovim sindromom in Hashimotovim tiroiditisom.*
Avtoimunske bolezni sprožijo nastanek avtoprotiteles, ki so usmerjena proti elementom apoptotičnih celic. Antiendometrijska protitelesa razreda IgG in IgM so prisotna pri 60 % bolnic z endometriozo in se značilno vežejo z žleznim epitelom in stromo. Antiendotelna protitelsa se vežejo na žilni endotel in so skupaj z antiendometrijskimi protitelesi delno odgovorna za neuspelo ugnezedenje jajčne celice in posledično neplodnost, ki je pogosta pri bolnicah z endometriozo. Za številne avtoimnuske bolezni je značilna tvorba antijedrnih protiteles, pri 29 do 47 % pa jih najdemo tudi pri bolnicah z endometriozo.[4] Nastanek teh protiteles pri endometriozi je dejavnik tveganja za razvoj ostalih avtoimunskih bolezni pri ženskah v reproduktivni dobi. Raziskave so pokazale nasprotujoča si mnenja o prisotnosti anti-ovarijskih protiteles v serumu bolnic in v peritonealni tekočini. Njihova prisotnost je tudi eden od možnih vzrokov neplodnosti.

Zaključki *Ne moremo še zanesljivo trditi, da je endometrioza res avtoimunska bolezen, vendar zadnje raziskave nakazujejo, da obstajajo podobnosti med endometriozo in ostalimi avotimunskimi boleznimi, kot so revmatoidi artritis, sistemski lupus eritematozus, Sjögrenov sindrom in ostale. Pomembna skupna značilnost je prisotnost različnih avtoprotiteles. Avtoimunska teorija torej pomeni izziv in hkrati odpira možnost za nov pristop k zdravljenju endometrioze z imunomodulacijskimi zdravili.*

Ključne besede *endometrioza; antiovarijska protitelesa; antiendometrijska protitelesa; antiendotelna protitelesa; antijedrna protitelesa*

Abstract

Background *Endometriosis is a comon, complex gynecological syndrom defined as the growth of endometrial glands and stroma in an extra-uterine location. It affects 5 – 20 % of women of reproductive age.[1] Nowadays, prevailing opinion about endometriosis is based on presumption, that endometriosis is a result of changed immune system, according to autoimmune theory.[2, 3] Characteristics of autoimmune disease that are also found in endometriosis are female preponderance, multiorgan involvement, family occurence, possible genetic basis, response to hormonal manipulation, tissue damage, polyclonal B lymphocite activation, immunological abnormalities in T lymphocite and B lymphocite function and associated autoimmune disease. Women with endometriosis are more frequently affected by asthma,*

rheumatoid arthritis, systemic lupus erythematosus, Sjögren syndrom and Hashimoto's thyroiditis.
Autoimmune disease is characterized by the production of autoantibodies against components of apoptotic cells. Anti-endometrial antibodies of IgG and IgM classes could be detected in 60 % of endometriosis patients. They show reactivity in glandular epithelium and stroma. Anti-endothelial antibodies specifically react with vascular endothelium and might be with anti-endometrial antibodies partially responsible for failure of implantation leading to infertility, wich is common in endometriosis patients. Anti-nuclear antibodies are frequent serological findings in patients with autoimmune disease, and could be detected in 29–47 % of women with endometriosis.[4] Generation of anti-nuclear antibodies is a risk factor for development of other autoimmune disease in women of reproductive age. Studies have shown conflicting results on the presence of anti-ovarian antibodies in the serum of endometriosis patients and in the peritoneal fluid. Their presence is one of the possible causes of infertility.

Conclusions *Ethiopathogenesis of endometriosis still remains uncelar but currently available data suggest that there are many similarites between endometriosis and such autoimmune diseases as rheumathoid arthritis, systemic lupus erythematosus, Sjögren syndrom etc. Important similarity is the presence of auto-antibodies. Autoimmune theory represents a challenge and at the same time opens the possibility of a new mode of treatement of endometriosis with immunomodulators.*

Key words *endometriosis; anti-ovarian antibodies; anti-endometrial antibodies; anti-endothelial antibodies; anti-nuclear antibodies*

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VPLIV SARTANOV NA NOSEČNOST

THE EFFECT OF SARTANS ON THE PREGNANCY

Marta Cvijič,[1] Mirjam Horvat,[1*] Petra Jernejčič,[1*] Ksenija Geršak[2]*

[1] Medicinska fakulteta Ljubljana, Vrazov trg 2, 1000 Ljubljana
[2] Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1525 Ljubljana
[*] Avtorice si delijo mesto prve avtorice

Izvleček

Izhodišča *Sartani so pogosto predpisovana zdravila za zdravljenje arterijske hipertenzije v splošni populaciji. V literaturi zasledimo malo podatkov o toksičnem delovanju na plod. Prvi primer je bil opisan leta 2001. Poznano je, da ima zdravljenje s sartani v drugem in tretjem trimesečju nosečnosti nefrotoksični učinek na plod, ki se kaže kot oligohidramnij, povzroča fetalno hipertenzijo, ledvično odpoved ter smrt ploda oziroma novorojenca. Uporabo sartanov v nosečnosti zasledimo le pri ženskah z že obstoječno kronično hipertenzijo, kjer so sartani njihovo primarno zdravljenje.*
Naš namen je predstavitev potekov nosečnosti in vpliv na plod pri ženskah, ki so v nosečnosti prejemale sartane.

Metode *Iz obdobja med letoma 2002 in 2006 smo pregledali porodne zapisnike nosečnic obravnavanih na Ginekološki kliniki v Ljubljani in analizirali potek nosečnosti pri tistih, ki so prejemale sartane.*

Rezultati *V preučevanem obdobju smo zasledili pet primerov uporabe sartanov med nosečnostjo. Pri dveh, ki sta jih prejemali le v prvem trimesečju, je bil potek nosečnosti normalen. Rodili sta zdravega donošenega otroka. Tudi tretja nosečnica je zdravilo prejemala v enakem obdobju, donošen otrok pa se je rodil s polidaktilijo.*
Pri četrti nosečnici so zdravljenje z irbesartanom prekinili v drugem trimesečju ob ultrazvočno ugotovljenem oligohidramniju. Po prekinitvi se je količina plodovnice normalizirala. Zaradi patološkega kardiotokograma je bil indiciran carski rez v 29. tednu. Novorojenček je kazal znake nezrelosti.
Zadnja nosečnica je bila bolnica s kronično ledvično odpovedjo in hipertenzijo, ki je poleg losartana prejemala še kalcijev antagonoist. Zdravili sta bili ukinjeni konec drugega trimesečja ob diagnosticirani nosečnosti in hkrati ugotovljenem oligohidramniju, ki je vztrajal vse do spontanega poroda v 27. tednu. Poleg znakov nezrelosti so pri nedonošenki ugotavljali ledvično okvaro, ki se je med hospitalizacijo popravila.

Zaključki *Pri naših nosečnicah, ki so prejemale sartane le v prvem trimesečju, je bil izid nosečnosti ugoden. Tudi iz maloštevilnih primerov v doslej objavljenih člankih jemanje sartanov v prvem trimesečju najverjetneje ni povezano s povečanim tveganjem za večje prirojene malformacije.*
Pri nosečnicah, ki sta jemali sartane še v drugem trimesečju, je bil ugotovljen oligohidramnij, ki se je v enem primeru po ukinitvi zdravljenja popravil, pri zadnjem primeru pa je novorojenček imel zmanjšano ledvično funkcijo še krajši čas po porodu. Tudi v literaturi so navedeni podatki o nefrotoksičnem učinku sartanov na plod pri jemanju v drugi polovici nosečnosti. Okvara ledvične funkcije ploda je v nekaterih opisanih primerih popravljiva, pri drugih pa vztraja tudi po ukinitvi zdravljenja s sartani.
Na podlagi virov iz literature in opisanih petih primerov lahko povzamemo, da naj se ženske v rodnem obdobju, ki se zdravijo s sartani zaradi kronične hipertenzije poučijo o možnih teratogenih učinkih, zdravljenje pa naj se v primeru nenačrtovane nosečnosti ukine takoj ob postavitvi diagnoze nosečnost.
Za natančnejšno oceno vpliva sartanov na potek nosečnosti bi bile potrebne obsežnejše študije.

Ključne besede *nosečnost; hipertenzija; sartani; teratogenost*

Abstract

Background

Sartans are commonly prescribed drugs for treatment of hypertension among general population. Data on their fetal toxicity are limited to small uncontrolled series and case reports; first such case was described in 2001.
It is a well known that sartans therapy in the second and third trimesters of pregnancy is associated with nephrotoxic effect on fetus which results in oligohydramnios, fetal hypertension, renal insufficiency and fetal or neonatal death. Therapy with sartans is found only among pregnant women with diagnose of preexistent chronic hypertension and where sartans were prescribed as primary chosen therapy.
Our aim is to describe samples of pregnant women who received sartans during their pregnancy.

Methods

We looked over labour and delivery records of all pregnant women, who delivered during the year 2002 and 2006 at Department of Obstetrics and Gynecology, University Medical Center Ljubljana. We analyzed courses of pregnancy for those women who received sartans during pregnancy.

Results

During the period we identified five hypertensive women who were exposed to sartans in pregnancy. Two of them were taking medications in the first trimester, course of their pregnancy was normal and the baby was delivered healthy and at term. Another pregnant woman who was also treated with sartans in the first trimester gave birth to a term baby with polydactyly.
In our fourth case the therapy with irbesartan ceased in the second trimester of pregnancy when oligohydramnios was described. After stopping the drug, amniotic fluid volumes returned to normal. At 29 gestational weeks, a pathological cardiotocogram was noted and an emergency caesarean section was performed. The baby suffered from severe immaturity.
The last case was a pregnant woman with chronic renal failure and arterial hypertension. Therapy with losartan and nifedipine was stopped at the end of second trimester. At the time oligohydramnios was also diagnosed. It persisted until spontaneous delivery at 27 gestational weeks. Aside from immaturity, the newborn suffered from transitional renal impairment.

Conclusions

All three pregnancies, where sartans were administrated during the first trimester, ended favorably. From relatively adverse reports we gather that sartan therapy during first trimester of pregnancy probably does not present a higher risk for fetal malformations.
Both other pregnancies, where therapy with sartans was stopped in the second trimester were complicated by oligohydramnios. In one of the two, oligohydramnios regressed spontaneously after the therapy had been stopped. In the last case reduced amniotic fluid persisted and it resulted in reversible renal insufficiency of the newborn.
A literature review of recent articles reveal the risk of fetal nephrotoxicity due to sartans administered to the mother still during second half of the pregnancy. Renal insufficiency may be reversible or it may persist after cessation of sartan therapy.
Based on data available from the literature and from our own five case reports, we can conclude that women who are treated with sartan at the childbearing age should be very well informed of possible teratogenic effects of the therapy. In case of unplanned pregnancy the therapy should be stopped as soon as the pregnancy is documented.
However, additional studies are needed to better define the effect of sartans on the pregnancy.

Key words *pregnancy; hypertension; sartans; teratology*

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RAZVOJ OTROK, SPOČETIH S POSTOPKOM ICSI IN PSIHOSOCIALNE ZNAČILNOSTI NJIHOVIH DRUŽIN

PSYCHOSOCIAL CHARACTERISTICS OF FAMILIES WITH ICSI CHILDREN AND THESE CHILDREN'S DEVELOPMENT

Vislava Globevnik-Velikonja, Adela Pislak-Bali, Branko Zorn, Ivan Verdenik
Ginekološka klinika, Univerzitetni klinični center Ljubljana, Šlajmerjeva 3, 1000 Ljubljana

Izvleček

Izhodišča *Z raziskavo smo želeli ugotoviti, ali se otroci, spočeti z metodo ICSI, in njihove družine razlikujejo od otrok, rojenih v normalno plodnih družinah.*

Metode *V študijsko skupino (ŠS) smo zajeli 41 triletnih otrok, spočetih z ICSI: 22 dečkov, 19 deklic, 6 parov dvojčkov, v kontrolno skupino (KS) pa 41 otrok, spočetih po naravni poti, ki so bili izenačeni po starosti, spolu in številu dvojčkov. Z vprašalnikom smo zajeli podatke o značilnostih družine, načinu oploditve, poteku nosečnosti, porodu in poporodnem obdobju. Razvoj otrok smo ocenjevali z razvojnim testom Čuturić, starši so izpolnili vprašalnik iz SPP-3 (Sistematski psihološki pregled triletnih otrok) o znakih neustreznega prilagajanja pri otroku, za oceno materine osebnosti smo uporabili vprašalnik BFQ (Big Five Questionnaire). Razlike med skupinama smo analizirali s statističnim paketom SPSS za Windows.*

Rezultati *Primerjava med ŠS in KS je pokazala naslednje statistično pomembne razlike: matere v ŠS so bile starejše, otroci po ICSI so bili večkrat edinci, družine v ŠS so imele boljši socialno-ekonomski položaj. Povprečno trajanje zdravljenja neplodnosti je bilo 4 leta, večina žensk je zanosila v tretjem poskusu ICSI. Ženske po ICSI so bile v primerjavi s KS do nosečnosti manj ambivalentne, odnos med partnerjema se je med nosečnostjo izboljšal, po porodu pa se je njihovo duševno počutje poslabšalo: bolj jih je bilo strah, da bo z otrokom kaj narobe, kakovost življenja po otrokovem rojstvu pa se je izboljšala. Matere svoje otroke po ICSI opisujejo kot bolj nemirne in občutljive, večkrat so ti otroci v varstvu staršev in starih staršev, medtem ko so otroci v KS večkrat vključeni v vrtec. Razvoj vseh otrok je bil normalen. Kljub temu, da v vsoti znakov neustreznega prilagajanja med skupinama statistično ni pomembnih razlik, pa so otroci ICSI imeli bolj intenzivno izražene posamezne znake. Faktorska analiza kaže zelo heterogeno latentno stukturo z veliko faktorji, ki pojasnjujejo majhen del variance, kljub temu pa je jasna povezava med znaki neustreznega prilagajanja pri otroku in značilnostmi materine osebnosti. Matere v ŠS so na BFQ dosegle statistično pomembno nižji rezultat na lestvici sprejemljivosti ($p = 0.025$) in odprtosti ($p = 0.008$) ter višji rezultat na lestvici neiskrenosti ($p = 0.001$), kar govori o tem, da so bolj toge, nestrpne, manj sprejemajoče, težijo k popolnosti in dajanju bolj socialno sprejemljivih odgovorov. Osebnostne značilnosti so v visoko pomembni korelaciji z izkušnjo neplodnosti kot izjemnega stresa in pogojene tudi s starostjo mater.*

Zaključki *Razvoj otrok, spočetih z ICSI, je v mejah normale, nakazuje pa se težnja k povečanemu tveganju za kasnejše čustvene težave. Obstaja povezava med otrokovimi značilnostmi in materino osebnostjo, ki jo označujeta izkušnja neplodnosti in višja starost.*

Ključne besede *neplodnost; ICSI; razvoj otrok; družinsko okolje*

Abstract

Background *The aim of the study was to find whether children conceived through ICSI and their families differ from the children conceived in normally fertile families.*

Methods *The study group (SG) consisted of 41 children aged 3 years conceived through ICSI: 22 boys, 19 girls, 6 pairs of twins, and the control group (CG) of 41 children matched for sex, age and*

twin pairs. Family characteristics were assessed using a self-administered questionnaire on family characteristics, conception, pregnancy, labour and delivery, and postpartum period. The children's development was assessed using the Developmental Čuturić Scale, and the parents filled in the questionnaire from SPP-3 on signs of inadequate child's adaptation. The mother's personality was assessed using the BFQ. Differences between the groups were analyzed using SPSS for Windows.

Results

Comparison between the SG and CG showed the following statistically significant differences: in the SG mothers were older, the ICSI child was more frequently the only child, the mean duration of infertility treatment was 4 years, in most couples pregnancy occurred by the 3rd ICSI attempt, the family had a better socio-economic status. During the pregnancy, the SG mothers were less ambivalent towards pregnancy and the relationship between the partners improved, after delivery their psychic condition deteriorated, they were more concerned whether their child would develop normally. In the SG parents' opinion, the quality of life improved after their baby's birth; they described their children as more demanding and more restless. More ICSI children were cared after by their grand parents than their CG peers that mostly attended kindergarten. The development of all children was normal. Although the sum of signs of inadequate adaptation was comparable between the groups, the ICSI children demonstrated stronger intensity of individual sings. Factor analysis showed very heterogenic latent structure with many components that explained low percentage of variance; there was a clear connection between child's signs of inadequate adaptation and maternal personality characteristics. The SG mothers achieved on BFQ a statistically lower score in agreeableness (P = 0.025) and openness (P = 0.008), and a higher score in the unsincerity scale (P = 0.001), i.e. they were more rigid, less open to diversity, less tolerant, tending more to perfection and providing more socially acceptable answers. These characteristics highly correlated with experiencing infertility as an extreme stress and were also in relationship with maternal age.

Conclusions

The development of ICSI children is within the normal range; however, they tend to be at increased risk for emotional problems. There exists a strong correlation between the child's characteristics and the mother's personality that has been marked with the experience of infertility and their age.

Key words *infertility; ICSI; child's development; family environment*

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KAKOVOST ZARODKA IN POJAVNOST SPONTANEGA SPLAVA PO PRENOSU ENE ALI DVEH BLASTOCIST

EMBRYO QUALITY AND SPONTANEOUS MISCARRIAGE AFTER SINGLE AND DOUBLE BLASTOCYST TRANSFER

Marko Došen, Veljko Vlaisavljević, Borut Kovačič

Oddelek za reproduktivno medicino in ginekološko endokrinologijo, Klinika za ginekologijo in perinatologijo, UKC Maribor, Ljubljanska 5, 2000 Maribor

Izvleček

Izhodišča *Spontani splav (SS) ni nepričakovan zaplet tako v zgodnji spontani nosečnosti kot v nosečnosti po postopkih oploditve z biomedicinsko pomočjo (OBMP). Dokazano je nekoliko višje pojavljanje SS pri nosečnostih po postopkih OBMP kot pri spontanih nosečnostih, tudi po upoštevanju materine starosti in preteklih SS. V naši raziskavi smo želeli dokazati vpliv kakovosti zarodkov na pojavljanje SS po prenosu ene ali dveh blastocist.*

Materiali in metode *Retrospektivno smo analizirali 1433 spodbujenih ciklusov IVF in ICSI, opravljenih na našem oddelku leta 2001 in 2002, pri katerih smo prenašali eno (PEB) ali dve blastocisti (PDB). V zaključno analizo smo uvrstili 418 ciklusov s PEB ali PDB in so imeli pozitiven βhCG ter so bili znani podatki o poteku nosečnosti.*

Rezultati *Povprečna starost bolnic je bila 32,2 let ± 4,5 let. V 133 primerih smo uporabili klasični postopek IVF, v 285 pa postopek ICSI. V 69 primerih smo prenesli eno, v 349 primerih pa dve blastocisti. Po PEB je delež SS znašal 11,6 %, po PDB pa 12,0 %. V skupini PEB nismo dokazali značilne povezave med kakovostjo blastociste in SS (logistična regresija: $\chi 2 = 0,88$; $p > 0,05$). V tej skupini tudi s standardnimi statističnimi testi nismo našli značilne razlike v deležu SS po prenosu optimalne ali suboptimalne blastociste (test $\chi 2$ z Yatesovo korekcijo: $p > 0,05$, Studentov t-test: $p > 0,05$). V skupini PDB smo dokazali značilno povezavo med kakovostjo prenesenih blastocist in SS ($\chi 2 = 10,12$; $p < 0,01$). S standardnimi testi smo potrdili značilnost razlike med skupinami z blastocistami različne kakovosti: po prenosu dveh blastocist optimalne kakovosti je znašal delež SS 8,6 %, pri preneseni optimalni in suboptimalani blastocisti 10,1 % in ob prenosu dveh suboptimalnih blastocist 25,4 % (Kruskal-Wallisov test: $p < 0,001$; enosmerna ANOVA: $p < 0,001$). Starost bolnic je visoko značilno povezana z deležem SS ($\chi 2 = 14,57$; $p < 0,0001$).*

Zaključki *V naši raziskavi je delež SS znašal 11,9 %, kar je nižje kot v že objavljenih raziskavah in celo na spodnji meji deleža SS v splošni populaciji. Navedeno protislovje si razlagamo kot pozitivno posledico selekcije zarodkov med kultiviranjem in vitro. Nismo dokazali značilne povezave med SS in kakovostjo blastociste po PEB, kar je verjetno posledica premajhnega vzorca. V skupini PDB smo dokazali značilnost povezave med kakovostjo blastociste in SS. Še enkrat smo potrdili zmerno značilno povezavo med starostjo bolnic in SS.*

Ključne besede *spontani splav (SS); oploditev z biomedicinsko pomočjo (OBMP); kakovost zarodka; prenos ene blastociste (PEB); prenos dveh blastocist (PDB)*

Abstract

Background *Spontaneous miscarriage isn't an unexpected complication either in early spontaneous or in ART pregnancy. Previous studies showed that incidence of SM was slightly increased in ART pregnancies in comparison with spontaneous ones after adjusting for maternal age and previous SM. Our objective was to examine the relationship between SM and embryo quality after transfer of one or two blastocysts.*

Materials and methods

The total of 1433 stimulated IVF and ICSI cycles achieved in our center in the period from 2001 to 2002 after SBT or DBT were retrospectively analyzed. Of these, in the final analysis we included only cases with positive βhCG for which complete data on pregnancy outcome were available – 418 cycles in total.

Results

The mean age of patients was 32.2 ± 4.5 years. IVF was performed in 133 cases and ICSI was performed in 285 cases, SBT in 69 and DBT in 349. After SBT, SM rate was 11.6 % and after DBT it was 12.0 %. In SBT group we didn't find significant relationship between embryo quality and SM (logistic regression: $\chi 2 = 0.88$; $p > 0.05$). In this groups, using standard statistical tests, we also couldn't find significant difference in SM rate between subgroups where optimal or suboptimal quality blastocyst was transferred (Yates corrected $\chi 2$ test: $p > 0.05$, Student's t-test: $p > 0.05$). In DBT group, we found a strong relationship between embryo quality and SM (logistic regression: $\chi 2 = 10.12$; $p < 0.01$). After standard analysis, we confirmed significant difference between subgroups with different combinations of blastocyst quality: after transfer of both optimal blastocysts SM rate was 8.5 %, after transfer of optimal and suboptimal blastocyst SM rate was 10.1 % and after transfer of both suboptimal blastocyst SM rate was 25.4 % (Kruskal-Wallis test: $p < 0.001$; one-way ANOVA: $p < 0.001$). We confirmed strong relationship between age of the patients and SM (logistic regression: $\chi 2 = 14.57$; $p < 0.0001$).

Conclusions

In our study SM rate was 11.9 % which was lower than in previous reports; it was even at the lower limit of expected SM rate in general population. This discrepancy was probably the consequence of longer selection period of blastocysts in in vitro conditions. We didn't find a significant relationship between SM and blastocyst quality after SBT, which was probably due to the small sample size. A strong relationship between SM and blastocyst quality after DBT was proved. We also confirmed a strong relationship between age of the patients and SM.

Key words *spontaneous miscarriage (SM); assisted reproductive technology (ART); embryo quality; single blastocyst transfer (SBT); double blastocyst transfer (DBT)*

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