VITRIFIKACIJA, NOVA METODA ZAMRZOVANJA ZARODKOV: MARIBORSKE IZKUŠNJE

VITRIFICATION, NEW METHOD OF EMBRYO CRYOPRESERVATION: MARIBOR EXPERIENCE

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Izvleček

Izhodišča *Vitrifikacija je nov, enostavnejši in racionalnejši način krioprezervacije nadštevilnih zarodkov v programu oploditve z biomedicinsko pomočjo (OBMP). Namen naše raziskave je bil uvesti postopek vitrifikacije blastocist v klinično prakso in primerjati učinkovitost dveh komercialnih krioprotektantov.*

Metode *Vitrifikacijo blastocist smo začeli v letu 2008. Uporabili smo dva komercialna vitrifikacijska protokola, in sicer Vitrification Cooling/Warming (MediCult, Danska) – (MC) in Vitrification Freeze/Thaw (IrvineScientific, ZDA) – (IS). Gojišče IS vsebuje dva krioprotektanta: dimetilsulfoksid (DMSO) in etilen glikol, MC pa le etilen glikol. Med 1030 ciklusi OBMP smo v 404 (39,2 %) primerih nadštevilne blastociste po vitrifikaciji shranili v tekočem dušiku. V začetnem obdobju smo v 253 ciklusih blastociste vitrificirali po protokolu MC, kasneje v 151 ciklusih pa po protokolu IS. Doslej smo opravili 127 prenosov 248 devitrificiranih blastocist po protokolu MC in 71 prenosov 124 blastocist po protokolu IS. Primerjali smo stopnjo preživetja vitrificiranih blastocist, delež kliničnih in ultrazvočno (UZ) potrjenih vitalnih nosečnosti ter spontanih splavov. Posebej smo evaluirali cikluse z vsaj eno vitrificirano optimalno blastocisto.*

Rezultati *Preživetje blastocist, vitrificiranih po protokolu IS je bilo statistično značilno boljše od preživetja po protokolu MC (88,7 % oziroma 77 %; P = 0,0103). Delež vgnezditve devitrificiranih blastocist je bil po protokolu IS in protokolu MC primerljiv (22,7 % oziroma 17,8 %). Delež spontanih splavov je enak v obeh skupinah (18,2 % oziroma 16,7 %). Pri kliničnih (31,8 % oziroma 24 %) in z UZ potrjenih vitalnih nosečnostih (26,1 % oziroma 20 %) ni statistično značilnih razlik med protokoloma IS in MC. Delež zanositev v ciklusih z vsaj eno devitrificirano optimalno blastocisto je bil v skupini IS 45,7 %, v skupini MC pa 36,4 %. V istih ciklusih je bil delež spontanih splavov 5,7 % po protokolu IS in 4,5 % po protokolu MC.*

Zaključki *Z uporabo gojišča IS smo uspeli dobiti višje vrednosti vseh spremljanih parametrov v primerjavi z gojiščem MC, čeprav razlike zaradi majhnega števila ciklusov niso bile statistično značilne. Edina statistično potrjena razlika med protokoloma je bila v deležu preživetja v prid protokolu IS. Raziskava se nadaljuje.*

Ključne besede *blastociste; vitrifikacija; stopnja preživetja; vgnezditev; zanositev*

Abstract

Background *Vitrification is a new, simpler and more rational way of cryopreservation of redundant embryos in in vitro fertilisation. The purpose of this study was to introduce vitrification of blastocysts in clinical practice and compared two commercial cryoprotectants.*

Methods *We started vitrifying blastocysts in 2008. Two commercial vitrification protocols were used, Vitrification Cooling/Warming (MediCult, Denmark) – (MC), and Vitrification Freeze/Thaw (IrvineScientific, ZDA) – (IS). IS medium includes two cryoprotectants: dimethylsulfoxide (DMSO) and ethylene glycol, meanwhile MC medium contains only ethylene glycol. Among*

1030 in vitro fertilizated cycles, we preserved redundant blastocysts in 404 (39.2 %) cycles in liquid nitrogen. At the begining MC vitrification protocol was used in 253 cycles and later IS protocol in 151 cycles. 127 transfers (248 devitrified blastocysts) were performed using MC protocol and 71 transfers (124 blastocysts) using IS protocol. We compared the survival rate of blastocysts, rate of clinical and ongoing pregnancies and miscarriages. Cycles with at least one optimal blastocyst were evaluated separately.

Results

Survival rate of vitrified blastocysts by IS protocol was statistically significantly higher than survival rate by MC protocol (88.7 % or 77 %; P = 0.0103). Implantation rate of devitrified blastocysts by IS and MC protocol are comparable (22.7 % or 17.8 %). The rate of miscarriages does not statistically differ between the protocols (18.2 % or 16.7 %). There are no statistically significant differences between IS and MC protocols in clinical (31.8 % or 24 %) and ongoing pregnancies (26.1 % or 20 %). Pregnancy rate in cycles with at least one optimal devitrified blastocyst is 45.7 % by IS protocol and 36.4 % by MC protocol. In the same cycles, the rate of miscarriages is 5.7 % by IS and 4.5 % by MC protocol.

Conclusions

Higher values in all parameters were by IS media, even though the differences were not statistically significant because of low number of cycles. The only statistically significant difference between protocols was in survival rate in favor of IS protocol. The study continues.

Key words *blastocysts; vitrification; survival rate; implantation; pregnancy rate*

Literatura

1. Liebermann J, Tucker MJ. Comparison of vitrification and conventional cryopreservation of day 5 and day 6 blastocysts during clinical application. Fertil Steril 2006; 86: 20–6.
2. Youssry M et al. 2008. Current aspects of blastocyst cryopreservation. Reproductive BioMedicine Online 2008; 16: 311–20.
3. Loutradi KE et al. Cryopreservation of human embryos by vitrification or slow freezing: a systematic review and meta – analysis. Fertil Steril 2007; 90, 186–93.

SERTOLI-LEYDIGOV TUMOR; REDEK PRIMER PRI POMENOPAVZNI BOLNICI – PRIKAZ PRIMERA

SERTOLI-LEYDIG CELL TUMOR; A RARE CASE IN A POSTMENOPAUSAL PATIENT – CASE REPORT

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Izvleček

Izhodišča *Sertoli-Leydigovi tumorji sodijo v skupino stromalnih tumorjev jajčnikov. So zelo redki; predstavljajo le 0,5 % vseh tumorjev jajčnikov. Najpogosteje se pojavljajo pri mladih bolnicah med 20. in 30. letom starosti. Lahko secernirajo androgene in povzročajo virilizacijo. V pomenopavzi se skoraj ne pojavljajo.*

Metode *V našo ustanovo smo sprejeli 73-letno bolnico, napoteno zaradi nespecifičnih bolečin v trebuhu in rasti obsega trebuha. Ob pregledu smo v trebuhu ugotavljali veliko nepremakljivo tumorsko maso v mali medenici, premera približno 20 cm, ter povišan tumorski označevalec CA 125 221,3 U/ml. Ultrazvočno je bil ugotovljen velik cistično solidni tumor, najverjetneje ovarijskega izvora, brez znakov ascitesa. Hormonski profil je bil v mejah normale, bolnica pa ni kazala znakov virilizacije.*

Pri bolnici je bila opravljena laparotomija, pri kateri smo odstranili kompleksen tumor, izhajajoč iz levega ovarija, premera 30 × 27 × 15 cm. Zmrzli rez je ugotavljal maligni tumor neznanega porekla, zaradi česar smo opravili radikalen operativni poseg. Definitivni histološki izvid je potrdil zmerno diferenciran maligni Sertoli-Leydigov tumor. Vse ostalo odstranjeno tkivo je bilo brez prisotnosti malignih celic. Bolnica je ves čas zdravljenja prejemala zaščitni odmerek NMH.

Zgodnji pooperativni potek je bil brez posebnosti, 10. pooperativni dan je bila odpuščena domov, nato pa 16. dan ponovno sprejeta zaradi proksimalne tromboze vene saphene magne. Zaradi tega je pričela dobivati NMH v terapevtskem odmerku, kasneje pa Marivarin do zaključenih 6 tednov po operaciji.

16 mesecev po operaciji se je simptomatsko zdravila zaradi mikrocitne anemije. Preiskave niso pokazale znakov recidiva.

27 mesecev po operaciji je bila urgentno operirana zaradi ileusa tankega črevesa, ob čemer so iz trebuha odstranili obsežne tumorske mase in naredili transverzostomo. Histološki izvid odstranjenega tkiva je govoril za recidiv malignega Sertoli-Leydigovega tumorja, ki infiltrira tanko črevo. Ugotovljen je bil tudi porast CA 125.

Zaključki *Predstavljamo klinični primer pomenopavzne bolnice s Sertoli-Leydigovim tumorjem, ki se je zdravila v naši ustanovi.*

Ključne besede *jajčnik; Sertoli-Leydigov tumor; pomenopavza*

Abstract

Background *Sertoli-Leydig cell tumors belong to the group of sex cord stromal tumors of the ovary. They account for less than 0.5 % of all ovarian tumors and occur primarily in young women between 20 and 30 years of age. This type of tumors can secrete androgens, causing virilisation, and are extremely rarely presented in postmenopausis.*

Methods *A 73-year old multiparous woman was presented to our institution with complaints of abdominal distention and abdominal pain in her lower abdomen. On physical examination, she had a large, fixed palpable abdominal mass, approximately 20 cm in diameter, arising*

from the pelvis. The laboratoric tests revealed an elevated level of CA125 of 221.3 U/ml of serum. The ultrasound showed a complex cystic and solid pelvic tumor. There was no sign of ascites. Her hormonal status was within normal range and she also showed no signs of virilisation.
On laparotomy a complex left ovarian mass, measuring 30 × 27 × 15 cm was found and sent to frozen section. The result of frozen section was a malignant tumor of unknown origin, therefore a radical surgical procedure was performed. The histopathological examination established the diagnosis of a malignant Sertoli-Leydig cell tumor of the left ovary, of intermediate differentiation. Other removed tissue was free of malignant cells.
The early postoperative course was uneventful and the patient was released from hospital 10 days after surgery. However, she returned to our institution 16 days after surgery due to a proximal thrombosis of v. saphena magna. The patient was treated with low-molecular-weight heparin and later warfarin for 6 weeks post operation.
16 months after the operation she was symptomatically treated for severe microcytic anemia. She showed no signs of a relapse.
27 months after primary surgery she was operated for the second time due to acute bowel obstruction. She had large masses of necrotic tumor removed from abdomen and transversostomia was performed. It was found to be a relapse of the malignant Sertoli-Leydig tumor, infiltrating the small intestines; the level of serum CA 125 also showed an increase.

Conclusions *We describe a case of a Sertoli-Leydig cell tumor in a postmenopausal woman, treated in our institution.*

Key words *ovary; Sertoli-Leydig cell tumor; postmenopause*

Literatura

1. Caringella A, Loizzi V, Resta L, Ferreri R, Loverro G. A case of Sertoli-Leydig cell tumor in a postmenopausal women. Int J Gynecol Cancer 2006; 16: 435–8.
2. Nicoletto MO, Caltarossa E, Donach M, Nardelli GB, Parenti A, Ambrosini A. Sertoli cell tumor: a rare case in an elderly patient. Eur J Gynaec Oncol 2006; 27: 86–7.
3. Chen FY, Sheu BC, Lin MC, Chow SN, Lin HH. Sertoli-Leydig cell tumor of the ovary. J Formos Med Assoc 2004; 103: 388–91.

TRILETNE IZKUŠNJE Z ANTERIORNO TRANSOBTURATORNO MREŽICO (ATOM) IN POSTERIORNO ISHIOREKTALNO MREŽICO (PIRM)

A THREE-YEAR EXPERIENCE WITH ANTERIOR TRANSOBTURATOR MESH (ATOM) AND POSTERIOR ISCHIORECTAL MESH (PIRM)

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Izvleček

Izhodišča *Nove uroginekološke kirurške tehnike omogočajo, da se z uporabo neresorbilnih tkivnih mrežnih vsadkov odpravi motena funkcija in porušena statika na prizadetem delu medeničnega dna z minimalno invazivnim igelnim transvaginalnim posegom, kot sta na primer anteriorna transobturatorna mrežica (ATOM) in posteriorna ishiorektalna mrežica (PIRM).*

Metode *V 3 letih, od aprila 2006 do maja 2009, smo opravili pri 184 ženskah korekcijo prolapsa medeničnih organov in disfunkcije medeničnega dna z mrežnimi tkivnimi vsadki (Tab. 1). K tem posegom nismo prišteli 83 bolnic, pri katerih smo v tem času opravili operacijo s prolenskim trakom (TVT-O oz. Monarc) kot samostojno operacijo zaradi stresne inkontinence brez napredovalega prolapsa.*
V 97 % operacij z mrežico smo uporabili Gynemesh 10 × 15 cm. Za korekcijo prolapsa sprednje vaginalne stene z ATOM posegom smo Gynemesh ukrojili v mrežico s šestimi kraki – trakovi za transobturatorno vstavitev in z vrhnjim nenapetostnim ovratnikom. Z IVS (Intravaginal sling) 04 Tunneller (Tyco) igelnim sistemom smo nenapetostno uvedli vseh 6 trakov transobturatorno skozi 4 kožne reze (2 desno in 2 levo). Sprednjo kolpotomijo smo naredili z dvema ločenima minimalnima rezoma vaginalno.
Za korekcijo prolapsa zadnje vaginalne stene s postopkom PIRM smo Gynemesh ukrojili v mrežico s 4 trakovi in nenapetostnim vrhnjim ovratnikom. Dva ishiorektalna dolga trakova za nenapetostno vstavitev skozi ishiorektalno foso – levo in desno in dva perinealna krajša kraka za vstavitev v perinealno telo, prav tako levo in desno. Za nenapetostno vstavitev vseh 4 trakov smo uporabili IVS 02 Tunneller (Tyco) igelni sistem skozi 4 kožne reze (2 desno in 2 levo).

Rezultati *Pri vseh 184 bolnicah je bil poseg opravljen sorazmerno varno. Pri 9 operacijah ATOM smo perforirali mehur, v 5 primerih pri vstavitvi zgornje igle, v 3 primerih pri vstavitvi spodnje igle in v enem primeru s pinceto ob nenapetostni vstavitvi vrhnjega ovratnika v lateralni rob veziko-vaginalnega prostora. Pri 2 operacijah PIRM smo perforirali črevo. V vseh 11 primerih smo poškodbo popravili med posegom in mrežice nismo odstranili; pooperativni potek je bil brez zapletov. Glede na celotno skupino mrežnih operacij je hospitalizacija trajala 4 do 5 dni. Kratkoročni rezultati (2–3 mesece po operaciji) so zelo dobri. V 14 primerih je prišlo do male vaginalne erozije na mestu zgornje vaginalne incizije pri posegu ATOM. Vse erozije so se zacelile spontano po odstranitvi neresorbilnega (Etibond 1/0; Ethicon) šiva oziroma odkritega dela mrežice (manj kot 1 mm^2) brez anestezije in brez dodatnih šivov vagine.*

Zaključki *Nove metode in materiali omogočajo, da se integriteta medeničnega dna vrne v fiziološko stanje tudi pri popolnoma izpadli maternici brez odstranitve sicer zdrave maternice ter z ohranitvijo primerne prostornine in osi nožnice. Korekcije statike medeničnega dna s tkivnimi vsadki, pri katerih se praviloma maternica ne odstrani, so časovno krajše in sodijo med minimalno invazivne posege. Kakovost življenja žensk se je po posegu močno izboljša. Ženske lahko po posegu dejavno zaživijo, saj so odpravljene težave, ki so jih omejevale. Dobre obete, da bo korekcija trajna, dajejo naši in tuji večletni rezultati na tem področju.*[1–8]

To pričakujemo tudi za bolnice, ki smo jim mrežico vstavili s pomočjo igelnih aplikatorjev pri ATOM in/ali PIRM posegu.[9, 10]

Ključne besede *prolaps ženskih spolnih organov; korekcija z mrežico; cistokela; rektokela*

Abstract

Background *Use of alloplastic mesh implantates allow a new urogynecologycal surgical techniques achieve a marked improvement in pelvic organ static and pelvic floor function with minimally invasive needle transvaginal intervention like an anterior transobturator mesh (ATOM) and a posterior ischiorectal mesh (PIRM) procedures.*

Methods *In three years, between April 2006 and May 2009, we performed one hundred and eighty-four operative corrections of female pelvic organ prolapse (POP) and pelvic floor dysfunction (PFD) with mesh implantates. The eighty-three patients with surgical procedure TVT-O or Monarc as solo intervention indicated by stress urinary incontinence without POP, are not included in this number.*
In 97 % of mesh operations, Gynemesh 10 × 15 cm was used. For correction of anterior vaginal prolapse with ATOM procedure, Gynemesh was individually trimmed in mesh with 6 free arms for tension-free transobturator application and tension-free apical collar. IVS (Intravaginal sling) 04 Tunneller (Tyco) needle system was used for transobturator application of 6 arms through 4 dermal incisions (2 on right and 2 on left). Minimal anterior median colpotomy was made in two separate parts.
For correction of posterior vaginal prolapse with PIRM procedure Gynemesh was trimmed in mesh with 4 free arms and tension-free collar. Two ischiorectal long arms for tension-free application through fossa ischiorectale – right and left, and two short arms for perineal body also on both sides. IVS 02 Tunneller (Tyco) needle system was used for tension-free application of 4 arms through 4 dermal incisions (2 on right and 2 on left) in PIRM.

Results *All 184 procedures were performed relatively safely. In 9 cases of ATOM we had perforation of bladder, in 5 by application of anterior needle, in 3 by application of posterior needle and in one case with pincette when collar was inserted in lateral vesico – vaginal space. In 2 cases of PIRM we had perforation of rectum. In all 11 cases correction was performed during the operation, mesh was kept in place and postoperative course of treatment went without complications. Mean hospitalization time for mesh operation was 4 to 5 days. Short term results, 2 to 3 months after the operation, are very good both for pelvic organ static, and for pelvic function. In 14 cases we had small vaginal erosion in place of upper vaginal incision by ATOM. All erosions were cured spontaneously after removing of unresorptive suture (Etibond 1/0; Ethicon) and/or excision of small denudated mesh part (< 1 mm^2) without any anesthesia and vaginal sutures.*

Conclusions *New methods and materials allow return of pelvic floor integrity to physiological condition without hysterectomy of otherwise healthy uterus also in state of totally uterine prolapse. Corrections of POP with mesh procedures and without hysterectomy present a minimally invasive surgery with short hospitalization and reconvalescence. Quality of life markedly improved after operation because the preoperative problems were eliminated.*
Our and foreign experiences on these field[1–8] *give us a promise for long duration of good results which we also expect for women after needle implanted mesh in ATOM and/or PIRM procedure.*[9, 10]

Key words *female genital prolapse; mesh; cystocele; rectocele*

Literatura

1. Lužnik M. Uporabnost propilenske mrežice pri motnjah funkcije medeničnega dna. In: Kralj B, Denona V, eds. Zbornik 2. kongres ginekologov in porodničarjev Slovenije z mednarodno udeležbo; 2000 nov 19–22; Portorož. Ljubljana: Združenje ginekologov in porodničarjev Slovenije; 2000. p. 133.
2. Petros PE. Vault prolapse II: restoration of dynamic vaginal supports by infracoccygeal sacropexy, an axial day-case vaginal procedure. Int Urogynecol J Pelvic Floor Dysfunct 2001; 12: 296–303.
3. Lužnik M. Tension-free vaginal tape (TVT) in combination with reconstructive pelvic floor operation. In: Abstract book of the World congress on gynecological endoscopy, 1st Croatian congress on gynecological endoscopy; 2002 May 15–18; Dubrovnik. Dubrovnik: Croatian society of gynecological endoscopy; 2002. p. 30.

4. Lužnik M. Mrežna krpa za korekcijo velike rektokele: prve izkušnje. Zdrav Vestn 2002; 71: 23–6.
5. Lužnik M. A four-year experience in use of mesh patch for correction of female pelvic organ prolapse (POP) and pelvic floor dysfunction (PFD): A vaginal approach. In: Lukanovič A, Tamussino K, eds. Urogynecology today. Joint meeting of Slovene urogynecological society and Austrian society for urogynecology and pelvic reconstructive surgery, Portorož, September 24–25; 2004. p. 181–2.
6. Jordaan DJ, Prollius A, Cronje HS, Nel M. Posterior intravaginal sling plasty for vaginal prolapse. Int Urogynecol J Pelvic Floor Dysfunct 2006; 17: 326–9.
7. Lužnik M. Pooperativno ovrednotenje nenapetostnega vaginalnega traku (TVT) 2 do 6 let po posegu: raziskava na osnovi ankete. Zdrav Vestn 2006; 75: 817–22.
8. Vardy MD, Brodman M, Olivera CK, Zhou HS, Flisser AJ, Bercik RS. Anterior intravaginal slingplasty tuneller device for stress incontinence and posterior intravaginal slingplasty for apical vault prolapse: a 2-year prospective multicenter study. Am J Obstet Gynecol 2007; 104: e1–e8.
9. Lužnik M. Anterior transobturator mesh (ATOM) and/or posterior ischiorectal mesh (PIRM) for correction of female pelvic organ prolapse and pelvic floor dysfunction. Gynecol Surg 2007; 4 Suppl 1: S31.
10. Lužnik M. Needle implanted mesh for correction of female pelvic organ prolapse and pelvic floor dysfunction: anterior transobturator mesh (ATOM) and/or posterior ischiorectal mesh (PIRM). CD – Abstract Presentations; IUGA 2009 Italy: 34th Annual IUGA Meeting, Lago di Como, 16–20 June 2009: Abstract No: 424; 276–7.

Tab. 1. *Število in tip posega z mrežico za korekcijo prolapsa medeničnih organov (POP) od aprila 2006 do maja 2009.*

Table 1. *The number of different types of procedures performed for pelvic organ prolapse (POP) correction between April 2006 and May 2009.*

	Korekcija prolapsa vaginalnega krna Correction of vaginal cuff prolapse	Korekcija POP brez histerektomije Correction of POP without hysterectomy	Korekcija POP s histerektomijo Correction of POP with hysterectomy	Σ
ATOM	10	122	12	144
PIRM	9	8	0	17
ATOM + PIRM	5	13	5	23
Skupaj / Total	24	143	17	184

Legenda: ATOM = anteriorna transobturatorna mrežica, PIRM = posteriorna ishiorektalna mrežica
Legend: ATOM = anterior transobturator mesh, PIRM = posterior ischiorectal mesh

SPONTANA EVISCERACIJA JAJCEVODA PRI PROCIDENCIJI IN PERFORIRAJOČEM KARCINOMSKEM ULKUSU VAGINE – PRIKAZ PRIMERA

SPONTANEOUS FALLOPIAN TUBE EVISCERATION IN PROCIDENTIA AND PERFORATING CARCINOMATOUS VAGINAL WALL ULCER – CASE REPORT

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Izvleček

Izhodišča

Popolni prolaps ženskih spolnih organov ni samo boleč in neprijeten zaradi otežene mikcije in defekacije, temveč je lahko tudi nevaren, saj je izpadla nožnica lahko sprejemljivo mesto za razjedo in/ali rupturo različne etiologije z evisceracijo trebušne vsebine. Incidenca evisceracij je sicer redka, v teh primerih pa je nujno hitro ukrepanje. Najpogosteje izpade tanko črevo, redkeje omentum in zelo redko druge abdominalne strukture. Niti v literaturi niti na medmrežju nismo zasledili primera, da bi izpadel jajcevod, kar ne bi bila posledica predhodne ginekološke operacije.

Vsebina

77-letna bolnica je bila napotena v specialistično ginekološko ambulanto z diagnozo prolapsus uteri totalis in dolores abdominalis. V anamnezi izvemo, da je 20 let opažala za jabolko veliko izboklino pred spolovilom, ki se je ob ležanju zmanjšala. Pred 3 dnevi se je ob napenjanju izboklina močno povečala in se tudi v ležečem položaju ni več zmanjšala. Otežena je bila hoja in onemogočeno sedenje. Mikcije in defekacije so bile izvedljive le v stoječem položaju. Tudi namestitev na ginekološki preiskovalni stol je bila močno otežena, saj je bolnica imela med nogami 14 × 10 × 9 cm^3 veliko kepo izpadle vagine, iz katere je v srednjem delu, v levo in nazaj, visel nabrekel jajcevod (Sl. 1). Na najbolj izbočenem delu popolno zdrsnjene maternice in vagine se je dalo prepoznati zunanje ustje cervikalnega kanala. Izboklina je bila v celoti napeta in boleča, tako da je nismo niti poskušali reponirati. V predelu, kjer je izstopal jajcevod, je bila vaginalna sluznica pordela, grobo nagubana, nabrekla in ranljiva (Sl. 2).

V ambulanti smo izpadli jajcevod in zdrsnjeno vagino z vsebino aseptično oskrbeli in nanesli kremi Dalacin in Ortho Gynest. Vstavili smo Foleyev kateter. Tudi po tem, ko smo izpraznili mehur, je izpadla vagina z uterusom in ostalo vsebino ostala tako napeta, da je ni bilo mogoče reponirati.

Operacijo smo izvedli s Stecklovim rezom tako, da smo se delu vagine z opisano spremembo na mestu izpadlega jajcevoda na široko izognili. Jajcevoda nismo poskušali reponirati, temveč smo odprli najprej Douglasov prostor, nato pa še pliko vezikouterino. Odstranili smo maternico in obojne adnekse in situ ter vagino skoraj v celoti. V spodnjem delu trebuha ni bilo posebnosti. Peritonealno votlino smo zaprli z mošnjatim šivom. Opravili smo vezikorafijo v treh slojih in minimalno rektorafijo s kolpoperineoplastiko. Pooperativni potek je bil brez posebnosti in po osmih dneh je bila bolnica odpuščena iz bolnišnice.

Patohistološki izvid: invazivni skvamozni karcinom vagine, velikocelični, poroženevajoči. Invazivna rašča je prisotna v okolici odprtine, skozi katero prominira del maternice. Maksimalna debelina invazivne rašče znaša 0,8 cm. Resekcijski robovi potekajo v zdravem.

Glede na patohistološki izvid smo bolnico napotili na ginekološko-onkološki konzilij Ginekološke klinike v Ljubljani.

Diagnoza: Ca. vaginae stadij I.. Stanje po vaginalni histerektomiji s kolpektomijo. Sprememba je odstranjena v zdravem.

Zdravljenje: Glede na leta bolnice se konzilij odloči le za opazovanje.

Zaključki *Zaradi perforirane nožnice in odprte poti v trebuh je bila v opisanem primeru huda motnja statike ženskih medeničnih organov, kot je popolni prolaps uterusa – procidencija, življenjsko ogrožajoč. Izpadli jajcevod je to komunikacijo vsaj delno zmanjšal, hkrati je pa deloval kot zagozda, da se prolabirani uterus in vagina nista več mogla reponirati. Potrebno je bilo hitro ukrepanje. S primerno operativno intervencijo smo uspešno razrešili procidencijo in odstranili rakasto raščo.*

Ključne besede *evisceracija tube uterine; popolni prolaps ženskih spolnih organov; karcinom vagine; vaginalni operativni poseg*

Abstract

Background *Total prolapse of female pelvic organs is not only painful and troublesome because of difficulties with micturition and defecation but it could be very dangerous since prolapsed vagina presents a predilection area for ulcer and/or rupture of different etiology and with evisceration of abdominal content. Eviscerations usually occur rarely, but when they do occur, it is important to intervene quickly. Most frequent is the evisceration of small bowel, rarely omentum and sporadically other abdominal structures. Neither in literature nor on the internet there were not any examples of primary eviscerated fallopian tube which was not a consequence of preceeding gynecological-surgical procedure found.*

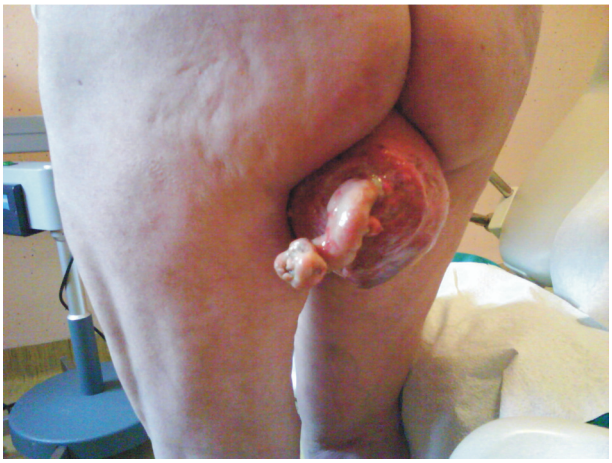
Methods *77-year-old woman was appointed to our out patient department with diagnosis of Prolapsus uteri totalis and Dolores abdominalis. In history there was prevulvar bulge in the size of an apple, which persisted for 20 years, and almost disappeared when lying supine. Three days before admission to the hospital the bulge was exceedingly enlarged by straining and did not diminish when lying supine. The patient walked only hardly and could not sit. Micturition and defecation was possible only in the upright position. There were also difficulties while placing the patient on a gynecologic chair, because between her legs there was a bulge in the size of 14 × 10 × 9 cm^3 with fallopian tube hanging out (Figure 1). On the outermost part of total uterovaginal prolapse the outer ostium of the cervical canal was recognizable. The bulge was fully stretched, painful and unreponible. Around a hole where a fallopian tube exits, vagina was eritematous, rough folded – swollen and vulnerable (Figure 2).*
In outpatient department eviscerated fallopian tube and prolapsed vagina with its contents were aseptically treated and Dalacin and Orho Gynest crème were applicated. Foley catheter was inserted.
Prolapsed vagina with uterus and other contents remained stretched even after catheterization and unreponible likewise.
In surgical procedure Steckel´s incision was used to avoid widely the area of vagina where tube exits. We did not try to repone the tube, so pouch of Douglas was opened first and after that uterovesical pouch as well. Hysterectomy with bilateral adnexectomy in situ and almost total vaginectomy has been made. In lower part of abdominal cavity there were not any pathological signs. Peritoneal cavity was closed with circular suture. Vesicorrhaphy in three layers and minimal rectorrhaphy with kolpoperineoplasty were made. Postoperative course of treatment was without complications. After eight days our patient has been discharged from the hospital.
Pathohistologic findings were: Invasive squamous cell carcinoma of the vagina, large cell and keratinizing. Invasive growth is present near the opening through which a part of the uterus prominates. Maximal thickness of invasive growth is 0.8 cm, on the borders there is not any cancerous tissue left.
Considering the pathologic findings, the patient has been appointed to the Gynecologic – oncologic counsel at University Department of Gynecology, Ljubljana.
Diagnosis was Ca. vaginae stadium I.. State after vaginal histerectomy with colpectomy. The lesion removed with safety border.
As for therapy; considering the age of the patient, consilium decided for observation.

Conclusions *Because of the perforated vagina and opened path to the abdominal cavity the total uterine prolapse in this case was a life-threatening emergency. The fallopian tube partly closed the communication and it also acted as a wedge so the prolapsed uterus and vagina could not repone. An urgent operation has been necessary – we resolved the procidentia and removed the cancer.*

Key words *Fallopian tube evisceration; complete uterovaginal prolapse – procidentia; vaginal carcinoma; vaginal surgical procedure*

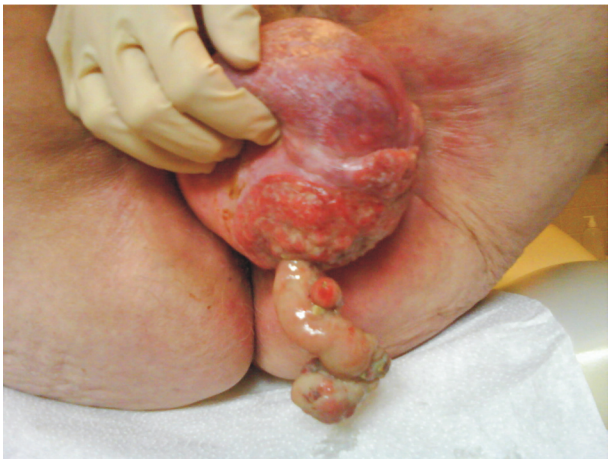
Literatura

1. Powell JL. Transvaginal evisceration after hysterectomy. Am J Obstet Gynecol 1995; 115: 1656.
2. Cardosi RJ, Hoffman MS, Roberts WS, Spellacy WN. Vaginal evisceration after hysterectomy in premenopausal women. Obstet Gynecol 1999; 94: 859.
3. Narducci F, Sonoda Y, Lambaudie E;Leblanc E, Querleu D. Vaginal evisceration after hysterectomy: the repair by a laparoscopic and vaginal approach with a omental flap. Gynecol Oncol 2003; 89: 549–51.
4. Iaco P, Ceccaroni M, Alboni C et al. Transvaginal evisceration after hysterectomy: Is vaginal cuff closure associated with a reduced risk? Eur J Obstet Gynecol Reprod Biol 2006; 125: 134–8.



Sl. 1. *Spontano eviscerirani jajcevod pri procidenciji.*

Figure1. *Spontaneously eviscerated fallopian tube with procidentia.*



Sl. 2. *Spremembe sluznice vagine okoli odprtine z izpadlim jajcevodom.*

Figure 2. *Changes of vaginal mucosa around a hole where a fallopian tube exits.*

TOTALNA PREDLEŽEČA POSTELJICA IN PERIPARTALNA HISTEREKTOMIJA – PRIKAZ PRIMERA

TOTAL PLACENTA PREVIA AND PERIPARTUM HYSTERECTOMY – CASE REPORT

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Izvleček

Izhodišča *Poporodna krvavitev največkrat nastane zaradi atonije maternice, adherentne posteljice, placente akrete, koagulopatije ali rupture uterusa. Pri totalni predležeči posteljici se poporodne krvavitve pojavljajo pogosteje in so ponavadi močnejše.*

Klinični primer *Prikazali smo primer hude poporodne krvavitve pri porodnici po načrtovanem carskem rezu zaradi totalne predležeče posteljice, ki se je končal s histerektomijo.*

Zaključki *Pri poporodni krvavitvi je zdravljenje konzervativno. Če to ni uspešno, je potrebno pravočasno kirurško zdravljenje. Abdominalna histerektomija je zadnji ukrep, ki ob masivni poporodni krvavitvi rešuje življenje porodnici.*

Ključne besede *predležeča posteljica; carski rez; histerektomija; hemoragični šok*

Abstract

Background *Postpartum haemorrhage usually occurs due to uterus atonia, adherent placenta, placenta accreta, coagulopathy or uterus rupture. In total placenta previa haemorrhage occurs more often and usually is more severe.*

Case report *We presented the example of severe postpartum haemorrhage with parturient woman after scheduled Caesarean section, due to total placenta previa, which was ended by performing hysterectomy.*

Conclusions *In postpartum haemorrhage, the treatment is conservative and if there is no improvement timely surgery is required. Abdominal hysterectomy is the final option and in case of severe haemorrhage it proved to be life saving for parturient woman.*

Key words *placenta praevia; Caesarean section; hysterectomy; shock haemorrhagicum*

Uvod

Totalna predležeča posteljica (PP) v celoti prekriva notranje maternično ustje. Etiologija je neznana, navajajo pa se razni vzroki: hiter transport oplojenega jajčeca, prejšnja poškodba endometrija in slaba vaskularizacija, zmanjšana invazivnost trofoblasta, mnogoplodne nosečnosti z velikimi posteljicami.

Plod ni akutno ogrožen, perinatalna umrljivost gre predvsem na račun nedonošenosti. Nekateri avtorji opisujejo pri otrocih akutne krvavitve, IUGR zaradi slabše posteljične perfuzije in povečano incidenco kongenitalnih anomalij. Najbolj ogrožena je mati zaradi možne poporodne krvavitve, večja je tudi incidenca placente akrete. Poporodne krvavitve pri totalni PP se pojavljajo pogosteje in so močnejše.

Carski rez je način dokončanja poroda pri totalni PP.

Prikaz primera

Na Ginekološko-porodniški oddelek Splošne bolnišnice Celje so sprejeli 32-letno nosečnico v 27. tednu nosečnosti zaradi totalne PP. Pred tremi leti je imela carski rez v 40. tednu nosečnosti zaradi kefalopelvičnega nesorazmerja (višina bolnice 145 cm, otrok 3440 g).

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Ob sprejemu je nosečnica brez težav, krvavela ni, CTG je reaktiven, ultrazvočno je vidna posteljica spredaj in zadaj čez maternično ustje, spremenljiva lega otroka. Vaginalno ni pregledana. Zaradi slabokrvnosti uvedemo terapijski odmerek pripravka železa, potem damo betametazon 14 mg/24 h v mišico (2-krat) .
Do 38. tedna nosečnosti spremljamo CTG, ultrazvočni pregled enkrat tedensko, kontrole hemograma.
Carski rez je bil narejen v splošni endotrahealni anesteziji v 38. tednu nosečnosti, operater in prva asistentka sta izkušena operaterja porodničarja. Po ponovni laparotomiji po Joel Cohenu najdemo prirasel uterus in mehur na sprednjo trebušno steno, zato povečamo rez z medialno spodnjo laparatomijo. Na uterusu napravimo vzdolžno cerviko-korporalni rez. Otroka izvlečemo, nato izluščimo posteljico, ki je prirasla v istmičnem delu, na sprednjo in zadnjo steno in povsem prekriva maternično ustje. Krvavitev iz maternice je močna. Zaustavimo jo s šivanjem ležišča posteljice in uterotoniki. Zašijemo rez na uterusu.
Nato se vaginalno pojavi močna krvavitev zaradi atonije maternice v spodnjem segmentu (tam je bilo ležišče posteljice). Kljub masaži maternice, uterotonikom, pospeševani transfuziji in vbrizgavanjem rakombinantnega faktorja VII a se razvija hemoragični šok, zato se odločimo za totalno histerektomijo brez adneksov, ki je tehnično bolj zapletena zaradi stanja po predhodnem carskem rezu.
Bolnica je med posegom prejela: uterotonike (Syntocinon 20 E v inf. in 5 × 1ml carboprost i.m. in intrauterino), 11 vrečk koncentriranih eritrocitov, 10 vrečk suhe zmrznjene plazme, terapijski odmerek 8 vrečk trombocitne plazme, 7,2 mgr Fa VII, 2000 ml plazma ekspanderja, 3500 ml kristaloidov, antibiotsko zaščito.
Pooperativni potek je bil brez posebnosti, rana se je takoj zacelila. Osmi dan po operaciji je bila odpuščena domov.
Rojen je bil zdrav deček, Apgar 8/9, pH 7,27, teža 2720 g, poporodni potek je brez posebnosti, razen odziva na sluh desno.
Naknadno pridobimo histološki izvid: cerviks brez posebnosti, v kavumu so ostanki tkiva posteljice.

Zaključki

Poporodna krvavitev je eden od glavnih vzrokov za maternalno umrljivost. Najpogostejši vzroki za poporodno krvavitev so: atonija maternice, adherentna posteljica, placenta akreta, koagulopatije in ruptura uterusa. Abdominalna histerektomija je zadnji ukrep, ki ob masivni poporodni krvavitvi rešuje življenje materi. Incidenca poporodne histerektomije se po podatkih iz literature giblje med 1/330 in 1/5000 porodov. Vodilni vzrok v razvitem svetu je placenta akreta.
Peripartalna histerektomija je povezana s predhodnim carskim rezom. Tveganje se povečuje s številom predhodnih carskih rezov, pa tudi z naraščajočo starostjo matere (nad 35 let) in večjim številom porodov (nad 3).
Posledice PP so: visoka obolevnost (najpogosteje pride do febrilnega stanja, sledijo krvavitve, ileus, pljučna embolija, poškodba sečnega mehurja in ostali), izguba plodnosti ter telesna in duševna travma bolnice.
Pri opisani porodnici je šlo za carski rez »na hladno« zaradi totalne PP, ki se je zaradi hude krvavitve končal s histerektomijo. Pooperativno ni bilo zapletov.

Literatura

1. Pajntar M, Novak-Antolič Ž. Nosečnost in vodenje poroda. 2. dopolnjena izd. Ljubljana: Cankarjeva založba, 2004.
2. Juvan-Kramer K, Cerar V, Šurlan M, Verdenik I. Poporodna histerektomija. Zdrav Vestn 2006; 75: 17–21.
3. Jacobs AJ. Peripartum hysterectomy. Uptodate oktober 2008. Dosegljivo na: http://www.uptodate.com
4. Knight M, Kurinczuk JJ, Spark P, Brocklehurst P; United Kingdom Obstetric Surveillance System Steering Committee. Cesarean delivery and peripartum hysterectomy. Obstet Gynecol 2008; 111: 97–105.
5. Premru-Sršen T, Pajntar M. Hemorrhage as a cause for postpartum hysterectomy. In: Walcher W, Rosegger H, eds. Preeclampsia, perinatal hemorrhage and hemostatic problems. Abstracts. 13th congress of perinatal medicine, 21st Alpe Adria meeting; 1999 Oct 7-9; Graz. Graz: Department of obstetrics and gynecology, University hospital Graz; 1999. p. 70.

PARAVAGINALNI IN RETROPERITONEALNI HEMATOM PO PORODU

PARAVAGINAL AND RETROPERITONEAL HAEMATOMA POST PARTUM

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Izvleček

Izhodišča *Vzrok povečane poporodne krvavitve so lahko raztrganine porodne poti in okolnih tkiv. Vidne raztrganine po porodu oskrbimo in zašijemo. Če so raztrganine pod kožo ali sluznico, je iztok krvi na prosto moten. Tvorijo se manjši ali večji hematomi, ki razrivajo rahlo podkožno tkivo, parakolpij ali pa gredo v parametrije in lahko zadržujejo večjo količino krvi.*

Metode. *Enainštiridesetletna drugorodka s carskim rezom ob prejšnjem porodu je ob epiduralni analgeziji in stimulaciji popadkov z infuzijo Syntocinona rodila dečka. Placenta se je porodila spontano in je bila cela, poporodno rupturo perineja II. stopnje smo oskrbeli.*
Po porodu je otročnica tožila zaradi vse močnejših bolečin v področju jajčnikov, ki so se kljub analgetiku stopnjevale. Ob pregledu smo ugotovili večji paravaginalni hematom zadaj in desno, z ultrazvokom smo za cerviksom in istmusom maternice videli številne koagule oziroma kri. Zaradi suma na rupturo uterusa (stanje po carskem rezu) smo se odločili za revizijo z laparotomijo.
Ob ponovni laparotomiji smo v trebušni votlini našli le sled krvi. V retroperitoneju male medenice so bile vidne obsežne sufuzije oziroma hematom, ki je prehajal tudi na mezosigmoidalni del črevesja. Rupture uterusa nismo našli. Ob hkratnem vaginalnem pregledu smo izpraznili paravaginalni in pararektalni hematom, ga prešili in uredili hemostazo. Med operacijo je bolnica dobila dve dozi kompatibilnih koncentriranih eritrocitov, težo koagulov v izpraznjenem delu hematoma smo ocenili na 400 do 500 g. Na koncu smo še enkrat pregledali trebušno votlino in ugotovili, da so bile sufuzije okoli črevesja za približno 50 % manjše. Krvni tlak in utrip srca sta bila ves čas v mejah normale. Pred operacijo je bil Hb 96 g/l, hematokrit 0,30, 6 ur po operaciji in dveh transfuzijah pa Hb 93 g/l, hematokrit 0,28. Razen anemije je bil pooperativni potek brez posebnosti, 6. dan je bila otročnica odpuščena.

Zaključki *Čeprav se na prvi pogled zdi oskrba z opravljeno ponovno laparotomijo pretirana, je bilo le tako možno izključiti rupturo uterusa po carskem rezu in hematom primerno oskrbeti. Danes bi morda lahko za nazaj sprejeli očitek, da je bil retroperitonealni hematom na UZ pregledu napačno predpostavljen kot intraabdominalna krvavitev, a je njuno razlikovanje izredno težko. Morda bi v neakutni situaciji oboje razlikovala preiskava z računalniško tomografijo (CT), s katero bi bilo morda mogoče izključiti tudi rupturo uterusa kot vzrok krvavitve.*

Ključne besede *porod; hematom; zapleti; krvavitev*

Abstract

Background *Postpartum haemorrhage from ruptured tissues can usually be diagnosed and managed properly. A problem exists with the occult haemorrhage without evident tissue trauma in which case a haematoma develops.*

Methods *After a normal delivery of the 41 years old secundipara after a previous caesarean in epidural analgesia a boy was born. Placenta was delivered spontaneously and perineal rupure sutured properly.*
About an hour after the delivery heavy pain was noted in the lower abdomen. Pelvic exam revealed a paravaginal haematoma and ultrasound scan coagulated and fresh blood be-

hind the uterus. Rupture of the uterus was suspected and laparotomy revision performed. During the laparotomy there was no haemorrhage in the pelvic cavity, no uterine rupture but a large retroperitoneal haematoma extending to mesosigmoidal part of intestinum. Paravaginal heamatoma was evacuated vaginally and after half an hour the retroperitoneal haematoma diminished by 50 %. The patient received two blood transfusions. The blood loss was estimated as about 500 grams. The pulse and blood pressure were normal all the time. The laboratory values of haemoglobin was 96 g/l, haematocrit 0.30 before the operation and 93 g/l and 0.28 respectively 6 hours after. Beside anaemia the postoperative course was uneventful and the patient was dismissed from the hospital the 6th day postpartum.

Conclusions *Although the laparotomy seems an excessive treatment it was the only way to exclude uterus rupture after a previous caesarean, heavy pain in the lower abdomen and blood behind the uterus noted on the ultrasound scan. In the non-urgent situation a CT scan could be performed to locate the blood accumulation and possibly exclude uterine rupture.*

Key words *delivery; haematoma; complications; haemorrhage*

Literatura

1. Pajntar M. Poporodne krvavitve. In: Pajntar M, Novak-Antolič Ž, eds. Nosečnost in vodenje poroda. 2. dopolnjena izdaja. Ljubljana: Cankarjeva; 2004. p. 231–6.
2. Fieni S, Berretta R, Merisio C, Melpignano M, Gramellini D. Retzius' space haematoma after spontaneous delivery: a case report. Acta Biomed 2005; 76: 175–7.
3. Bienstman-Pailleux J, Huissoud C, Dubernard G, Rudigoz RC. Management of puerperal hematomas. J Gynecol Obstet Biol Reprod. V tisku 2008.

PRIMERJAVA UČINKOVITOSTI IN SPREJEMLJIVOSTI DVEH SELEKTIVNIH ANTAGONISTOV M_3 RECEPTORJEV SOLIFENACINA IN DARIFENACINA PRI ŽENSKAH S PREKOMERNO AKTIVNOSTJO MEHURJA – RAZISKAVA SOLIDAR

COMPARISON OF EFFICACY AND TOLERABILITY OF TWO SELECTIVE M_3 RECEPTOR ANTAGONISTS SOLIFENACIN AND DARIFENACIN IN WOMEN WITH OVERACTIVE BLADDER – THE SOLIDAR STUDY

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Izhodišča

Ugotoviti klinično učinkovitost in sprejemljivost solifenacina in darifenacina pri ženskah s prekomerno aktivnostjo mehurja (PAM) s poudarkom na urgenci. Oceniti tudi vpliv antiholinergikov na kakovost življenja bolnic in oceniti tudi uspeh zdravljenja (objektivna in subjektivna ocena izboljšanja).

Metode dela

Multicentrična, prospektivna, randomizirana, primerjalna, odprta, pilotska raziskava pri 100 bolnicah s PAM. Bolnice smo naključno razvrstili v dve skupini, 50 naj bi jih prejelo solifenacin, 50 pa darifenacin. Raziskava je potekala 3 mesece, bolnice so prihajale na kontrolo po 1 in 3 mesecih in vedno izpolnjevale dnevnik uriniranja, vprašalnike o urgenci, vprašalnika Urogenital Distress Inventory (UDI) in Incontinence Impact Questionnaire (IIQ) ter na koncu ocenile uspeh zdravljenja na podlagi lestvice VAS.

Rezultati

V raziskavo smo uspeli vključiti le 77 bolnic. Njihova povprečna starost je znašala 54,8 let, njihov indeks telesne mase (BMI) 27,6 kg/m2, simptomi PAM so trajali v povprečju 86.0 mesecev, urgentna inkontinenca pa 46,5 mesecev. 40 bolnic je prejelo solifenacin, 37 pa darifenacin. Bolnice obeh skupin se med sabo niso značilno razlikovale v nobenem parametru.

Raziskave ni dokončalo 16 bolnic (8 solifenacin, 8 darifenacin), večinoma zaradi stranskih učinkov (8 bolnic). Po 3-mesečnem zdravljenju se je pri obeh zdravilih značilno zmanjšala jakost, pogostost in druge težave zaradi urgence, značilno so se izboljšali tudi ostali simptomi PAM (Tab. 1). Objektivno izboljšanje po 1 mesecu je bilo večje pri bolnicah s solifenacinom ($p = 0.033$); te bolnice so imele tudi značilno manj iritativnih simptomov ($p = 0.034$). Razlike v subjektivnem izboljšanju med obema zdraviloma pri enem mesecu ni bilo. Po treh mesecih je bila kakovost življenja značilno boljša v obeh skupinah bolnic, razlike v kakovosti življenja med zdraviloma pa ni bilo ($p = 0.174$). V skupini solifenacina sta bili značilno višji objektivna ocena uspeha zdravljenja (3.8 proti 3.2, $p = 0.047$) in tudi ocena zdravljenja po VAS (74.4 proti 54.1, $p = 0.010$). Bolnice s solifenacinom so po treh mesecih porabile značilno manj vložkov (Graf 1). Pogost stranski učinek zdravljenja z obema antiholinergikoma so bila le suha usta (32 % bolnic). V Grafu 2 prikazujemo pojavnost različnih težav oz. stranskih učinkov na začetku raziskave in po trimesečnem zdravljenju. Po 3-mesečnem zdravljenju je 65,6 % bolnic ostalo na istem odmerku solifenacina (37.9 % pri darifenacinu), višji odmerek pa je prejelo 44.8 % na darifenacinu (12.5 % pri solifenacinu).

Raziskavo sta odobrili Komisija za medicinsko etiko pri Ministrstvu za zdravje in Strokovni svet UKC Maribor.
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Zaključki *Oba antiholinergika značilno izboljšata urgentno inkontinenco in ostale simptome PAM in s tem značilno izboljšata kakovost življenja bolnic. Naše ugotovitve so skladne s strokovno literaturo.[1] Pogost stranski učinek so suha usta, ki so se bodisi pojavila ali pa se je suhost poslabšala pri tretjini bolnic. Objektivna in subjektivna ocena uspeha zdravljenja sta bili višji pri bolnicah, ki so prejemale solifenacin. Morda je razlog za to njegova 3,5-krat višja koncentracija v urinu v primerjavi z darifenacinom.[2, 3] Potrebna je izvesti raziskavo na večjem vzorcu, ki bo preverila naše zaključke.*

Ključne besede *čezmerno aktiven sečni mehur; selektivni antagonist M_3 receptorjev solifenacin; darifenacin*

Abstract

Background *To assess clinical efficacy and tolerance of solifenacin and darifenacin in women with OAB with urgency as primary end point. To estimate the impact of anticholinergic drugs on quality of life of patients and to assess treatment outcome (objective and subjective improvement).*

Methods *Multicentric, prospective, randomized, head to head, open label pilot study in 100 women with OAB. Patients were randomly assigned into two groups, 50 of them received solifenacine and the remaining 50 patients darifenacin. Study duration was 3 months, patients came to the office 1 and 3 months after inclusion in the study and they always filled out voiding diaries, urgency perception questionnaires as well as the Urogenital Distress Inventory (UDI) and Incontinence Impact Questionnaires (IIQ). At the end of the study all patients estimated the success of treatment on the basis of VAS scale.*

Results *Only 77 patients were enrolled into study. Their average age was 54.8 years, and their BMI amounted to 27.6 kg/m2. The average duration of OAB symptoms and urge urinary incontinence was 86.0 and 46.5 months, respectively. 40 patients received solifenacin and remaining 37 patients darifenacin. Before treatment patients from both groups did not differ statistically significant in any of observed variables. 16 patients did not finish the study (8 solifenacin, 8 darifenacin), mainly due to side effects (8 patients). After 3 months of treatment we observed a significant improvement in severity, frequency and botherness of urgency in all patients, significantly improved were also other OAB symptoms (Table 1). Objective improvement after 1 months was greater in patients with solifenacin (p = 0.033), these patients also experienced significantly less irritative symptoms (p = 0.034). There was no difference in subjective improvement score between both drugs. Quality of life was better after three months in both groups of patients and there was no significant difference between both drugs with this regard (p = 0.174). However, we observed a significantly higher objective improvement score (3.8 vs. 3.2, p = 0.047) as well as the subjective improvement VAS score (74.4 vs. 54.1, p = 0.010) in solifenacin group.*
Patients receiving solifenacin used significantly less pads after three montha (Figure 1). Common side effect with both drugs was dry mouth (32 % of patients). In Figure 2 we are presenting the prevalence of different difficulties and side effects in the beginning of the study and after 3-month treatment. After 3-month treatment 65.6 % of patients received the same dose of solifenacin (37.9 % in darifenacin group), higher dose received 44.8 % patiens with darifenacin (12.5 % in solifenacin group).

Conclusions *Both anticholinergics significantly improved urgency as well as other OAB symptoms and thus significantly improved the quality of life of patients. These observations are, however, in accordance with literature.[1] Common side effect was dry mouth which developed or worsen in one third of patients. Objective and subjective treatment outcome were higher in patients receiving solifenacin, the reason for later probably being 3.5-times higher solifenacin concentration in urine as compared to darifenacin.[2, 3] We feel that a greater study population is needed to confirm our preliminary results.*

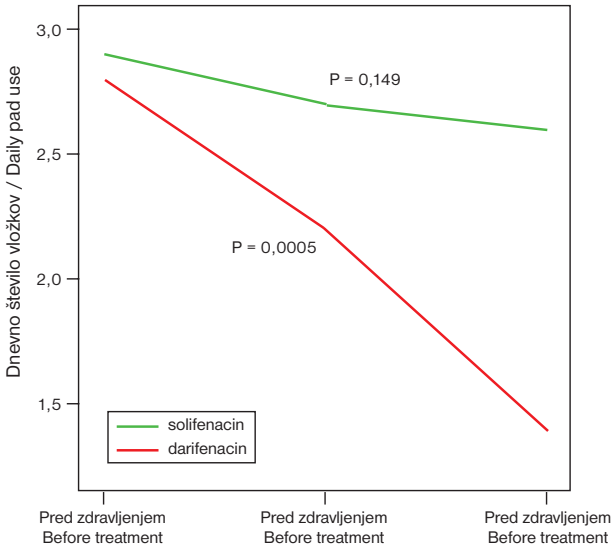
Literatura

1. Nabi G, Cody JD, Ellis G, Herbison P, Hay-Smith J. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. Cochrane Database Syst Rev 2006: CD003781.
2. Haab F, Stwart L, Dwyer P. Darifenacin, an M3 selective receptor antagonist, is an effective and well tolerated once-daily treatment for overactive bladder. Eur Urol 2004; 45: 420–9.
3. Chapple CR, Rechberger T, Al-Shukri S, Meffan P, Everaert K, Huang M, et al. Randomized, double-blind, placebo- and tolterodine controlled trial of the once-daily antimuscarinic agent solifenacin in patients with symptomatic overactive bladder. BJU Int 2004;93:303–10.

Tab. 1. *Učinkovanje antiholinergikov na simptome PAM.*

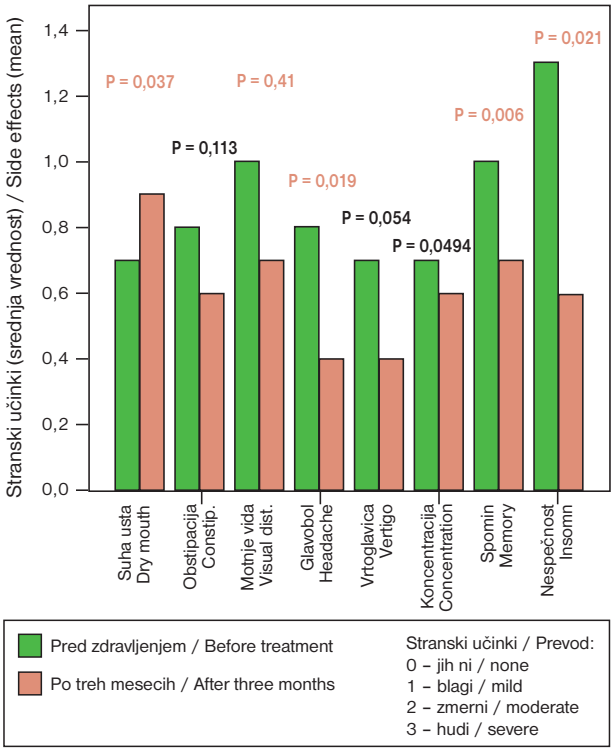
Table 1. *Effect of anticholinergics on OAB symptoms.*

	Pred zdravljenjem Before treatment	Po zdravljenju After treatment	
	Srednja vrednost Mean (SD)	Srednja vrednost Mean (SD)	p
Jakost urgentnosti (1–4) / Severity of urgency	3,1 ± 0,6	2,2 ± 0,9	< 0,0005
Pogostost urgentnosti / Frequency of urgency	5,8 ± 12	4,0 ± 2,2	< 0,0005
Koliko urgentnost moti (VAS %) / Botherness of urgency	73,0 ± 18	44,5 ± 26	< 0,0005
Frekvenca / Urinary frequency	9,1 ± 3,6	7,1 ± 2,8	< 0,0005
Nokturija / Nocturia	2,6 ± 1,4	1,4 ± 1,3	< 0,0005
Dnevna UI / Daytime UI	2,5 ± 3,4	1,5 ± 2,3	0,001
Nočna UI / Nightime UI	0,6 ± 0,9	0m3 ± 0,7	0,001
Število vložkov / Number of pads	2,8 ± 2,6	2,0 ± 2,4	< 0,0005



Sl. 1. *Poraba vložkov pri zdravljenju z antiholinergikoma.*

Figure 1. *Pad use during anticholinergic treatment.*



Sl. 2. *Pojavnost različnih težav in stranskih učinkov na začetku raziskave in po trimesečnem zdravljenju.*

Figure 2. *Prevalence of different difficulties and side effects at the beginning of the study and after 3-month treatment.*