นิพนธ์ต้นฉบับ • **Original Article**

การศึกษาเปรียบเทียบอัตราการตั้งครรภ์ระหว่างการฉีดน้ำอสุจิเข้าสู่โพรงมดลูกท่อนำไข่ ช่องท้อง และการฉีดน้ำอสุจิเข้าสู่โพรงมดลูก : รายงานเบื้องต้น

สุรางค์ทิพย์ ตั้งวิจิตร, สุพัชญ์ สีนะวัฒน์, กนก สีจร, ธนิดา พงษ์ศรีทัศน์
ภาควิชาสูติศาสตร์และนรีเวชวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น จ.ขอนแก่น ประเทศไทย 40002

Comparison of Intrauterine Tuboperitoneal Insemination and Intrauterine Insemination on Pregnancy Rate : Preliminary Report

Surangtip Thangwijitra, Supat Sinawat, Kanok Seejorn,Thanida Pongsritasana
Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand 40002

หลักการและวัตถุประสงค์: การฉีดน้ำอสุจิที่เตรียมแล้วเข้าสู่โพรงมดลูก หลังการกระตุ้นรังไข่ด้วยยาโคลมิฟีนซิเตรท (clomiphene citrate) เป็นที่นิยมอย่างแพร่หลายในการรักษาภาวะมีบุตรยากที่ไม่ได้มีสาเหตุมาจากภาวะท่อนำไข่อุดตัน เพราะเป็นวิธีที่ง่าย ไม่ยุ่งยาก ค่าใช้จ่ายไม่สูง อัตราการตั้งครรภ์ต่อรอบของการฉีดน้ำอสุจิเข้าสู่โพรงมดลูกโดยทั่วไปประมาณ ร้อยละ 8-15 แม้ว่าจะได้จำนวนฟองไข่หลายใบ แต่อัตราการตั้งครรภ์ก็ยังไม่เป็นที่น่าพอใจ ส่วนที่คลินิกมีบุตรยากโรงพยาบาลศรีนครินทร์ อัตราการตั้งครรภ์ทางคลินิกต่อรอบประมาณ ร้อยละ 3.08 การศึกษาหาวิธีเพิ่มอัตราการตั้งครรภ์ก่อนที่จะรักษาด้วยเทคโนโลยีการเจริญพันธุ์จะช่วยลดค่าใช้จ่ายประหยัดเวลาและเลี่ยงภาวะแทรกซ้อนที่อาจเกิดขึ้นได้ ดังนั้นการศึกษาครั้งนี้เป็นโครงการนำร่องเปรียบเทียบอัตราการตั้งครรภ์ระหว่างการฉีดน้ำอสุจิเข้าสู่โพรงมดลูกท่อนำไข่ ช่องท้อง กับการฉีดน้ำอสุจิเข้าสู่โพรงมดลูก

วิธีการศึกษา: ทำการศึกษาตั้งแต่ 1 พฤษภาคม พ.ศ. 2550 ถึง 31 มีนาคม พ.ศ. 2551 ที่คลินิกมีบุตรยาก โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น โดยอาสาสมัครที่ทำการศึกษาเป็นสตรีมีบุตรยากที่มิได้มีสาเหตุมาจากภาวะท่อนำไข่อุดตันที่มารับการรักษาเป็นครั้งแรก และตรงกับเกณฑ์ที่คัดไว้ (ภาวะมีบุตรยากโดยไม่ทราบสาเหตุ ภาวะเยื่อบุโพรงมดลูกเจริญผิดที่ชนิดเล็กน้อย ภาวะมีตัวอสุจิจำนวนน้อยไม่รุนแรง) โดยสตรีจำนวน 28 ราย ได้รับการสุ่มเข้าสู่การศึกษาและถูกจัดเข้าสู่ กลุ่ม A (Intrauterine

Background and objective: Intrauterine insemination (IUI) after ovarian stimulation with clomiphene citrate has been a mainstay of therapy for couples suffering from non-tubal infertility because IUI is a simple, non-invasive, and cost-effective technique. Pregnancy rates after IUI were 8% to 15% on the average. Although the number of available follicles was increased by ovarian stimulation, the results are still not very promise. Because the clinical pregnancy rate of IUI in Srinagarind Hospital was 3.08%. The new insemination method for improving the clinical pregnancy rate was considered to be an alternative way technique which could be reduced cost and duration of treatment and avoid complication of the assisted reproductive technology. A preliminary RCT compared the clinical pregnancy rate of IUTPI and IUI was the main objective of the study.

Methods: The study was conducted from April 1, 2007 to March 31, 2008 at Infertility clinic, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University. The volunteers were women with non-tubal infertility who met the inclusion criteria (unexplained infertility, minimal-mild endometriosis, mild oligozoospermia) and undergoing first treatment cycle were randomized to the study. Twenty eight women were randomized to the study and allocation to group A (IUTPI) or group B (IUI) on the day of insemination followed the ovarian stimulation with clomiphene citate

tuboperitoneal insemination:IUTPI) หรือ กลุ่ม B (Intrauterine insemination:IUI) ในวันที่จะฉีดน้ำอสุจิ ซึ่งเป็นวันหลังจากได้รับการกระตุ้นรังไข่ด้วยยา clomiphene citrate และฉีดยา hCG ไปแล้ว 36-40 ชั่วโมงเมื่อฟองไข่สุก การฉีดน้ำอสุจิเข้าสู่โพรงมดลูก ท่อรังไข่ ช่องท้อง (IUTPI) ใช้สาย pediatric Foley's catheter ขนาด 8 F ฉีดน้ำอสุจิที่เตรียมด้วยปริมาตร 10 มิลลิลิตร การฉีดน้ำอสุจิเข้าสู่โพรงมดลูก (IUI) ใช้สาย IUI ที่เตรียมเองฉีดน้ำอสุจิที่เตรียมด้วยปริมาตร 0.5 มิลลิลิตร

ผลการศึกษา: มีการรักษาทั้งสิ้น 28 รอบการรักษาที่ให้การรักษาและติดตามผลได้ครบถ้วน (IUTPI มี 16 รอบการรักษา และ IUI มี 12 รอบการรักษา) อัตราการตั้งครรภ์ทางคลินิกต่อรอบสำหรับ IUTPI=6.3%(1/16) และ IUI=0%(0/12), p=1.00 อัตราการตั้งครรภ์ต่อเนื่องต่อรอบสำหรับ IUTPI=6.3%(1/16) และ IUI=0%(0/12), p=1.00 ไม่พบการตั้งครรภ์แฝด การตั้งครรภ์นอกมดลูกกลุ่มอาการรังไข่ถูกกระตุ้นมากเกินไปและการติดเชื้อเกิดขึ้นในระหว่างการศึกษา

สรุป: การศึกษาเบื้องต้นนี้พบว่าการฉีดน้ำอสุจิเข้าสู่โพรงมดลูกท่อนำไข่ ช่องท้อง หลังการกระตุ้นรังไข่ด้วยยา clomiphene citrateอาจจะไม่ได้ให้อัตราการตั้งครรภ์เหนือไปกว่าวิธีมาตรฐานเดิมคือการฉีดน้ำอสุจิเข้าสู่โพรงมดลูกสำหรับคู่สมรสที่มีภาวะมีบุตรยากที่ไม่ได้มีสาเหตุมาจากภาวะท่อนำไข่อุดตัน

คำสำคัญ: การฉีดน้ำอสุจิเข้าสู่โพรงมดลูก ท่อนำไข่ ช่องท้อง การฉีดน้ำอสุจิเข้าสู่โพรงมดลูก อัตราการตั้งครรภ์ทางคลินิกต่อรอบ อัตราการตั้งครรภ์ต่อเนื่องต่อรอบ

(CC). On the day of 36-40 hours after hCG administration, IUTPI was performed by using a pediatric Foley's catheter size 8 F inseminating with 10 mL of sperm suspension and IUI was performed with 0.5 mL of sperm suspension by using the household IUI catheter.

Results: A total of 28 cycles was completed treatment and followed up (16 IUTPI cycles and 12 IUI cycles).The clinical pregnancy rate per cycle was 6.3%(1/16) for IUTPI and 0%(0/12) for IUI, p=1.00. The ongoing pregnancy rate per cycle was 6.3%(1/16) for IUTPI and 0%(0/12) for IUI, p=1.00. No multiple pregnancy, ectopic pregnancy, ovarian hyperstimulation syndrome and infection were occurred.

Conclusion: This preliminary result of IUTPI after ovarian stimulation with clomiphene citrate might not be advantage over the standard IUI for couples with non-tubal infertility on pregnancy rate.

Keywords: Intrauterine tuboperitoneal insemination, intrauterine insemination, clinical pregnancy rate, ongoing pregnancy rate

ศรีนครินทร์เวชสาร 2553; 25(4): 298-305 • Srinagarind Med J 2010; 25(4): 298-305

Introduction

Intrauterine insemination (IUI) with ovarian stimulation by clomiphene citrate or gonadotropin is commonly offered to couples with a variety of infertility factors. Because IUI is a simple, non-invasive, and cost-effective technique, which has been a mainstay of therapy for couples suffering from non-tubal infertility prior to considering the more invasive and expensive method as IVF (in vitro fertilization).[1] Pregnancy rates after IUI were 8% to 15% on the average.[2,3] Although the number of available follicles was increased by ovarian stimulation, the results are still not very promise, mainly because of low sperm count, suboptimal spermatozoa or total absence of spermatozoa at the site of fertilization.[4] Mortimer et al showed that there is a reduction in sperm number of five to six orders of magnitude along the length of the female reproductive tract, so in the normal fallopian tubes a maximum of only 200 spermatozoa are present in the ampulla.[5,6] Ripps et al[7] showed that the number of spermatozoa in the pouch of Douglas after IUI was very low. However, the number of spermatozoa can be significantly increased with uterotubal flushes.[7] Another simple non-invasive method was introduced as fallopian tube sperm perfusion (FSP) by Kahn et al.[8] The technique was developed to ensure the presence of higher sperm densities in the fallopian tubes at the time of ovulation than standard IUI provides which flushing the uterine cavity and the tubes with 4 mL of sperm suspension by using an Allis clamp placed on the cervix.[8] However, clamping of the cervix produced some discomfort or even pain and occasionally bleeding from the cervix.[8] The pregnancy rate per treatment was 26.9% with unexplained

infertility.[8] Kahn concluded that FSP is easy to perform and is less expensive than other methods of assisted conception, such as in vitro fertilization (IVF) and gamete intra-fallopian transfer (GIFT).[8] Cantineau et al[9] reported a systematic review based on meta-analysis of FSP compared with IUI and concluded that unclear whether fallopian tube sperm perfusion (FSP) is better than intrauterine insemination (IUI) for non-tubal infertility but FSP may be better for unexplained infertility. The previous study reported the possible therapeutic effect of 10 ml of contrast medium using in hysterosalpingography (HSG) results in increasing of the rate of live births after HSG, especially in patients with unexplained infertility, supporting the hypothesis that tubal "plugs".[10-12] Mamas L et al[13] reported RCT compared the results of fallopian tube sperm perfusion (FSP) with 4 mL of sperm suspension and intrauterine tuboperitoneal insemination (IUTPI) with 10 mL of sperm suspension by using the DNB speculum cervical clamp. The study showed that the clinical pregnancy rate per cycle was 17.6% for FSP (n=199) and 29.4% for IUTPI (n =204), p<0.007. Three of twin pregnancies and 3 of quadruplets occurred in FSP group and 5 of twin pregnancies and 5 of quadruplets occurred in IUTPI group. None of ectopic pregnancy and infection was observed. There was not report about pain during insemination but a large volume of 10 mL sperm suspension was sufficient to fill the uterine cavity, pass through the fallopian tubes, and finally reach peritoneal cavity.

Because the clinical pregnancy rates of IUI in the previous studies[2,3] and in Srinagarind Hospital, Faculty of Medicine, Khon Kaen University from 1997 to 2004 (3.08%) were quite low for couples with non-tubal infertility. The new insemination method for improving the clinical pregnancy rate was considered to be an alternative way prior move to the more invasive and expensive technique. A preliminary RCT compared the clinical pregnancy rate of IUTPI and IUI was the main objective of the study.

Materials and Methods

The study was conducted from April 1, 2007 to March 31, 2008 at the infertility clinic of Srinagarind Hospital, under the Ethics Committee of Faculty of Medicine, Khon Kaen University that was followed in accordance with the Helsinki Declaration of 1975 on human experimentation. The financial was supported by Faculty of Medicine Research Grant Khon Kaen University, Khon Kaen, Thailand. The basic infertility investigations such as semen analysis[14], transvaginal ultrasonography (TVS), hysterosalpingography (HSG), blood test for CBC, Anti-HIV, HBsAg, VDRL, TSH and prolactin level were performed. The participants with mild oligozoospermia[15] (initial sperm count $\geq$10 million/mL to <20 million/mL), unexplained infertility[16] (diagnosed when all of the standard elements of infertility evaluation yield normal result), minimal and mild endometriosis[17] (stages I endometriosis with ASRM scores 1-5 and stages II endometriosis with ASRM scores 6-15) were included to the study after receiving the information about risk and benefit of the treatment study, and participants signed informed consent forms. The exclusion criteria were participants with unilateral or bilateral tubal obstruction and intrauterine abnormality. Participants undergoing first cycle treatment were allocated randomly to group A (IUTPI) or group B (IUI) by choosing the sealed envelopes on the day of insemination.

Ovarian stimulation: All women underwent the same ovarian stimulation with clomiphene citrate (CC) 100 milligrams per day, started on 3rd day of menstrual cycle and continued for 5 days. TVS was performed on day 12th of menstrual cycle for assessment numbers and diameter of the dominant follicles, endometrial thickness and endometrial morphology. Serial TVS was performed and 5,000 IU of hCG (human chorionic gonadotropin) was administered for triggered ovulation when the diameter of the leading follicle was 18 mm at least. If four matured follicles or more were found, the treatment cycles were cancelled because of the risk of multiple gestation and ovarian hyperstimulation syndrome (OHSS is an exaggerated response to ovulation induction therapy).[18]

Sperm Preparation: Husband semen was collected by masturbation into a sterile container followed 2-3 days of sexual abstinence. Semen analysis was evaluated after liquefaction according to the World Health Organization 1992 criteria.[14] A two-layer gradient technique was used for sperm preparation. One milliliters of 45% SpermGrad diluted with Ham's F-10 was layered over 1 mL of 90% SpermGrad, in a 15-mL conical centrifuge tube. The semen was layered over this gradient and the tube was centrifuged for 15 minutes at 350g. The supernatant was discarded and the pellet diluted

in 5 mL of Ham's F-10 and centrifuged for 5 minutes at 350g. The supernatant was discarded after centrifugation and the remaining final pellet was re-suspension with Ham's F-10 to be a sperm suspension of 0.5 mL and 10 mL for IUI and IUTPI, respectively. All solutions were also analyzed to evaluate the total inseminated sperm count and motility.

Insemination: A single insemination was performed 36-40 hours after hCG administration. **IUTPI** was performed by using a size 8 F pediatric Foley's catheter (figure 1) after removed mucus with cotton soaked normal saline solution. The catheter was gently inserted through the cervix into the uterine cavity and the balloon was inflated with 1.0 mL of normal saline solution and gently pressed back against the internal os to avoid fluid reflux. Ten milliliters of sperm suspension were slowly infused in the rate of 4 mL per minute by using 10 mL sterile syringe. Immediately after insemination, the catheter was clamped with uterine packing forceps to avoid semen reflux for 2 minutes. The catheter was deflated the balloon after 2 minutes of clamping. The patient remained lying for approximately 15 minutes after insemination. **IUI** was performed by using a household IUI catheter (a three centimeters tip of the size 5 F feeding tube connected with an outer sheath of IV Catheter 18G) (figure 2). A one milliliter insulin syringe was used for infused. After removed any mucus with cotton soaked normal saline solution, the catheter was passed through the cervix and 0.5 mL of the sperm suspension was slowly infused for 30 seconds in the upper part of the uterine cavity before withdrawal. The patient remained lying for approximately 15 minutes after insemination.

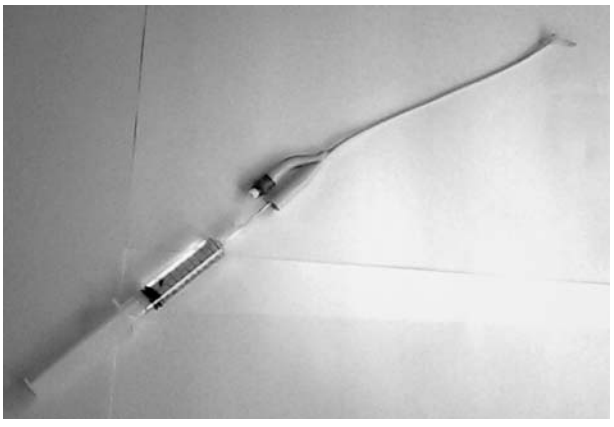

Figure 1 IUTPI catheter

Figure 2 IUI catheter

Participants were followed up after 2 weeks of insemination for the urinary pregnancy test (UPT). If the urinary pregnancy test was positive, TVS was performed when the gestational age was about 6 weeks by the last menstrual period (LMP) to confirm clinical pregnancy (positive intrauterine gestational sac with fetal heart motion). The second transvaginal ultrasonography (TVS) was performed on the 12^{th} week gestation to confirm ongoing pregnancy. The clinical pregnancy rate per cycle was defined by number of clinical pregnancy divided by number of treatment cycle. The ongoing pregnancy rate per cycle was defined by number of ongoing pregnancy divided by number of treatment cycle.

The SPSS version 11.5 program was used for analysis. Continuous variables from the two groups were compared by the two-tailed Student's *t*-test for independent data and the Mann-Whitney test was used if the data did not distribute normally. Categorical variables from the two groups were compared by the Chi-square(x^2) test and the Fisher's exact test was used if there were more than 25% of the expected count <5 in each cell. The clinical pregnancy rates were compared by the Chi-square(x^2) test at α=0.05 considered statistical significance.

Results

During the study period, 28 women were systematically randomized to the study, 16 participants were allocated to group A (IUTPI) and 12 to group B (IUI). All of these were completed treatment and followed up. Demographic characteristics of both groups are shown in Table 1. There were not statistically differenced in body mass index (BMI), menstrual cycle interval, duration of infertility, causes of infertility in the two groups. The mean age of group A (IUTPI) and group B (IUI) were significant difference (31.9$\pm$3.8 years vs. 35.5$\pm$4.2 years, p=0.02).

Number of the dominant follicles (≥18 mm), mean of follicular diameter, endometrial thickness, endometrial patterns and Husband semen sperm count before and after semen preparation in both groups were not statistically differenced. Although sperm motility before sperm preparation was statistically difference between the two groups, but after sperm preparation there was not difference significantly. The clinical pregnancy rate per cycle was 6.3% (1/16) for group A (IUTPI) and 0% (0/12) for group B (IUI), p=1.00. The ongoing pregnancy rate per cycle was 6.3% (1/16) for group A (IUTPI) and 0% (0/12) for group B (IUI), p=1.00 (Table 2). In the IUTPI group there was singleton pregnancy. None of ovarian hyperstimulation syndrome (OHSS) and infection was occurred in both groups.

The presence of blood on catheter after insemination in group A (IUTPI) and group B (IUI) were 81.3% and 50%, respectively (p=0.08). Pain during insemination was found 81.3% and 0% in the IUTPI group and the IUI group, respectively (p=<0.001). Regurgitation of sperm suspension after catheter withdrawal was no difference in both groups (43.8% vs. 25.0%, p=0.31) (Table 3).

Table 1 Patient demographic characteristics.

Characters	IUTPI (n = 16)	IUI (n = 12)	p-value
Age(years)	31.9±3.8	35.5±4.2	0.02 [a]
BMI(kg/m^2)	20.6±2.2	21.0±3.8	0.75 [b]
Menstrual cycle interval(days)	29.1±2.2	30.3±2.6	0.21 [a]
Duration of infertility(years)	4.8±3.0	5.8±3.3	0.38 [b]
Causes of infertility			
Mild oligozoospermia	14 (87.5)	11 (91.7)	1.00 [d]
Unexplained infertility	2 (12.5)	0 (0.0)	0.49 [d]
Minimal to mild endometriosis	4 (25.0)	2 (16.7)	0.67 [d]

Note: Data are presented as mean±SD and numbers (%).

[a] Student's *t*-test, [b] Mann-Whitney test, [c] Chi-square test, [d] Fisher's exact test

Table 2 Characteristics of treatment cycle and pregnancy rate.

Characters	IUTPI (n = 16)	UI (n = 12)	p-value
Number of follicles(≥18 mm diameter)	1.8±0.7	2.0±0.9	0.52 [b]
Mean of follicular diameter(mm)	21.1±2.8	20.8±3.2	0.75 [b]
Endometrial thickness(mm)	9.1±3.1	8.7±4.3	0.77 [a]
Endometrial pattern			0.49[d]
Triple lines	13 (81.3)	12 (100.0)	
Hyperechoic	2 (12.5)	0 (0.0)	
Heteroechoic	1 (6.3)	0 (0.0)	
Initial semen analysis			
Sperm count (million/ml)	62.4±25.9	59.8±35.8	0.82 [a]
Sperm motility (%, grade a+b)	68.2±9.2	56.3±17.1	0.03 [a]
Post preparation inseminate			
Total sperm count (million)	34.8±25.2	30.8±25.9	0.69 [b]
Sperm motility (%, grade a+b)	98.8±5.0	91.3±13.7	0.05 [b]
Clinical pregnancy rate per cycle (%)	1 (6.3)	0 (0.0)	1.00 [d]
Ongoing pregnancy rate per cycle (%)	1 (6.3)	0 (0.0)	1.00 [d]

Note: Data are presented as mean±SD or numbers (%).

[a] Student's *t*-test, [b] Mann-Whitney test, [c] Chi-square test, [d] Fisher's exact test

Table 3 Events during insemination.

Events	IUTPI (n = 16)	IUI (n = 12)	p-value
Presence of blood on catheter			0.08
Present	13 (81.3)	6 (50.0)	
Absent	3 (18.8)	6 (50.0)	
Pain			<0.001
Present	13 (81.3)	0 (0.0)	
Absent	3 (18.8)	12 (100.0)	
Regurgitation of sperm suspension			0.31
Present	7(43.8)	3 (25.0)	
Absent	9 (56.3)	9 (75.0)	

Note: Data are presented as mean±SD and numbers (%).

[a] Student's *t*-test, [b] Mann-Whitney test, [c] Chi-square test, [d] Fisher's exact test

Discussion

The study presents the preliminary results of intrauterine tuboperitoneal insemination (IUTPI) compared with intrauterine insemination (IUI) in non-tubal infertility participants (mild oligozoospermia, unexplained infertility, minimal to mild endometriosis). The pregnancy rate of IUTPI was quite low when compared to IUI (in the present study, Dodson's study[2] and Peterson's study[3]). There were the factors might be influenced the pregnancy outcomes such as flushing out of oocyte by a large volume of IUTPI method. A large volume of 10 ml possible directed flushing the oocyte out of fallopian tube and might be stimulated abnormal tubo-muscular contraction resulting in expulsion of the oocyte from the tube with subsequent failure of fertilization as the conclusion of Nuoja-Huttunen et al about the study of fallopian tube sperm perfusion.[19] Blood presence on catheter after withdrawal was not significantly difference in the two groups. The possible endometrial injury caused by the compressive effect of the balloon of Pediatric Foley's catheter in fallopian tube sperm perfusion (FSP) was the disadvantage of the method, but this was not influence the clinical pregnancy rate as Li et al reported.[20] In Kahn's study[8], using an Allis clamp placed on the cervix produced occasionally bleeding but this was not cause adverse effect on pregnancy. Nuoja-Huttunen et al[19] reported that the inflated balloon of the Foley's catheter and abnormal intrauterine pressure during FSP could be damage the endometrial architecture, thus reducing the chance of embryo implantation.

The difference in ovarian stimulation protocol, combined clomiphene citrate with exogenous gonadotropin was used in Mamas's study[13] and clomiphene citrate was used in the author's study may be result the difference in pregnancy rate. Using the DNB speculum cervical clamp in Mamas's study[13] during intrauterine tuboperitoneal insemination was more advantage than Pediatric Foley's catheter with ballooning in the present study. External pressure on the cervix with DNB speculum cervical clamp can avoid endometrial trauma and bleeding. A significance of pain during IUTPI was more disadvantage than the standard IUI as the studies of FSP by Kahn et al[8] and Li et el[20], but in Mamas's studies[13,21] were not mention about this. In Mamas's study there were 3 twin pregnancies occurred in group A (FSP) and 5 in group B (IUTPI), as well as a set of quadruplets.[13] Three cases of mild ovarian hyperstimulation syndrome (OHSS) occurred in both groups in Mamas's study.[13] None of multiple pregnancies or ovarian hyperstimulation syndrome were occurred in the present study may be indicate that ovarian superovulation with clomiphene citrate resulting fewer mature follicles.[18] Numerous causes of infertility might be influenced the present study results. Further study should be designed for treatment with one specific cause of infertility.

Conclusion

Intrauterine tuboperitoneal insemination (IUTPI) after ovarian stimulation with clomiphene citrate by using pediatric Foley's catheter for insemination might not be advantage over the standard IUI treatment for couples with non-tubal infertility (mild oligozoospermia, minimal-mild endometriosis and unexplained infertility) on pregnancy rate. Because a large volume of 10 ml possibly directed flushing the oocyte out of fallopian tube and might be stimulated abnormal tubo-muscular contraction resulting in expulsion of the oocyte from the tube with subsequent failure of fertilization and damaging endometrial might be reduced the chance of embryo implantation. The other disadvantage of IUTPI was the pain during insemination.

Acknowledgements

The present study has been supported by Faculty of Medicine Research Grant Khon Kaen University, Khon Kaen, Thailand. The authors thank advising staff; Professor Jadsada Thinkhamrop, Assisted Professor Srinaree Kaewrudee and staff of both Division of reproductive medicine of Khon Kaen University and Chiang Mai University for correcting the sample size calculation and statistic analysis; and also thank; the nurses, the technicians, and the ultrasonographic staff of Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University for assistance in the completion of the treatment program.

References

1. Hughes EG. The effectiveness of ovulation induction and intrauterine insemination in the treatment of persistent infertility: a meta-analysis. Hum Reprod 1997; 12:1865-72.
2. Dodson WC, Haney AF. Controlled ovarian hyperstimulation and intrauterine insemination for the treatment of infertility. Fertil Steril 1991; 55:457-67.
3. Peterson CM, Hatasaka HH, Jones KP, Poulson AM Jr, Carrel DT, Urry RL. Ovulation induction with gonadotropins and intrauterine insemination compared with in vitro fertilization and no therapy: a prospective, non-randomized, cohort study and meta-analysis. Fertil Steril 1994; 62:535-44.
4. Mamas L. Higher pregnancy rates with a simple method for fallopian tube sperm perfusion, using a cervical clamp double nut bivalve speculum in the treatment of unexplained infertility: a prospective randomized study. Hum Reprod 1996; 11: 2618-22.
5. Mortimer D, Templeton AA. Sperm transport in the human female reproductive tract in relation to semen analysis characteristics and time of ovulation. J Reprod Fertil 1982; 64:401-8.
6. Mortimer D. Sperm transport in the human female reproductive tract. Oxford Rev Reprod B 1983; 5:30-61
7. Ripps BA, Minhas BS, Carson SA, Buster JE. Intrauterine insemination in fertile women delivers larger numbers of sperm to the peritoneal fluid than intracervical insemination. Fertil Steril 1994; 61:398-400.
8. Kahn JA, von During V, Sunde A, Sordal T, Molne K. Fallopian tube sperm perfusion: first clinical experience. Hum Reprod 1992; 7(Suppl 1):19-24.
9. Cantineau AE, Heineman MJ, Al-Inany H, Cohlen BJ. Intrauterine insemination versus fallopian tube sperm perfusion in nontubal subfertility: a systematic review based on a Cochrane review. Hum Reprod 2004; 19:2721-19.
10. Shalev J, Krissi H, Blankstein J, Meizner I, Ben-Rafael Z, Dicker D. Modified hysterosalpingography during infertility work-up: use of contrast medium and saline to investigate mechanical factors. Fertil Steril 2000; 74:372-5.
11. Spring DB, Barkan HE, Pruyn SC. Potential therapeutic effects of contrast materials in hysterosalpingography: a prospective randomized clinical trial. Kaiser Permanente Infertility Work Group. Radiology 2000; 214:53-7.
12. Johnson N, Vandekerckhove P, Watson A, Lilford R, Harada T, Hughes E. Tubal flushing for subfertility. Cochrane Database Syst Rev 2002; 3: CD003718.
13. Mamas L. Comparison of fallopian tube sperm perfusion and intrauterine tuboperitoneal insemination: a prospective randomized study. Fertil Steril 2006; 85:375-40.
14. World Health Organization. WHO laboratory manual for the examination of human semen and sperm-cervical mucus interaction. 3rd ed. New York: Cambridge University Press, 1992.

15. Hirsh A. Male subfertility. BMJ 2003; 327:669-72.
16. Speroff L, Fritz MA. Female infertility. In : Speroff L, Fritz MA, editors. Clinical gynecology endocrinology and infertility. 7th ed. Philadelphia : A Wolters Kluwer company, 2005 : 1053-6.
17. American Society for Reproductive Medicine (ASRM). Revised American Society for Reproductive Medicine classification of endometriosis. Fertil Steril 1997; 67:817-21.
18. Practice Committee of the American Society for Reproductive Medicine (ASRM). Ovarian hyperstimulation syndrome. Fertil Steril 2006; 86(Suppl 4): S178-83.
19. Nuojua-Huttunen S, Tuomivaara L, Juntunen K, Tomas C, Martikainen H. Comparison of fallopian tube sperm perfusion with intrauterine insemination in the treatment of infertility. Fertil Steril 1997; 67:939-42.
20. Li TC. A simple non-invasive method of Fallopian tube sperm perfusion. Hum Reprod 1993; 8:1848-50.
21. Mamas L, Faye R, Eudoxia M, Kalogirou I, Chandakas S, Polyzos P. A new method of intrauterine insemination: 6 years experience of intrauterine tuboperitoneal insemination (IUTPI). Fertil Steril 2008; 90(Suppl 1): S384.