Thai Journal of Obstetrics and Gynaecology
December 2003, Vol. 15, pp. 223-229

GYNAECOLOGY

Comparison of Tom Cat and PIVET Catheter for Intrauterine Insemination

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ABSTRACT

Objective To compare immediate endometrial changes after IUI, pregnancy rates and difficulty in performing insemination using either Tom Cat or PIVET catheter.

Design A randomized trial.

Setting University Hospital.

Patients and Intervention Infertile couples (n=163) participated in 239 cycles of ovarian stimulaton and intrauteine insemiantion (IUI). Patients with bilateral tubal obstruction and severe male factor were excluded. Eligible patients were stratified into 2 groups by sonographic endometrial pattern (triple layer pattern present or absent). Patients in each group were randomized to either Tom Cat or Pivet catheters. Transvaginal sonography was repeated immediately after IUI in the former group and endometrial changes were recorded. All patients were followed for the outcomes of treatment.

Main outcome measurement Ultrasonographic endometrial changes, clinical pregnancy rates, technical difficulties and complications in performing IUI.

Results Pregnancy rates in both groups were not statistically different (12.9% in Tom Cat and 11.4% in PIVET group, p=0.714). Endometrial triple-layer pattern remained intact in 76.6% and 72.6% of cases after insemination using Tom Cat and PIVET catheter respectively (p=0.214). Difficulties and complications were not statistically different. Endometrial thickness $\geq$ 7.5 millimeters was the only factor that significantly predicted success of IUI (p=0.042, odds ratio = 3.7; 95% CI = 1.1 - 11.9).

Conclusion Tom Cat and PIVET catheters are equally effective for IUI.

Key words: intrauterine insemination, Tom Cat, PIVET catheter

Superovulation with intrauterine insemination (IUI) is now widely practiced as a treatment option for nontubal infertility because it is simple, less costly and less invasive than the more complex assisted reproduction techniques.[1] The precise mechanism that this method enhances the conception rate is still

unknown. It is likely that it works through a combination of actions, including correction of the erratic LH patterns, normalization of follicular growth, increasing the number of available oocytes and spermatozoa at the site of fertilization and correction of luteal phase defect.[1-4]

There is considerable variation in the reported cycle fecundity rates,[4] which could be due to multiple factors such as heterogeneity of patient population, variable number of motile sperm inseminated, difference in ovulation induction protocol, etc.[1,2,4] A report by Lavie et al.[5] suggested that success of IUI might be affected by the type of catheter used. Specifically, they found total destruction of the endometrial triple-layer pattern in 12.5% of the cycles when Wallace catheters were used, compared with 50% when Tom Cat catheters were used. Although pregnancy rates were not statistically different, there was a trend in favor of those with intact endometrial triple-layer pattern.

Since we routinely use Tom Cat catheters for IUI and PIVET catheters for embryo transfer, we feel that a randomized clinical trial is needed to re-examine our position regarding the appropriate choice of catheters for IUI. The objectives of this study are to compare immediate endometrial changes after IUI, pregnancy rates, and difficulty in performing insemination using these two types of catheters.

Material and methods

This study was approved by the Ethical Committee of the Faculty of Medicine, Chiang Mai University. Subjects were recruited from infertility clinic at Maharaj Nakorn Chiang Mai Hospital between March 13, 1998 to May 25, 2000. Couples were included if they had indications for IUI and gave their informed consents. They were excluded if: 1) the female partner was more than 42 years old; or 2) she had bilateral tubal obstruction; or 3) the male partner had sperm concentration less than 10×10^6 spermatozoa per milliliter.

All female partners received 1 of the 3 ovulation induction regimens: 1) clomiphene citrate (Duinum, Medline); 2) clomiphene citrate plus human menopausal gonadotropin (hMG, Humegon, Organon) or recombinant follicle stimulating hormone (rFSH, Puregon, Organon); and 3) HMG or rFSH. The choice was decided by the couples and their physicians after consideration of factors such as cost, success rate and complication. In the clomiphene protocol, the female partners received 100 mg per day of clomiphene citrate for 5 days starting from cycle day 3. In the clomiphene citrate plus HMG/FSH group, a daily dose of 100 mg of clomiphene citrate was given from day 3 to day 7, followed by 75 IU of HMG or 50 IU of rFSH daily from cycle days 8-10. In the group that received only HMG/rFSH, a daily dose of 150-225 IU of HMG or 100-150 IU of rFSH was given, starting on cycle day 3 until at least 1 follicle reached a diameter of 17 millimeters or more. Transvaginal sonography was performed to measure follicular size. If the average diameter of the leading follicle was greater than 17 millimeters, 5,000 IU of human chorionic gonadotropin (hCG; Pregnyl, Organon or Profasi, Serono) was injected intramuscularly. Intrauterine insemination (IUI) was scheduled 38-40 hours after hCG injection.

Sperm preparation was processed in andrology laboratory by using discontinuous 90%:40% Percoll gradient (Percoll, Sigma Chemical, USA). The pellet was washed twice in Earle's balanced salt solution (EBSS, Gibco, USA) The final pellet was resuspended in 0.4 ml of EBSS and used for insemination. Just before IUI transvaginal sonography (Aloka SSD620, with a 5 MHz transvaginal probe) was performed by the attending gynecologist to measure endometrial thickness and to assess endometrial echoic pattern. Subjects were classified into 2 groups: triple-layer present (group I) or triple-layer absent (group II). Subjects in each group were randomized separately, by using a table of random number, to either Tom Cat (Sherwood Medical, U.S.A) or PIVET catheter (Cook IVF, Australia). The insemination was performed by 4 infetility

specialists. Procedural difficulty and patient discomfort were recorded. In group I (triple-layer present) transvaginal sonography was repeated after IUI to assess the degree of endometrial destruction as: 1) intact; if the triple-layer remained intact with traces of inseminated fluid near the fundus; 2) partial destruction; if some part of triple-layer pattern was still seen; and 3) complete destruction: if the triple-layer could no longer be demonstrated.

In this study, procedural difficulty in catheter insertion was defined as present when: 1) several attempts were needed to pass the catheter through the cervical canal into the uterine cavity; or 2) when teneculum was needed to stretch the cervical and uterine axis; or 3) cervical dilatation either by uterine sound or Hegar dilator was done.

Clinical pregnancy was diagnosed when fetal heart activity could be demonstrated by transvaginal sonography at a gestational age of 6-7 weeks. Patients, who were not pregnant or had abortion, were retreated with the same type of catheters until they completed 3 cycles of treatment or were pregnant or were lost from the study.

Ages of the female partners, types and duration of infertility, indication for IUI, types of ovulation induction, numbers of follicles greater than 14 millimeters, number of motile sperm used for IUI, endometrial echoic patterns, endometrial thickness and outcomes of the treatment were recorded. Stata program (College Station, Texas) was used for statistical analysis. Chi^2 and t-tests were used for comparison of proportions and means as appropriate. Life table was used for calculation of cumulative pregnancy rates. Cox regression model was used to determine factors that affected the success of treatment. A p-value < 0.05 was considered statistically significant.

Results

During the study period, 245 couples underwent IUI but only 163 met eligibility criteria and gave their informed consent. Seventy seven couples were randomized to Tom Cat and 86 to PIVET catheters. Baseline characteristics of subjects were comparable except for infertility status. The proportion of cases with primary infertility was higher in the PIVET than in the Tom Cat group (84.9% vs 68.8%; p=0.015). (Table 1)

A total of 239 IUI cycles were performed in 163 subjects. Triple-layer pattern was present in 122 cycles (60 cycles in Tom Cat and 62 cycles in PIVET group). Triple-layer pattern was absent in 117 cycles (56 cycles in Tom Cat and 61 cycles in PIVET group). There was no difference in the ovulation induction regimen, number of follicles $\geq$ 14 m.m., endometrial pattern, endometrial thickness, and the number of motile sperm inseminated. (Table 2).

In patients with triple-layer endometrial pattern, the degree of endometrial destruction after insemination was comparable in the Tom Cat and PIVET groups. (Table 3) The endometrium remained intact in 76.6% and 72.6% of cases in the Tom Cat and PIVET group respectively (p=0.214).

The overall clinical pregnancy rate in this study was 12.1% per IUI cycle (29 pregnancies from 239 IUI cycles) or 16.6% per subject (27 out of 163 subjects). Cumulative pregnancy rate calculated by life-table analysis was 32.9% (95% CI = 19.0% - 52.9%) after 3 treatment cycles. Eighty-two couples, who did not meet eligibility criteria or refused to participate in the study, underwent a total of 125 IUI cycles during the same period. There were only 4 clinical pregnancies in this group, giving a clinical pregnancy rate of 3.2% per cycle)

Clinical pregnancy rates per cycle in the Tom Cat and PIVET groups were not significantly different (12.9% and 11.4% respectively, p=0.714). Clinical pregnancy rates per patient were also comparable (19.5% and 14.0% respectively, p=0.423). Cumulative pregnancy rates after 3 treatment cycles were also similar (30.6%; 95% CI = 18.0%-49.0% in Tom Cat and 34.5%; 95% CI = 14.5%-68.1% in PIVET group). Pregnancy rates in patients with or without triple-layer endometrial pattern were similar (10.7% and 13.7% respec-

tively, p=0.475). Of 29 pregnancies, there were 8 abortions (27.6%), 2 ectopic pregnancies (6.9%) and 3 multifetal pregnancies (2 twins and 1 triplet; 10.3%).

There was no significant difference in procedural difficulty in the Tom Cat and PIVET groups (16.4% and 17.1% respectively, p=0.886). Teneculum was used in 15.5% of Tom Cat and 9.8% of PIVET group, p=0.179). Cervical dilatation was performed in 1.7% in Tom Cat and 1.6% in PIVET group (p=0.953). Discomfort reported by patients during the procedure was also not different (29.3% in Tom Cat and 26.8% in PIVET group, p=0.882). (Table 4)

The following variables were used in a Cox regression model as covariates to predict the success of IUI: ages of female partner, infertility status, duration of infertility, indication for IUI, ovulation induction regimens, number of follicles $\geq$ 14 millimeter, duration between hCG injection and IUI, number of motile sperm inseminated, type of catheter, endometrial thickness and endometrial pattern. Endometrial thickness was found to be the only factor that significantly predicted a clinical pregnancy after IUI (p=0.042). From ROC curve, the cut-off value for endometrial thickness that predicted success after IUI was $\geq$7.5 millimeter (odds ratio = 3.71; 95% CI = 1.15 - 11.92)

Only 58 subjects were treated with more than one IUI cycle (44 subjects with 2 cycles and 14 with 3 cycles), In this group we found that endometrial pattern remained the same in all cycles in 43 cases (74.1%). There were only 15 cases (25.9%) whose endometrial pattern changed. Subjects with or without triple-layer pattern had the same endocmetrial echoic pattern in all subsequent cycles in 75.0% and 72.7% respectively, p=0.848).

Discussion

A pregnancy rate of 12.1% per IUI cycle in our study was comparable to those reported by others (10.5-15%).[6-10] However, we could not confirm the results of Lavie et al.[5] who claimed that Tom Cat catheter caused total destruction of endometrial pattern in up to 50 % of cases. The percentages of patients who had destruction of endometrial triple layer pattern after IUI were comparable in the Tom Cat and PIVET groups (23.4% and 27.4% respectively). Clinical pregnancy rates per IUI cycle in the 2 groups were also similar (12.9% and 11.4% respectively). Subjects without triple-layer pattern had a slightly higher pregnancy rate than those with triple-layer pattern (13.7% and 10.7% respectively), but this was not statistically significant.

Subjects in this trial had a much higher pregnancy rate per IUI cycle than those who did not participate in the study (12.1% vs 3.2%). This could be due to the fact that noneligible patients were older or had severe male factor infertility. Indeed, Stone et al.[7] reported that pregnancy rate in IUI was dependent on ages of the female partners, number of follicles, and the number of inseminated spermatozoa. In our study, the lowest concentration at which a pregnancy was achieved was 3.6 million spermatozoa/ml. This was comparable to around 4 million spermatozoa/ml reported by others.[6,7,11] Most of the pregnancies occurred in couples with unexplained infertility, which agreed with the study by Stone et al.[7]

Our regression model showed that endometrial thickness was a good predictor of IUI success. A cut-off value of $\geq$7.5 m.m. was consistent with a study by Router et al.,[12] who found that endometrial thickness less than 8 m.m. was associated with a decreased chance of pregnancy. In our model, ages of the female partners and the number of follicles did not stand out as significant predictors. It was possible that this could be due to a small sample size of only 239 cycles as compared to 9,963 cycles in a study by Stone et al.[7] A borderline p value (0.07) associated with ages in our model could become significant if the sample size was larger.

A clinical abortion rate of 27.6% in our study was rather high but still within the ranges of 8% - 35% reported in the literature[10,13,14,15] In the study by Haebe et al.[10] spontaneous pregnancy loss

increased with maternal age from 29.6% in women <25 years old to 52.6% in women >40 years old. Perhaps a rather high mean age of 33 in our study population explained this increase. An ectopic pregnancy rate of 6.9% in our study was higher than those reported by others (2.3-4.3%).[10, 14-16] This could be due to the fact that we included women with pelvic pathology such as pelvic adhesion with unilateral blockade of one tube in our study. There was no case of ovarian hyperstimulation syndrome in our series. A multifetal preganancy rate of 10% compared favourably with a rate of 9.9% reported by Keck et al.,[17] but was much lower than those reported by Chang et al. (19.2%)[16] and Shelden et al. (27%).15 This was not surprising as more than 80% of subjects in this study received mild ovarian stimulation with either clomiphene citrate or clomiphene plus HMG/FSH. In conclusion, we found that PIVET or Tom Cat catheter had no influence on clinical outcomes. The choice of catheters, therefore, depends on its cost and ease of use. In this regard our team prefers Tom Cat to PIVET catheter for insemination.

Table 1. Baseline characteristics of infertile couples

	Tom Cat	**PIVET**
N (couple)	77	86
Age of female partners (years)	33.1 $\pm$ 4.4	32.9 $\pm$ 4.5
Duration of infertility (months)	50.9 $\pm$ 31.3	44.8 $\pm$ 32.2
Infertility status *		
Primary	53 (68.8%)	73 (84.9%)
Secondary	24 (31.2%)	13 (15.1%)
Indication for IUI		
Male factor **	15 (19.5%)	13 (15.1%)
Cervical factor	2 (2.6%)	0
Unexplained	40 (51.9%)	58 (67.5%)
Endometriosis	10 (13.0%)	7 (8.1%)
Others	10 (13.0%)	8 (9.3%)

* P = 0.015

** sperm count <20x10^6 but $\geq$10 x 10^6

Table 2. Baseline characteristics of treated cycles

	Tom Cat 116 (cycles)	**PIVET 123 cycles**
Ovulation induction regimen		
CC 9 (7.8%)	11 (8.9%)	
CC + hMG/FSH	89 (76.7%)	88 (71.6%)
HMG/FSH	18 (15.5%)	24 (19.5%)
Number of follicles with a diameter $\geq$ 14 mm.		
1 follicle	18 (15.5%)	16 (13.0%)
2-3 follicles	55 (47.4%)	71 (57.7%)
$\geq$ 4 follicles	43 (37.1%)	36 (29.3%)

	Tom Cat 116 (cycles)	PIVET 123 cycles
Endometrial pattern		
Triple layer present	60 (51.7%)	62 (50.4%)
Triple layer absent	56 (48.3%)	61 (49.6%)
Endometrial thickness (mm.)	8.79 ± 2.53	9.16 ± 2.49
Number of motile sperm inseminated ($x10^6$)	23.1 ± 16.1	24.8 ± 18.3

Table 3. Immediate endometrial changes after IUI

	Intact	Partial destruction	Complete destruction
Tom Cat	46 (76.6%)	10 (16.7%)	4 (6.7%)
PIVET	45 (72.6%)	7 (11.3%)	10 (16.1%)

Table 4. Procedural difficulties and discomfort

	Tom Cat	PIVET
Difficulty in catheter insertion	19 (16.4%)	21 (17.1%)
Teneculum used	18 (15.5%)	12 (9.8%)
Cervical dilatation needed	2 (1.7%)	2 (1.6%)
Discomfort		
No	82 (70.7%)	90 (73.2%)
Mild	28 (24.1%)	29 (23.6%)
Moderate	4 (3.5%)	3 (2.4%)
Severe	2 (1.7%)	1 (0.8%)

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