

Assisted Reproduction Technology: Comparison of Anesthetic Techniques for Oocyte Retrieval in a Tertiary Health Facility in Ilorin, Nigeria

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Abstract

Background: Transvaginal ultrasound-guided oocyte retrieval (TUGOR) technique is minimally invasive and requires shorter time compared to previous techniques. Yet, it is a potentially stressful and painful procedure and thus requires some form of analgesia with or without sedation. The effects of various anesthetic techniques used for TUGOR on reproductive outcomes remain controversial. **Aims and Objectives:** This study aimed at comparing the efficacy of paracervical block (PCB) and conscious sedation for pain relief and pregnancy outcomes during TUGOR. **Materials and Methods:** This is a cross-sectional comparative study of 137 eligible clients that underwent assisted reproduction program in our facility. All clients were treated with antagonist protocol for controlled ovarian hyperstimulation. The choice of analgesia for TUGOR was influenced by clients' and/or clinicians' preference. PCB and conscious sedation were administered for TUGOR in 66 and 71 clients, respectively. Pain was assessed using a 10-cm Visual Analog Scale (VAS), while clients' overall satisfaction was rated using Likert scoring system. **Results:** There was no statistically significant difference in the clinical pregnancy, miscarriage, and live birth rates between the two groups. The mean VAS 10-point scores at 1, 6, and 24 h postretrieval and on the day of embryo transfer were significantly higher for paracervical group. The mean Likert score for conscious sedation group was significantly higher than that of paracervical group. **Conclusion:** Conscious sedation is superior to PCB as anesthetic/analgesic agent for pain relief and clients' satisfaction for TUGOR. However, a multimodal approach to anesthesia/analgesia for TUGOR is suggested to further improve overall clients' satisfaction.

Keywords: Assisted reproduction technology, conscious sedation, oocyte retrieval, paracervical block

INTRODUCTION

Assisted reproduction technology is the highest breakthrough in the medical treatment of infertility in the whole world.^[1] It offers a chance at parenthood to couples, who until recently would have had no hope of having a "biologically related" child.^[1] Anesthesia during assisted reproductive technique is generally required during oocyte retrieval, which forms one of the fundamental steps during the entire procedure.^[2]

In the 1980s, there existed a drastic change from the use of laparoscope to transvaginal ultrasound-guided oocyte retrieval (TUGOR). Although this technique of TUGOR is less invasive and associated with higher pregnancy rates, it

still forms one of the most stressful and painful components of the entire assisted reproductive treatment.^[2,3]

Pain experienced during oocyte retrieval is identical to intensive menstrual pain caused by the puncture of the vaginal skin and ovarian capsule by the aspirating needle as well as manipulation within the ovary during the entire procedure,^[4] hence the need for the anesthetist to provide adequate pain relief to immobilize

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the patient and eliminate the danger of piercing any vessel during the process of oocyte retrieval. The ideal pain relief during oocyte retrieval should be effective and safe, easy to administer and monitor, short acting, and readily reversible with a few side effects.^[2,5]

Various anesthetic modalities and analgesic regimens have been tested in different studies, but no definite conclusion so far has been made regarding the preferred technique for anesthesia and pain relief for these procedures.^[2-5] Many anesthetic drugs have been detected in the oocyte follicular fluid and may potentially interfere with oocyte fertilization and implantation. Therefore, this study aimed at comparing the efficacy of paracervical block (PCB) and conscious sedation for pain relief during TUGOR and pregnancy outcomes at the Assisted Reproductive Technology unit of University of Ilorin Teaching Hospital, Ilorin, Nigeria.

MATERIALS AND METHODS

This is a cross-sectional comparative study of 137 eligible patients that underwent assisted conception program (*in vitro* fertilization [IVF]/intracytoplasmic sperm injection [ICSI]) at the Assisted Reproductive Technology unit of University of Ilorin Teaching Hospital, Ilorin, between January 1, 2013, and December 31, 2017. Patients were recruited using convenience sampling method. Investigation results, i.e., transvaginal/saline infusion sonography, hormonal profile, and/or laparoendoscopic findings were noted and necessary interventions, were instituted prior to recruitment. Information on bio-social variables, gender-factor infertility, types of stimulation protocols, duration of follicle-stimulating hormone (FSH) used/dosage, endometrial thickness at embryo transfer (ET), types of anesthesia/analgesia used for oocyte retrieval, Visual Analog scale (VAS) at 1, 6, 24 h, and on the day of ET, Likert score, and pregnancy outcomes was properly documented.

Clients' were counseled on the available methods of anesthesia/analgesia for TUGOR and the choice of analgesia was influenced by clients' and or clinicians' preference. Informed consent was obtained from each patient and protection of personal data and confidentiality were prioritized. Inclusion criteria were normoresponders (age <40 years), clients' with normogonadotrophic normogonadism, first attempt at TUGOR, and those consented to participate in the study, while the exclusion criteria included clients' who are allergic to anesthetic agents, with cardiopulmonary compromise, thyroid dysfunction, whose TUGOR exceeded >30 min, and those required other forms of analgesia for pain relief during TUGOR.

Seminal fluid analysis was conducted for male partners. The criteria for men were a sperm count of at least 20 million cells per milliliter of semen and progressive sperm motility of 50% or greater. Male partners with semen count and/or motility less than the cutoff values were offered ICSI unless the sperm count was zero after centrifugation; therefore, donor sperm was used for IVF.

All clients had a body mass index (calculated as weight in kilograms divided by the square of height in meters) ranging between 18 and 30 with a mean of $24 \pm 4 \text{ kg/m}^2$. All had antagonist protocol for controlled ovarian hyperstimulation. Their infertility evaluation results were normal. Furthermore, all had oral contraceptive pills for menstrual cycle synchronization and precervical assessment (trial/dummy transfer) on day 2/3 of menses prior to commencement of stimulation.

Stimulation protocol

Clients were commenced on 150 IU (2 vials) of recombinant FSH Gonal F (Gonal F®; Merck Serono, Germany) and 75 IU (1 vial) highly purified FSH (Folliculin®; Barratt Pharmaceutical, India) on day 3 of menstrual cycle for 11–14 days. Transvaginal ultrasonographic scan was also done at interval from day 5/6 of stimulation to determine the numbers, size of follicles, and endometrial thickness. Subcutaneous 2.5 mg daily gonadotropin-releasing hormone antagonist (Cetrotide®; Merck Serono, Germany) was administered whenever the follicles have grown to 14 mm in size usually around day 6/7 of stimulation and was continued till the day of trigger to prevent premature luteinizing hormone surge. Eighty-three micrograms (2000 IU) of recombinant human chorionic gonadotropin (hCG: Ovitrelle®; Merck Serono, Germany) and 0.25 mg of buserelin (Suprecur®; Aventis Pharma, West Malling, UK) were administered subcutaneously for trigger whenever two or more follicles have grown to 18 mm or more and oocyte retrieval was carried out at 35.5 h thereafter.

Anesthesia/analgesia for oocyte retrieval

Two methods of anesthesia/analgesia were offered namely conscious sedation and PCB. All clients were counseled to fast overnight and 1 mg of atropine was administered intravenously as preanesthetic medication. Conscious sedation was achieved with 50 mg of pethidine and 2.5 mg of midazolam administered intravenously. Sedation was adjusted with 50 mg increments of pethidine and/or 2.5 mg of midazolam based on clinician perception of client's response to pain in the course of TUGOR. While PCB was carried out with the aid of specially designed needle, 10 ml of 1% lidocaine was injected into each lateral fornix between 3 and 4 o'clock and 8 and 9 o'clock positions after which TUGOR was commenced within 5 min of administration. Sixty-six clients had PCB, while 71 had conscious sedation.

Oocyte retrieval, insemination, embryo transfer, and luteal phase

Oocyte retrieval was done at 35.5 h of hCG injection by TUGOR with the aid of 17G needle (Cooper Surgical Fertility Companies, Origio, Denmark), and the aspirate in a test tube was transferred immediately to the laboratory for oocyte screening and pickup. Mature oocytes were inseminated with prepared sperm after 6 h of oocyte pickup and incubated. ICSI was done in cases of severe male-factor infertility. Best cleavage embryos were transferred on day 5 of oocyte retrieval usually at the blastocyst stage under transabdominal ultrasound guidance and the transfer catheters were checked to ensure

all the embryos were transferred. The number of embryos transferred was individualized, two or three in most cases. The luteal-phase support was conducted with progesterone (800 mg twice daily [Cyclogest pessaries®; Cox, Barnstaple, UK] and intramuscular 100 mg twice weekly [Gestone®; Ferring Pharmaceutical, Mumbai, India]). Serum pregnancy test was carried out 2 weeks after ET and subsequently transvaginal ultrasound at 6th week for detection of gestational sac and/or viability of the fetus.

Visual Analog Scale and Likert score

Following TUGOR, clients had self-administered questionnaire administered to assess their perception of pain using VAS scoring system^[6] on a scale of 0–10 cm at 1, 6, and 24 h and on the day of ET, and their responses were properly documented. VAS scoring was graded as follows: 0 – no pain, 1–3 – mild pain, 4–6 – moderate pain, and 7–10 – severe pain. Furthermore, overall clients' satisfaction was assessed through Likert scoring system^[7] on a scale of 1–5 categorized as 1 – poor, 2 – fair, 3 – satisfactory, 4 – very good, and 5 – excellent.

Statistical analysis

Statistical analysis was done using Epi-info version 7.1.3.0 (Centers for Disease Control and Prevention, Atlanta, USA). Categorical data were expressed as numbers and percentages, while numerical data were expressed as mean and standard deviation. Associations of categorical variables were tested using Chi-square test, while statistical significance was set at $P \leq 0.05$. Results were presented in tables.

RESULTS

Table 1 characterizes the women undergoing the IVF-ET cycles and their spouses. The clients' mean age, duration of infertility, FSH ampoule used, and endometrial thickness were 33.15 ± 4.2 versus 32.78 ± 3.4 , 4.49 ± 2.9 versus 4.64 ± 2.4 , 32.57 ± 5.1 versus 32.68 ± 4.8 , and 8.59 ± 2.0 versus 8.80 ± 2.1 for conscious sedation and paracervical group, respectively. There were no statistically significant differences in age, duration of infertility and mean FSH ampoule used, duration of FSH, and endometrial thickness between the two groups. The groups were subdivided by the type of anesthesia used for oocyte retrieval. There was no statistically significant difference in the mean number of oocytes retrieved, mean number of oocytes fertilized, mean number of embryo transferred, and cycle cancellation rates between the two groups [Table 2].

There was no difference in the clinical pregnancy rate and live birth rate between the groups, although the miscarriage rate for the PCB group is higher (25%) than that of the conscious sedation group (11%), but it was not statistically significant. When comparing patients' perception of pain using the VAS score and Likert scale between the groups [Table 3], the mean VAS score at 1 h post-oocyte retrieval for the conscious sedation group was significantly lower (4.94 ± 1.74) than the PCB group (7.08 ± 1.07) ($P < 0.05$). In addition, the mean VAS score

Table 1: Sociodemographic characteristics

Variables	Types of anesthesia	
	C/sedation (n=71)	P/block (n=66)
Mean age	33.15±4.2	32.78±3.4
Mean age (spouse)	38.70±4.5	38.67±4.4
Mean duration of infertility	4.49±2.9	4.64±2.4
Mean duration of FSH	13.67±1.8	14.33±1.9
Mean FSH ampoule used	32.57±5.1	32.68±4.8
Mean ET	8.59±2.0	8.80±2.1

FSH: Follicle-stimulating hormone, ET: Embryo transfer

Table 2: Types of anesthesia used and *in vitro* fertilization outcomes

Outcome measures	Type of anesthesia		
	C/sedation (n=71)	P/block (n=66)	P
Mean number of oocytes retrieved	11.36±5.54	9.97±4.3	0.6803
Mean number of oocytes fertilized	7.44±3.5	6.11±3.2	0.5284
Mean number of embryos transferred	4.72±2.5	3.97±2.3	0.3001
Cycle cancellation rate	5 (7.04)	7 (10.61)	0.7491
Pregnancy rate	34 (47.89)	24 (41.38)	0.3657
Miscarriage rate	4 (11.76)	6 (25.00)	0.1036
Live birth rate	30 (88.24)	18 (75.00)	0.1936

Table 3: Visual Analog Scale and Likert score of the types of anesthesia

Mean score	Types of anesthesia used		
	C/sedation	P/block	P
VAS 1 h	4.94±1.74	7.08±1.67	0.000
VAS 6 h	2.54±1.22	4.57±1.41	0.000
VAS 24 h	1.34±0.89	2.76±1.4	0.000
VAS ET	0.48±0.61	0.96±0.93	0.000
Likert	3.8±1.09	2.39±0.77	0.000

VAS: Visual Analog Scale, ET: Embryo transfer

at 6 and 24 h post-oocyte retrieval and VAS score on the day of ET were significantly higher for PCB group (4.57 ± 1.41 , 2.76 ± 1.4 , and 0.96 ± 0.93 , respectively) than that of the conscious sedation group (2.54 ± 1.22 , 1.34 ± 0.89 , and 0.48 ± 0.61 , respectively, $P = 0.000$). The mean Likert score for the conscious sedation group is significantly higher (3.8 ± 1.09) than the PCB group (2.39 ± 0.77 , $P = 0.000$).

DISCUSSION

Assisted reproduction technology is increasingly being practiced in different parts of the world.^[8]

Anesthesiologists are faced with peculiar challenge to determine anesthetic technique for oocyte retrieval that allays patient anxiety with adequate pain relief and yet avoiding any

deleterious effect on the outcome of successful pregnancy.^[2-5] This study compared the efficacy of PCB and conscious sedation for pain relief during TUGOR and pregnancy outcomes. In this study, preference for conscious sedation by clinician and clients is slightly higher than that of PCB (71 vs. 66). This may be related to the fact that conscious sedation allows patient cooperation to be maintained and the procedure to be conveniently performed in the outpatient setting devoid of intensive monitoring. This is inconsonance with the reports from the UK and the USA where 84% and 95% of IVF clinics, respectively, have adopted conscious sedation for oocyte retrieval.^[2]

Our findings revealed no significant association in the mean number of oocyte retrieved, oocyte fertilized, embryo transferred, cycle cancellation rate, clinical pregnancy, miscarriage rate, and live birth rate. However, there exist controversies regarding the effects of anesthetic agents administered during TUGOR on fertilization, embryonic development, and conception rate.^[9-11] Anesthetic drugs have been detected in follicular fluid, and a longer period of exposure in the general anesthesia group may have enhanced the deleterious effects of these drugs on the oocyte and/or follicular structures, thereby interfering with the reproductive process.^[12,13] Halogenated agents have been associated with reduced reproductive success in clinical practice and must therefore be used with caution.^[9]

Opioids and benzodiazepines, most especially midazolam, do not seem to affect reproductive success.^[14] Minimal doses of midazolam and pethidine were administered in this study.

Exposure to high concentrations of different local anesthetic agents adversely affects fertilization and embryonic development.^[11] However, given that much lower concentrations of lignocaine were administered in this study and that oocytes were washed after retrieval, the clinical effects of using local anesthetics should be limited and probably no adverse effects should occur.^[15] This might account for insignificant differences on reproductive outcomes between the groups in our series. Furthermore, limited sample size could be contributory.

The mean VAS scores at 1, 6, 24 h, and on the day of ET for conscious sedation group of 4.94 ± 1.74 , 2.54 ± 1.22 , 1.34 ± 0.89 , and 0.48 ± 0.61 were comparable to 2.83 ± 1.67 , 0.78 ± 1.04 , 0.39 ± 1.09 , and 0.14 ± 0.58 , respectively, obtained in a previous study conducted in Tamil Nadu, India.^[16] In addition, the mean VAS scores for paracervical group were significantly higher than that of conscious sedation group.^[17] This is in consonance with findings from a previous study which showed that patients who received only PCB during oocyte collection experienced 2.5 times higher levels of vaginal and abdominal pain than those who received conscious sedation and/or PCB. More so, conscious sedation (opioids in combination with benzodiazepines) was reported to be a safe, well-tolerated, and cost-effective method of anesthesia for oocyte retrieval and does not require highly specialized equipment for monitoring.^[14]

On the contrary, Kwan *et al.* did not find one particular modality of pain relief better than other and overall satisfaction level was high among women irrespective of the pain relief method used during TUGOR and that the optimal method could be decided depending on the woman and clinician's preferences, with resource availability being another important factor.^[18] In this study, overall clients' satisfaction was assessed using Likert scoring system. The mean Likert score for the conscious sedation group was significantly higher (3.8 ± 1.09) than that of the PCB group (2.39 ± 0.77 , $P = 0.000$). This is comparable to Likert score of 3.65 ± 0.82 obtained in a previous study.^[16]

CONCLUSION

Conscious sedation is the most common method of pain relief used during TUGOR and was found to be superior to PCB in our series with regard to pain relief and overall clients' satisfaction. We suggest the need for a multimodal approach to anesthesia/analgesia during TUGOR to further enhance clients' satisfaction. Furthermore, randomized prospective studies with larger sample sizes are recommended to validate our findings.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Omokanye LO, Olatinwo AW, Durowade KA, Biliaminu SA, Salaudeen AG, Panti AA. Pregnancy outcome following assisted reproduction technologies for infertile women at a public health institution in Nigeria. *Trop J Health Sci* 2015;22:1-6.
2. Jain D, Kohli A, Gupta L, Bhadoria P, Anand R. Anaesthesia for *in vitro* fertilisation. *Indian J Anaesth* 2009;53:408-13.
3. Trout SW, Vallerand AH, Kemmann E. Conscious sedation for *in vitro* fertilization used in paracervical block during oocyte retrieval. *J Assist Reprod Genet* 2003;20:8-12.
4. Stener-Victorin E. The pain-relieving effect of electro-acupuncture and conventional medical analgesic methods during oocyte retrieval: A systematic review of randomized controlled trials. *Hum Reprod* 2005;20:339-49.
5. Sator-Katzenschlager SM, Wölfler MM, Kozek-Langenecker SA, Sator K, Sator PG, Li B, *et al.* Auricular electro-acupuncture as an additional perioperative analgesic method during oocyte aspiration in IVF treatment. *Hum Reprod* 2006;21:2114-20.
6. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. *J Clin Nurs* 2005;14:798-804.
7. Fiebai PO, Ogunmokin AA, Ajayi RA. Experience with conscious sedation for oocyte retrieval in Nigeria. *Afr J Reprod Health* 2008;12:30-4.
8. Omokanye LO, Olatinwo AW, Saadu LO, Biliaminu SA, Durowade KA, Panti AA. Assisted reproduction technology: Experience from a public tertiary institution in North-central, Nigeria. *Afr J Infertil Assist Concept* 2016;1:23-6.
9. Wilhelm W, Hammadeh ME, White PF, Georg T, Fleiser R, Biedler A. General anesthesia versus monitored anesthesia care with remifentanyl for assisted reproductive technologies: Effect on pregnancy rate. *J Clin Anesth* 2002;14:1-5.
10. Gonen O, Shulman A, Ghetler Y, Shapiro A, Judeiken R, Beyth Y, *et al.* The impact of different types of anesthesia on *in vitro* fertilization-embryo transfer treatment outcome. *J Assist Reprod Genet* 1995;12:678-82.
11. Casati A, Valentini G, Zangrillo A, Senatore R, Mello A, Airaghi B, *et al.* Anaesthesia for ultrasound guided oocyte retrieval:

- Midazolam/remifentanyl versus propofol/fentanyl regimens. *Eur J Anaesthesiol* 1999;16:773-8.
12. Imoedemhe DA, Sigue AB, Abdul Ghani I, Abozeid MA, Abdel Halim MS. An evaluation of the effect of the anesthetic agent propofol (Diprivan) on the outcome of human *in vitro* fertilization. *J Assist Reprod Genet* 1992;9:488-91.
 13. Boyers SP, Lavy G, Russell JB, DeCherney AH. A paired analysis of *in vitro* fertilization and cleavage rates of first- versus last-recovered preovulatory human oocytes exposed to varying intervals of 100% CO₂ pneumoperitoneum and general anesthesia. *Fertil Steril* 1987;48:969-74.
 14. Trout SW, Vallerand AH, Kemmann E. Conscious sedation for *in vitro* fertilization. *Fertil Steril* 1998;69:799-808.
 15. Wikland M, Evers H, Jakobsson AH, Sandqvist U, Sjöblom P. The concentration of lidocaine in follicular fluid when used for paracervical block in a human IVF-ET programme. *Hum Reprod* 1990;5:920-3.
 16. Singhal H, Premkumar PS, Chandy A, Kunjummen AT, Kamath MS. Patient experience with conscious sedation as a method of pain relief for transvaginal oocyte retrieval: A cross sectional study. *J Hum Reprod Sci* 2017;10:119-23.
 17. Garg R, Dali J. Assisted reproductive technology and anesthetic considerations: Review of literature. *Internet J Anesthesiol* 2007;18:1-8.
 18. Kwan I, Bhattacharya S, Knox F, McNeil A. Pain relief for women undergoing oocyte retrieval for assisted reproduction. *Cochrane Database Syst Rev* 2013;1:CD004829.