Original Article

Conscious sedation for oocyte retrieval: Experience at a tertiary health facility in North-Central, Nigeria

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ABSTRACT

Background: A variety of anesthetic techniques have been used to make transvaginal oocyte retrieval (TVOR) safe and efficient. The optimal anesthetic technique during TVOR should provide safe, effective analgesia, few side effects, a short recovery time, and be nontoxic to the oocytes that are being retrieved. The concept of conscious sedation is widely accepted for the short-term management of pain.

Objective: This study assessed patient's perception of pain using conscious sedation and in-vitro fertilization (IVF) outcomes.

Materials and Methods: A cross sectional study of 71 eligible patients that underwent assisted reproduction program in our facility. All clients were treated with antagonist protocol for controlled ovarian hyperstimulation. Self-administered questionnaires were used as the research instrument. Pain was assessed using a 10 cm visual analogue scale (VAS), while client's overall satisfaction was rated using Likert scoring system.

Results: Client aged 33.2 ± 4.2 years. Most of them had primary infertility with mean duration of 4.5 ± 2.9 years. Unexplained infertility was the commonest cause of infertility. The pregnancy rate per embryo transfer was 47.9%, miscarriage rate was 5.6%, while the live birth rate was 42.3%. The mean VAS scores at 1 h, 6 h, 24 h and at embryo transfer were 4.9 ± 1.7, 2.5 ± 1.2, 1.3 ± 0.9, and 0.5 ± 0.6, while the Likert score was 3.8 ± 1.1.

Conclusion: Conscious sedation with Midazolam and Pethidine is a safe, effective, and acceptable method of analgesia/anesthesia for TVOR. However randomized prospective studies with larger sample sizes are recommended.

Key words: Conscious sedation; Nigeria; oocyte retrieval; tertiary health facility.

Introduction

Oocyte retrieval is one of the fundamental steps in in-vitro fertilization/embryo transfer (IVF/ET) treatment. It was previously done through laparoscopy but is now being done less invasively through the vagina with the aid of an ultrasound scan.[1,2] TVOR may be the most painful procedure performed during IVF/ET treatment.[3]

A variety of anesthetic techniques have been used to make TVOR safe and efficient.The optimal anesthetic technique

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during TVOR should provide safe, effective analgesia, few side effects, a short recovery time, and be nontoxic to the oocytes that are being retrieved.[3,4]

Types of pain relief used for TVOR include conscious sedation, local, epidural, spinal and general anaesthesia. General anesthetic agents traverse easily into follicular fluid and may have detrimental effects on cleavage rates of embryos and pregnancy rates, and as such are not popular in IVF.[2] The concept of conscious sedation is widely accepted for the short-term management of pain, defined as a technique in which the use of a drug or drugs produces a state of depression of the central nervous system enabling treatment to be carried out, but during which verbal contact with the patient is maintained throughout the period of sedation.[5] It is the most common methodof pain relief used for TVOR by IVF units worldwide.[2]

Studies suggest higher pregnancy and delivery rates if conscious sedation or epidural anesthesia is used instead of general anesthesia.[2,5] We present our experience with conscious sedation for TVOR on clients' pain perceptions and IVF outcomes

Materials and Methods

This is a cross-sectional study of 71 eligible clients' that underwent assisted conception program (IVF/ICSI) at the assisted reproductive technology (ART) unit of university of Ilorin teaching hospital, Ilorin between 1st January 2013 and 31st December 2017. Investigation results, i.e. transvaginal/saline infusion sonography, hormonal profile, and/or laparo-endoscopic 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 FSH used/dosage, endometrial thickness at embryo transfer, types of anaesthesia/analgesia used for oocyte retrieval, visual analogue scale (VAS) at 1 h, 6 h, 24 h and on the day of embryo transfer, Likert score and pregnancy outcomes were properly documented.

Clients' were counseled on conscious sedation for TVOR. Informed consent was obtained from each patient and protection of personal data and confidentiality were prioritized. Inclusion criteria were normo-responders (age < 40 years), clients' with normogonadotrophic normogonadism, first attempt at TVOR and those consented to participate in the study while the exclusion criteria included clients' who were allergic to general anesthetic agents, with cardiopulmonary compromise, thyroid dysfunction, whose TVOR exceeded more than one hour and those that required other forms of analgesia for pain relief during TVOR.

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 cut-off values were offered intracytoplasmic sperm injection (ICSI) unless the sperm count was zero after centrifugation in which case donor sperm was used for *in vitro* fertilization.

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

Stimulation protocol

Clients were commenced on 150 IU (2vials) of recombinant FSH Gonal F (Gonal F®; Merckserono, Germany) and 75 IU (1 vial) highly purified FSH (Folliculin®; Barrat pharmaceutical, India) on day 3 of menstrual cycle for 11–14 days. Transvaginal ultrasonographic scan was also done at intervals from day 5/6 of stimulation to determine the numbers, size of follicles, and endometrial thickness. Subcutaneous 2.5 mg daily GnRH antagonist (Cetrotide®; merckserono, Germany) was administered whenever the follicles have grown to 14 mm size usually around day 6/7 of stimulation and was continued till the day of trigger to prevent premature LH surge. In total 83 μg (83μg [2000IU]) of recombinant human chorionic gonadotrophin (hCG: Ovitrelle; merckserono, Germany) and 0.25mg of buserelin (Supricure®; Aventis Pharm, West Malling, UK) were administered subcutaneously for trigger whenever 2 or more follicles have grown to 18mm or more and oocyte retrieval was carried out at 35.5 h thereafter.

Anaesthesia/analgesia for oocyte retrieval

All clients were counseled to fast overnight and 1 mg of Atropine was administered intravenously as pre-anaesthetic 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 TVOR to a maximum dose of 200 mg and 10 mg for Pethidine and Midazolam respectively over an hour period.

Oocyte retrieval, insemination, embryo transfer and luteal phase

TVOR was done at 35.5 h of hCG injection with the aid of 17G needle (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 six (6) hours 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 trans-abdominal ultrasound guidance and the transfer catheters were checked to ensure all the embryos were transferred. The number of embryos transferred was individualized, 2 or 3 in most cases. The luteal phase support was conducted with progesterone (800 mg twice daily [cyclogest pessaries®; Cox, Brarnstaple, UK] and Intramuscular 100 mg twice weekly [Gestone®;Ferring, pharmaceutical, Mumbai, India]). Serum pregnancy test was carried out two weeks after embryo transfer and subsequently transvaginal ultrasound scan at 6th weeks for detection of gestational sac and/or viability of the fetus.

Visual analog scale and Likert score

Following TVOR, clients had self-administered questionnaires administered to assess their perception of pain using VAS scoring system[6] on a scale of (0-10cm) at 1 h, 6 h, 24 h, and on the day of embryo transfer respectively and their responses were properly documented. VAS scoring was graded as 0- no pain, 1-3 – mild pain, 4-6 – moderate pain and 7-10 – severe pain. Also overall clients' satisfactions were 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 (Centres for Disease Control and Prevention-CDC, 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 shows the characteristics of the women undergoing IVF-ET and their spouses. The mean age of the women and their spouses were 33.2 ± 4.2 years and 38.7 ± 4.5 years respectively. The mean duration of infertility was 4.5 ± 2.9 years. Most (52.9%) of the couple had primary infertility while unexplained infertility was the commonest cause of infertility (39.4%).

The mean duration of FSH, Mean FSH ampoule used and endometrial thickness were 13.7 ± 1.8, 32.6 ± 5.2 and 8.6 ± 2.0 respectively.The mean number of oocyte retrieved and mean number of oocyte fertilized were 11.4 ± 5.5 and 7.3 ± 3.5 respectively [Table 2]. The clinical pregnancy rate per embryo transferred was 47.9%, miscarriage rate was 5.6%, while the live birth rate was 42.2% [Table 3].

Table 4 shows clients' perception of pain and satisfaction. The mean VAS scores at 1hour, 6 h, 24 h and at embryo transfer were 4.9 ± 1.7, 2.45 ± 1.2, 1.3 ± 0.9 and 0.5 ± 0.6. The mean Likert score was 3.8 ± 1.1

Table 1: Socio-demographic characteristics

Variables	Frequency (*n*=71)	Percentage
Age		
25-29	13	18.3
30-34	33	46.5
35-39	18	25.4
40-44	5	7.0
45-49	2	2.8
Mean= 33.2±4.2 years	Range=27-46	
Age (Spouse)		
30-34	11	15.5
35-39	30	42.3
40-44	19	26.8
45-49	10	14.1
50-54	1	1.4
Mean=38.7±4.5 years	Range=32-50	
Parity		
0	41	57.8
1	18	25.4
2	7	9.9
3	4	5.6
4	1	1.4
Duration of infertility		
1-5	50	70.4
6-10	19	26.8
11-15	1	1.4
16--20	1	1.4
Mean= 4.5±2.9 years	Range=1-18	
Type of infertility		
Primary	42	59.2
Secondary	29	40.8
Cause of infertility		
Male factor	11	15.5
Female factor	18	25.4
Male/female factor	14 19.7	
Unexplained	28	39.4

Table 2: Stimulation cycle characteristics of the clients

Variables	Mean
Duration of FSH (days)	13.7±1.8
FSH ampoule used	32.6±5.1
Endometrial thickness	8.6±2.0
No. of oocyte retrieved	11.4±5.5
No. of oocyte fertilized	7.43±3.51

Table 3: Clinical outcomes

Outcome	Frequency (n=71)	Percentage
Clinical Pregnancy	34	47.9
Miscarriage rate	4	5.6
Live birth rate	30	42.3

Table 4: Clients' perception of pain and satisfaction

VAS score	Mean
VAS at 1 h	4.9±1.7
VAS at 6 h	2.5±1.2
VAS at 24 h	1.3±0.9
VAS at ET	0.5±0.6
Likert	3.8±1.1

Discussion

In this study, the mean age of the clients and the mean number of oocytes retrieved were 33.2 ± 4.2 and 11.4 ± 5.5. This is in consonance with the mean age of 33.7 ± 4.9 and mean number of oocytes retrieved of 13.31 ± 9.04 obtained in a previous study in Nigeria.[2]Also, unexplained infertility was the commonest cause of infertility in our series. On the contrary combined male and female factors predominate in an earlier study at Tamil, India.[6] However, varied geographical locations of both studies could be responsible for the difference.

The clinical pregnancy rate of 47.9% is comparable to 40.7% recorded in a similar study in India.[6] However, there are controversies regarding the effects of anaesthetic agents administered during TVOR onfertilization, embryonic development and conception rate.[7-9] Some anaesthetic drugs mostespecially halogenated agents have been found in the follicular fluid and these could have deleteriouseffects on the oocyte and/or follicular structures, thereby interfering with the Reproductive process,[7,10,11] conversely, conscious sedation (opiods in combination with Benzodiazepines) which wasemployed in our series was reported to be a safe, well tolerated and cost effective method of anaesthesia for oocyteretrieval devoid ofinterference with reproductive process.[12-15] These couldbe responsible for the clinical pregnancy rate of 47.9% reported in this study. However, no single method of anaesthesia/analgesia for TVOR appeared superior for pregnancy rates and pain relief asobserved in a randomized controlled trial.[5] Thus the need for a multimodal approach to anaesthesia/analgesia for oocyte retrieval.

The mean VAS scores at 1 h, 6 h, 24 h and at embryo transfer of 4.9 ± 1.7, 2.5 ± 1.2,1.3 ± 0.9, and 0.5 ± 0.6 were comparable with 2.8 ± 1.7, 0.78 ± 1.04, 0.39 ± 1.09, and 0.14 ± 0.58, respectively obtained in a similar study at Tamil Nadu India.[6]Similarly, Fiebai *et al*. inNigeria reported a one-point post TVORlow mean VAS score of 3.89 ± 1.98 following use ofconscious sedation (Midazolam and Pethidine) with most clients expressing satisfaction and 94% indicating a preference for it in any subsequent procedure.[2]

In this study over all clients' satisfaction was assessed using Likert scoring system. The mean Likert score of (3.8 ± 1.1) ranging between satisfactory and very good is in keeping with findings from a similar study in Tamil Nadu, India that reported a meanlikert score of (3.6 ± 0.8) with high clients' satisfaction and acceptance of Midazolam and Pethidine combination for TVOR.[6]

Conclusion

Conscious sedation with Midazolam and Pethidine is a safe, effective and acceptableanalgesia/anaesthetic option for transvaginal oocyte retrieval. Randomized controlled trials on variedcombination of medications for conscious sedation and by extension a multimodal approach ofanalgesia/anaesthesia for transvaginal oocyte retrieval is recommended to further improve on clientssatisfaction.

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Conflicts of interest
There are no conflicts of interest.

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