Anaesthetic Issues in In-vitro Fertilisation

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Abstract

Background: Ultrasonically guided transvaginal oocyte retrieval is a relatively short procedure that is performed on an outpatient basis. Any anaesthetic technique may interfere with certain aspects of human oocyte fertilisation or embryo implantation. The optimal anaesthetic technique should allow good surgical anaesthesia with minimal side effects, a short recovery time and high rate of successful pregnancy.

Method: We present our experience and evaluation of the various techniques studied to carry out this technique.

Results and Conclusion: Amongst the various available total intravenous anaesthesia options, propofol/ remifentanyl or fentanyl technique of sedation appears to be safe and effective.

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Key Words : Anaesthesia; In vitro fertilisation; Total intravenous anaesthesia

Introduction

The first successful live birth following in-vitro fertilisation (IVF) of a human oocyte was performed in 1978 by Steptoe and Edwards. Since then, the transvaginal ultrasound guided oocyte retrieval (TUGOR), a relatively invasive procedure generally performed under light anaesthesia with local anaesthetics, opioids, hypnotics or benzodiazepines has increased exponentially. In recent years several opioids, such as, pethidine, morphine, fentanyl and remifentanyl, have been used as a part of conscious sedation and monitored anaesthesia care [1,2]. Technological advances have improved the success of the technique with a more than 25-30% chance of pregnancy after a cycle of hormonal stimulation [2]. More and more patients, however, are requesting sedation or anaesthesia for ultrasound-guided oocyte retrieval.

Materials and Methods

A total of one thousand four hundred ninety six patients scheduled to undergo invitro fertilisation formed the study sample in this retrospective analysis (Jan 2003 - Oct 2006). All the patients were unpremedicated patients, having American Society of Anaesthesiologists (ASA) class I or II physical status. The demographic profile of patients in the study is shown in Table 1.

The inclusion criteria were first IVF attempt, age less than forty two and normal responders. The exclusion criteria were age above forty two, history of psychiatric illness and secondary infertility due to correctable surgical cause.

All patients were day case surgeries and the techniques

used are given in Table 2. The induction agents used were either thiopentone (n=404), propofol (n=806), midazolam (n=190) or ketamine (n=96). The conventional dosages were used and loss of eyelash reflex was taken as the end point.

After induction, the face mask (FM) group was managed with oxygen and volatile inhalational agent (isoflurane). In the endotracheal tube (ETT) and laryngeal mask airway (LMA) groups after induction, placement of the tube was facilitated using succinylcholine as muscle relaxant and anaesthesia was maintained on inhalational agents (isoflurane) and oxygen. The endotracheal group was allowed spontaneous ventilation and no non depolarizing muscle relaxants were used. The total intravenous anaesthesia (TIVA) group (n=670) were given maintenance dose of propofol (1%) by a continuous infusion syringe pump @ 2-4 mg/ kg weight.

Analgesia was provided with opioids using pethidine 0.4-0.5 mg/kg (n=384), morphine 0.08-0.1 mg/kg (n=608), fentanyl 0.5-1.0 µg/ kg (n=486) and pentazocine 0.2-0.3 mg (n=18). All cases were administered the analgesic only as a single dose and post operative analgesia was provided if required either by intramuscular injection of diclofenac 50-75 mg or oral paracetamol or ibuprofen or both.

The monitoring consisted of three lead electrocardiograph, heart rate (HR), end tidal carbon dioxide (ETCO₂), pulse oximetry (SpO₂), respiratory rate (RR) and noninvasive blood pressure measurement. The procedure lasted an average of 18-28 minutes. Post procedure all cases were monitored for 45 to 60 minutes before being sent to ward.

Results

The age of patients varied between 23 to 42 years. The age and weight was comparable in all the groups as shown in

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Table 1. The causes of infertility were tuboperitoneal in majority (68%), while the rest were male related causes, anovulation, unexplained and mixed aetiologies. The various therapies included intracytoplasmic sperm injection (ICSI), embryo reduction, testicular sperm aspiration and cyst aspiration. These various therapeutic interventions were carried out under either inhalational anaesthesia or total intravenous anaesthesia as shown in Table 2.

Sedation was assessed clinically and the aim was to achieve a state in which the patient slept but easily woken up. In all groups when the sedation was deep, with respiratory rate of less than eight breaths per minute, oxygen saturation less than 94% and end tidal carbon dioxide concentration higher than 50 mmHg. Respiration was supported with manual ventilation/ oxygenation/ stopping of the infusion. Similarly when sedation was light, respiratory rate was higher or if the blood pressure and heart rate increased by 20% above the basal levels, the anaesthesia was managed by either increasing the concentration of the inhalational agents or by increasing the intravenous drug delivery for optimal response.

There were no significant differences in MAP, HR, EtCO₂, and saturation levels in various groups throughout the procedure. There were clinically insignificant fluctuations in SpO₂ and ETCO₂ values through out the procedure. Side effects in the form of nausea, vomiting, dysphagia, nystagmus, muscular rigidity and headache were assessed post operatively (Table 3). The three groups of FM, ETT and LMA were taken as inhalational anaesthesia and compared with TIVA. There were fewer incidences of postoperative nausea vomiting, dysphagia and sore throat, headache, shivering in TIVA group as compared to other groups, adding to patient satisfaction. However, incidence of pruritus, nystagmus and muscle rigidity was higher, though transient in nature and did not adversely affect patient recovery.

Post operative nausea and vomiting (PONV) is a common and is related to peak plasma level of oestradiol and patient's previous experience of anaesthesia. Higher incidence of PONV was observed following inhalational anaesthesia for IVF procedures as compared to TIVA. The anti emetic property of propofol explains the reduced incidence of associated post operative nausea and vomiting[3].

Table 1
Demographic characteristics

Group	Mean	Total number
Age: (years)		
Face Mask	28.27± 5.1	315
ETT	27.90± 6.4	405
LMA	28.67± 6.8	106
TIVA	27.68± 5.7	670
p = 0.27 (NS)		
Weight : (Kgs)		
Face Mask	51.96± 7.83	315
ETT	52.23± 8.23	405
LMA	53.67± 7.96	106
TIVA	53.20± 8.62	670
p = 0.06 (NS)		

All patients were assessed post operatively based on a recovery scale of R1 and R2 time pattern. R1 is the time from cutting off the agent (either inhalational or the intravenous agent) to the time for opening eyes on command and R2 is time from beginning of R1 till the execution of command. The recovery times in all the groups (averaged) are represented in Table 4. The results were statistically analysed using Anova with multiple comparison test and p value < 0.05 was considered significant. R1 was least for TIVA group. Significant p values were found when R1 in TIVA was compared with R1 in FM and ETT groups. R1 for LMA and TIVA were comparable and statistically insignificant. R2 was least in TIVA group, which was statistically significant as compared to other three groups.

Early awakening, orientation to time, place and return of normal psychomotor performance are the essential prerequisites of the expanding outpatient surgical concept. Drugs with larger elimination t_{1/2} time have prolonged residual effects and hence delay recovery. Propofol is rapidly metabolized in the liver, which accounts for rapid weaning from anaesthesia. Propofol clearance rate of 20-30 ml kg/min exceeds the hepatic blood flow. Thus propofol has advantage of rapid recovery as compared to other IV anaesthetic agents. Isoflurane was used in our study because of its low blood gas solubility as compared to halothane, which permits rapid elimination from the central nervous (CNS).

Patient satisfaction was assessed by the fact if they would prefer the same anaesthesia protocol for a similar procedure in future. The analysis revealed that majority preferred the intravenous technique as compared to others.

The pregnancy success rates were of 391/1496 (26%) and the delivery rate stood at 314/1496 (21%). The abortion rate in our series was at 5-8% in the first trimester, for which no significant cause or correlation with anaesthetic techniques could be found.

Discussion

Exposure to high concentrations of different local anaesthetics adversely affects fertilisation and embryonal development [4]. However, given that much lower concentrations are achieved clinically and that oocytes are washed after retrieval, the clinical effects of using local anaesthetics should be limited and no adverse effects have been reported in human trials [4]. Nitrous oxide adversely influences DNA synthesis in animals and humans by reducing methionine synthetase

Table 2
Details of general anaesthesia used for IVF (n = 1496)

Number of patients (percentage)	Type
315 (21.05%)	Face Mask - /Oxygen/ Isoflurane
405 (27.07%)	Endotracheal Tube/Oxygen/ Isoflurane
106 (7.08 %)	Laryngeal Mask Airway/Oxygen/ Isoflurane
670 (44.78%)	Total Intravenous Analgesia-Propofol/ Fentanyl/Pethidine / Morphine

Table 3**Incidence of side effects**

Side effect	Inhalational group				TIVA group (n=670)	p value
	(FM (n=315))	ETT (n=405)	LMA (n=106)	Total (n=826)		
Nausea	12	16	02	30	14	0.08
Nausea + vomiting	08	10	02	20	08	0.08
Dysphagia	00	05	02	07	00	0.02*
Pruritus	00	00	00	00	05	0.02*
Headache	03	04	02	09	08	0.85
Shivering	04	07	03	14	07	0.29
Nystagmus	00	05	00	05	12	0.03*
Muscle rigidity	02	04	00	06	08	0.35

* p value < 0.05 is significant

Table 4**Time for recovery**

Average time (in minutes)	Face mask	ETT	LMA	TIVA	p value
R1	4.65 ± 1.3	5.12 ± 2.3	4.14 ± 1.8	3.70 ± 2.4	0.001*
R2	7.54 ± 2.8	9.12 ± 3.4	9.01 ± 2.1	5.97 ± 1.3	0.001*

1) * p value < 0.05 is significant

2) The p values for recovery times shown above pertain to intergroup comparison between all the four groups.

activity. Therefore, this agent cannot be recommended despite the lack of data indicating that it reduces the success rate of fertility treatment [5]. Halogenated agents have been associated with reduced reproductive success in clinical practice and must therefore be used with caution [6,7]. Opioids, and especially fentanyl and remifentanyl, do not seem to affect reproductive success [7]. In addition, midazolam and ketamine seem to be acceptable drugs for use during assisted reproduction [8,9]. Recent data also suggest that propofol may be a safe alternative for use during assisted reproduction [10-12]. Currently, in our institution a fentanyl / propofol based technique involving optimal sedation has been the technique of choice for all invitro fertilisation procedures. This method has been reported to be safe and effective [13] and institutional experience seems to confirm this finding with no differences in oocyte fertilisation rate or subsequent successful pregnancy outcome as compared to general anaesthesia. Electro-acupuncture appears to be an effective alternative to conventional anaesthesia during egg collection (ovum pickup) for in vitro fertilisation [14]. recently Para cervical block (PCB) has been used in combination with opioids, hypnotics, sedatives, and acupuncture with or without premedication during transvaginal ultrasound guided oocytes retrieval [15-17]

The most important complication associated with IVF is the ovarian hyper stimulation syndrome, usually seen after transfer of fertilised oocytes manifesting as abdominal discomfort, ovarian enlargement, ascites, haemorrhage, ruptured follicle, pleural effusion and thromboembolism, which has no relation to the

anaesthetic procedure per se [18]. No other untoward complications of clinical significance were noticed in this retrospective study. Amongst the various available TIVA options, propofol/ remifentanyl or fentanyl technique of sedation has been opted as a safe and effective anaesthetic for in vitro fertilisation [19].

Conflicts of Interest

None identified

Intellectual Contribution of Authors

Study Concept : Col TVSP Murthy, Col RK Sharma

Drafting & Manuscript Revision : Col TVSP Murthy

Statistical Analysis : Col TVSP Murthy, P Gupta

Technical Support : Col TVSP Murthy

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CORP NEWS

SCIENTIFIC SESSIONS ON SELECTED PROFESSIONAL PAPERS

57TH ARMED FORCES MEDICAL CONFERENCE: 2009

1. It has been decided to organise two scientific sessions on selected professional papers during the above conference scheduled to be held at the Armed Forces Medical College, Pune in the month of **February 2009**. The details are as under:-
 - (a) Medicine and allied subjects including Pathology, Preventive and Social Medicine, Hospital Administration and Nursing.
 - (b) Surgery and allied subjects including Dental Surgery and Nursing.
2. The scientific sessions mentioned at para 1(a) will include presentation of papers by medical, dental and MNS officers on original work on various aspects of work done in clinical disciplines, development of new diagnostic/therapeutic techniques/equipments/aids etc. Each paper will be allotted 12 minutes including the time for discussion.
3. The criteria for selection of papers, for scientific sessions in general, will be in terms of originality, scientific content and methodology adopted. Rejection of paper should not be regarded as a reflection of its merit, since diversity and balance are also considered in the selection of papers for presentation.
4. Wide publicity may please be given on this subject matter and medical, dental and MNS officers be encouraged to prepare papers of high quality which are worthy of presentation in the above scientific sessions.
5. Papers for presentation should be submitted in an article format as per the guidelines to authors printed in Jan 2008 issue of Medical Journal Armed Forces India. The first page of paper must bear a heading **Paper for Scientific Session** [indicating the session (Medicine/Surgery)]. Papers received in conformity with the correct format will only be taken up for consideration. **Seven copies** of each scientific paper are to be submitted through proper channel so as to reach this office latest by **31 Aug 2008**.