

Anesthesia and assisted reproductive technology: A literature review

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Abstract

Assisted reproductive technology or *in vitro* fertilization (IVF) is a method used to achieve pregnancy by artificial methods. It includes four steps which are: Induction of ovulation, picking up of mature ovum, injection of sperm microscopically into the mature ovum, and then transferring of fertilized ovum, as embryo, to the uterus. The procedure of IVF demonstrates pain during ovum pickup through aspiration technique using vaginal ultrasound probe which supersedes the laparoscopic retrieval oocyte. The bulk of cases present with anxiety and other psychological disorders related to their infertility. These factors perpetuate pain associated with the procedure. Consequence of this, the role of anesthetist will be of great importance to deal with these challenges. Different modalities and methods of anesthesia could be used during IVF. Clinician should adapt to familiar one. Counseling of patients has a major role. However, written guidelines and protocol may be helpful and of great benefit.

Key words: Anesthesia, assisted reproductive technology, fertilization, *in vitro*, *in vitro* fertilization

INTRODUCTION

Assisted reproductive technology or *in vitro* fertilization (IVF) is a method used to achieve pregnancy by artificial methods. It includes four steps. which are: Induction of ovulation, picking up of mature ovum, injection of sperm microscopically into the mature ovum, and then transferring of fertilized ovum, as embryo, to the uterus. In mid-1978, Louise Brown did the first successful test tube baby. However, the pioneers of IVF are Robert Edwards and Patrick Steptoe.^[1] The procedure of IVF demonstrates pain during ovum pickup through aspiration technique using vaginal ultrasound probe which supersedes the laparoscopic retrieval oocyte. However, it may approach

natural fecundity when there are favorable patient and embryo characteristics.^[2-4]

ANESTHESIA

The bulk of cases present with anxiety and other psychological disorders related to their infertility. These factors perpetuate pain associated with the procedure. In addition to these factors and family stress on some women, the chance of becoming pregnant is only 30% or even less. Consequence of this, the role of anesthetist will be of great importance to deal with these challenges.^[3]

No ideal or superior technique of anesthesia for IVF even many modalities of anesthesia has been used. There is some controversy regarding the effect of anesthetic agents on fertilization, embryo division, and the rate of pregnancy.

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Comparing a remifentanyl-based monitored anesthesia care technique with general anesthesia, pregnancy rates were found to be higher. More rationale anesthesia in IVF nowadays is used due to generation of new drugs. This mandates more service in this up growing field.^[5,6]

Methods of anesthesia during *in vitro* fertilization

- General anesthesia
- Central neuraxial anesthesia
- Regional block
- Procedural sedation/analgesia
- Patient-controlled analgesia
- Electropuncture
- No anesthesia.

GENERAL ANESTHESIA

A lot of regimen and combinations of drugs can be used to conduct general anesthesia. While general anesthesia offers a complete muscle relaxation, amnesia, and analgesia, the rate of complications is higher compared with other types.

Propofol characterizes by rapid induction and recovery with less hangover. These features make it suitable for day care IVF procedures.^[7] It is safe to use propofol as there is no effect on the ovum fertilization or embryo. No detrimental effects of propofol have been found of the rising concentrations of follicular fluid on oocyte quality. However, the possibility of that may be due to the short duration of retrieval procedures and the consequent low follicular fluid propofol concentrations.^[8]

Fentanyl and alfentanil have a potent analgesic effect with short duration. Recently, they are used in combination with other agent such as propofol or ketamine. Follicular fluid level of both was found to be low.^[6-8]

Isoflurane and sevoflurane used with other agent to maintain anesthesia. They have rapid effect and elimination. Among halogenated anesthetic agents, there was agreement that halothane is an unwise choice for IVF.^[6,9]

Midazolam which is a short-acting benzodiazepine is used commonly in combination with other inhalational and intravenous agents. It characterizes with a retrograde amnesia and short duration. Small amount of midazolam was found in follicular fluid with no determinant effect has been established.^[6]

Ketamine which is a unique anesthetic agent having a potent analgesic, anesthetic, and amnesic effect. Ketamine alone is rarely used nowadays due to its unpleasant adverse effects mainly hallucination and bad emergence phenomena.^[6,10] Ketamine and propofol are used in combinations by many

practitioners. Ketofol as combination of 50% propofol and 50% ketamine (5 mg/ml of each) now is widely used for procedural sedation analgesia with high satisfaction and effectiveness.^[11,12] Literature regarding its use in IVF is still deficient. Ketofol characterizes with less hemodynamic instability and a decreased ketamine adverse effects. Another combination which is also effective is fentanyl which is calculated the dose of propofol and fentanyl.

General anesthesia with fentanyl, propofol, and isoflurane results in similar pregnancy rate when was compared with ketamine and midazolam for sedation.^[8] Conscious sedation using opioid combined with benzodiazepines was found to be safe and cost effective.^[13] Combination of propofol, fentanyl, and midazolam is relatively safe and easy to use to obtain conscious sedation.^[14]

High patients' satisfaction was obtained during patient-controlled analgesia compared with physician-administered method. However, patients demonstrated more need for supplemental analgesics.^[4] In 2001, Martin premedicated patient with 4 mg of midazolam and 25 mcg of fentanyl. Then, analgesia was maintained with the patient using infusion pump (patient-controlled analgesia).^[8]

DELETERIOUS EFFECTS OF ANESTHETIC AGENTS ON *IN VITRO* FERTILIZATION

While there is no strong evidence, double-blind control studies, some anesthetics have been detected in follicular fluids which raised the suggestion of deleterious effect on ovum, embryos, success rate of pregnancy, abortion, and congenital anomalies. Nitrous oxide was found to be hazardous on IVF outcome due to its effect on DNA synthesis while another study did not prove that.^[15] However, fentanyl and remifentanyl revealed no deleterious side effects.^[16]

CENTRAL NEURAXIAL BLOCK: SPINAL/ EPIDURAL

Spinal anesthesia

No doubt, spinal anesthesia compared with general anesthesia has less complications rate. Spinal anesthesia offers a high rate of success and outcome in IVF procedure when compared with general anesthesia.^[17] Spinal anesthesia increases the chance of fertilization by 27%.^[18] Endler *et al.* 1985 induced pregnancy in three out of four patients of them two ended with full healthy term infants.^[19]

Low dose of lidocaine (45 mg) with small dose of fentanyl (10 mcg) can achieve comfortable anesthesia. No differences were found between small dose of hyperbaric bupivacaine (3.75 mg of 0.75%) combined with 25 mcg

of fentanyl compared with lidocaine 30 mg of 1.5% with 25 mcg fentanyl.^[20,21]

Procedural sedation with alfentanil and midazolam when compared with 50–80 mg of 5% lidocaine for spinal anesthesia revealed no differences regarding reproductive outcome. However, recovery time was found to be longer in intravenous group.

Epidural analgesia

Epidural analgesia compared with intravenous sedation, combined with face mask, has no superiority. Botta *et al.* 1995 found that fertilization, cleavage, and pregnancy rate were 67.2%, 92%, and 20%, respectively, in epidural anesthesia compared with 69.3%, 93%, and 19.6% in sedation groups.^[22]

PARACERVICAL BLOCK

Paracervical block with bupivacaine or lidocaine can be used. It was found to be effective and offers good analgesia. However, it was not the same as by Ng *et al.* in 2001 when he compared it alone with conscious sedation combined paracervical block. A 2.5 times in vaginal and abdominal pain were demonstrated when paracervical block was used alone. They recommended only 50 mg lidocaine as high doses demonstrated no improvement in analgesia beside the risk of side effects.^[20,23-25]

No strong evidences support the adverse effects of local anesthetics on fertilization and embryo development.^[14,15] These may be due to short procedure and repeated washing of the ovum. Motivation of patients also plays a role in the analgesic properties of paracervical block.

CONCLUSION

Different modalities and methods of anesthesia could be used during IVF. Clinician should adapt to familiar one. Counseling of patients has a major role. However, written guidelines and protocol may be helpful and of great benefit.

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Conflicts of interest

There are no conflicts of interest.

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