



The effect of spinal anesthesia versus general anesthesia on oocyte and embryo quality and pregnancy success rate during in-vitro fertilization.

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ABSTRACT

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Women who have transvaginal oocyte retrieval feel nervous and have mild to moderate pain because a needle is used to poke holes in the vaginal skin and ovarian capsule to get the oocytes. The aim of this study is compare between general and spinal anesthesia effect on ICSI outcome. A cross-sectional study was conducted in the High Institute of Infertility Diagnosis and Assisted Reproductive Technologies/ Al-Nahrain University, from first April 2021 to the first of February 2022. Patients were randomized blindly at time of oocyte retrieval for types of anesthesia given: (50 women subjected to spinal anesthesia and 50 women subjected to general anesthesia). All females were subjected to flexible antagonist protocol. Also, all of them had the same surgical procedure by the same physicians. ICSI outcome was compared between the groups. The study showed there was non-significant difference ($p>0.05$) between the two groups regarding pregnancy rate with higher oocyte number in women subjected to spinal anesthesia than those who were under the general anesthesia although the difference was not statistically significant. The fertilized oocyte number was non significantly higher in spinal anesthesia group than the general anesthesia. So; spinal anesthesia and general anesthesia have comparable ICSI outcome.

KEYWORD

IVF; Spinal Anesthesia; Oocyte; General anesthesia.

1. Introduction

Infertility is a disease of the reproductive system, defined by the failure to achieve a pregnancy after at least one year of regular unprotected sexual intercourse in women < 35 years not using contraception and after six months in women > 35 years or due to an impairment of a person's capacity to reproduce, either as an individual or with his/her partner, it affects about 10-15% of couples (Gambineri *et al.*, 2019 [1]; Omani-Samani *et al.*, 2019 [2]). The chance of having a baby is 85%-90% in a year, and the rest is infertile because it depends on the length of sexual exposure, frequency of coitus, and the couple's age. According to the World Health Organization (WHO) definition, a couple is considered infertile if, after two years of regular sexual intercourse without contraception, the woman has not become pregnant (Yun *et al.*, 2019 [3]). Infertility is classified as primary (no pregnancy in the past) or

secondary (pregnancy has occurred in the past, not necessarily leading to live birth). According to the WHO, most infertile couples around the world suffer from primary infertility, which means that the woman has never conceived. On the other hand, secondary infertility may occur at any time in a woman's life after the first pregnancy (Eccles, 2018 [4]). The causes of infertility can be generally classified into four groups: male, female, combined (both male and female), and unexplained (Yun *et al.*, 2019 [3]). Some additional factors that may contribute to female infertility are behavioural factors such as diet, exercise, smoking, alcohol, and drug use (De Geyter, 2019 [5]). Combined infertility arises from the combination of male and female causes, and it may be that each partner is independently fertile, but the couple cannot conceive together without assistance (Malhotra *et al.*, 2018 [6]). Nowadays, progress in assisted reproductive technology (ART) has enabled the clinicians to

treat many types of infertility. Assisted reproduction is a complicated process involving multiple stages like ovarian stimulation, ovum pick up, and then fertilization of these oocytes, embryo cleavage and implantation (Montgomery *et al.*, 2016 [7]). The ultimate goal of all these procedures is to get a viable intrauterine pregnancy as a step to get a healthy baby (Bai *et al.*, 2020 [8]). Intra-cytoplasmic sperm injection (ICSI) refers to the technique of assisted reproduction, include injecting a single sperm into the center (cytoplasm) of the egg (Kawwass and Badell, 2018 [9]). Women who have transvaginal oocyte retrieval feel nervous and have mild to moderate pain because a needle is used to poke holes in the vaginal skin and ovarian capsule to get the oocytes. Often, people have to try many times before they succeed (Buisman *et al.*, 2022 [10]). So, it's important to make sure they're in a comfortable place that reduces their pain and anxiety and makes them more willing to work with

you. For these reasons, these procedures have used sedation alone or in combination with painkillers, as well as different types of anesthesia, such as general anesthesia, regional anesthesia, and an alternative medicine approach. All of the above methods require the help of an anesthesiologist to make sure that transvaginal oocyte retrieval is safe and effective for both women and doctors. Even though it is used in most fertility centers, (Matsota *et al.*, 2021 [11]) there is debate about the type of anesthesia used during OPU for IVF. Some anesthetics, like Remifentanyl, were found in the follicular fluid. This was compared to the effect of spinal anesthesia. The aim of this study was to demonstrate which is the better technique to get best oocytes quality and ICSI outcome with higher pregnancy rate by comparing two groups of infertile women during oocytes retrieval, One group under general anesthesia and the other group under spinal anesthesia.

2. Patients and Methods

A cross-sectional study was conducted in the High Institute of Infertility Diagnosis and Assisted Reproductive Technologies/ Al-Nahrain University, from first April 2021 to the first of February 2022. Verbal consent agreements from all subject will be obtained prior to the collection of samples. Patients during their IVF course randomized blindly at time of oocyte retrieval, two types of anesthesia given to two groups: (50 women subjected to spinal anesthesia and 50 women subjected to general anesthesia). All couples subjected to a full history taking, complete general examination, complete gynecological examination and infertility workup including: husband's seminal fluid analysis, basal hormonal analysis, uterine cavity assessment by ultrasound and tubal patency evaluation by hystrosalpingogram. All the patients had the same therapeutic protocols for ovum retrieval; which was the long

protocol. Also, all of them had the same surgical process with the same physicians. For assuring the oneness of the surgeon, all the patients were operated by only one of the surgeons. Also, all the patients underwent the same procedure to ensure the oneness of the surgical procedure. For anesthesia, the first group, received spinal anesthesia for performing In Vitro Fertilization (IVF), and the other group received general anesthesia for this purpose. In the spinal anesthesia group, the patients first were monitored using standard electrocardiography, noninvasive blood pressure, pulse oximetry and heart rate monitoring. Then, 500 mL of isotonic saline was administered, and while a guardian nurse was holding the patient, in the sitting position and under sterile conditions, between the 3rd and 4th lumbar interspaces, a number 25 Quincke needle was introduced and 75 mg of pure 2% lidocaine, without any additive or preservatives was injected into the subarachnoid space. The

patients were turned immediately to supine position to gain a T10 (10th thoracic) level of anesthesia. The anesthesia level and the blood pressure were checked continually. For the general anesthesia (GA) group, each patient was in supine position in operation room. Then, standard monitoring was used including pulse oximetry, pulse rate, noninvasive blood pressure (NIBP) monitoring and 3 lead electrocardiogram monitoring. Also, clinical monitoring of respiratory status was constantly performed. Afterwards, using fentanyl (1 µg/kg) and midazolam (30µg/kg) intravenously as premedication drugs, induction of GA was administered by incremental intravenous doses of thiopental (4 mg/kg) and atracurium (0.5 mg/kg). The trachea was intubated using a low pressure high volume tube (size 7) by direct laryngoscopy. The tracheal tube cuff was filled by air to 15-20 cm-H₂O pressure until minimal leak occurred. The anesthesia was maintained by isoflurane (0.8-1 MAC). The residual

of muscle relaxant was reversed by atropine (0.03 mg/kg) and neostigmine (0.07 mg/kg) after detection of minimal muscle contractions at the end of the procedure. The patients were extubated in fully awake and stable clinical condition. Patient evaluation for the results of pregnancy outcome was performed by a different team who were unaware of patient group allocation. The evaluating teams were different from the executive team and evaluated the patients separately at two weeks and six weeks after IVF accordingly. The patients were evaluated regarding the pregnancy outcome using serum β-hCG test two weeks after IVF and sonographic evaluation six weeks after IVF. All the evaluations were performed by the same setting. Pregnancy confirmation was performed after approval of the two tests. The number of fertilized oocytes and embryos transferred in each group and also, the duration in which embryos were outside the

controlled environments were kept similar as much as possible.

Technique

After obtaining their informed consent, the patients received 2 ml of glucose and preservative-free lidocaine 2% at room temperature (density at $37^{\circ}\text{C} = 1.0003 \text{ g. ml}^{-1}$, baricity at $37^{\circ}\text{C} = 1.0000$, $\text{pH} = 4.7$). Baseline blood pressure and heart rate were recorded. All the patients were prehydrated with 1500 ml Ringer's lactate solution IV warmed to 37°C . The fluids were administered over 15-20 min. With the patient in the sitting position, lumbar puncture was performed at the L3-L4 inter-space using a 23-gauge needle with its bevel facing laterally. Once free flow of cerebrospinal fluid was obtained, lidocaine was injected without barbotage at a rate of 1 ml per five seconds. The solution injected in each patient was determined from a

random list and was known only to the anaesthetist performing the block. Immediately after the injection, the patients were placed in the supine position with a further 500 ml Ringer's solution was infused during the following 30 min.

3. Results

The study showed that the pregnancy rate was 20% in a woman under spinal anesthesia as compared with 16.67% in women under general anesthesia although there was non-significant difference between the two groups, Table 1. The study showed that 23.33% of women under General anesthesia where with G1 plus G2 compared with 20% of women under spinal anesthesia, while 50% of women with spinal anesthesia where within G1 class although the difference was nonsignificant between the two groups.

(Table 1): Pregnancy rate comparison

Pregnancy rate	Spinal Anesthesia	General Anesthesia
Positive	6 (20)	5 (16.67)
Negative	24 (80)	25 (83.33)
Total	30 (100)	30 (100)

P- value: >0.05

(Table 2): Comparison of embryo status in women under SA and GA

Grade	General Anesthesia	Spinal Anesthesia
0	3 (10)	1 (3.33)
G 1	14 (46.67)	15 (50)
G 2	6 (20)	8 (26.67)
G 1 & G 2	7 (23.33)	6 (20)
Total	30 (100)	30 (100)

P- value: >0.05

The study showed that the oocyte number after IVF in women after spinal anesthesia was more than oocyte number in women who under the general anesthesia although the difference was not statistically significant. Table 3

(Table 3): Comparison of oocyte number between studied groups

Type of Anesthesia	Oocyte number		P-value
	Mean	SD	
General Anesthesia	12.33	7.55	0.31
Spinal Anesthesia	12.97	5.70	

4. Discussion

The comparison of Number of fertilized oocytes, number of oocytes, estrogen level at cycle day 2 and preoperational estrogen level between women with General Anesthesia and women with Spinal Anesthesia were shown in Table 1. The study showed no significant differences between women under spinal anesthesia and general anesthesia regarding number of fertilized oocytes, number of oocytes, estrogen level at day two of Menstrual cycle and pre-operational estrogen level.

Inducing analgesia for oocyte retrieval may reduce the success rate of an IVF program (Scanlon and Green, 2021 [12]). Regarding its safety, specialists usually prefer regional analgesia more. There are three methods for regional analgesia: paracervical block, SA, and epidural analgesia (Beck *et al.*, 2020 [13]). Because of technical acceptability and simplicity, SA is used more than the other two methods in

gynecology and obstetrics (Jain *et al.*, 2013 [14]). Another method which is still widely used is GA; GA is inherently associated with high risks of respiratory complications, aspiration, prolonged duration of hospitalization, and it probably affects its outcome (Hwang and Kim, 2022 [15]). The current study showed that the pregnancy rate was 20% in a woman under spinal anesthesia as compared with 16.67% in women under general anesthesia. Since successful fertilization is dependent on several different and even unknown factors, some studies have been conducted to investigate the effective factors to improve fertilization, but more investigations must be done focusing on the type of analgesia method selected as well as considering temporal and spatial conditions (Cai *et al.*, 2011 [16]). In agreement with our finding, Aghaamoo *et al.*, (2014) showed poor quality of GA compared with SA to achieve successful IVF outcome (Aghaamoo *et al.*, 2014 [17].

Moreover, it is recommended to use SA for oocyte retrieval instead of GA. Adjusting the number of transferred embryos as well as fetus grade (Cai *et al.*, 2011[16]) it was found that practicing SA is twice as much as GA related to increased chance of chemical pregnancy. Additionally, Azmude *et al.*, (2013) in similar study demonstrated that spinal anesthesia can increase the chance of fertilization success and suggested that the method of anesthesia could affect the outcome of pregnancy in IVF patient, due to the effects of anesthetic drugs and the effects of the anesthesia on the physiologic status of the patients (Azmude *et al.*, 2013 [18]). In a study performed on fifty patients scheduled for IVF by Circeo *et al.*, (2011) it was demonstrated that “there was no need to use midazolam or larger doses of fentanyl to obtain patient comfort and prevent recall” and this finding implies that patients undergoing general anesthesia or intravenous sedation receive extra doses of anesthetic

agents; while there is no need for it and patients undergoing regional anesthesia would not receive such doses to be protected from the anesthetic drug side effects (Circeo *et al.*, 2011 [19]). But Kim *et al.* in 2000 meta-analyzed four studies with distinct general and loco-regional anesthesia to evaluate the prospective trials comparing GA vs. spinal anesthesia on reproductive outcomes (pregnancy rate) for IVF and concluded that there was no significant difference in both groups of GA and spinal anesthesia. The study showed that 23.33% off four men under General anesthesia where with G1 plus G2 compared with 20% off women under spinal anesthesia, while 50% of women with spinal anesthesia where within G1 class although the difference was nonsignificant between the two groups (Kim *et al.*, 2000 [20]). Azmude *et al.*, (2013) and Aghaamoo *et al.*, (2014), showed that number of good embryos higher in women undergone IVF with SA method compared to GA method

(Aghaamoo *et al.*, 2014 [17] and Azmude *et al.*, 2013 [18]). The study showed that the oocyte and fertilized number after IVF in women after spinal anesthesia was more than oocyte number in women who under the general anesthesia although the difference was not statistically significant. Spinal anesthesia increased significantly the chance of IVF success in a randomized prospective trial by Azmude *et al.*, (2013) in similar study demonstrated oocyte and fertilized number after IVF in women after spinal anesthesia was more than oocyte number in women who under the general anesthesia Azmude *et al.*, 2013 [18]). According to a cohort study based on analysis of patient records at Mirza Kochak Khan Hospital, Tehran University of Medical Sciences by Aghaamoo *et al.*, (2014), it was recommended to use spinal anesthesia instead of GA for oocyte retrieval, to achieve successful in vitro fertilization outcome (Aghaamoo *et al.*, 2014 [17]).

6- Conclusion

In summary, the use of SA for oocyte retrieval can be suggested instead of GA to achieve successful IVF outcome. Further investigation should be done on SA to clarify the underlying mechanisms of action and the likelihood of negative effects or benefits on the reproductive outcome.

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Author Contribution

Farah M. Mohammed, performed the study, Mufeda A. Jwad, Raed G. Reshan, supervised the work .

Conflict of Interest

The authors declare no conflict of interest .

Ethical Clearance

The study was approved by the Ethical Approval Committee.

Financial Disclosure

There is no financial disclosure.

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