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Study some parameters in women underwent in-vitro fertilization with spinal anesthesia compared with general anesthesia

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Abstract---Background: 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 Aim of the study: 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 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. 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. 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. Results: There was no significant difference in age, mean body mass index (BMI), mean duration of infertility, type of infertility, educational level, smoking and menstrual cycle regularity. The comparison of serum hormonal levels between women with General Anesthesia and women with Spinal Anesthesia were shown in Table 2. There was no significant difference in mean basal serum hormonal levels, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and preoperational E2 between women with General Anesthesia and women with Spinal Anesthesia. 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. The study showed non significant differences between women under general anesthesia and women under spinal anesthesia regarding blood pressures while the study showed that woman under SA have high mean of SPO2 and lower hear rate than women under general anesthesia. The study showed that the time used to perform IVF in women under spinal anesthesia was less than the time spent in women who under the general anesthesia, although the difference was not statistically significant

Keywords---IVF, spinal anesthesia, oocyte, general anesthesia.

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 ; Omani-Samani *et al.*, 2019). 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 couple's age. According to World Health Organization (WHO) definition, a couple is considered infertile if, after 2 years of regular sexual intercourse, without contraception, the woman has not become pregnant (Yun *et al.*, 2019). Infertility 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). The causes of infertility can be generally classified into four groups: male, female, combined (both male and female) and unexplained (Yun *et al.*, 2019). Some additional factors that may contribute to female infertility are behavioural factors such as diet, exercise, smoking, alcohol and drug use (De Geyter, 2019). 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). 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, then fertilization of these oocytes, embryo cleavage and implantation (Montgomery *et al.*, 2016). 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). 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). 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). 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) 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.

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 hysterosalpingogram. 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 (30 µg/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.

Results

The comparison of demographic characteristics between women with General Anesthesia and women with Spinal Anesthesia were shown in Table 1. There was no significant difference in age, mean body mass index (BMI), mean duration of infertility, type of infertility, educational level, smoking and menstrual cycle regularity. ($p > 0.05$).

Table 1: Comparison of demographic characteristics of the studied groups

Parameters	General Anesthesia	Spinal Anesthesia	P-value
Age (years)	n(%)	n(%)	
<30	11 (36.67)	6(20)	>0.05
30-40	16(53.33)	22(73.33)	
>40	3(10)	2(6.67)	
Total	30(100)	30(100)	
Mean±SD	32.55±4.67	33.7±4.23	>0.05

Educational level			
primary	11(36.67)	5(16.67)	>0.05
secondary	13(43.33)	12(50)	
College	6(20)	13(43.33)	
Type of infertility			
Primary	21(70)	22(73.33)	>0.05
Secondary	9(30)	8(26.67)	
Smoking			
Yes	2(6.67)	11(36.67)	>0.05
No	28 (93.33)	19(63.33)	
Menstrual cycle			
Regular	22(73.33)	16(53.33)	>0.05
Irregular	8(26.67)	14(46.67)	
Obesity			
Normal	5(16.67)	4(13.33)	0.051
Overweight	24(80)	16(53.33)	
Obese	1(3.33)	10(33.33)	
Mean±SD	27.3±2.88	28.51±3.44	>0.05
Duration of infertility			
Mean±SD	8.87±5.92	7.57±5.22	>0.05

The comparison of serum hormonal levels between women with General Anesthesia and women with Spinal Anesthesia were shown in Table 2. There was no significant difference in mean basal serum hormonal levels, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and preoperational E2 between women with General Anesthesia and women with Spinal Anesthesia ($p > 0.05$).

Table 2: Comparison of serum hormonal levels between studied groups

Hormones (Mean±SD)	General Anesthesia	Spinal Anesthesia	P-value
LH at CD2	4.29±2.24	5.2±2.8	>0.05
FSH at CD2	5.12±1.89	5.34±3.41	>0.05
E2 at CD2	47.9±22.1	55.8±18.8	>0.05
preoperational E2	2074±1023	1624±748	>0.05

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 3. 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.

Table 3: Comparison of fertilization parameters and E2 between studied groups

Characteristic	General Anesthesia	Spinal Anesthesia	P-value
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No. of fert. oocyte	6.73±4.09	6.87±5.21	>0.05
No. of oocyte	12.63±7.55	12.67±5.71	>0.05
E2 at CD2	47.9±22.1	55.8±18.8	>0.05
preoperational E2	2074±1023	1624±748	>0.05

The study showed non significant differences between women under general anesthesia and women under spinal anesthesia regarding blood pressures while the study showed that woman under SA have high mean of SPO2 and lower hear rate than women under general anesthesia as shown in table 4

Table 4: Comparison of serum blood pressure parameters between studied groups

Blood pressure parameters	General Anesthesia	Spinal Anesthesia	P-value
Systolic BP	73.63±7.43	70.9±10.1	>0.05
Diastolic BP	119.5±10.2	120.7±11.1	>0.05
Heart rate	90.07±7.92	96.67±9.66	0.045
SPO2	95.45±12.3	99.81±6.46	0.041

The study showed that the time used to perform IVF in women under spinal anesthesia was less than the time spent in women who under the general anesthesia, although the difference was not statistically significant. Table 5

Table 5: Comparison of operation time between studied groups

Type of Anesthesia	operation time (minutes)		P-value
	Mean	SD	
General Anesthesia	14.40	3.68	0.15
Spinal Anesthesia	12.23	6.79	

Discussion

The comparison of demographic characteristics between women with General Anesthesia and women with Spinal Anesthesia were shown in Table 1 There was no significant difference in age, mean body mass index (BMI), mean duration of infertility, type of infertility, educational level, smoking and menstrual cycle regularity. ($p > 0.05$). Ghaffari *et al.*, (2018) also showed no significant difference between general anesthesia and spinal anesthesia groups in baseline demographic and obstetric data for the women in their study. In point of fact, the available published articles contain substantial reports about the association between the fertility outcome following assisted reproductive technologies (ARTs) and demographic characteristics (Hwang and Kim, 2022). Many articles say that a woman's age is the most important factor in predicting whether or not she will get pregnant after having IVF (Scanlon and Green, 2021; Cai *et al.*, 2011). Low ovarian reserve, low number of retrieved oocytes, poor oocyte quality, poor embryo quality, less fertilization rate, and less implantation rate are all things that may be linked to a woman's age making it much harder for her to get pregnant (Khadra *et al.*, 2018).

Both obesity and underweight have been linked to decreased fertility in assisted reproduction patients. The mechanisms by which BMI affects reproduction are anovulation and menstrual irregularity; nevertheless, normal current ARTs can resolve these issues (Bellver *et al.*, 2013). Due to alterations in hormonal levels and metabolic processes (LH, ovarian and adrenal androgens, sex binding globulin and insulin resistance) as well as unfavorable effects on endometrial receptivity, a high BMI may have a negative effect on reproductive success in IVF/ICSI cycles (Bhojwani *et al.*, 2016). Thus, this lack of significant difference may lead to avoidance of any bias in fertility outcome related to younger age, shorter duration of infertility, optimum BMI or variation in causes of infertility which will limit the explanation of any possible difference in fertility outcome or other fertility parameters to variation General Anesthesia and Spinal Anesthesia. The comparison of serum hormonal levels between women with General Anesthesia and women with Spinal Anesthesia were shown in Table 4.2. There was no significant difference in mean basal serum hormonal levels, follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2) and preoperational E2 between women with general anesthesia and spinal anesthesia ($p > 0.05$). These findings also provide support for statistical matching between the groups used general anesthesia versus spinal anesthesia, which allows for the scientific avoidance of any bias in the outcome of the IVF procedure that could be attributed to variation in the serum hormonal concentrations of infertile women. Indeed, a number of authors (Scanlon and Green, 2021; Hwang and Kim, 2022), have written about the association between IVF outcome and serum hormonal levels in infertile women undergoing In addition to the substantial contribution that gonadotrophins make to the development and maturation of oocytes, as well as the subsequent processes of fertilization and implantation, the role that gonadotrophins play in the regulation of both ovarian and endometrial responses that are included in the female menstrual cycle is well known and established. Regarding estradiol, research conducted by Siddhartha et al. (2016) found that a high serum level of estradiol was substantially associated with a bigger number of oocytes, improved oocyte quality, and an increased implantation rate. The study showed non significant differences between women under general anesthesia and women under spinal anesthesia regarding blood pressures while the study showed that woman under SA have high mean of SPO2 and lower hear rate than women under general anesthesia. In agreement of our findings, Circeo *et al.*, (2011) also Found that women who under spinal anesthesia have more preferable conditions of hypertension parameters than woman under general anesthesia. The study showed that the time used to perform IVF in women under spinal anesthesia was less than the time spent in women who under the general anesthesia, although the difference was not statistically significant. In agreement of our findings, Circeo *et al.*, (2011) explained that "Oocyte retrieval though being a short procedure is preferably performed in ambulatory setting and would necessitate rapid recovery from anesthesia with short recovery and minimal side effects".

Conclusions and Recommendations

In summary. The study showed that woman under SA have high mean of SPO2 and lower hear rate than women under general anesthesia and less than the time

spent in women who under the general anesthesia. Large sample size in further prospective study are required to discuss the SA negative effects or benefits.

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