

# Effect of conscious anesthesia with remifentanil versus general anesthesia with propofol on embryo quality and pregnancy rate in ICSI

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## Abstract

**Background:** Anesthesia is a corner of stone in invitro fertilization method for infertile couple and can be detrimental on the any results of reproduction due to potential toxicity run into by the anesthetic medications used. **Objective:** To assess the effect of conscious anesthesia with remifentanil versus general anesthesia with propofol on embryo quality and pregnancy rate in ICSI. **Material and methods:** Comparative cross-sectional study that's enrolled Seventy infertile female who were enduring intra cyto-plasm sperm injection technique (ICSI) at the infertility center of High Institute for In-fertility Diagnosis and Assisted Reproductive Technique /Al-Nahrain University / Baghdad / Iraq, during a period from November 2021 until May 2022. The present study enrolled Seventy infertile females undergoing ICSI cycles with an age range of 19 to 40 years and an infertility duration ranging from 2 years to 10 years.

**Results:** Mean level of day of embryo transferred was  $2.5 \pm 0.662$  in conscious group and  $2.59 \pm 0.56$  in GA group with no significant difference ( $p=0.5$ ), mean of number of embryos transferred was  $2.9 \pm 0.995$  in conscious group and  $2.78 \pm 0.706$  in GA group with no significant difference ( $p=0.5$ ), and grade of embryo transferred mean level was  $1.67 \pm 0.685$  in conscious group and  $1.52 \pm 0.601$  in GA group with no significant difference ( $p=0.3$ ). Pregnancy in conscious group happened in 13 (37.1%) and 12 (34.3%) of patients in GA group.

**Conclusion:** Conscious anesthesia remifentanil with had better reproductive outcome on fertilization rate cleavage and grade 1 embryo rate with significant higher pregnancy rate than general anesthesia with propofol.

**Keywords:** Vitro Fertilization (IVF), conscious anesthesia, general anesthesia; Propofol; remifen-tanil.

## INTRODUCTION

T Transvaginal ultrasound oocyte retrieval is an outpatient procedure and can be performed under different technique of anesthesia such as sedation and general or regional anesthesia. In in vitro fertilization treatments, one of the necessary steps is follicular puncture or ovarian puncture. It consists of the extraction of the ovules from the follicles of the ovary through a puncture made through the vagina and under ultrasound control. This process is performed in the operating room, usually under anesthesia and usually lasts around 10-15 minutes (2).

The anesthesia used in most centers and occasions is sedation. It is a general anesthesia, always performed by an Anesthetist, in which the patient is completely asleep but intubation is not necessary since she is able to breathe spontaneously. The immobility of the patient is essential to minimize complications during the surgical act (3).

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Sedation avoids the patient's pain during the surgical process and facilitates the intervention of the gynecologist who performs the ovarian puncture. After it, the patient usually goes back to her room practically awake. It is the anesthetic technique of choice in most centers due to its low rate of complications, safety and comfort for both the patient and the doctor who performs the puncture (4).

**Aim of the study:** To compare the effect of analgesia with remifentanil versus anesthesia with propofol on IVF outcome in terms of their impact on fertilization rate, cleavage rate, implantation rate, pregnancy rate, and embryo quality.

## PATIENTS' MATERIAL AND METHODS

The study comparative cross sectional study, held at the high institute of infertility and assisted reproductive technique in Al-Nahrin Medical University in Baghdad, the study was started at the November 2021 till June 2022, 70 patients subjected to ICSI for infertility treatment were included in our study after taking a written informed consent from them for their participation in the study.

### Inclusion criteria:

1. Females underwent antagonist protocol.
2. Infertile women aged 18-40 years
3. Infertility (prim./sec.)
4. Couples with unexplained
5. BMI 19-30
6. Expected normal ovarian response.
7. The patient underwent transvaginal oocyte retrieval with GA and Conscious sedation method.

### Exclusion Criteria:

1. Age more than 40 years
2. The patient underwent transvaginal oocyte retrieval with anesthesia methods other than GA and Conscious sedation.
3. Diminished ovarian reserve.
4. Patient underwent transvaginal oocyte retrieval with anesthetic method other than G.A. and Conscious sedation.

70 patients were evaluated initially during their IVF/ICSI cycle for hormonal and ultrasound examination they

start their controlled ovarian stimulation with gonadotrophin, the response for treatment was monitored by repeated ultrasound and estradiol level measurements, when the largest follicles was 14 mm antagonist 0.25mg was administered daily until at least three follicles reach 18mm in size, when oocyte maturation was triggered by 10000IU sub-cutaneous HCG.

Anesthesia and analgesia during Oocyte Retrieval

All patients were fasted and unpremedicated, and received midazolam 2 mg intravenous (iv) just before

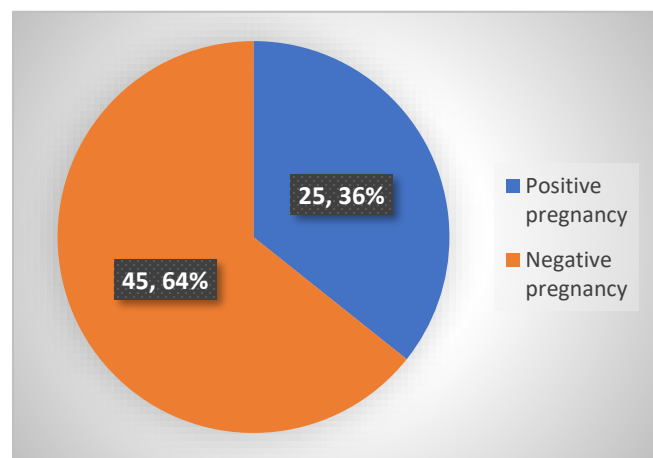
starting the procedure. Afterwards, women were assigned into two groups, and received

either analgesia with remifentanil or anesthesia with propofol.

Oocyte retrieval guided by ultrasound anesthesia or analgesia were done after 34-36 hours. Measurements of vital signs including pulse rate, blood pressure and respiratory rate. At the embryology laboratory assessment of total number of oocytes. Oocyte denudation is done and number of MII and MI assessed and abnormal oocyte including GV, mature oocyte were inseminated by ICSI, 18 hours after, assessment for fertilization and assessment for grade of pronuclei, then daily follow up for number of blastomeres, degree of fragmentation, and grading of embryo. Embryo transfer after 48-72 hours, all patients have one or two Grade 1 embryo transferred, this is determined according to the grades and numbers of embryo available, then luteal phase support by cyclogest suppositories twice daily and primolut depot ampoules 250 µg I.M. twice weekly, 2 weeks later checking for pregnancy is done by serum measurement of hCG.

### Results:

The current study shows that pregnancy was occurred in 25 (36%) of the patients in the studied groups and 45 (64%) with negative pregnancy (Figure 1). Pregnancy in conscious group happened in 13 (37.1%) and 12 (34.3%) of patients in GA group, while negative pregnancy occurred in 22 (62.9%) of patients in conscious group and 23 (65.7%) in GA group (Table 1 and figure 2).

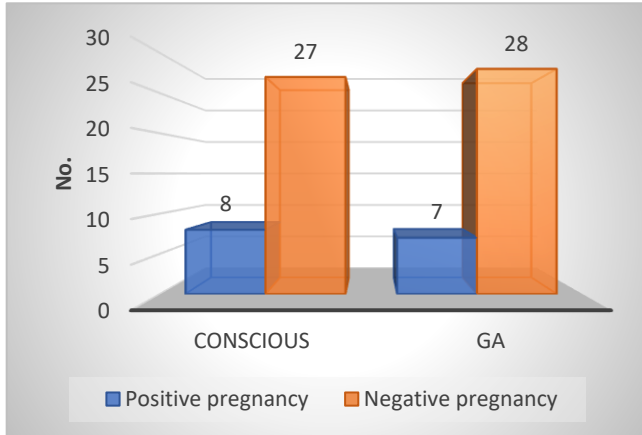


**Figure 1:** Pregnancy outcome in the studied groups

**Table 1:** Comparison between Conscious and general anesthesia groups according to pregnancy outcome

Parameters		Conscious (n=35)		GA (n=35)		P. value
		No.	%	No.	%	
Pregnancy outcome	Positive (n=25)	13	37.1	12	34.3	0.8 ns*
	Negative (n=45)	22	62.9	23	65.7	

\*: Chi square test, ns: not significant



**Figure 2:** Distribution of the studied groups according to pregnancy outcome

Mean level of day of embryo transferred was  $2.5 \pm 0.662$  in conscious group and  $2.59 \pm 0.56$  in GA group with no significant difference ( $p=0.5$ ), mean of number of embryos transferred was  $2.9 \pm 0.995$  in conscious group and  $2.78 \pm 0.706$  in GA group with no significant difference ( $p=0.5$ ), and grade of embryo transferred mean level was  $1.67 \pm 0.685$  in conscious group and  $1.52 \pm 0.601$  in GA group with no significant difference ( $p=0.3$ ) (Table 2).

**Table 2.** Comparison between Conscious and general anesthesia groups according to embryo in Pre OPU serum

Parameters	Conscious (n=35)	GA (n=35)	P. value
	Mean± SD	Mean± SD	
Day of transferred embryo	$2.5 \pm 0.662$	$2.59 \pm 0.56$	0.5 ns*
Number of embryos transferred	$2.9 \pm 0.995$	$2.78 \pm 0.706$	0.5 ns*
Grade of transferred embryo	$1.67 \pm 0.685$	$1.52 \pm 0.601$	0.3 ns*

\*: Independent t-test, ns: not significant.

## DISCUSSION

The oocyte retrieval might be quite painful procedure therefore, women should offer pain relief, therefore, opioids are used during these procedures for analgesic effect. Remifentanil used due to its pharmacokinetic characteristics that provide rapid anesthet-ic effect, hence, there is a strong clinical evidence that remifentanil is superior and the outcomes of IVF are better than that of other opioids such as fentanyl (5). On the other hand, no significant difference was found between remifentanil analgesia and anesthe-sia with propofol used for oocyte retrieval procedures (2)

The explanation for this higher rates of pregnancies and embryo transfer attributed to the fact that the uterus is more relaxed during general anesthesia with propofol, and the use of remifentanil which lead to technically so easier aspiration.

Additionally, patients experience was good and high satisfaction level and acceptance rates were reported in patients with conscious sedation (6).

Oliveira et al., reported better rates of pregnancy, as well as fertilized oocytes and em-bryos obtained with the use of opioid and propofol against cervical blockad (7). Similar results were obtained in by Saxena in 2016, in which it was shown that the cervical block is ineffective as a single technique for performing puncture (8). On the other hand, in a prospective study conducted by Rolland et al., the effect of anesthetic agents on the patients satisfaction, pain experienced by the patients and birth rates after 22 weeks-gestation were assessed, Rolland et al. found no significant difference in the birth rates between general anesthesia group compared to the cervical block group. However, they reported that after cervical block, the vaginal and abdominal

pain experienced was underestimated by medical personnel. (9).

From other point of view, there is a transition in oocyte retrieval from laparoscopic method to less invasive via vaginal procedure which is very stressful and painful to women. Additionally, it had been observed that during oocyte retrieval under general anesthesia, stress increases the serum prolactin level by almost 50 fold, that may affect the outcome of IVF/ICSI, also repeated exposure of anesthesia may be needed until the success of oocyte retrieval procedure which further increase the anxiety and stress of the patient (10). Another explanation would be that the greater the anesthetic time, the greater the suppression of secretion

Furthermore, the dose of propofol has to be increased in some patients with higher BMI; Saxena et al. reported that for every 1% increase in BMI, an additional 14 mg of propofol is needed. This increase in the dose of propofol will extend the recovery time that may affect the ICSI outcome (Saxena et al., 2017) (11)

In a systemic review, Matsota et al. analyzed results of 14 clinical trials and concluded that only two studies reported a significant difference in the number of collected oocytes, where the total number of oocytes was significantly higher with general anesthesia than with sedation (2).

Interestingly, some studies compare defect of remifentanil on the ICSI outcomes, for instance, Mohsin et al. from Iraq, compare the effect of remifentanil to that of Ketamine on the outcome of ICSI among 60 Iraqi women aged 19-44 years who had different causes of infertility. They concluded that remifentanil was superior to ketamine where significantly higher fertilization rate has been reported in remifentanil group than ketamine group, however, they did not find significant difference between both groups in the cleavage rates but the positive pregnancy rates was significantly higher in remifentanil group than ketamine group, 46.7% vs. 20%, respectively. On the other hand, the Iraqi study documented that the time of procedure was not significantly different but the recovery time was longer in ketamine group than remifentanil, therefore, Mohsin et al. concluded that remifentanil was superior to ketamine in ICSI procedures due to high rates of fertilization and positive pregnancy with shorter recovery time (12)

From other point of view, a double-blind clinical trial conducted in Turkey by Sarikaya et al, compared the effect of two different doses of remifentanil infusion, 0.1 mcg/kg/min and 0.15 mcg/kg/min infusion for sedation during IVF procedures among 86 ASA I-II grade women aged 18-40 years managed with IVF procedures. Sarikaya et al. assessed vital signs total required doses of remifentanil, fertilization rate, cleavage rate and pregnancy rates and all these rates were not significantly different between the two groups however, the anesthesiologist satisfaction was higher with lower dose of remifentanil while surgeon satisfaction was higher in the second group with higher dose of

remifentanil, but patients satisfaction was good in both groups. Authors concluded that both doses of remifentanil associated with stable hemodynamics and rapid recovery without complications (8).

## Conclusion

Conscious anesthesia remifentanil with had better reproductive outcome on fertilization rate cleavage and grade 1 embryo rate with significant higher pregnancy rate than general anesthesia with propofol.

## Conflict of interest

There is no conflict of interest

Source of funding: self

Ethical clearance: was approved by Iraqi Ministry of health-scientific committee

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