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Analysis of the applied technique of intravenous anesthesia for *in vitro* fertilization in obese and patients with normal body mass index

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SUMMARY

Introduction/Objective In this study, the effects of applied anesthetic techniques were investigated in a retrospective analysis of obese patients and those with normal body mass index undergoing *in vitro* fertilization, using bispectral index as an indicator of anesthetic depth.

Methods In total 116 patients with normal body mass index were allocated to group N. Another 116 patients with body mass index > 30 kg/m² were allocated to group O. Anesthetic protocol comprised midazolam for premedication, diclofenac for pre-emptive analgesia, propofol for induction and maintenance, alfentanil for analgesia, suxamethonium for muscle relaxation. We recorded and compared the monitored parameters using t-test and χ^2 test.

Results Procedure duration and recovery time were significantly longer in O group ($p < 0.01$). There is a statistically significant difference ($p = 0.000181$) in the number of patients requiring mechanical ventilation after induction of anesthesia. Propofol consumption was significantly higher ($p < 0.0001$) in O group (2.7 ± 1.6 mg/kg) as compared to group N (2.1 ± 0.4 mg/kg). The incidence of postoperative nausea and vomiting was observed in six patients in N group (5.17%) and nine patients in O group (7.76%). Pain intensity was found higher in group O compared to group N ($p < 0.0001$). Assessment of patients' sedation using verbal scale reported no statistically significant difference between N and O groups ($p = 0.2548$).

Conclusion Induction and maintenance of anesthesia in obese patients results in increased consumption of propofol and the need for muscle relaxation. The statements of the patients who underwent the procedure under intravenous propofol and alfentanil serve as the best recommendation for clinical practice.

Keywords: oocyte retrieval; pain; propofol; alfentanil; body weight

INTRODUCTION

In vitro fertilization (IVF) is an assisted reproductive technology characterized by letting the fertilization of male and female gametes (sperm and egg) occur outside the female body, in the laboratory; created embryos are then transferred into the woman's womb. Stages in IVF procedure are as follows:

- Indications for IVF and preparation for treatment,
- Ovulation induction and monitoring,
- Oocyte retrieval,
- Insemination and fertilization,
- Embryo-transfer.

The role of anesthesiologist is associated to the phase of oocyte retrieval with follicle aspiration. In this stage of the procedure, it is necessary to induce analgesia for pain relief, and in this way to provide the optimal conditions for the gynecologist to perform the procedure.

Oocyte retrieval involves direct ultrasound guidance, i.e. a needle is passed through the top of the vagina to reach the follicles. Pain during oocyte retrieval is caused by the punc-

ture of the vaginal skin and ovarian capsule by the aspirating needle, as well as manipulation within the ovary during the entire procedure [1]. The number of follicles and duration of the oocyte retrieval procedure may affect the pain intensity. Single follicle aspiration would take lesser time and cause less pain as compared to multiple follicle aspirations [2]. In addition, the pain intensifies with difficult ovarian access (for instance congenital and acquired anomalies, obesity, etc.) that requires external compression of the lower anterior abdominal walls external abdominal compression. Insufficiently deep anesthesia in these cases can lead not only to the onset of intense pain but also to the reflex movements of patients that can disturb manipulation of aspiration needle and the whole procedure.

Obese patients undergoing IVF present a challenge not only for gynecologists, but also for anesthesiologists, who are to provide adequate anesthesia to make transvaginal oocyte retrieval a safe and effective procedure. Obesity is often accompanied by a series of possible complications on cardiovascular and respiratory systems, increased incidence of

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thrombosis, difficulties related to airway management and the more emphasized adverse pathophysiological effects of the gynecological position [3]. Varieties of anesthetic techniques and modalities have been used in the history of IVF. The procedure necessitates a short-acting anesthetic approach with minimal side-effects. The various anesthetic modalities used for transvaginal oocyte retrieval include monitored anesthesia care, conscious sedation, general anesthesia, regional anesthesia, local injection as a paracervical block, epidural block, subarachnoid block, total intravenous anesthesia, patient-controlled analgesia, and acupuncture [4, 5, 6].

In our study, we investigated the effects of applied anesthetic techniques using propofol and alfentanil (hemodynamic and respiratory stability of patients, the occurrence of perioperative complications associated with anesthetic technique, duration of intervention, anesthetic consumption per patient, length of stay in post-anesthesia care unit, presence and intensity of pain after intervention, postoperative nausea and vomiting, degree of patient satisfaction with anesthesia) in a retrospective analysis of anesthetic and post-anesthetic records of obese and patients with normal body weight undergoing IVF, using bispectral (BIS) index as an indicator of anesthetic depth.

METHODS

The study was conducted in accord with standards of the institutional Committee on Ethics of the Faculty of Medicine Priština – Kosovska Mitrovica and Spebo Medical fertility clinic in Leskovac. Written consents to the administration of intravenous anesthesia were obtained from the patients. The study (retrospective, randomized) included subjects who underwent IVF in the Spebo Medical specialist medical center for fertility treatment in the period 2010–2017. A total of 950 patients with normal BMI (18.5–24.9 kg/m²) were recorded to have undergone IVF procedure under intravenous anesthesia with propofol and alfentanil. Of these, 116 subjects were randomly assigned following simple randomization procedures (computerized random numbers) to group N (normal BMI). In the same timeframe (2010–2017), 184 patients with BMI > 30 kg/m² received intravenous propofol – alfentanil during IVF procedure. Of them, 116 were included in the study and assigned to group O (obese). Data analysis was performed for each patient based on medical records, anesthesia charts, and post-anesthetic monitoring sheets. The anesthesia chart for oocyte retrieval procedure was completed

by the anesthetist who administered intravenous anesthesia; whereas the sheets of post-anesthetic monitoring were completed by another anesthetist the patient was handed over to on admission to the post-anesthesia care unit (PACU). All patients were classified according to the American Society of Anesthesiologists (ASA) classification system I–II. Age varied from 18 to 45. The study excluded patients with cardiorespiratory disorders, diabetes, thyroid disorders, chronic opioid and sedative use, allergic reactions to administered anesthetics, opioids, sedatives and nonsteroidal anti-inflammatory drugs.

Anesthetic protocol

All patients underwent a uniform anesthetic protocol. The minimum fasting period was four hours prior to the procedure. Patients preoperatively received low molecular weight heparin for the prevention of thromboembolism. A cubital vein cannula was used to administer premedication.

Hydration was provided by continuous infusion of Ringer lactate solution (10 ml/kg body weight [b. w.]). After positioning, the patient is linked to the mandatory standard monitoring for this type of intervention listed below. After recording the monitoring parameters from pre-induction stage, patients were premedicated with 0.02 mg/kg b. w. intravenous midazolam and 1 mg/kg b. w. diclofenac sodium with 100 ml saline infusion. Anesthesia was induced with propofol 2 mg/kg b. w. and alfentanil 0.01 mg/kg b. w. (Table 1).

Additional propofol was administered to maintain BIS values within the target range (40–60). When needed, muscle relaxation was achieved by intravenous administration of suxamethonium chloride.

In the incidence of apnoea after induction of anesthesia, patients were mechanically ventilated through a facemask or a cuffed oropharyngeal airway with tidal volume of 8 ml/kg b. w. The inspiratory mixture of oxygen and medical air delivered the inspired oxygen concentration of 40% (FiO₂ 0.4).

Monitoring

The standard monitoring included: BIS index, pulse oximetry (SaO₂), level of (partial pressure) of carbon dioxide released at the end of expiration (EtCO₂), peak inspiratory pressure (P_{peak}), plateau airway pressure (P_{plato}), tidal volume (Vt), mean arterial blood pressure (ABP) and electrocardiography (EKG). EtCO₂, P_{peak}, P_{plato} and Vt were determined only in patients where intermittent positive-pressure

Table 1. Anesthetic protocol

Premedication and <i>preemptive analgesia</i>		Induction of anesthesia		Maintenance of anesthesia	
Drugs	Dose (mg/kg b. w.)	Drugs	Dose (mg/kg b. w.)	Drugs	Dose (mg/kg b. w.)
Midazolam	0.02	Propofol	2	Propofol	0.5
Diclofenac	1	Alfentanil	0.01	Suxamethonium chloride	1.5
<i>Ringer's solution</i>				10 ml/kg b. w.	

b. w. – body weight

Table 2. Demographic characteristics, ASA affiliation, procedure, and recovery time

Variables	Group N	Group O	p-value (t-test)
Age (years \pm SD)	34.2 \pm 8.7	33.5 \pm 8.5	0.4471
Body weight (kg \pm SD)	53.4 \pm 14.7	73.5 \pm 23.4	< 0.0001
Body height (cm \pm SD)	162.7 \pm 17.8	163.9 \pm 13.8	0.5055
ASA I affiliation	80 (68.96%)	41 (35.34%)	0.003828 (χ^2 test)
ASA II affiliation	36 (31.04%)	75 (64.66%)	0.002182 (χ^2 test)
Procedure time (min. \pm SD)	17.6 \pm 7.3	24.2 \pm 5.6	< 0.0001
Recovery time (min. \pm SD)	8.5 \pm 4.2	15.3 \pm 3.1	< 0.0001

ASA – American Society of Anesthesiologists; SD – standard deviation; min. – minutes

p > 0.05 – non-significant

p < 0.05 – significant

p < 0.01 – highly significant

ventilation (IPPV) was applied. Parameters were analyzed at following intervals: T_0 – baseline, T_1 – after induction to anesthesia, and T_2 – at the end of the procedure. Clinical parameters were measured by vital sign monitor (BIS™ Complete 2 Channel Monitor, Covidien, Minneapolis, MN, USA) (Medtronic and Monitor Infinity Gamma XL, Dräger, Lübeck, Germany) and anesthesia machine (Fabius Tiro Anesthesia Machine, Dräger).

BIS index is processed electroencephalographs monitor which measures the effects of sedatives and anesthetics on the brain; a new vital sign that allows clinicians to deliver anesthesia with more precision and to assess and respond more appropriately to patients changing condition during surgery [7]. The BIS monitor provides a single number, which ranges from 0 to 100 where the value between 40 and 60 indicates an appropriate level for general anesthesia [8].

Recovery Room / Post-Anesthesia Care Unit

Post-anesthetic monitoring included the following parameters:

- The need for additional analgesia;
- Presence and intensity of pain (we used a modified visual analogue scale (VAS) where pain descriptors were assigned an intensity value. Categories proposed were: 0 – no pain, 1–30 mild, 40–60 moderate, 70–90 severe, 100 – extreme);
- Presence of postoperative nausea and vomiting (PONV);
- The need for administration of ondasetron;
- The length of stay in PACU;
- The overall patient satisfaction with analgesia and sedation (overall anesthetic experience) was assessed by a second anesthesiologist before discharge using a 4 – point verbal scale ranging from very satisfied to very dissatisfied (1 – very dissatisfied, 2 – dissatisfied, 3 – satisfied, 4 – very satisfied).

Statistical Analysis

The analysis of obtained data was performed using the IBM SPSS Statistics software for Windows (IBM Corp. Version 22.0. Armonk, NY, USA) as well as Microsoft Excel 2010. Descriptive statistics was used to determine the relative numbers and measures of the central tendency:

the arithmetic mean (X), a measure of variability, standard deviation (SD) and the relative proportions (percentages).

The monitored parameters were recorded and compared using the Student's t-test and χ^2 test. P-values > 0.05 were considered statistically non-significant, p-values < 0.05 were considered statistically significant, and p-values < 0.01 were considered statistically highly significant for all comparisons.

RESULTS

Data analysis reported no statistical difference ($p > 0.05$, t-test; Table 2) between the groups with respect to age (group N: 34.2 \pm 8.7; group O: 33.5 \pm 8.5) and height (group N: 162.7 \pm 17.8 cm; group O: 163.9 \pm 13.8). The χ^2 test revealed a significant difference ($p < 0.01$; Table 2) between the two groups in the ASA classification. There was a statistically significant difference ($p < 0.01$, t-test; Table 2) between the groups with respect to weight, length of surgery, and recovery time.

Table 3 shows the values of the BIS index, hemodynamic and respiratory parameters (ventilation and oxygenation) obtained during monitoring intervals (T). A comparative analysis (t-test) between the tested groups reported a statistically significant difference, except for the BIS index and pulse values at the T_0 time interval ($p > 0.05$). The χ^2 test reported a statistically significant difference ($p = 0.000181$) with respect to the number of patients requiring IPPV for anesthesia maintenance after introduction. Mechanical ventilation was delivered in 82 patients of group N, compared to 33 patients of group O.

Propofol consumption was statistically higher ($p < 0.0001$, t-test; Table 4) in group O (2.7 \pm 1.6 mg/kg b. w.) compared to group N (2.1 \pm 0.4 mg/kg b. w.). Twenty-four patients in group O required muscle relaxation with suxamethonium to create the state of complete immobilization and optimal conditions for the performance of transvaginal aspiration of ovarian follicles by a gynecologist. In contrast, in group N, suxamethonium was administered to only five patients ($p = 0.000852$, χ^2 test; Table 4).

After induction to anesthesia with propofol (2 mg/kg b. w., intravenous), sufficient spontaneous breathing was preserved in 18 patients in group N and 46 in group O ($p = 0.001855$, χ^2 test; Table 5). Assisted ventilation was

Table 3. Bispectral index, hemodynamic and parameters of ventilation and oxygenation through determining time intervals (T)

T – intervals and parameters	T ₀			T ₁			T ₂		
	Group N	Group O	p-value (t-test)	Group N	Group O	p-value (t-test)	Group N	Group O	p-value (t-test)
BIS index	98.4 ± 1.7	97.7 ± 3.8	0.0714	45.3 ± 5.9	54.1 ± 7.4	< 0.0001	48.4 ± 6.7	57.8 ± 8.9	< 0.0001
Pulse	96.4 ± 12.3	93.1 ± 15.7	0.0761	65.4 ± 11.4	73.5 ± 13.1	< 0.0001	73.8 ± 15.7	83.9 ± 16.3	< 0.0001
ABP _{mean} (mmHg)	82.7 ± 14.1	93.4 ± 11.5	< 0.0001	67.2 ± 9.4	84.4 ± 11.3	< 0.0001	73.9 ± 14.6	91.5 ± 15.2	< 0.0001
SaO ₂ (%)	99.4 ± 0.7	95.3 ± 1.7	< 0.0001	98.5 ± 1.2	95.6 ± 2.1	< 0.0001	98.7 ± 1.7	95.4 ± 2.4	< 0.0001
EtCO ₂ (mmHg – IPPV)	-	-	-	28.4 ± 6.3	35.1 ± 5.5	< 0.0001	27.9 ± 4.8	36.6 ± 4.9	< 0.0001
P _{peak} (mbar – IPPV)	-	-	-	11.3 ± 2.4 (n – 82)*	17.6 ± 1.9 (n – 33)*	< 0.0001	12.5 ± 1.6 (n – 82)*	18.6 ± 2.3 (n – 33)*	< 0.0001
P _{plato} (mbar – IPPV)	-	-	-	9.8 ± 1.8 (n – 82)*	14.4 ± 1.6 (n – 33)*	< 0.0001	10.4 ± 1.6 (n – 82)*	16.5 ± 1.9 (n – 33)*	< 0.0001
Abdominal pressure							11 (9.48%)	46 (39.6%)	0.000029 (χ ² test)

T₀ – baseline; T₁ – after induction to anesthesia; T₂ – at the end of the procedure; Group N – patients with normal body mass index; Group O – obese patients; BIS index – bispectral index; ABP_{mean} – arterial blood pressure; SaO₂ – pulse oximetry; EtCO₂ – carbon dioxide released at the end of expiration; IPPV – intermittent positive pressure ventilation; P_{peak} – peak inspiratory pressure; P_{plato} – plateau airway pressure; p > 0.05 – non-significant; p < 0.05 – significant; p < 0.01 – highly significant

Table 4. Total anesthetics and drugs consumption

Variables (mg/kg b. w.)	Group n	Group O	p-value (t-test)
Propofol	2.1 ± 0.4	2.7 ± 1.6	< 0.0001
Alfentanil	0.01	0.01	-
Suxamethonium chloride	1.5 (n – 5)	1.5 (n – 24)	For n: 0.000852 (χ ² test)
Midazolam	0.02	0.02	-
Diclofenac	1	1	-
Solution of lactated Ringer	10 ml/kg b. w.	10 ml/kg b. w.	-

Data are presented as mean ± standard deviation or n (number of patients); p > 0.05 – non-significant; p < 0.05 – significant; p < 0.01 – highly significant

required in 16 patients in group N and 37 patients in group O (p = 0.009063, χ² test; Table 5). The depressive effect of propofol on the respiratory center caused apnoea in 82 patients of group N and 33 in group O (p = 0.000161, χ² test; Table 5) and here it was necessary to perform IPPV using an anesthesia machine ventilator.

Anesthesia and controlled ventilation were delivered via a facemask. After induction to anesthesia, hypopharyngeal obstruction from tongue displacement was handled with the use of oropharyngeal airway in 24 patients in group N and 88 in group O (p < 0.01, χ² test; Table 5). At the end of the surgery, no statistical differences were reported with respect to applied mode of ventilation. There was no need for endotracheal intubation or placement of a laryngeal mask to maintain an open airway.

Post-operatively, additional analgesic administration (one intravenous dose) was required in 13 (11.2%) patients in group N. In group O, an additional intravenous dose of analgesics was required in 48 (39.66%) patients (p = 0.000113, χ² test; Table 6).

PONV occurred in six patients (5.17%) in group N and nine (7.76%) in group O after applying ondansetron hydrochloride. Comparison of the obtained data using

χ² test did not show a statistically significant difference (p = 0.452795; Table 6).

Duration of PACU stay was longer in group O (13.7 ± 6.3 min.) compared to group N (19.6 ± 7.3 min.). Here, the Student's t-test reported a statistically significant difference (p < 0.0001; Table 6).

Measurement of pain intensity after admission and before discharge to PACU, using the combination of visual and numeric analogue scales, reported higher values in group O compared to group N (p < 0.0001, t-test; Table 6).

Scores based on Satisfaction with Anesthesia Scale revealed no statistical significance between the groups (p = 0.2548, t-test; Table 6).

DISCUSSION

The ideal anesthetic technique for IVF should provide good surgical anesthesia with minimal side effects, a short recovery time, high rate of successful pregnancy, and shortest required duration of exposure. The preferred method of anesthesia and analgesia should be individualized [9].

Using BIS monitor to guide anesthetic administration would allow optimization of drug delivery to the individual needs of each patient in order to avoid unnecessarily deep or too light anesthesia due to overdosage or underdosage of the hypnotic medications [10]. BIS values in both groups signifies that increasing depth of anesthesia was associated with a decrease in BIS values and the decreasing level of anesthesia was associated with increasing BIS values [11].

Benzodiazepines are used for premedication, procedural sedation, and supplementation of general or regional anesthesia. A common sequel to intravenous administration of benzodiazepines is anxiety and anterograde amnesia. These two main characteristics of these drugs make them suitable for patients undergoing unpleasant or repeated procedures, like oocytes retrieval. In both tested groups, premedication with midazolam was found to be

Table 5. The ventilation model and the way of establishing and maintaining the airway

T – intervals and ventilation	T ₀			T ₁			T ₂		
	Group N	Group O	p-value (χ ² test)	Group N	Group O	p-value (χ ² test)	Group N	Group O	p-value (χ ² test)
Spontaneous breathing	116 (100%)	116 (100%)	1	18 (15.5%)	46 (39.6%)	0.001855	83 (71.6%)	68 (58.6%)	0.341715
Assisted ventilation	-	-	-	16 (13.8%)	37 (31.9%)	0.009063	25 (21.6%)	32 (27.6%)	0.405993
Controlled ventilation (IPPV)	-	-	-	82 (70.7%)	33 (28.4%)	0.000161	8 (6.9%)	16 (13.8%)	0.119869
Face mask	-	-	-	116 (100%)	116 (100%)	1	116 (100%)	116 (100%)	1
Oropharyngeal airway	-	-	-	24 (20.7%)	98 (84.5%)	< 0.01	24 (20.7%)	98 (84.5%)	< 0.01
Laryngeal mask	-	-	-	-	-	-	-	-	-
Endotracheal tube	-	-	-	-	-	-	-	-	-

T₀ – baseline; T₁ – after induction to anesthesia; T₂ – at the end of the procedure; Group N – patients with normal body mass index; Group O – obese patients; IPPV – intermittent positive pressure ventilation; p > 0.05 – non-significant; p < 0.05 – significant; p < 0.01 – highly significant

Table 6. Postoperative outcome measures

Variables	Group N	Group O	p-value
Oocytes retrieved (n ± SD)	10.3 ± 3.1	7.6 ± 2.8	< 0.0001 (t-test)
The need for additional analgesia	13 (11.2%)	46 (39.66%)	0.000113 (χ ² test)
Postoperative nausea and vomiting	6 (5.17%)	9 (7.76%)	0.452795 (χ ² test)
Average postoperative VAS pain scores (0–100 mm ± SD) (entrance/exit PACU)	14.7 ± 7.1 / 21.4 ± 12.3	26.8 ± 12.2 / 47.2 ± 13.4	< 0.0001 / < 0.0001 (t-test)
Ondansetron hydrochloride	6 (5.17%)	9 (7.76%)	0.452795 (χ ² test)
Length of PACU stay (min. ± SD)	13.7 ± 6.3	19.6 ± 7.3	< 0.0001 (t-test)
Patient satisfaction score (1–4 ± SD)	3.4 ± 0.5	3.3 ± 0.8	0.2548 (t-test)

SD – standard deviation; min. – minutes; PACU – post-anesthesia care unit; p > 0.05 – non-significant; p < 0.05 – significant; p < 0.01 – highly significant

an adequate means to address fear and anxiety and create optimal conditions for puncture and aspiration of ovarian follicles. Although minimal amounts of this benzodiazepine were found in follicular fluid, no detrimental effects have been proven so far [12]. Furthermore, midazolam enhances the postoperative analgesic effects of diclofenac when used before the onset of noxious stimuli [13].

The pain during oocyte retrieval is caused by the puncture of the vaginal skin and ovarian capsule by the aspirating needle as well as manipulation within the ovary during the entire procedure [14]. Here it becomes customary for the anesthetist to provide adequate pain relief to immobilize the patient and eliminate the danger of piercing any vessels during the process of oocyte retrieval. The ideal pain relief during oocyte retrieval should be effective and safe, easy to administer and monitor; short acting and readily reversible with few side effects [15, 16].

There are animal studies that bring impressive evidence of the efficacy of prior administration of non-steroidal anti-inflammatory analgesics in treatment of inflammatory diseases [17]. Preemptive administration of non-steroidal anti-inflammatory drugs reduces the average perioperative consumption of opioid analgesics. In their retrospective study, Mialon et al. [18] compared two analgesic protocols: paracetamol/alprazolam and nefopam/ketoprofen on IVF outcomes. They found that both groups had similar IVF

outcomes and nefopam/ketoprofen protocol enhanced patient comfort without jeopardizing the IVF success rates. Women can be offered adequate pain relief. Opioids are used in oocyte retrieval procedure primarily for their analgesic effects. The most frequently used are fentanyl, alfentanil, and remifentanyl, because of their pharmacokinetic profile that enhances fast track anesthesia.

Pethidine is used in some cases as an agent of premedication. The amount of alfentanil is not associated with adverse effects on fertilization rate, embryo development, or clinical pregnancy rate [19]. Both of the groups received propofol for induction and maintenance of anesthesia. Propofol is the most commonly used intravenous anesthetic agent in sedation and general anesthesia. Its pharmacokinetic profile makes propofol anesthetists' first choice. It provides rapid induction and easy maintenance in continuous infusion or fractionated doses.

Several studies investigate the effect of this agent on IVF success with conflicting results [20–25]. Of the studies investigating toxicity, two of them relate propofol with negative effects on the reproductive outcome, and five studies conclude with the opposite result [20–25].

According to these findings, propofol is probably a safe choice, but caution is recommended since Propofol also accumulates in the follicular fluid [24]. Its hemodynamic effect results in a decrease in arterial blood pressure and

pulse [26]. However, in both groups of subjects, this decrease was within physiological limits. Increased values of arterial blood pressure and pulse in obese patients should be associated to increased sensitivity to pain during aspiration of ovarian follicles. This is conditioned by the difficulty in accessing ovaries in obese women, when surgeons often require assistance by compressing the lower abdomen. These additional manipulations can lead to unconscious movement of patients and in this way increase the risk of aspiration needle damaging the surrounding anatomical structures. In order to prevent this, it is often necessary to administer additional dose of propofol and sometimes use short-acting muscle relaxants such as suxamethonium. This may explain the higher consumption of propofol (mg/kg b. w.) and the more frequent use of relaxants in obese patients. The administered induction dose of propofol (2 mg/kg b. w.) in certain patients of both groups, resulted in the cessation of breathing or decreased pulmonary ventilation, to the extent that it was necessary to apply assisted or controlled ventilation.

Propofol is widely used for anesthesia and sedation purposes because of its amnesic effect, fast recovery, and low incidence of nausea and vomiting. Propofol, however, has the shortcoming of severe respiratory depression, including a decrease in ventilatory response to hypoxia and in tidal and minute volumes [27].

The problem of securing and maintaining an open airway has been known. In this study, for the purpose of securing the airway and providing adequate ventilation, it was necessary to use an oropharyngeal tube in almost two-thirds (84.5%) of obese patients. There was no need for laryngeal mask and endotracheal intubation in neither of groups of patients. Delivering controlled ventilation using an anesthesia machine ventilator through the full-face mask with or without the assistance of an oropharyngeal airway was accompanied with statistically higher values of ventilation parameters (EtCO_2 , P_{peak} and P_{plato}) in group O compared to group N. Abdominal compression caused an increase in intra-abdominal pressure, cranial displacement of the diaphragm, decrease in lung and chest wall compliance, and an increase in airway resistance, which, paired with obesity, resulted in significantly higher P_{peak} and P_{plato} values in O group.

REFERENCES

1. Kwan I, Bhattacharya S, Knox F, McNeil A. Pain relief for women undergoing oocyte retrieval for assisted reproduction. *Cochrane Database Syst Rev.* 2013; 1:CD004829.
2. Gejervall AL, Stener-Victorin E, Möller A, Janson PO, Werner C, Bergh C. Electro-acupuncture versus conventional analgesia: A comparison of pain levels during oocyte aspiration and patients' experiences of well-being after surgery. *Hum Reprod.* 2005; 20(3):728–35.
3. Girish PJ. Perioperative Management of an Adult Obese Patient for Ambulatory Surgery: An Update. *Curr Rev Nurs Anesth.* 2013; 36(15):181–92.
4. Aghaamoo S, Azmoodeh A, Yousefshahi F, Berjis K, Ahmady F, Qods K, et al. Does Spinal Analgesia have Advantage over General Anesthesia for Achieving Success in In-Vitro Fertilization? *Oman Med J.* 2014; 29(2):97–101.
5. Jarahzadeh MH, Davar R, Hajiesmaeili MR, Entezari A, Musavi F. Remifentanyl versus fentanyl for assisted reproductive technologies: effect on hemodynamic recovery from anesthesia and Outcome of ART Cycles. *Int J Fertil Steril.* 2011; 5(2):86–9.
6. Ben-Shlomo I, Moskovich R, Golan J, Eyal V, Tabak A, Shalev E. The effect of propofol anaesthesia on oocyte fertilization and early embryo quality. *Hum Reprod.* 2000; 15(10):2197–9.
7. Johansen JW, Sebel PS, Sigl JC. Clinical impact of hypnotic-titration guidelines based on EEG bispectral index (BIS) monitoring during routine anesthetic care. *J Clin Anesth.* 2000; 12(6):433–43.
8. Circeo L, Grow D, Kashikar A, Gibson C. Prospective, observational study of the depth of anesthesia during oocyte retrieval using a total intravenous anesthetic technique and the Bispectral index monitor. *Fertil Steril.* 2011; 96(3):635–7.

The difficulty in accessing ovarian follicles in obese women requires additional surgical manipulations, resulting in additional administration of analgesics during the patient's stay at PACU. This may partly explain the higher PONV rate and the need for introducing antiemetics in O group.

As an intravenous anesthetic, propofol shows a rapid rate of metabolism, resulting in quick recovery from anesthesia with few side effects. Because of the low incidence of nausea and vomiting, propofol is commonly used for anesthesia induction and maintenance in ambulatory surgery.

An anesthetic protocol that involved the use of sedatives (midazolam), intravenous anesthetics (propofol) and opioids (alfentanil) resulted in a high degree of patient satisfaction with anesthesia. Developments in medical technology have resulted in a rapid increase in the use of ambulatory surgery. The use of fast- and short-acting anesthetics, analgesics, and muscle relaxants, as well as improved brain monitoring techniques, has reduced anesthetic complications during recovery. Additionally, improvements in surgical techniques have allowed surgeons to perform more invasive surgical procedures and complex medical procedures on an ambulatory basis [28].

CONCLUSION

Intravenous anesthesia with propofol and alfentanil has created adequate conditions for the aspiration of ovarian follicles. Midazolam was found to be the ideal means for premedication and creation of favorable conditions for the patient to undergo the procedure. Preemptive administration of diclofenac reduced the preoperative consumption of alfentanil. During their stay in PACU, these patients experienced mild, or no pain. Induction and maintenance of anesthesia for IVF in obese patients results in increased consumption of propofol and a more frequent need for muscular relaxation. However, the recovery was fast and followed by a low PONV rate. Therefore, the very first assessment of the patients who underwent the procedure under intravenous anesthesia with propofol and alfentanil is the best recommendation for clinical practice.

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9. Sharma A, Borle A, Trikha A. Anesthesia for in vitro fertilization. *J Obstet Anaesth Crit Care*. 2015; 5(2):62–72.
10. Sebel PS. Can we monitor depth of anesthesia? *Anesth Analg*. 2001; 93(6):94–8.
11. Liu J, Singh H, White PF. Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. *Anesth Analg*. 1997; 84(1):185–9.
12. Liang FG, Shi YS, Ding H, Zhou W, Gu MN. Application of subclinical doses of pentazocine and propofol in painless vaginal egg retrieval. *NanFang Yi Ke Da Xue Xue Bao*. 2011; 31(2):373–6.
13. Hasani A, Maloku H, Sallahu F, Gashi V, Ozgen SU. Preemptive analgesia with midazolam and diclofenac for hernia repair pain. *Hernia*. 2011; 15(3):267–72.
14. Stener-Victorin E. The pain-relieving effect of electro-acupuncture and conventional medical analgesic methods during oocyte retrieval: a systemic review of randomized controlled trials. *Hum Reprod*. 2005; 20(2):339–49.
15. Cerne A, Bergh C, Borg K, Ek I, Gejervall AL, Hillensjo T, et al. Pre-ovarian block versus paracervical block for oocyte retrieval. *Hum Reprod*. 2006; 21(11):2916–21.
16. Katzenschlager SMS, Wolfer MM, Langenecker SAK, Sator K, Sator PG, Li B, et al. Auricular electro-acupuncture as an additional perioperative analgesic method during oocyte aspiration in IVF treatment. *Hum Reprod*. 2006; 21(8):2114–20.
17. Kissin I. Preemptive analgesia. *Anesthesiology*. 2000; 93(4):1138–43.
18. Mialon O, Delotte J, Lehert P, Donzeau M, Drici M, Isnard V, et al. Comparison between two analgesic protocols on IVF success rates. *J Gynecol Obstet Biol Reprod*. 2011; 40(2):137–43.
19. Gejervall AL, Lundin K, Stener-Victorin E, Bergh C. Effect of alfentanil dosage during oocyte retrieval on fertilization and embryo quality. *Eur J Obstet Gynecol Reprod Biol*. 2010; 150(1):66–71.
20. Piroli A, Marci R, Marinangeli F, Paladini A, Di Emidio G, Giovanni Artini P, et al. Comparison of different anaesthetic methodologies for sedation during in vitro fertilization procedures: effects on patient physiology and oocyte competence. *Gynecol Endocrinol*. 2012; 28(10):796–9.
21. Vincent Jr RD, Syrop CH, van Voorhis BJ, Chestnut HD, Sparks TEA, McGrath MJ, et al. An evaluation of the effect of anesthetic technique on reproductive success after laparoscopic pronuclear stage transfer. Propofol/nitrous oxide versus isoflurane/nitrous oxide. *Anesthesiology*. 1995; 82(2):352–8.
22. Huang HW, Huang FJ, Kung FT, Tsai MY, Lin H, Chang SY. Effects of induction anesthetic agents on outcome of assisted reproductive technology: a comparison of propofol and thiopental sodium. *Chang Gung Med J*. 2000; 23(9):513–19.
23. Jarahzadeh MH, Jouya R, Mousavi FS, Dehghan-Tezerjani M, Behdad S, Soltani HR. Propofol or Thiopental sodium in patients undergoing reproductive assisted technologies: differences in hemodynamic recovery and outcome of oocyte retrieval: a randomized clinical trial. *Iran J Reprod Med*. 2014; 12(1):77–82.
24. Matsota P, Sidiropoulou T, Batistaki C, Giannaris D, Pandazi AE, Krepi H, et al. Analgesia with remifentanyl versus anesthesia with propofol-alfentanil for transvaginal oocyte retrieval: a randomized trial on their impact on in vitro fertilization outcome. *Middle East J Anaesthesiol*. 2012; 21(5):685–92.
25. Christiaens F, Janssenswillen C, Verborgh C, Verborgh C, Moerman I, Devroey P, et al. Propofol concentrations in follicular fluid during general anaesthesia for transvaginal oocyte retrieval. *Hum Reprod*. 1999; 14(2):345–8.
26. de Wit F, van Vliet AL, de Wilde RB, Jansen JR, Vuyk J, Aarts LP, et al. The effect of propofol on haemodynamics: cardiac output, venous return, mean systemic filling pressure, and vascular resistances. *Br J Anaesth*. 2016; 116(6):784–9.
27. Lee MH, Yang KH, Lee CS, Lee HS, Moon SY, Hwang SI, et al. The effect-site concentration of propofol producing respiratory depression during spinal anesthesia. *Korean J Anesthesiol*. 2011; 61(2):122–6.
28. Lee JH. Anesthesia for ambulatory surgery. *Korean J Anesthesiol*. 2017; 70(4):398–406.

Анализа примењене технике интравенске анестезије за вантелесну оплодњу код гојазних болесница и болесница са нормалним индексом телесне масе

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САЖЕТАК

Увод/Циљ Ретроспективно се анализирао примењена интравенска анестезија пропофолом и алфентанилом у вантелесној оплодњи код гојазних болесница и болесница са нормалним индексом телесне масе коришћењем биспектралног индекса као индикатора дубине анестезије.

Метод Групу *N* сачињавало је 116 болесница са нормалним индексом телесне масе, а групу *O* 116 болесница са индексом телесне масе > 30 kg/m². Протокол анестезије састојао се од мидазолама за премедијацију, диклофенака за пре-емптивну аналгезију, индукције и одржавања анестезије пропофолом, аналгезије алфентанилом, суксаметионијума за мишићну релаксацију уколико је неопходна. Мониторовани параметри били су забележени и упоређивани коришћењем *t*-теста и χ^2 теста.

Резултат Трајање процедуре и опоравак дужи су у групи *O* ($p < 0,01$). Статистички високо значајна разлика ($p = 0,000181$) постоји при упоређивању броја болесница из испитиваних

група којима је била неопходна механичка вентилација након индукције у анестезију и њеном одржавању. Потрошња пропофола је статистички значајно већа ($p < 0,0001$) у групи *O* ($2,7 \pm 1,6$ mg/kg) у поређењу са групом *N* ($2,1 \pm 0,4$ mg/kg). Постоперативна мучнина и повраћање јавили су се код шест (5,17%) болесница групе *N* и девет (7,76%) болесница групе *O*. Интензитет бола је већи у групи *O* у односу на групу *N* ($p < 0,0001$). Вербална скала задовољства болесница анестезијом и седацијом није дала статистичку значајност између група *N* и *O* ($p = 0,2548$).

Закључак Индукција и одржавање анестезије код гојазних болесница резултира већом потрошњом пропофола и потребом за мишићном релаксацијом. Сама оцена болесница примењене технике интравенске анестезије пропофолом и алфентанилом њена је најбоља препорука за клиничку праксу.

Кључне речи: аспирација јајних ћелија; бол; пропофол; алфентанил; телесна тежина