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# Efficacy of bispectral index monitoring for prevention of anesthetic awareness and complications during oocyte pick-up procedure

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**Background/aim:** This study was planned by considering that the use of bispectral index (BIS) monitoring ensures sufficient depth of anesthesia and avoids anesthetic awareness and patient movement in the oocyte pick-up (OPU) procedure.

**Materials and methods:** Ninety-eight patients undergoing OPU were randomly divided into 2 groups as the control group (n = 48) and BIS group (n = 50). After propofol and remifentanil induction, the control group was given additional propofol according to reaction response, while the BIS group was given propofol at BIS values of 60 and above with the aim that BIS values be 40–60. Total procedure time, recovery time, patient movement, additional propofol consumption, total number of oocytes, and awareness during anesthesia were recorded.

**Results:** Demographic data were similar in the two groups ($P > 0.05$ for all). The recovery time in the BIS group was significantly shorter compared to the control group ($P < 0.001$) while additional propofol consumption was found to be significantly lower ($P < 0.001$). Baseline BIS values fell compared to all other times after induction significantly ($P < 0.001$). No patient had anesthesia awareness.

**Conclusion:** During the OPU procedure BIS monitoring is considered to prevent anesthesia awareness, intraoperative movement, and complications caused by insufficient anesthetic use as it ensures optimal doses of anesthetic agents used and early recovery.

**Key words:** Oocyte pick-up, bispectral index, anesthesia awareness, intraoperative patient movement

## 1. Introduction

Defined as the collection of oocytes after controlled overstimulation, the oocyte pick-up (OPU) procedure constitutes an important stage of in vitro fertilization (IVF) treatment. Previously this procedure was only performed with laparoscopy under general anesthesia, but currently it is completed with transvaginal ultrasound guidance (1). Anesthetic options for the procedure can be vary from minimal sedation (known as conscious sedation) to deep sedation, or general anesthesia or regional anesthesia techniques may be used (2). Though regional methods where the patient is awake or conscious sedation where the patient can cooperate appear to be the most appropriate, high anxiety levels in patients may lead to the selection of deep sedation or general anesthesia methods (2,3). Whatever the method chosen, in addition to reliable effective analgesia and anesthesia, the aim should be patient discharge with rapid recovery and minimal side effects (4).

During OPU, complications that develop may be linked to sterility or anesthetic administration, or may occur linked to injury of the neighboring pelvic organs and veins by the aspiration needle during the procedure (2,5). While it may appear to be a surgical complication, this situation may occur due to insufficient anesthetic level during the procedure not preventing patient movement, increasing the importance of anesthetic administration. Another complication related to insufficient anesthesia level is anesthesia awareness. This situation, defined as the patient clearly remembering sensory perception during general anesthesia, occurs in procedures with short operation time just as it does in other operations (6). While intraoperative anesthetic depth was previously evaluated with clinical findings like blood pressure and heart rate, since 1998 electroencephalogram-based bispectral index (BIS) monitoring showing cerebral cortex activity entered use for this purpose with Food and Drug Administration approval (7). While it was determined that propofol consumption, extubation time, and recovery period were reduced with BIS monitoring (8), broader series studies have shown that BIS monitoring prevents nearly 80% of awareness in paralytic patients (cesarean, cardiac surgery,

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bronchoscopy, etc.) where neuromuscular blockage is used and anesthetic awareness is commonly observed (9,10).

This study was completed by considering that the use of BIS monitoring for the OPU procedure under general anesthesia will ensure appropriate anesthetic depth with the use of sufficient anesthetic medication, and also may prevent both anesthetic awareness and patient movement, thus increasing the success rate of the procedure and preventing complications.

## 2. Materials and methods

### 2.1. Patients

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethics committee approval was received for this study from the Scientific Research Ethics Committee of Kahramanmaraş Sütçü İmam University (Protocol No: 224, 2015/17). Informed consent was obtained from all individual participants included in the study. The study included patients above the age of 18 years applying for IVF to the assisted reproduction treatment center undergoing the OPU procedure under general anesthetic before the IVF procedure with physical status I–II according to American Society of Anesthesiologists (ASA). Exclusion criteria included any comorbid disease, chronic medication use, and body mass index of ≥30. Between 28.11.2015 and 15.02.2016, 102 patients met the criteria and 4 of those patients did not agree to participate, so the remaining 98 patients provided written consent and were included in the study. Randomization of patients before anesthesia was completed by pulling numbered balls from a bag. The patients were divided into 2 groups as a control group (n = 48) and the BIS group (n = 50) (Figure 1). Patients were given noninvasive blood pressure (NIBP), heart rate (HR), pulse oximetry ($SpO_2$), and 3-lead ECG monitoring and baseline hemodynamic data and demographic data (age, weight, height, ASA status) were recorded. Before the anesthesia induction, patients in the BIS group had 4 BIS electrodes (BIS-XP Quatro Sensor) stuck on their foreheads and connected with a BIS device (BIS-XP, A-2000, Aspect Medical Systems, Newton, MA, USA) and baseline BIS values were recorded. Anesthesia induction used 2 mg/kg IV propofol (propofol 1% ampoule, Fresenius Kabi, Germany) and 1 μg/kg IV remifentanil (Ultiva 2 mg vial, Glaxo SmithKline, UK) as the standard with 2% sevoflurane (Sevorane liquid, Abbott, USA), and 50% / 50% $O_2$ / air administered through a face mask for anesthesia maintenance. It was decided that patients would have 10–20 mg propofol IV bolus additionally administered according to conventional reactional responses (sudden increase in blood pressure and pulse, spontaneous difficulty

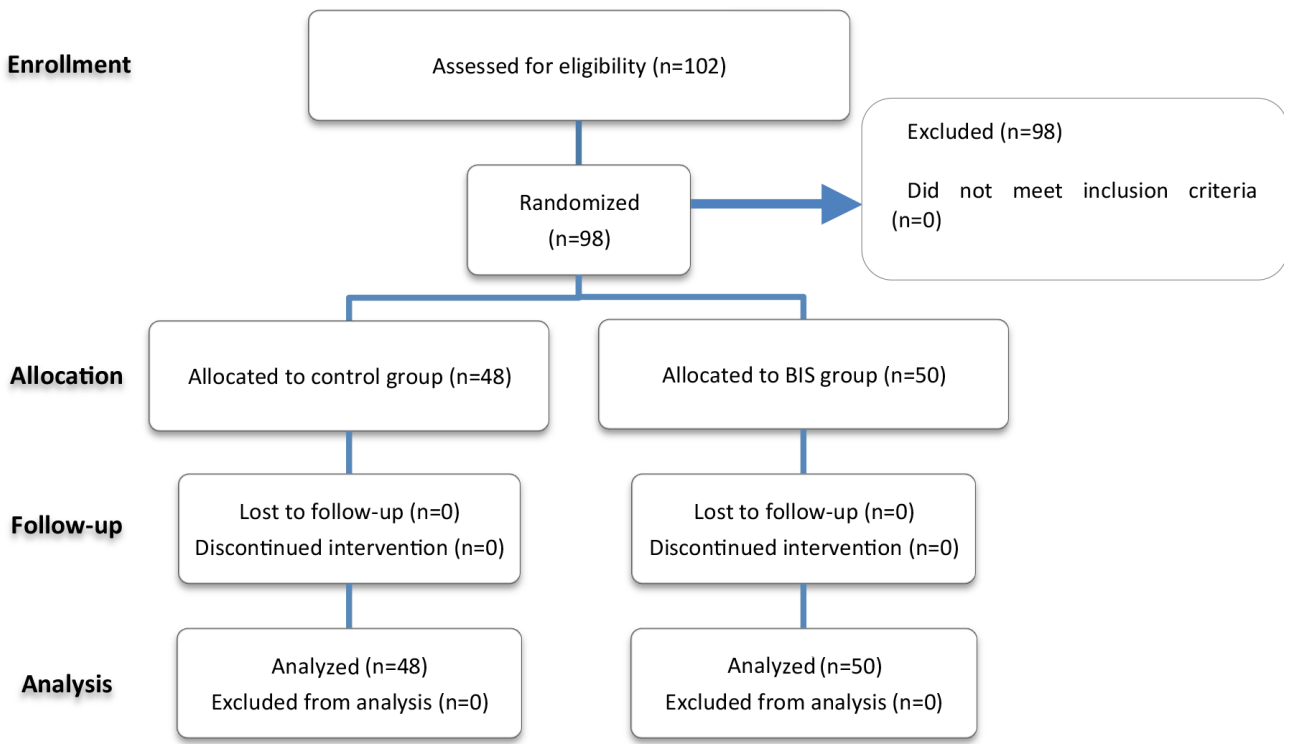


**Figure 1.** The randomized trial flow diagram, including enrollment, allocation, and analysis.

with respiration, recoil of extremities, etc.) in the control group patients, and the same was administered to patients with BIS values of 60 and above, aiming to have BIS values from 40 to 60 (11) in patients with BIS monitoring. BIS provides information about cortical activity on a scale from 100 to 0 with lower values showing increased level of hypnosis. Accordingly, patients with scores of 95–100 are awake, of 70–95 have minimal sedation, of 60–70 have deep sedation, and of 40–60 are under general anesthesia (9,12). A transvaginal ultrasound device was used and the OPU procedure was begun with aspiration using an oocyte aspiration needle on the follicles of both ovaries through the lateral vaginal fornix route. All patients had NIBP, HR, and $SpO_2$ values, and in the BIS group BIS values, recorded simultaneously preoperatively, immediately after anesthesia induction, at 5 and 15 min, and at the end of the procedure. Total procedure duration (beginning with IV anesthesia induction and ending when the patient awoke after anesthetics were ceased at the end of the OPU procedure), recovery duration (beginning when patients woke after the procedure until the modified Alderete score was ≥8 in the recovery unit), upper extremity patient movement in the intraoperative period during the procedure, additional propofol consumption, and collected oocyte numbers recorded. Anesthesia awareness was evaluated in the recovery room after the procedure. Patients were asked if they remembered the healthcare personnel talking to them during the procedure and if they awoke or not with pain during the procedure. Additionally, postoperative nausea-vomiting and side effects were recorded, and patients were also asked about anesthetic awareness. While all patients were administered 75 mg of IM diclofenac sodium (Diclomec 3 MI 75 mg amp., Abdi İbrahim, Turkey) intraoperatively for analgesia, patients with nausea-vomiting complaints were administered 10 mg of IV metoclopramide in the postoperative period. To prevent the surgical and anesthesia teams carrying out measurements from influencing each other, data were collected by a third person external to the study and data headings from both groups were sent for statistical assessment coded so that the third person not participating in the study could understand it.

### 2.2. Statistical analysis

Analysis of data was completed using SPSS 22.0 (IBM Corp., Armonk, NY, USA) and PAST 3 (https://folk.uio.no/ohammer/past/) programs. Normality of data was tested with the Lilliefors corrected Kolmogorov–Smirnov test for univariate data, while the Mardia test was used for multivariate data and variance homogeneity was assessed with the Levene test. Independent two-group comparison used the independent samples t-test bootstrap results while the Mann–Whitney U test used the Monte Carlo simulation technique. To investigate interactions between dependent variable groups, from parametric methods the general linear model-repeated ANOVA test was used, while for post hoc analysis the Bonferroni test was used. From nonparametric methods, Friedman's two-way test Monte Carlo simulation technique was evaluated and post hoc analyses used the nonparametric post hoc test and LSD test. Comparison of categorical variables was tested with the Fisher exact test results. Quantitative data are given in tables as mean ± standard deviation and median range (minimum–maximum), while categorical data are stated as n (number) and percentage (%). $P < 0.05$ was accepted as significant. In the power analysis (R 3.3.2 program language) conducted while planning the study, the power of the test obtained in respect to propofol values was at a significance level of 0.05 for a difference of 20 between the BIS and control groups and a power of 99.93% was obtained for a BIS group of n = 50 and a control group of n = 48.

## 3. Results

There was no statistical difference between patients in both groups with mean age, weight, height, mean total procedure time, and oocyte counts given in Table 1 (all $P > 0.05$). The baseline mean BIS values for patients in the BIS

**Table 1.** Demographic characteristics (age, height, weight, total procedure duration, number of oocytes, recovery duration) and additional propofol consumption.

| | Control (n = 48) | BIS (n = 50) | P-value |
|---|---|---|---|
| Age | 34.00 ± 5.73 | 34.80 ± 5.38 | 0.478 |
| Weight | 69.63 ± 8.59 | 69.84 ± 7.54 | 0.895 |
| Height | 160 (155–172) | 160 (155–170) | 0.780 |
| Total procedure duration (min) | 16 (12–20) | 16 (12–21) | 0.568 |
| Additional propofol consumption (mg) | 40 (0–100) | 20 (0–60) | <0.001 |
| Recovery duration (min) | 6 (4–8) | 5 (3–7) | <0.001 |
| Oocyte number | 8 (1–26) | 6 (0–31) | 0.598 |

Independent t-test (bootstrap) – Mann–Whitney U test (Monte Carlo); $P < 0.01$ = highly significant, $P > 0.05$ = nonsignificant.

group were between 95 and 98. Comparing BIS values after anesthesia induction with baseline values, at all times they were determined to fall by a significant amount (P < 0.001). Compared to baseline values, values at all times were low, with an increase identified over time in parallel to the level of anesthesia. There was no significant difference between the values after induction and in the intraoperative 5th minute (P > 0.05), with the increase in BIS values from the intraoperative 15th minute being statistically significant (P < 0.001) (Table 2; Figure 2). No patient participating in the study had anesthesia awareness.

When the patient recovery times were compared, in the BIS group they were significantly low compared to the control group (P < 0.001) (5 (3–7) min, 6 (4–8) min, respectively). Additional propofol consumption during the procedure was lower by a significant degree in the BIS group when compared with the control group (P < 0.001) (20 (0–60) mg, 40 (0–100) mg, respectively) (Table 1).

**Table 2.** Bispectral index scores of patients according to time.

| BIS score (n = 50) | | Median (min–max) | P-value | |
|---|---|---|---|---|
| Preoperative | = I | 98 (95–98) | I→II | <0.001 |
| | | | I→III | <0.001 |
| After induction | = II | 41 (30–54) | I→IV | <0.001 |
| | | | I→V | 0.002 |
| Intraop 5th min | = III | 46 (38–58) | II→III | >0.05 |
| | | | II→IV | <0.001 |
| Intraop 15th min | = IV | 50.5 (42–58) | II→V | <0.001 |
| | | | III→IV | <0.001 |
| End of procedure | = V | 81 (76–87) | III→V | <0.001 |
| | | | IV→V | <0.001 |

Friedman test (Monte Carlo) post hoc test: nonparametric post hoc test; P < 0.01= highly significant, P > 0.05= nonsignificant.

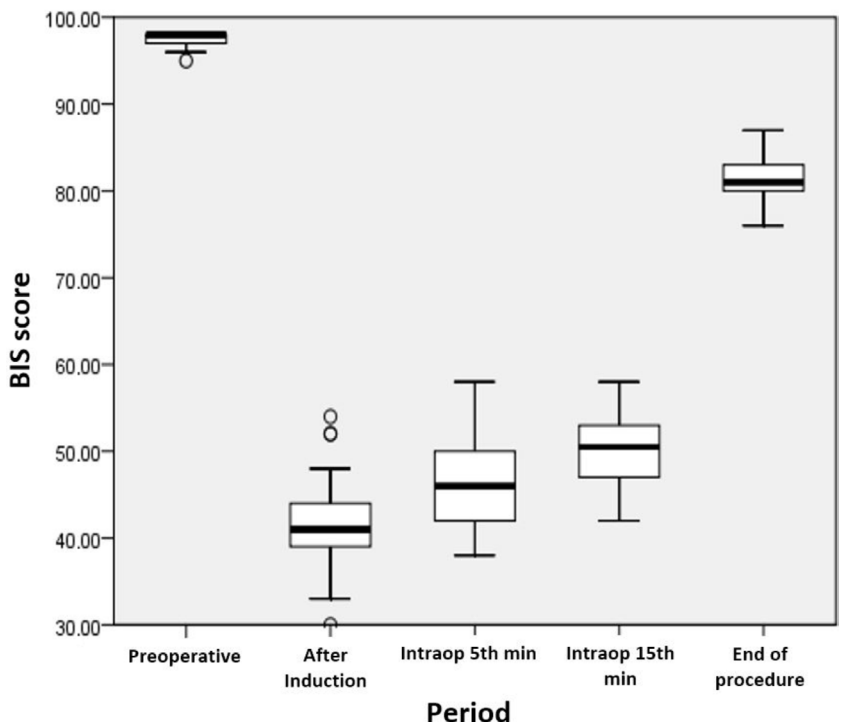


**Figure 2.** Change in bispectral index (BIS) scores depending on time.

When patient movement during the intraoperative period was examined, 9 patients in the control group had slight extremity movement while 2 patients did in the BIS group (P = 0.026).

When hemodynamic data were examined, there was no statistical difference in MAP, HR, and $SpO_2$ values at baseline, during the operation, or at the end of the procedure. During the whole procedure no emergency situation requiring medical intervention occurred.

In one patient in each of the control and BIS groups nausea-vomiting developed; however, this was not identified to be statistically significant. No patient had side effects like laryngeal-bronchial spasm or aspiration.

**4. Discussion**

The OPU is a short procedure completed using a variety of anesthetic methods in clinics. Generally in centers without an anesthesiologist, cooperation is established with the patient and a conscious sedation technique minimizing risk factors for the respiratory tract is chosen. Accompanied by anesthesiologists, regional anesthetic methods, deep sedation, and even general anesthesia administration are used at varying rates (2,4,13). Whichever method is chosen, the desired result is early recovery and early discharge with fewer side effects for the outpatient surgical procedure of OPU using appropriate short-effect anesthetic medications and methods (14). In parallel to the study by Hong et al., which found that the amount of propofol used for conscious sedation was higher in the high-anxiety group compared to the low-anxiety group (15), as the majority of patients at our center had high anxiety levels, deep sedation with a mask or general anesthesia methods are chosen for these patients. While the majority of anesthetic agents are IV agents used alone or with inhalation agents, propofol, remifentanil, and alfentanil are mainly chosen due to their short effect duration and rapid recovery properties (16). At our clinic, propofol, remifentanil, and an inhalation agent are administered together. As the procedure is short, it is difficult to optimize the dose of the anesthetic agents used, which may cause a range of problems linked to anesthetic awareness or not ensuring sufficient anesthetic depth. The most important clinical finding of inadequate anesthesia is patient movement and increased breathing rate due to response to nociceptive stimuli (6). However, patient movement during the OPU procedure when a needle is used to enter the vaginal fornix may cause injury and perforation of neighboring tissue and veins (2). This study used BIS monitoring aiming to prevent anesthetic awareness, ensure sufficient anesthetic depth by optimizing the dose of propofol, and prevent secondary complications linked to patient mobilization. Studies have reported positive effects of BIS monitoring under general anesthesia to ensure assessment of anesthetic depth, to limit insufficient or overdose amounts of anesthetic agents, and most importantly to prevent anesthesia awareness (17,18). In the study group the mean BIS values varied from 30 to 98 in the BIS group, while more importantly there was a significantly lower rate of intraoperative movement observed compared to the patients in the control group without BIS monitoring. Though in neither group did any complication linked to intraoperative movement of patients develop, the significantly lower rate of movement in the BIS group shows that BIS monitoring can reduce the development of complications. Additionally, the additional propofol consumption in the groups after induction was significantly lower in BIS group compared to control group, similar to the results of studies by Circeo et al. and Saleh et al. on BIS monitoring for OPU procedures (3,19). The recovery duration was significantly shorter in the BIS group compared to the control group. These results show that the use of BIS monitoring ensures optimization of anesthetic agents, prevents administration of unnecessary overdose or shallow anesthesia, and ensures a short recovery period for clinics with high patient circulation (3). The study determined that no patient had anesthetic awareness in the intraoperative period, even in patients with intraoperative movement observed. This situation shows that in OPU patients with intraoperative movement anesthesia awareness may not be present, but this does not mean that BIS monitoring has no benefit to prevent anesthetic awareness. Anesthetic awareness is observed in general anesthesia procedures where neuromuscular blockers are used and patients feel intraoperative sensory stimuli but cannot move (6). Similar to our administration, during the OPU procedure where neuromuscular blockers are generally not used, the cause of intraoperative movement observed in patients may be low anesthesia or analgesia levels and it is logical to say that the possibility of anesthetic awareness being observed among these patients is high.

The present study showed that there was no significant difference in the baseline, intraoperative, and postoperative hemodynamic parameters or postoperative nausea and vomiting. It is known that propofol has a particularly greater effect on hemodynamic parameters in the elderly or patients with disordered hemodynamics. It reduces cardiac output and systemic vascular resistance, lowering blood pressure in a dose-linked fashion (20). Here hemodynamic changes were not observed, which may be explained by the majority of patients undergoing OPU being relatively young patients with no comorbid diseases (4). Again the low nausea-vomiting rate may be explained by the procedure being short, the total anesthetic and analgesic amounts consumed being relatively low compared to other operations, and most importantly propofol having proven antiemetic efficacy (20).

A limitation of this study is that propofol and remifentanil, usually administered by total intravenous anesthesia (TIVA) and target-controlled infusion (13,14) for these types of procedures, were administered by intermittent IV push and as a result it appears that the anesthetic and analgesic consumption could not be calculated in a sensitive manner. The reason for choosing this method is that we wanted to avoid continuous medication administration using TIVA or target-controlled infusion. Some studies have identified that after anesthetic administration using IV analgesics like midazolam and propofol and opioids, they pass very quickly into the follicular fluid aspirated from the ovary and over time this amount increases (21,22). Although Bümen et al. (23) claimed that propofol and remifentanil do not change egg quality and fertilization rates, some studies have observed contrary harmful effects (24,25). In our study the anesthetic medication levels in aspirated follicular fluid were not examined; however, in patients in both groups similar numbers of eggs were recovered in accordance with the known follicle numbers in the preoperative period.

Anesthetic administration for OPU is a short-duration procedure where ensuring sufficient anesthesia levels is important for the success of the procedure and to prevent complications. With this aim, BIS monitoring ensures the use of anesthetic agents at optimal doses and as a result reduces the consumption of anesthetic agents, providing early recovery and preventing side effects linked to medication. It is considered to prevent anesthetic awareness caused by insufficient anesthetic agent use and prevent intraoperative movement and linked complications.

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