



Comparison of recovery time of ketamine versus nalbuphine used in combination with propofol in females undergoing in-vitro fertilization under intravenous sedation.

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INTRODUCTION

Day care surgery has become immensely popular throughout the world. The major advantage of the day care surgery is cost effectiveness, early discharge and less stress to the patient. Early recovery time from anesthesia is the main goal in day care surgeries.¹ There are many methods of anesthesia for patients undergoing day care surgeries like general anesthesia with inhalations or intravenous sedation, regional anesthesia or total intravenous sedation with analgesia. The ideal anesthetic technique for a day care surgery should provide good surgical anesthesia with minimum stress, a short recovery time, shortest duration of exposure and maximum comfort to patient along with less postoperative side effects.^{2,3} In-vitro fertilization is one of the procedure done as a day care surgery. Women coming for in-vitro fertilization are extremely anxious and under great stress. They also experience mild to moderate

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ABSTRACT... Objective: To compare the mean recovery time after administration of propofol-ketamine versus propofol-nalbuphine combination in patients undergoing in-vitro fertilization procedures under intravenous sedation. **Study Design:** Randomized control trial. **Setting:** Department of Anesthesiology, Hameed Latif Hospital, Lahore. **Period:** 14/11/2016 to 14/11/2017. **Material & Methods:** 60 Married females of age between 20 to 35 years undergoing elective in-vitro fertilization surgeries of ASA I and II with weight 50-70 kg were included. Group A was treated with nalbuphine and propofol while group B with ketamine and propofol and mean recovery time was calculated. **Results:** In this study there were total 60 cases, 30 in each group included. The mean age in group A was 27.53 ± 3.36 years while in group B was 26.33 ± 2.44 years. The mean weight in group A was 63.45 ± 3.21 years while in B was 62.78 ± 5.23 years. Recovery time was significantly better in group A (nalbuphine) where it was seen as 4.73 ± 0.98 minutes as compared to 7.17 ± 1.14 minutes in group B with $p = 0.01$. Recovery time was better in younger age groups (20-27) and again was significantly better in nalbuphine group revealing it in 4.43 ± 0.91 minutes with $p = 0.01$. **Conclusion:** The recovery time of nalbuphine is significantly better than ketamine group when combined with propofol.

Key words: Ketamine, Nalbuphine, Propofol, IVF.

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pain by the puncture of the ovarian capsule in order to take the oocytes, so anesthesiologists are increasingly being challenged by the peculiar nature of this procedure.⁴ A favorable analgesic regimen for oocyte retrieval must have no toxic effects on the oocytes with rapid onset, rapid recovery, ease of administration, and monitoring.^{2,4}

Different methods of conscious sedation and analgesia have been used for oocytes recovery for IVF techniques.⁴ Propofol, the most commonly used sedating agent, is suitable for day care IVF procedures as its a potent hypnotic agent with rapid onset of action and rapid recovery.⁵ But it is inadequate as sole agent as it lacks analgesic properties and so used with different agents.^{6,7} While opioid analgesics can be used as the solitary supplement they do not provide reliable sedation without considerable respiratory depression.⁸ Practicing combination of two agents increases

safety and efficacy, provides better patient control and allows the use of smaller doses of each single agent avoiding its undesirable effect^{9,10} Therefore opioids are most commonly used in conjunction with sedative drugs.⁸

Nalbuphine hydrochloride is a synthetic opioid agonist-antagonist. It is a potent analgesic that can be used as a supplement with propofol for balanced anesthesia, and for preoperative and postoperative analgesia.¹¹ It acts as a partial agonist at kappa receptors and an antagonist at μ receptors. It has minimal side effects, and exhibits a ceiling effect for respiratory depression.^{12,13}

Ketamine, an NMDA receptor antagonist is increasingly used for short term painful procedures in doses of 0.1-0.6 mg/kg.¹⁰ Currently, ketamine and propofol are used in the ED as a sedative drug in short procedures.¹⁴ The untoward effects of ketamine and propofol are reduced and balanced by each other as a combination producing synergistic, smoother sedation.⁷ Ketamine in combinations with propofol provide analgesic effect, shorter recovery time with decreased incidence of vomiting.^{10,15} Various combinations with propofol have been studied earlier but none has been done to compare propofol-ketamine with propofol-nalbuphine. Thus, the objective of this study was to compare the mean recovery time after administration of propofol-ketamine versus propofol-nalbuphine combination in patients undergoing in-vitro fertilization procedures under intravenous sedation.

MATERIAL & METHODS

After approval from Ethical Review Committee, 60 patients of ASA I and ASA 2 were selected using random number tables and patients were divided into two groups, A and B undergoing elective in-vitro fertilization procedures. An informed consent was taken from each patient, the relevant investigations were done after taking a detailed history and patients were kept nil per orally for 6 hours before procedure. All the patients were given inj. midazolam 0.03 mg/kg I/V 10 min before induction. Group A received a fixed dose of inj. nalbuphine 0.06 mg/kg along with inj. propofol with 20 mg initial bolus and later 10 mg for

supplemental drug doses as required to maintain deep sedation. Group B received a fixed dose of inj. ketamine 0.3 mg/kg along with inj. propofol with 20 mg initial boluses and 10 mg for later supplemental drug doses as required to maintain deep sedation. All patients were maintained on spontaneous ventilation using face mask. In cases of apnea, patients were manually ventilated till spontaneous ventilation was maintained. The recovery time was calculated from discontinuation of propofol till the eye opening of the patients on verbal command.

Statistical analysis was done using statistical package for social sciences (SPSS) version 24.

Quantitative data i.e. age, weight, recovery time were presented as mean and standard deviation. The two groups were compared by independent sample t test for recovery time, taking p-value equal or less than 0.05 as significant.

RESULTS

In this study there were total 60 cases, 30 in each group included. The mean age in group A was 27.53 ± 3.36 years while in group B was 26.33 ± 2.44 years (Table-I). The mean weight in group A was 63.45 ± 3.21 years while in group B was 62.78 ± 5.23 years as in Table-I. Recovery time was significantly better in group A (Nalbuphine) where it was seen as 4.73 ± 0.98 minutes as compared to 7.17 ± 1.14 minutes in group B with $p = 0.01$ as in Table-II. Recovery time was better in younger age groups (20-27 years) in Nalbuphine group (4.43 ± 0.91 minutes with $p = 0.01$) (Table-III). Patients weighing 50-59 kg and 60-70kg showed faster recovery time in group A as compared to group B. (Table-IV).

	Group A	Group B
Age	27.53 ± 3.36	$26.33 \pm .44$
Weight	63.45 ± 3.21	62.78 ± 5.23

Table-I

	Group A	Group B	P-Value
Recovery Time (minutes)	4.73 ± 0.98	7.17 ± 1.14	0.01

Table-II

Recovery Time (minutes)			
Age (years)	Group A	Group B	p-value
20-27	4.43±0.91	7.01±1.09	0.01
28-35	4.76±0.99	7.53±1.19	0.01

Table-III

Recovery Time (minutes)			
Weight (kg)	Group A	Group B	p-value
50-59	4.52±0.93	7.10±1.11	0.01
60-70	4.98±1.01	7.92±1.19	0.01

Table-IV

DISCUSSION

One of the most recent advances in the treatment of infertility is In vitro fertilization (IVF). For improved patient outcome, it has undergone various advances.¹⁶ The use of this technology is increasing day by day. These procedures are being performed as a day case procedure. Previously performed laproscopically, the oocyte retrieval is now performed through vagina which is much less invasive.¹⁷ This process required analgesia with or without sedation because it is very painful and stressful one.^{16,18} Different studies has used different anesthetic modalities and analgesic regimen but no definite conclusion so far been made regarding the preferred anesthetic and analgesic regimens for these procedures.¹⁹

Due to lower incidence of respiratory tract complications and advantages of verbal communications with the patient, regional methods with conscious sedation are preferred one. General anesthesia with sedation and analgesia has been found to be the superior method due to advantages of facilitating ovarian aspiration, reducing uterine tone, removing anxiety and preventing patient movements.^{20,21}

Deep level of sedation is obtained by adding small dose of propofol while ketamine gives good analgesia in small dose with minimal sedation.²² This combination of ketamine and propofol provides good sympathomimetic stability. Ketofol as combination of 50% propofol and 50% ketamine (5 mg/ml of each) is widely used for procedural sedation and analgesia with high

level of effectiveness and satisfaction.²² Opioid with propofol is also an effective combination. Propofol and fentanyl has been used in many studies but we used nalbuphine with propofol. Literature regarding use of these combinations in IVF is still deficient.

Recovery time in our study was significantly shorter in group A treated with nalbuphine (4.73±0.98 min) vs (7.17±1.14 min) in group B treated with ketamine (both in conjunction with propofol) (p value =0.01). When recovery time was compared in terms of age and weight, it was significantly decreased in Group A than group B. (p=0.01) There was no such one to one comparison of these two agents especially in cases with in vitro fertilization.

The results of a study by Mora-Gonzalez et al reported shorter time of recovery with propofol-- nalbuphine (11.3±4.3 min) than dexmedetomidine-fentanyl which was consistent to our study results.²³

In the study by Urfalioglu et al, the recovery time was statistically significantly shorter in propofol-remifentanil group in comparison to propofol-ketamine. (p<0.001) This was comparable to our study results where we also found propofol-nalbuphine better than propofol-ketamine combination. The difference was the type of opioid used and the time of recovery was determined as median. 6 mins (range, 3-9 mins) for Group P than that for Group PK of 7 mins (range, 5-10).²⁰

Studies done earlier show contrasting results which may be attributed to variation in dose and interpretation. In a study of Dexmedetomidine versus Ketofol Sedation for Outpatient Diagnostic Transesophageal Echocardiography by Sruthi et al, the recovery time was comparable among the two groups which was approximately 2.6min expressed as median. This was not consistent with our results as we reported the time in mean±sd.⁷

Ejaimi et al evaluated Ketamine/Propofol Combination for Deep Sedation and Analgesia in Minor Painful Operations and observed the time from the last dose to full recovery to range from 10

– 20 min. (mean: 15 minutes.) This was different from our results where the mean recovery time was 7.17min. This could be due to difference in doses of ketamine and propofol. They used 5mg/ml of each agent in combination whereas we used separately 0.3 mg/kg ketamine and 10mg initial bolus with 10mg supplemental propofol.²²

A study by Tajoddini et al revealed shorter recovery time (5.65 ± 0.35 min) with propofol- ketamine when compared to propofol-fentanyl for sedation and analgesia in emergency procedures. This difference in results could be due to different methodology.¹⁵

Panjabi et al did not find significant difference in the recovery time when comparing nalbuphine and fentanyl for post-operative pain relief in patient undergoing short surgical procedures. (8.8 ± 1.0 minutes vs 7.8 ± 1.5 min).²⁴ In another study by Madacsy et al no difference was seen in recovery time when propofol-nalbuphine was compared with propofol alone for deep sedation for colonoscopy (51.7 min \pm 23.4 vs. 49.5 min \pm 21.7, $p = 0.4$).²⁵

There were few limitations of the study. As this study did not look for the other parameters like pain relief, sedation scores and side effect profiles of the drugs used in both groups. Future studies need to be designed to investigate the effects of these drugs. In conclusion, our findings reveal that propofol-nalbuphine provides faster recovery time as compared to propofol-ketamine combination.






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3	Hamza Waheed	Data collections, Data analysis.	
4	Shamila Athar	Manuscript review, Literature & review.	
5	Zulqarnain Butt	Methodology, Proof reading.	
6	Mohsin Riaz Askri	Supervision, Methodology, Proof reading.	