The Journal of Obstetrics and Gynecology of India (January–February 2022) 72(1):59–65
https://doi.org/10.1007/s13224-021-01495-w

ORIGINAL ARTICLE

Opioid-free TIVA Improves Post- operative Quality of Recovery (QOR) in Patients Undergoing Oocyte Retrieval

Gurusanthiya Saravanaperumal[1] · **Prabha Udhayakumar**[1]

Received: 27 October 2020 / Accepted: 27 April 2021 / Published online: 22 May 2021

Abstract

Background Oocyte retrieval is a part of in vitro fertilisation (IVF) procedures performed on an ambulatory basis. Total intravenous anaesthesia (TIVA) with opioid is shown to improve quality of recovery (QOR) after ambulatory surgery. Opioid-free anaesthesia (OF) is gaining popularity in recent times as it is associated with lesser post-operative side effects related to opioids. Quality of recovery is considered as one of the principal end points in ambulatory surgery.

Aim To compare quality of recovery using QOR-15 questionnaire between opioid-free TIVA and opioid-based TIVA at 24 h after oocyte retrieval.

Settings and Design A prospective randomised control study.

Patients and Methods Sixty six patients undergoing oocyte retrieval were prospectively selected. They were randomised into two equal group. OF TIVA group with dexmedetomidine (D) and propofol or opioid-based TIVA with fentanyl (F) and propofol. The primary outcome measured was quality of recovery using QOR-15 at 24 h after oocyte retrieval. Secondary outcomes measured were incidence of bradycardia, post-operative nausea and vomiting, usage of rescue analgesia and total consumption of propofol.

Results A statistically significant difference in total QOR-15 was observed between two groups (p value = 0.021) at 24 h post-operatively. Usage of rescue analgesia and incidence of post-operative nausea and vomiting was less in opioid-free TIVA.

Conclusion Opioid-free TIVA improves post-operative QOR in patients undergoing oocyte retrieval.

Keywords Opioid-free anaesthesia · Oocyte retrieval · Quality of recovery · QOR-15

Introduction

Oocyte retrieval is a part of IVF which involves transvaginal ultrasound-guided aspiration of ovarian follicle. It is painful due to passage of needle through vaginal wall and mechanical stimulation of ovary. It is performed on an ambulatory basis. Complete recovery after anaesthesia is vital parameter in determining discharge following ambulatory surgery. The QOR-15 provided a valid, reliable, extensive and efficient evaluation of patient's QOR after anaesthesia and surgery [1].

Total intravenous anaesthesia (TIVA) is known to improve quality of anaesthesia in ambulatory surgery [2, 3]. The most common anaesthetic agents used for monitored anaesthesia care are midazolam, fentanyl and propofol. Opioids are associated with post-operative nausea and vomiting, pruritus and respiratory depression. The opioid-free (OF) anaesthesia is associated with lesser post-operative rescue analgesic usage and lesser side effects associated with opioids [2, 4, 5]. Dexmedetomidine is an important adjunct in opioid-free anaesthesia which is shown to have adequate analgesic effect (as a sole analgesic) in recent studies in patients undergoing laparoscopic surgery [2, 4, 5].

Aim: To compare quality of recovery using QOR-15 questionnaire at 24 h post-operatively between opioid-free (OF) TIVA and opioid-based TIVA in oocyte retrieval.

Group D (OF TIVA): propofol and dexmedetomidine.

Gurusanthiya Saravanaperumal— Registrar. Prabha Udayakumar—Head of Department.

✉ Gurusanthiya Saravanaperumal
gurusanthiya@gmail.com; gurusanthiya.anaes@gmail.com

Prabha Udhayakumar
prabhadr01@gmail.com

[1] Department of Anaesthesiology, Sri Ramakrishna Hospital, 394, Sarojini Naidu road, Siddhapudur, Coimbatore 641044, India

Group F (opioid-based TIVA): propofol and fentanyl.

Prospective randomised single-blinded study.

Objective:

Primary Outcome

To compare quality of recovery after anaesthesia between opioid-free TIVA and opioid-based TIVA.

Secondary outcomes

Total propofol consumption.

Incidence of bradycardia, nausea and vomiting.

Usage of rescue analgesic agents.

Materials and Methods

The study was conducted at Sri Ramakrishna Hospital, a tertiary care centre in Coimbatore, between June 2019 and September 2020 on patients for first cycle of oocyte retrieval. American Society of Anaesthesiologists (ASA) physical status I and II aged 23 to 38 years with ultrasound (USG) showing > 3 bilateral ovarian follicular response were included in the study.

Exclusion criteria were ASA III patients, history of cardiac/renal/liver disease, BMI > 35 kg/m^2, USG showing less than 3 dominant follicle.

Sample Size

Sample size was calculated from previous study with Q0R-15, the mean and standard deviation were 127 and 22, respectively, in minor surgery [6]. A sample size of 29 in each group was needed to detect a difference of 8 points, with a type I error of 5% and power of 80%. Thirty-three patients in each group were selected to include attrition.

Detailed Description

Institutional ethics committee clearance was obtained. All patients were evaluated preoperatively one day prior to procedure. All patients were familiarised about QOR-15 questionnaire. Written informed consent was obtained from all patients. Routine nil per oral guidelines were followed. All patients were re-evaluated on day of procedure. 20 gauge IV cannula was secured and Ringer lactate (according to Holliday Segar formula for per kg requirement) was started. Baseline measurements of heart rate (HR), non-invasive blood pressure (NIBP), respiratory rate, mean arterial blood pressure (MAP), room air oxygen saturation were noted. The patients were randomly (by computer-generated random numbers) allotted to group D receiving dexmedetomidine and group F receiving fentanyl.

Group D (OF) patients received 0.5 µg/kg of dexmedetomidine over 10 min in 100 ml of normal saline as infusion, about 10 min prior to procedure. At the start of the procedure, another 0.5 µg/kg of dexmedetomidine was given as infusion over 15 min.

Group F opioid-based patients received 1 µg/kg of fentanyl over 10 min in 100 ml of normal saline as infusion, about 10 min prior to procedure. At the start of the procedure, another 1 µg/kg of fentanyl was given.

Propofol 1.5 mg/kg was given initially to all patients in both groups at the start of procedure and additional doses of propofol 0.5 mg/kg was given if the patient exhibited kinetic response.

Oxygen was supplemented through Hudson mask at 6 L per minute. Nasal airway was used if airway obstruction occurred. During the procedure HR, NIBP, oxygen saturation (SpO2) were monitored every 5 min (Figs. 1 and 2).

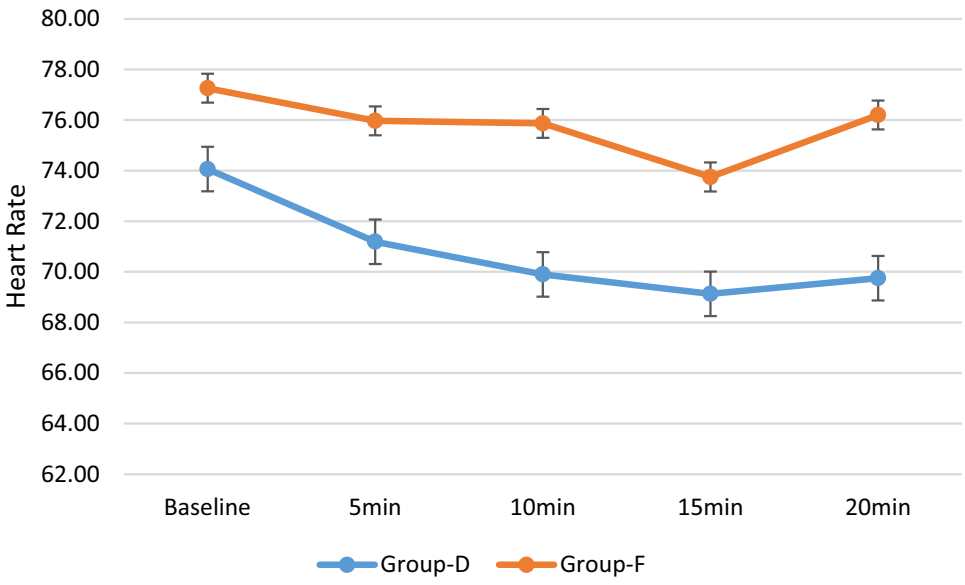

Fig.1 Changes in heart rate between two groups during intraoperative period.

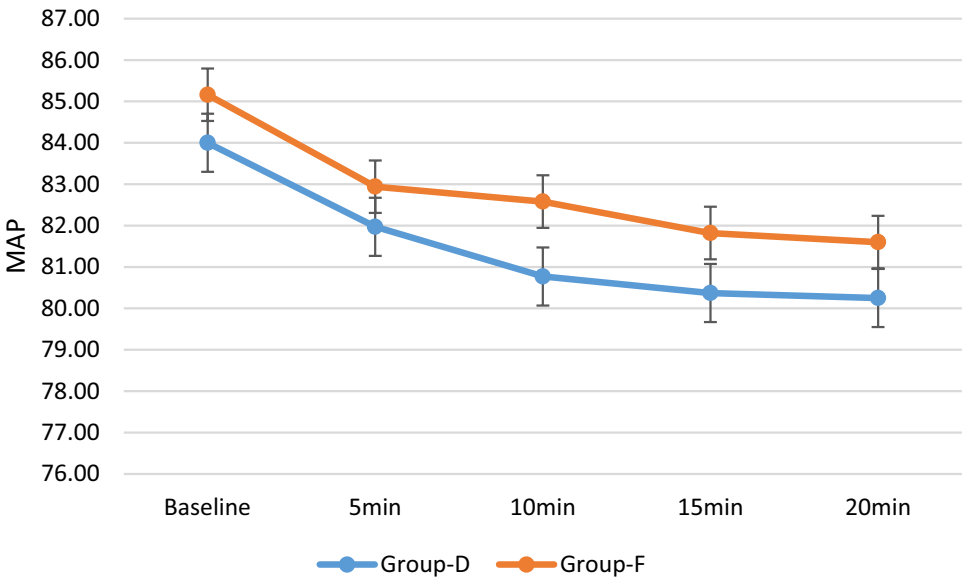

Fig. 2 Changes in mean arterial blood pressure (MAP) between two groups during intraoperative period.

Post-procedure HR,NIBP, oxygen saturation were recorded every 5 min up to 30 min and every 15 min until 2 h (Figs. 3 and 4). Total propofol consumption was noted. Number of oocytes retrieved were also noted. Bradycardia was defined as heart rate under 50 beats per minute and treated with atropine 0.6 mg IV. A drop in MAP of 20% was regarded as hypotension, treated with ephedrine bolus of 6 mg IV, while MAP value more than 20% is regarded as hypertension.

Post-operatively pain was assessed by numerical rating scale (NRS), (where 0 = no pain and 10 = worst imaginable pain) for every 10 min up to 30 min and every 30 min thereafter. When NRS is more than 3, rescue analgesia with injection Paracetamol 1 g was given IV. Post-operative nausea and vomiting were treated with ondansetron 4 mg IV. Incidence of bradycardia, nausea, vomiting and usage of rescue analgesia was also noted. Patients were discharged about 8 h post-procedure after active mobilization and diet. Patients were telephoned and asked to take QOR-15 questionnaire at 24 h post-procedure, and response was noted by researcher. QOR-15 categorised into 4 classes of recovery as excellent (135–150), good (122–135), moderate (90–121), poor (0–89) [6].

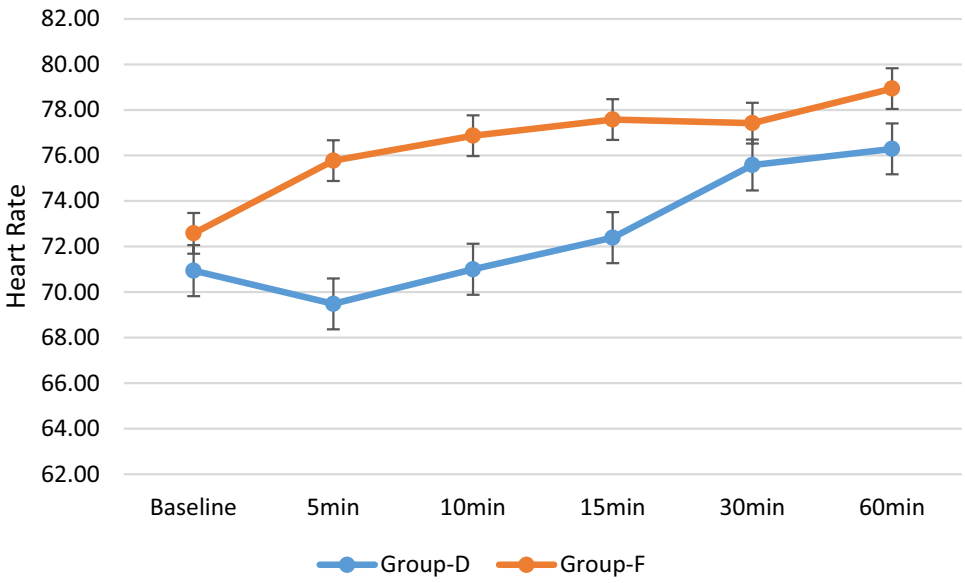

Fig. 3 Changes in heart rate between two groups during first hour of post-operative period.

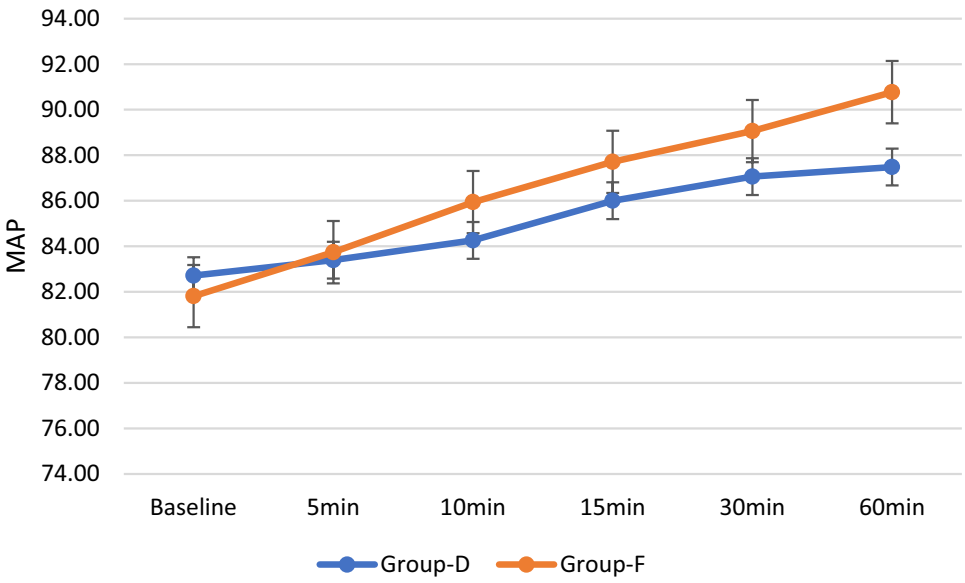

Fig. 4 Changes in mean arterial blood pressure between two groups during first hour of post-operative period.

Statistical Analysis

The sample size was calculated from previous study. Sixty-six patients were enrolled and randomised as 33 in each group. Statistical analysis performed using SPSS version 20. Data are presented as mean ± standard deviation, median, numbers and frequencies as appropriate. Comparison between two groups was made using Independent *t*-test for detecting differences in demographics, haemodynamic parameters and QOR-15. Chi-square analysis was used for categories of QOR-15. Statistical significance was determined at $p < 0.05$ and highly significant when $p < 0.01$.

Table 1 Demographic characteristics and duration of infertility

	Category	Mean	SD	*p* value
Age in years	Group D	30.55	2.77	0.209
	Group F	29.65	2.83	
Height in cm	Group D	161.94	6.52	0.712
	Group F	162.55	6.48	
Weight in kg	Group D	61.77	10.87	0.168
	Group F	65.80	11.85	
BMI in kg/m^2	Group D	23.39	2.90	0.075
	Group F	24.75	3.03	
Duration of Infertility in years	Group D	4.81	1.42	0.329
	Group F	5.19	1.66	

Data presented as mean ± SD. $p < 0.05$ considered significant
Group D-opioid-free TIVA, Group F-opioid-based TIVA group

Results

Sixty-six patients enrolled and randomised as 33 in each group for oocyte retrieval. Two patients in each group declined to complete the study and were excluded from statistical analysis. Hence, analysis was made for 31 patients in each group.

Demographic data (age, weight, height, body mass index and ASA) were comparable and no statistical differences were observed between groups. In addition, there was no significant difference between duration of infertility in each group. (Table 1).

The mean values of baseline HR (beats/min), MAP (mmHg) and SpO2 were comparable between two groups. (Table2).

There was a significant difference in intraoperative heart rate between two groups at 5 min, 10 min and at 15 min of the procedure. However, MAP was comparable (Table 3). Significant difference in heart rate was observed up to 15 min post-operatively while MAP was comparable. There were no significant difference in duration of procedure and number of oocytes retrieved in both groups (Tables 4 and 5).

NRS was significantly less up to first 20 min post-procedure in group D compared to group F and comparable later on (Table 6). Incidence of bradycardia ($p = 0.69$), PONV ($p = 0.236$) and usage of rescue analgesic ($p = 0.09$) were comparable between two groups (Table 5). However, the incidence of PONV was higher in opioid-based TIVA group (19.40%), usage of rescue analgesic was higher in opioid-based TIVA group (25.80%), (Table 5).

There was highly significant difference in propofol consumption with mean dosage of propofol 150 ± 32 mg in opioid-free TIVA group as opposed to 184 ± 18 mg in opioid-based TIVA group (Table4).The QOR-15 at 24 h post-operatively was significantly higher in opioid-free TIVA (Table 4). There was significant difference in QOR

Table 2 Preoperative haemodynamic parameters

	Category	Mean	SD	*p* value
Pre-OP HR Baseline beats/min	Group D	85.45	11.68	0.544
	Group F	87.26	11.60	
Pre-OP HR 5 min	Group D	79.87	8.08	0.361
	Group F	82.03	10.27	
Pre-OP HR 10 min	Group D	76.03	8.38	0.169
	Group F	79.29	9.98	
Pre-OP MAP Baseline in mmHg	Group D	88.10	13.02	0.500
	Group F	89.97	8.14	
Pre-OP MAP 5 min	Group D	88.52	9.64	0.262
	Group F	84.77	15.68	
Pre-OP MAP 10 min	Group D	86.10	8.87	0.285
	Group F	88.32	7.31	
Pre-OP SPO2 Baseline	Group D	99.19	0.60	0.545
	Group F	99.10	0.65	

Data presented as mean ± SD, Pre-OP-preoperative value, *HR*-heart rate, *MAP*-mean arterial blood pressure

$p < 0.05$ considered significant

Table 3 Intraoperative haemodynamic parameter

	Category	Mean	SD	*p* value
IOP HR Baseline in beats /min	Group D	70.06	8.88	0.0161*
	Group F	77.26	8.84	
Intraop HR 5 min	Group D	71.19	7.85	0.036*
	Group F	75.97	9.57	
Intraop HR 10 min	Group D	69.90	8.28	0.014*
	Group F	75.87	10.12	
Intraop HR 15 min	Group D	69.13	7.13	0.034*
	Group F	73.75	8.96	
Intraop HR 20 min	Group D	69.75	4.99	0.172
	Group F	76.20	7.16	
Intraop MAP Baseline mmHg	Group D	84.00	9.05	0.566
	Group F	85.16	6.59	
Intraop MAP 5 min	Group D	81.97	9.23	0.620
	Group F	82.94	5.65	
Intraop MAP 10 min	Group D	80.77	8.10	0.312
	Group F	82.58	5.64	
Intraop MAP 15 min	Group D	80.37	7.30	0.411
	Group F	81.82	5.96	
Intraop MAP 20 min	Group D	80.25	5.56	0.742
	Group F	81.60	6.11	
Intraop SPO2 Average	Group D	99.58	0.50	0.077
	Group F	99.35	0.49	

Data presented as mean ± SD, Intraop-intraoperative, SpO2-oxygen saturation; $p < 0.05$ significant

*$p < 0.05$

HR-heart rate, *MAP*-mean arterial pressure, group D-opioid-free, group F-opioid-based

Table 4 post-operative NRS, propofol consumption and QOR-15

	Category	Mean	SD	*p* value
Post-op NRS 30 min	Group D	1.45	1.26	0.369
	Group F	1.74	1.26	
Post-op NRS 1 h	Group D	1.13	0.43	0.057
	Group F	1.35	0.49	
Post-op NRS 2 h	Group D	1.10	0.60	0.082
	Group F	1.35	0.55	
Duration of Procedure in minutes	Group D	16.61	1.82	0.750
	Group F	16.77	2.14	
Dosage of Propofol in mg	Group D	150.00	32.76	0.000*
	Group F	184.84	18.05	
QOR 15	Group D	129.00	6.06	0.021*
	Group F	125.16	6.64	

Data presented as mean ± SD. Post-op- post-operative, *NRS*-numerical rating scale, *QOR*-quality of recovery. $p < 0.05$ considered significant.

* significant

Table 5 Usage of rescue analgesia

Rescue analgesia		Group D	Group F	Total
Used	N	3	8	11
	%	97.0%	25.80%	17.70%
Not Used	N	28	23	51
	%	90.30%	74.20%	82.30%
p value = 0.091				

Data presented as frequency and percentage. $p < 0.05$ considered significant

Table 6 QOR -15 Category

QOR Category		Group D	Group F	Total
Moderate	N	4	13	17
	%	12.90%	41.90%	27.40%
Good	N	21	17	38
	%	67.70%	54.80%	61.30%
Excellent	N	6	1	7
	%	19.40%	3.20%	11.30%
p value = 0.013*				

Data presented as frequency and percentage. $p < 0.05$ considered significant.

* significant

categories between two groups with opioid-free TIVA having excellent recovery of around 19.40% (Table 6). None of the patients in either group had poor quality of recovery.

Discussion

Transvaginal ultrasound-guided aspiration of oocytes is quite a painful procedure as needle passes through vaginal mucosa, ovarian capsule and oocytes are aspirated. Adequate analgesia and immobility of patient are primary requisite for this procedure.

Enhanced recovery after surgery (ERAS) is a multidimensional approach to reduce length of hospital stay involving a rational set of perioperative goals targeting early ambulation, gut motility, enhanced nutrition and goal directed fluid therapy and optimising perioperative haemodynamic parameters.

High dose opioid increases length of hospital stay, delays recovery and return to normalcy. Opioid free anesthesia (OFA) has favourable profile leading to early recovery and reduction in the incidence of post-operative hyperalgesia. Enhanced recovery pathway incorporating OFA provides a platform for addressing patients with opioid addiction and ensuring their safe transition into post-operative recovery. Goal of ERAS is to provide 'optimal analgesia' which optimises patient comfort, facilitates early functional recovery while minimising adverse effects of opioids [7, 8].

OF TIVA with dexmedetomidine is associated with early recovery, lesser post-operative analgesic requirements, better quality of recovery, better patient satisfaction while maintaining haemodynamic parameters [2, 4, 5, 7, 8, 9].

QOR-15 is a patient reported outcome measurement validated to measure QOR after surgery and anaesthesia. It ranges from 0 to 150 with a higher score indicating better recovery. Jakob et al. [6] classified quality of recovery into excellent (136–150), good (122–135), moderate (99–121), poor (0–89). QOR-15 questionnaire provided valid, extensive and efficient evaluation of post-operative QOR [1].

Our study showed significant difference in quality of recovery as assessed by QOR-15 questionnaire at the time of discharge in OF TIVA compared to those with opioid-based TIVA in patients undergoing oocyte retrieval. There was also significantly higher patients with excellent recovery profile in OF TIVA. Incidence of post-operative nausea and vomiting and rescue analgesia usage was also reduced in OF TIVA. Incidence of bradycardia between the two groups was comparable. Though the heart rate intraoperatively was significantly lower in OF TIVA group, MAP was maintained.

Hakim KY et al. [2] observed that OF TIVA during ambulatory gynaecological laparoscopy improved QOR post-operatively, prolonged post-operative analgesia, lowered the incidence of PONV and reduced the requirements of propofol while maintaining stable haemodynamic parameters.

Elnabtity AM et al. [10] compared dexmedetomidine and midazolam for conscious sedation in oocyte retrieval and stated that dexmedetomidine offered favourable analgesic effects and significantly less requirements for rescue propofol intraoperatively and paracetamol post-operatively. The number of oocytes retrieved, embryo transferred and percentage of pregnancy per embryo transfer were comparable in both groups.

Mayar et al. [11] compared emergence profile of propofol + dexmedetomidine and fentanyl + dexmedetomidine for oocyte retrieval and concluded that dexmedetomidine was associated with rapid onset of sedation, better analgesic effect with stable haemodynamic parameters, better preservation of respiratory function and rapid recovery.

Candiotti et al. concluded that dexmedetomidine is associated with lesser incidence of respiratory depression and significantly higher patient satisfaction score following monitored anaesthesia care [12].

Conclusion

Thus, we conclude that opioid-free TIVA with dexmedetomidine and propofol has better quality of recovery following oocyte retrieval compared to opioid-based TIVA with fentanyl and propofol.

Acknowledgements DR. M. S. Lakshmi MBBS, DNB (OG), Consultant in infertility. DR. R. Suganya MBBS, DNB (OG), Consultant in infertility.

Funding This study was not funded.

Declarations

Conflict of interest There are no conflicts of interest.

Ethical Approval Institutional ethical committee clearance obtained.

Informed Consent Informed written consent obtained from all participants undergoing the study.

References:

1. Stark PA, Myles PS, Burke JA. Development and psychometric evaluation of a postoperative quality of recovery score: the QoR-15. Anesthesiol. 2013;118(6):1332–40. https://doi.org/10.1097/ALN.0b013e318289b84b (**PMID: 23411725**).
2. Hakim KYK, Wahba WZB. Opioid-free total intravenous anesthesia improves postoperative quality of recovery after ambulatory gynecologic laparoscopy. Anesth Essays Res. 2019;13(2):199–203.
3. Lee WK, Kim MS, Kang SW, Kim S, Lee JR. Type of anaesthesia and patient quality of recovery: a randomized trial comparing propofol-remifentanil total iv anaesthesia with desflurane anaesthesia. Br J Anaesth. 2015;114(4):663–8. https://doi.org/10.1093/bja/aeu405 (**PMID: 25500679**).

4. Bhardwaj S, Garg K, Devgan S. Comparison of opioid-based and opioid-free TIVA for laparoscopic urological procedures in obese patients. J Anaesthesiol Clin Pharmacol. 2019;35(4):481–6. https://doi.org/10.4103/joacp.JOACP_382_18 (**PMID: 31920231, PMCID: PMC6939571**).
5. Tufanogullari B, White PF, Peixoto MP, Kianpour D, Lacour T, Griffin J, Skrivanek G, Macaluso A, Shah M, Provost DA. Dexmedetomidine infusion during laparoscopic bariatric surgery: the effect on recovery outcome variables. Anesth Analg. 2008;106(6):1741–8. https://doi.org/10.1213/ane.0b013e318172c47c (**PMID: 18499604**).
6. Kleif J, Gögenur I. Severity classification of the quality of recovery-15 score-an observational study. J Surg Res. 2018;225:101–7.
7. Kamdar NV, Hoftman N, Rahman S, Cannesson M. Opioid-free analgesia in the era of enhanced recovery after surgery and the surgical home: implications for postoperative outcomes and population health. Anesth Analg. 2017;125(4):1089–91. https://doi.org/10.1213/ANE.0000000000002122 (**PMID: 28922216**).
8. Brandal D, Keller MS, Lee C, Grogan T, Fujimoto Y, Gricourt Y, Yamada T, Rahman S, Hofer I, Kazanjian K, Sack J, Mahajan A, Lin A, Cannesson M. Impact of enhanced recovery after surgery and opioid-free anesthesia on opioid prescriptions at discharge from the hospital: a historical-prospective study. Anesth Analg. 2017;125(5):1784–92. https://doi.org/10.1213/ANE.0000000000002510 (**PMID:29049123;PMCID:PMC7402216**).
9. Bakan M, Umutoglu T, Topuz U, Uysal H, Bayram M, Kadioglu H, Salihoglu Z. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. Braz J Anesthesiol. 2015;65(3):191–9. https://doi.org/10.1016/j.bjane.2014.05.001 (**PMID: 25925031**).
10. Elnabtity AA, Selim M. A prospective randomized trial comparing dexmedetomidine and midazolam for conscious sedation during oocyte retrieval in an in vitro fertilization program. Anesth Essays Res. 2017;11(1):34.
11. The emergence profile of propofol sedation compared with dexmedetomidine injection during ultrasound-guided oocyte pickup for in-vitro fertilization Elsersi MH, Abuelghar WM, Makled AK-Ain-Shams J Anaesthesiol [Internet]. [cited 2020 Oct 26]. Available from: http://www.asja.eg.net/article.asp?issn=1687-7934;year=2015;volume=8;issue=3;spage=327;epage=333;aulast=Elsersi
12. Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY; MAC Study Group. Monitored anesthesia care with dexmedetomidine: a prospective, randomized, double-blind, multicenter trial. Anesth Analg. 2010;110(1):47–56. https://doi.org/10.1213/ane.0b013e3181ae0856 (**PMID: 19713256**).

About the Author

Gurusanthiya Saravanaperumal is from Coimbatore, India. She pursued her under graduation in medicine and Masters in Anaesthesiology from Madurai Medical College and passed out with honours from Institute of Anaesthesiology, Madurai. She is attached with the Department of Anaesthesiology in Sri Ramakrishna hospital, a 750 bedded multispecialty hospital in Coimbatore. Her areas of interest are obstetric, cardiovascular and paediatric anaesthesia. She is keen to research in areas that enhance perioperative outcomes in patients.