Eurasian Journal of
Anesthesiology & Intensive Care
Original Article
doi
10.51271/EAJAIC-0013

Comparing the effects of propofol dosing based on total body weight and lean body weight on hemodynamics and intraoperative awareness during sleeve gastrectomies

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Received: 20/05/2024 ◆ **Accepted**: 11/06/2024 ◆ **Published**: 06/08/2024

Cite this article: Yıldırım Ş, Kına SF, Özayar E. Comparison of the effects of dosing propofol according to total body weight and lean body weight on hemodynamics and intraoperative awareness in sleeve gastrectomies. *Eurasian J Anesthesiol Intens Care* . 2024;1(3):58-62.

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ABSTRACT

Aims: According to the World Health Organization, obesity is an abnormal or excessive fat accumulation in adipose tissue that impairs health. In recent years, due to the increase in the number of patients referred for surgery with diagnoses of obesity surgery or other clinical conditions, the perioperative evaluation and anesthesia management of these patients have become crucial. Obesity is associated with increased anesthesia risk due to its effects on metabolic, cardiovascular, and pulmonary functions. This study compares the effects of propofol dosing based on lean body weight (LBW) and total body weight (TBW) on hemodynamics and intraoperative awareness in patients undergoing laparoscopic sleeve gastrectomy.

Methods: This study is a prospective observational and randomized clinical trial. It included 54 patients aged 18-60 who underwent elective laparoscopic sleeve gastrectomy under general anesthesia at Ankara Keçiören Training and Researches Hospital. The patients were ASA I-III, with surgeries lasting less than 2 hours, and propofol was used for induction. Patients were randomized into Group LBW and Group TBW based on the calculation of the propofol dose according to their lean body weight and total body weight, respectively. Clinical, demographic, perioperative, and hemodynamic data were recorded for all patients. Additionally, all patients were assessed using the Appendix 1 questionnaire.

Results: The dose of propofol administered was higher in Group TBW than in Group LBW ($p<0.001$). When propofol was administered based on TBW, systolic blood pressure was significantly lower at the 1st and 2nd minutes of induction ($p<0.05$). There was no significant difference in systolic blood pressure recorded during the intraoperative period and post-extubation between the two groups. Diastolic blood pressure, mean arterial pressure, and heart rate were significantly lower in Group TBW post-extubation ($p=0.003$). Intraoperative BIS values were significantly lower in Group TBW at the 1st, 2nd, and 3rd minutes post-induction and post-extubation. No intraoperative awareness (IOA) was detected in either group according to the Appendix 1 questionnaire.

Conclusion: In obese patients undergoing sleeve gastrectomy, propofol doses calculated based on LBW during induction were associated with less hemodynamic instability compared to doses calculated based on TBW.

Keywords: Laparoscopy, obesity, total body weight, lean body weight, intraoperative awareness, sleeve gastrectomy

INTRODUCTION

Obesity is defined by the body mass index (BMI), which is the ratio of body weight (kilograms) to the square of height (meters). According to the World Health organization's classification, individuals with a BMI over 30 are considered obese.[1,2] The prevalence of obesity has increased in recent decades, particularly in the United States and Asian countries.[3,4] The rise in the number of obese patients has also led to an increase in obesity-related surgical procedures.[4-6] Due to the increase in the number of obese patients referred for surgery with diagnoses of obesity surgery or other clinical conditions, the preoperative evaluation and anesthesia management of these patients have become increasingly important.

The pharmacokinetic parameters of anesthetic drugs are affected by obesity due to their solubility in fat and distribution in tissues. Dose adjustments for these drugs should consider the volume of distribution for the loading dose and clearance

for the maintenance dose.[7] Obese individuals can metabolize lipophilic drugs to a greater extent compared to lean individuals.

Propofol is an intravenous (IV) anesthetic agent commonly used for induction of anesthesia. Although propofol has high fat solubility, its induction dose should be calculated based on lean body weight (LBW), whereas the maintenance dose should be adjusted according to total body weight (TBW) due to its high clearance.[1,4] Recent studies on anesthesia in obesity surgery have primarily focused on total IV anesthesia or specific infusion models like target-controlled infusion.[4,8] In rapid induction models, individuals receiving propofol based on TBW have faster induction times. When compared to normal-weight individuals, obese patients receiving propofol based on LBW during induction have similar times to loss of consciousness.[8,9] This can be explained by the unchanged initial volume of distribution in patients receiving propofol based on LBW. [8,9]

The primary aim of this study is to compare the hemodynamic parameters of groups by applying two different doses of propofol (TBW or LBW) during induction in obese patients. The secondary aim is to compare their intraoperative awareness (IOA).

METHODS

The study was carried out with the permission of Ethics Committe of the Keçiören Training and Researches Hospital Ethics (Date: 13.12.2017, Decision No: 1563). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study is a prospective observational randomized clinical comparison conducted in a tertiary education and research hospital and from the Turkish Medicines and Medical Devices Agency (decision number 93189304-514.05.01-E7287, dated 11.01.2018). Written informed consent was obtained from all patients participating in the study, and no interference was made in their perioperative management.

The study included patients aged 18-60 who were planned for elective laparoscopic sleeve gastrectomy at the General Surgery Clinic under general anesthesia, classified as American Society of Anesthesiologists (ASA) physical status I-III, with surgeries lasting less than 2 hours, and who consented to participate postoperatively. Exclusion criteria were patients who refused to participate, had a history of allergy to anesthetic drugs, had preoperative hemoglobin levels below 10 mg/dl, received premedication, were assessed as difficult intubation, developed intraoperative complications, had surgery lasting more than 2 hours, consumed alcohol daily, were diagnosed with severe anxiety, used benzodiazepines, opioids, sedatives, or anxiolytic drugs preoperatively, had stage 2-3 hypertension or any chronic disease, and had dementia.

Patients were randomized in the operating room using the sealed envelope draw method. They were divided into two groups: the group given propofol according to TBW (Group TBW) and the group given propofol according to LBW (Group LBW). The dose of propofol used for anesthesia induction in patients was calculated according to TBW and LBW, while other drugs used for anesthesia induction and maintenance were dosed according to LBW.

In patients included in the study, demographic information, BMI, ASA score, comorbidities, mechanical ventilator settings, administered drug doses, perioperative hemodynamic monitoring (Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), Mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2), End-tidal carbon dioxide (EtCO2)], Bispectral index (BIS) values, anesthesia and surgery duration, loss of consciousness time (time elapsed until loss of eyelash reflex after propofol administration), TOF unresponsiveness time (Time elapsed until TOF 0 after muscle relaxant administration), intubation time, insufflation and desufflation time, intraoperative inhalation anesthetic consumption measured by fresh gas flow method, and whether additional medication was used intraoperatively were evaluated. Additionally, the dose of medication used during extubation, time to reach TOF 90%, extubation time, and the time in the postoperative recovery unit (PACU) (when Aldrete score >9) were recorded. Patients were evaluated with the PO Appendix 1 questionnaire a total of 3 times: within the first 24 hours postoperatively, between 24-72 hours, and 30 days after the surgery. Patients were asked to answer these questions with 'Yes' or 'No'.

Statistical Analysis

The required sample size for each group was determined to be 27, with a total of 54 patients, based on BIS results from the study by Fai Lam et al., using the Minilab program with α 0.05 and β 0.10 for power analysis. Data were evaluated using SPSS (Statistical Package for Social Science) 22.0. Categorical data were presented as numbers (n) and percentages (%), and continuous numerical data were presented as mean± standard deviation (SD). The Kolmogorov-smirnov test was used to assess the normality of continuous data distribution. Student's t-test was used for group comparisons of normally distributed parameters, and paired t-test for within-group comparisons. The mann-whitney U test was used for group comparisons of non-normally distributed parameters, and the Wilcoxon test for within-group comparisons. Categorical data comparisons were made using the chi-square or Fisher's exact test. Results were considered significant at $p < 0.05$ within a 95% confidence interval.

RESULTS

Twenty-seven patients were assigned to each group, and the data of all 54 patients were analyzed. Demographic and preoperative assessment data of the groups were similar (Table 1). Induction doses of rocuronium and fentanyl, calculated according to LBW, were administered similarly in both groups. However, the propofol dose administered was significantly higher in Group TBW ($p<0.001$) (Table 2). No significant difference was found between the groups regarding the need for additional medication. Total nitrogen and sevoflurane consumption during maintenance of anesthesia, guided by BIS monitoring to maintain BIS values between 40-60, were similar between the groups.

There was no significant difference in the time of consciousness loss between the groups. Consequently, the time from anesthesia drug administration to intubation was also similar (Table 3).

Table 1. Distribution of some descriptive and clinical features among study groups

	Total body weight (n=27) group 1	Lean body weight (n=27) group 2	p
Age*	40.51±11.50	38.62±12.26	0.562
Gender, n(%)			
Woman	23 (85.2)	22 (81.5)	
Male	4 (14.8)	5 (18.5)	0.715
Height length (cm)*	162.33±9.11	166.03±6.65	0.094
Body Weight (kg)*	127.27±16.69	136.55±21.15	0.079
Body Mass Index (BMI)*	48.36±5.72	49.53±7.44	0.523
Lean Body Weight (kg)*	64.01±10.11	69.18±7.44	0.097
Comorbidity Status, n(%)			
None	19(70.4)	15 (55.6)	
There is	8(29.6)	12 (44.4)	0.260
Comorbidities, n(%)			
DM	6 (22.2)	14 (14.8)	0.484
H.T.	7 (25.9)	6 (22.2)	0.750
Obst . Akc . Hast	1 (3.7)	4 (14.8)	0.159
ASA Classification, n(%)			
I	19 (70.4)	15 (55.6)	
II	8 (29.6)	12 (44.4)	0.260
Anesthesia Duration (min)*	70.07±14.14	66.66±7.55	0.267
Surgery Time (min)*	55.22±13.98	48.74±9.25	0.051
*: mean±sd			

n : Number, ASA : American society of anesthesia , min : Minute, cm: Centimeter, kg: Kilogram, DM: Diabetes Mellitus , HT: Hypertension, mean : Median, sd : Standard deviation

Table 2. Intravenous Drug Doses Used During Induction

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Arrhythmal (mg)	40.55±4.00	40.37±1.97	0.829
Propofol (mg)	310.00±50.15	183.88±37.42	<0.001
Rocuronium (mg)	42.03±8.57	43.70±7.54	0.452
Fentanyl (mg)	132.18±25.71	141.11±23.91	0.192
*: mean±sd			

mg : Milligram, n: Number , mean : Median, SD : Standard deviation

Table 3. Induction times

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Duration of loss of consciousness (sec)	34.96±13.27	35.70±15.79	0.853
TOF non-response time (sec)	225.59±100.02	257.00±122.75	0.307
Intubation time (sec)	326.85±95.98	364.44±125.71	0.222
*: mean±sd			

n : Number, sec : Seconds, mean : Median, sd : Standard deviation

SAP was found to be significantly lower in Group TBW at the 1st and 2nd minutes of induction ($p<0.05$). No significant difference was found in SAP between the groups post-intubation intraoperatively and post-extubation. DAP and MAP values were found to be significantly lower in Group TBW post-intubation ($p=0.003$ and $p=0.001$, respectively). However, at 30-40-50 minutes post-intubation, DAP and MAP values were significantly higher in Group TBW ($p<0.05$).

Comparing HR at 1 minute post-induction, no significant difference was found, but HR was significantly lower in Group TBW at the 2nd and 3rd minutes post-induction, 20-30 minutes post-intubation, and post-extubation ($p<0.05$). No difference was found between the groups for SpO_2 and $EtCO_2$ values. BIS measurements at 1-2-3 minutes post-induction and during the intraoperative and post-extubation periods were significantly lower in Group TBW ($p<0.05$) (Table 4). The TOF values were similar preoperatively and postoperatively in both groups, with similar sugammadex doses, time to TOF 90%, and extubation times post-surgery. The average Modified Aldrete score in Group TBW post-extubation in the operating room was 7.22±1.01, compared to 6.62±1.07 in Group LBW ($p=0.046$). However, no difference was found between the groups in the PACU Modified Aldrete score (Table 5).

Appendix 1 questionnaire responses, collected at three different times with 16 questions, showed no statistical difference between the groups. Only the question "Do you remember the moment you fell asleep?" in the questionnaire administered within the first 24 hours showed that Group TBW significantly more often answered "yes" ($p=0.033$) (Table 6).

Table 4. Comparison of BIS values

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Preinduction	95.1481±8.45669	96.7778±5.24282	0.922
Induction 1 minute	36.9630±16.27996	47.0370±14.42349	0.005
Induction 2 min	33.4074±9.43504	50.4815±16.23475	<0.001
Induction 3 minutes	35.4800±11.99347	53.2692±11.44572	<0.001
Postintubation	42.0741±10.94717	62.5926±10.06998	<0.001
Intubation 10 minutes	44.7037±5.68273	50.8889±9.10762	0.006
Intubation 20 minutes	43.6296±7.14223	47.3704±6.98982	0.073
Intubation 30 minutes	42.8519±6.79198	45.7778±5.92474	0.049
Intubation 40 minutes	42.2308±5.27111	46.1538±6.03783	0.023
Intubation 50 minutes	42.7143±5.01142	48.8421±9.64517	0.025
Intubation 60 minutes	46.2667±5.84889	49.6667±6.15359	0.225
Intubation 70 minutes	40.7500±6.23832		
Intubation 80 minutes	46.0000±5.65685		
Intubation 90 minutes	42,0000		
Intubation 100 minutes	45,0000		
Postextubation	88.6296±15.79715	81.4444±6.29611	0.013

n : Number, min : Minute

Table 5. Postoperative recovery data

	Total Body Weight (n=27) Group 1	Lean Body Weight (n=27) Group 2	p
Extubation aldrete	7.22±1.01	6.62±1.07	0.046
Aldrete 9 time (min)	8.07±2.60	9.59±3.38	0.137
*: mean±sd			

mean : Median, sd : Standard Deviation , min : Minutes

Table 6. Appendix 1 survey 'Yes' answers comparison table

	0-24. HOUR			24-72.HOUR			POSTOP DAY 30		
	TVA n(%)	YVA n(%)	p	TVA n(%)	YVA n(%)	p	TVA n(%)	YVA n(%)	p
1	25 (92.6)	27 (100)	0.150	25 (92.6)	26 (96.3)	0.552	25 (92.6)	26 (96.3)	0.552
2	4 (14.8)	5 (18.5)	0.710	4 (14.8)	6 (22.2)	0.484	7 (25.9)	7 (25.9)	1.000
3	6 (22.2)	7 (25.9)	0.750	5 (18.5)	5 (18.5)	1.000	4 (14.8)	7 (25.9)	0.311
4	16 (59.3)	23 (85.2)	0 .033	17 (63)	20 (74.1)	0.379	18 (66.7)	18 (66.7)	1.000
5	0(0)	0(0)	1.000	0 (0)	0 (0)	1.000	0 (0)	1 (3.7)	0.313
6	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	1(3.7)	-
8	0(0)	0 (0)	1.000	0 (0)	0(0)	1.000	0(0)	0(0)	1.000
9	1 (3.7)	0 (0)	0.313	1 (3.7)	0(0)	0.313	1(3.7)	2(7.4)	0.552
10	0(0)	0 (0)	1.000	0(0)	0(0)	1.000	0(0)	1(3.7)	0.313
11	0(0)	0 (0)	1.000	0(0)	0(0)	1.000	1(3.7)	0(0)	0.313
12	-	-	-	-	-	-	-	-	-
13	0(0)	0 (0)	1.000	1 (3.7)	0(0)	0.313	0(0)	0(0)	1.000
14	0(0)	0 (0)	1.000	0(0)	0(0)	1.000	0(0)	0(0)	1.000
15	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-

TVA: Total body weight, YVA: Lean body weight, n:Number

Appendix 1. Intraoperative awareness appendix 1 survey	
1	Do you remember being transferred to the operating room and being prepared for anesthesia?
2	Do you remember the end of the operation?
3	Do you remember sleeping during the operation?
4	Do you remember the moment of falling asleep?
5	Do you remember the dreams you had while you were under anesthesia?
6	If yes; Were they pleasant dreams?
7	If yes; Were they disturbing unpleasant dreams?
8	Did you feel pain during anesthesia?
9	Do you remember not being able to breathe during anesthesia?
10	Do you remember anything from the operation?
11	Did you hear anything during the surgery?
12	If yes; Can you specify if it is a personal conversation?
13	Did you hear any noise during surgery?
14	Did you feel anything during the surgery?
15	If yes; Did you feel any touch?
16	If yes; Did you feel anything in your throat or mouth?

DISCUSSION

The increase in the prevalence of obesity has led to a rise in obesity-related surgical procedures.(4-6) Compared to the normal population, anesthesia complications are higher in obese patients, causing confusion regarding the dose-effect strategy of anesthetic drugs due to their pharmacokinetic and pharmacodynamic interactions. Propofol is a frequently used drug with high fat solubility. Besides providing rapid loss of consciousness, it has cardiac effects such as hypotension and myocardial depression due to its redistribution.[10,11] In this prospective observational clinical study compared the hemodynamic effects and IOA in patients administered propofol doses based on TBW and LBW. According to this study, it was shown that dosing propofol according to LBW during induction had significantly better results on hemodynamic parameters.

In a similar study by Ingrande et al. with 60 morbidly obese patients (BMI > 40), propofol doses calculated according to TBW and LBW were administered by infusion. The time to loss of consciousness was defined as the moment the patient dropped a small object from their hand, and the propofol infusion was stopped. A significant difference was found between the amounts of propofol administered in the groups (TVA:244.7 mg LBW: 183.3 mg, p=0.0002).[12] The time to loss of consciousness was shorter in Group TBW (65.86 s vs 94 s, p=0.0001). Another study by Fai Lam et al.,[4] similar to our study, administered propofol as a rapid single bolus and found a significant difference in propofol amounts between the groups during induction (TVA - LBW; 217.3 ± 39.1 mg-189.5±36.3 mg, p=0.03). No difference was found in the time to loss of consciousness and the need for additional drugs, similar to our study.

There are studies in the literature investigating BIS monitoring. Ibraheim et al. examined the effect of BIS monitoring on PO recovery and IO sevoflurane consumption in morbidly obese patients undergoing laparoscopic gastric banding and found higher sevoflurane consumption in the group without BIS monitoring (19.60 ml vs 15.66 ml, p<0.05).[13] Tong J. Gan et al.[14] compared the amounts of propofol, alfentanil, and nitrous oxide used in normal-weight individuals and found significantly lower anesthetic consumption in the BIS-monitored group. In our study, BIS monitoring was applied to all patients. Inhaled anesthesia was administered to maintain BIS values between 40-60. Despite the different propofol doses administered, BIS monitoring allowed balanced and safe anesthesia maintenance without significant differences in inhaled anesthetic doses between the groups.

Ingrande et al., Kazama et al., and Fai Lam et al. found a dose relationship between the rate and amount of propofol administration and hypotension. Particularly, in the absence of surgical or anesthetic complications, a decrease in MAP of more than 40% within 5 minutes post-induction was defined as post-induction hypotension. In the control group, hypotension was observed in 3 patients, 5 in the LBW group, and 9 in the TBW group, with no significant statistical difference.[5] In Fai Lam et al.'s study, propofol administered based on TBW allowed for rapid loss of consciousness accompanied by hypotension, with at least 83% of patients experiencing hypotension and at least 44% experiencing significant hypotension. Another study by Kazama et al.[15] found that propofol administration leading to SAP <75 mm Hg or a decrease of more than 40% was associated with the relationship between propofol plasma concentration and infusion rate and lean body mass.

In our study, the decrease in SAP and greater impact on Group TBW were attributed to propofol's effects on the cardiovascular system. Administering propofol based on LBW was shown to cause less cardiac instability, similar to other studies. The significant differences in SAP, DAP, and MAP at the 30th minute measurements between the groups were not associated with propofol's pharmacodynamics and pharmacokinetics. Propofol undergoes biotransformation in the liver and is excreted by the kidneys. Its effect begins within seconds and ends rapidly due to its short distribution half-life (2-8 minutes). Patients included in our study were selected to be free of liver and kidney dysfunction, eliminating factors that could affect propofol's duration and elimination. Therefore, the changes in SAP, DAP, and MAP during the IO period were not related to the propofol induction dose but rather to surgical conditions or inhalation anesthetic dose adjustments.

Ingrande et al.,[16] Kazama et al., and Fai Lam et al.[17] found no significant statistical difference in HR changes due to propofol in their studies. The lack of similar changes in HR despite observed SAP changes was attributed to propofol's inhibition of baroreflex response, which normally occurs due to decreased systemic vascular resistance, cardiac contractility, and preload. However, in our study, we observed a greater decrease in MAP (Mean arterial pressure) after induction in Group TVA and considered that it might be due to cardiac depression associated with the high dose of propofol used in obese patients.

BIS can be used for IOA diagnosis. Differences have been found between groups with and without BIS monitoring in the literature. In our study, preoperative BIS averages were the same in both groups, but a greater decrease was observed post-induction in Group TBW. Particularly, BIS averages below 40 were found in Group TBW at 1-2-3 minutes post-induction, indicating deep hypnosis and brain activity close to an isoelectric EEG, which is considered unsafe.[18] In Group LBW, BIS values between 40-60 during the first 1-2-3 minutes post-

induction indicated sufficient hypnosis for safe anesthesia and rapid recovery. A significant difference was found between the groups in BIS values at 1-2-3 minutes post-induction and post-intubation.

In our study, comparison of postoperative effectiveness between the groups was limited to 30 days and did not assess long-term effects and complications. New studies with larger sample sizes are needed to evaluate long-term effects and complications.

CONCLUSION

There is no consensus on the dose-effect strategy for propofol in obese patients in the literature. Our study demonstrated that using propofol doses calculated based on LBW during induction in obese patients undergoing sleeve gastrectomy resulted in less hemodynamic instability. Based on our findings, sufficient and safe anesthesia depth can be achieved with BIS monitoring, with no IOF detected. Administering propofol doses based on TBW in obese patients may negatively affect hemodynamic responses, predispose to cardiovascular complications, and lead to unnecessary costs. Further studies with larger sample sizes, different surgical types, and various weight scales are needed to determine the optimal dose.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethics Committe of the Keçiören Training and Researches Hospital Ethics (Date: 13.12.2017, Decision No: 1563).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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