



The Assessment of Muscle Relaxation and Anesthesia Depth in Morbidly Obese Patients: Should We Determine Drug doses According to Lean Body Weight (LBW)?

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NCD and NKO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors BK and KI managed the analyses of the study. Author IB managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: To give a good planned anesthesia to a morbidly obese patient, it is better to have knowledge about morbid obesity's interaction and impact on drug dosages. For safe drug dosing, not only increased body weight and changed body composition but also physiological changes and comorbid conditions have to be considered.

In this study, we aimed to examine the adequacy of the associated drug with the BIS and TOF monitoring for patients who are scheduled the surgical intervention due to morbid obesity in anesthesia induction. The induction of drug doses were calculated based on LBW; were compared

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with the calculated dose based on IBW and TBW and were evaluated statistically.

Methods: Study was carried out at 35 patients who undergone bariatric surgery. Induction was done with thiopental, rocuronium and fentanyl according to the estimation of lean body weight (LBW). Later, whether enough muscle relaxation and anesthesia depth occurred or not at expected normal period of time, was observed with bispectral index (BIS) and train of four (TOF) monitorization.

Results: According to estimated lean body weight at morbidly obese patients, 5 mg/kg thiopental, 0.6 mg/kg rocuronium and 2 mcg/kg fentanyl found to be not enough for BIS, TOF and intubation quality at any of patients. According to LBW with 8 mg/kg thiopental, 1 mg/kg rocuronium and 2 mcg/kg fentanyl, enough depth of anesthesia and muscle relaxation and good quality of intubation were shown by evaluation of BIS and TOF.

Conclusion: At morbidly obese patients LBW can be estimated by Janmahasatian formula. After administration of 8 mg/kg thiopental, 1 mg/kg rocuronium and 2 mcg/kg fentanyl according to patients' lean body weights that estimated with this formula; evaluation with BIS and TOF have shown that enough depth of anesthesia and muscle relaxation. When intubation quality was evaluated, it was revealed that good and perfect intubation quality.

Keywords: Morbid obesity; lean body weight; BIS; TOF.

1. INTRODUCTION

Nowadays, obesity is among the most significant health problem in both developed and developing countries. According to 2008 data of the World Health Organization (WHO), 1.4 billion adults are overweight people and some of which more than males of 200 million and females of 300 million have obesity disease, i.e. there is an obesity situation for more than 10% of the total adult population all over the world. According to data that was come from 2011, more than 40 million children who are under age 5 are overweight [1,2]. In Obesity Prevalence Study (TURDEP I), the prevalence of obesity was found as 22.3% in Turkey [3,4]. In the TURDEP II study conducted in 2001, it was found that the obesity rate in Turkey have risen 32% This remarkable rapid rise is the alarm attribute [5].

Obesity disease impacts to the many organs. Diabetes, hypertension, increased incidence of obstructive sleep apnea and cardiopulmonary disease narrows the safety margin of anesthetic agents in the morbidly obese. Rational perioperative anesthetic agent selection and application need the knowledge about how obesity affects the pharmacology of drugs which are used in morbid obesity. In morbidly obese, augmented cardiac output, augmented lean body weight (LBW), augmented fat and augmented extracellular fluid volume are the factors which influence pharmacokinetics and pharmacodynamics. Wrong dose application causes the perioperative complications [6,7,8].

Drug doses, which are calculated according to Total body weight (TBW), are applicable to patients of normal weight. However, adipose tissue increases proportionally with TBW in morbidly obese people, lean body weight per kilogram of total body weight percentage reduces. These alterations change the distribution of medication [7]. Ideal body weight defines ideal weight which is involved in maximum life expectancy according to the certain height and body shape [7].

Lean body weight is calculated by subtracting body fat weight from total body weight. Many metabolic activity takes place in lean tissue. Therefore, the dose of lean body weight is the current scale to grade. Janmahasatian et al. have been derived the equation of lean body weight for patients who have weight between 60 and 220 kg patients and height between 150 and 200 cm [9].

In this study, we aimed to examine the adequacy of the associated drug with the BIS and TOF monitoring for patients who are scheduled the surgical intervention due to morbid obesity in anesthesia induction.

2. MATERIALS AND METHODS

This study was conducted in 35 patients undergoing the bariatric surgery in operating room of general surgery, after obtaining the approval of the Ethics Committee Antalya Education and Research Hospital. Morbidly obese patients between 21-59 years of age which are in ASA I-II group were included.

Table 1. The quality of intubation

Mouth opening	Vocal cords	Intubation response	Score	The quality of intubation
Impossible	Full closed	Severe jump	0 Poor	0
Difficult	Half closed	Light jump	1 Weak	0
Middle	Moving	Diaphragm movement	2 Good	13 (%38)
Easy	Open	No response	3 Excellent	22 (%62)

In pre- operation, patients were given information about BIS and TOF monitoring and were taken the written consent associated with work. Before surgery, patients were taken to the premedication room and intravenous cannula was opened with a 20-gauge in antecubital region or hand over for patients, 8-10 ml/kg/hr infusion rate of 0.9% NaCl was initiated.

BIS values of patients were followed with TM 2000 BIS Monitor, USA. GA anesthesia monitor was used for monitorization of (ECG), heart rate (HR), noninvasive systolic arterial pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and peripheral oxygen saturation (SpO2) with standard DII derivation for patients taken to the operating room. Vascular and blood pressure cuff on the same arm and the other arm were also prepared to aim for neuromuscular monitoring. TOF WATCH®-SX (Organon, 27, Ireland) instrument was used for monitoring of neuromuscular transmission.

In our study, the following formula is used in the calculation of IBW [9];

$$\text{Men IBW (kg)} = 50 + 2.3 [\text{height (inches)} - 60]$$

$$\text{Women IBW (kg)} = 45.5 + 2.3 [\text{height (inches)} - 60]$$

In our study, according to the Janmahasatian formula that we used to calculate the LBW [10];

Lean Body Weight for Men (kg):

$$\frac{9270 \times \text{Total Vücut Ağırlığı (kg)}}{6680 + 216 \times \text{Vücut Kitle İndeksi (kg/m}^2\text{)}}$$

Lean Body Weight for Women (kg):

$$\frac{9270 \times \text{Total Vücut Ağırlığı (kg)}}{8780 + 244 \times \text{Vücut Kitle İndeksi (kg/m}^2\text{)}}$$

All patients received 3 minutes 100% oxygen for the preoxygenization. For induction, the lean

body mass (LBW) which was calculated according to Janmahasatian formula patients were performed to induction of anesthesia with 8 mg/kg thiopental sodium, 1 mg/kg rocuronium bromide, 2 mcg / kg by fentanyl. After completion of the injection of thiopental in 30 seconds, the stopwatch is recorded as long as the BIS score below 60 value. After loss of eyelash reflex, it was run a second time piece made of rocuronium injection in 10 seconds. After the calibration of the TOF device for each patient, by starting the perpetual TOF stimulation with determined supramaximal stimulation for 2 Hz at 12 second intervals when TOF was 0.2, the patient's orotracheal intubation was performed. Endotracheal intubation was performed by the same anesthesiologist and the quality was assessed using intubation scale [10,11]. If the total score was 8-9 intubation, it was assessed as excellent; if it was 6-7, it was assessed as good; if it was 3-5, it was assessed as poor and if it was 0-2 are, it was assessed as bad (Table 1). Recorded time with the stopwatch for thiopental and rocuronium were statistically compared with the expected duration of the normal muscle relaxation and hypnosis.

2.1 Statistical Analysis

Data were analyzed with using PASW 18 (SPSS/IBM, Chicago, IL, USA) for statistical analysis. Data were expressed as the mean \pm standard deviation, number and percent. BIS and TOF time were evaluated with using hypothesis tests for a single sample. The level of significance was accepted as $p < 0.05$.

3. RESULTS

Our study was conducted in 35 patients that were scheduled bariatric surgery under general anesthesia and those were between 21-59 years old, ASA I-II risk group, and have the BMI of 40 or above this. 81% of patients were female (28 patients), 18% of patients were male (7 patients). The average age of patients in the study was found as 36 ± 9 years (min. 21, max. 59 years); the average height was found as 160

± 10 cm (min. 148 cm, max. 190 cm); the average weight was found as 125 ± 18 kg (min. 100, max. 180 kg); the average BMI was found as 45 ± 5 (min. 40 kg / m², max. 68 kg / m²); LBW average was found as 61 ± 12 kg (min. 48 kg, max. 87 kg) (Table 2).

Table 2. Demographic datas, BMI, LBW and ASA (mean \pm standart deviation)

	Mean	SD
Age (year)	36	9
Gender	Male	7 (%18)
	Female	28 (%81)
Height (cm)	160	10
Weight (kg)	125	18
BMI	45	6
LBW	61	12
ASA	I	20 (%56)
	II	15 (%44)

Average thiopental dose used for induction was found as 487 ± 98 mg (min. 385 mg, max. 700 mg); the rocuronium dose used for induction was found as 61 ± 12 mg (lowest 48 mg, the highest 87 mg). The average fentanyl dose used was 129 ± 32 mcg. Duration of the falls of BIS values below 60 within 30 seconds after injection of 8 mg/kg thiopental calculated based on LBW was found as 36 ± 12 sec. (min. 20 sec, max. 75 sec).

Duration of the falls of TOF values below 0.2 within 10 seconds after injection of 1 mg/kg rocuronium calculated based on LBW was found as 61 ± 12 sec. (min. 30 sec, max. 120 sec) (Table 2,3).

Table 3. The induction doses determined by LBW (mean \pm standart deviation)

	Mean	SD
Thiopental	487 mg	98 mg
Rocuronium	61 mg	12 mg
Fentanyl	129 mcg	32 mcg

BIS durations when compared with sufficient time for 60 seconds, which is normally expected depth of anesthesia was found statistically significant with a test for one sample ($p < 0.0001$). When 8 mg/kg of thiopental calculated dose according to LBW was injected in 30 seconds during induction, it has been seen that this thiopental concentration concluded the sufficient hypnotic level. In 32 of 35 patients, BIS value fell below the 60 before 60 seconds. In other 3 patients adequate anesthetic depth was

achieved at the latest within 75 seconds. Thus, in 92% of patients was achieved sufficient anesthetic depth within the first 75 seconds; in the remaining 8% of patients was achieved that within the first 75 seconds. BIS scores of the patients continued to remain below the 60 until the end of intubation time. After intubation, volatile anesthetics were continued by hypnosis (Table 4).

Table 4. The mean duration of TOF and BIS (mean \pm standart deviation)

	Mean	SD
BIS	36 sn	12 sn
TOF	61 sn	12 sn

TOF durations when compared with sufficient time for 60 seconds, which is normally expected muscle relaxiton was found statistically insignificant with a test for one sample ($p < 0,98$). When 1 mg/kg of rocuronium calculated dose according to LBW was injected in 10 seconds during induction, it has been seen that this rocuronium concentration did not conclude the sufficient muscle relaxiton for intubation. In 8 of 35 patients adequate muscle relaxation was achieved in longer than 60 seconds. In 3 patients adequate muscle relaxation was provided between 60 and 90 seconds. In the remaining 5 patients, adequate muscle relaxation was reached between 90 and 120 seconds. The longest obtained muscle relaxation duration was found as 120 seconds (Table 4).

TOF times was statistically significant when it was compared with the normal muscle relaxation which was 90 seconds ($p < 0.0001$). When 1 mg/kg of rocuronium calculated dose according to LBW was injected in 90 seconds during induction, it has been seen that this rocuronium concentration concluded the sufficient muscle relaxiton for intubation.

Table 5. The drug doses determined by TBW (mean \pm standart deviation)

	Mean	SD
Thiopental	997	147
Rocuronium	124	18
Fentanyl	258	42

Patients were evaluated intubation made by the same anesthesiologist. When evaluated according to intubation quality scale; No patients were not included in the group of weak or bad. In 22 of the patients intubation was assessed as

excellent, 13 of them were considered as well (Table 1).

Table 6. The drug doses determined by IBW (mean±standart deviation)

	Mean	SD
Thiopental	457	83
Rocuronium	57	10
Fentanyl	120	21

In the study, the total weight of morbidly obese patients we observed if 8 mg/kg thiopental, 1 mg/kg rocuronium and 2 mcg/kg fentanyl had been made; mean thiopental dose would be 997 ± 147 mg, mean dose rocuronium would be 124

± 18 mg, the mean fentanyl dose would be 258 ± 42 mcg. These doses were significantly high and significant compared with the LBW doses statistically ($p < 0.0001$) (Table 5, Table 6).

According to the ideal weight of morbidly obese patients if 8 mg/kg thiopental, 1 mg/kg rocuronium and 2 mcg/kg fentanyl had been made; mean thiopental dose would be 457±83 mg, mean dose rocuronium would be 57±10 mg, the mean fentanyl dose would be 120±21 mcg. These doses were found to be highly significant and low compared separately with TBW and LBW statistically ($p < 0.0001$, $p < 0.0001$) (Fig. 1, Fig. 2, Fig. 3).

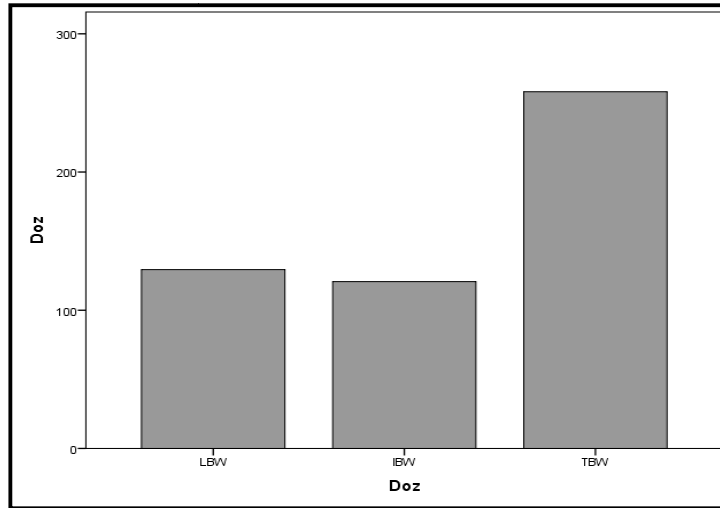


Fig. 1. The comparison of fentanyl dose according to TBW, IBW and LBW

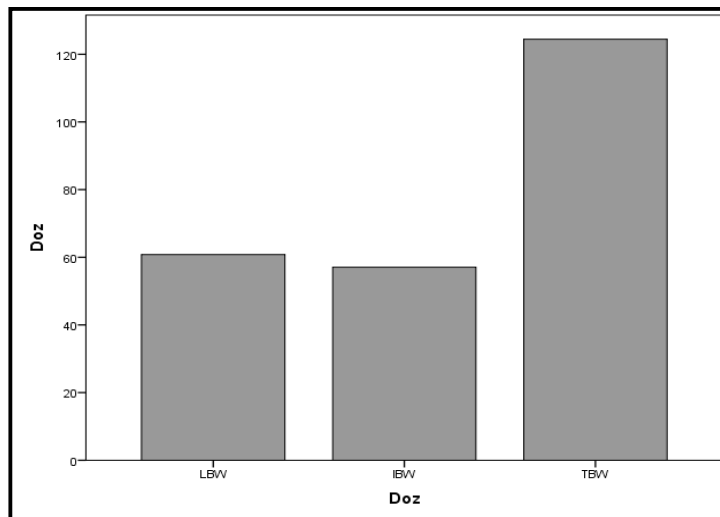


Fig. 2. The comparison of rocuronium dose according to TBW, IBW and LBW

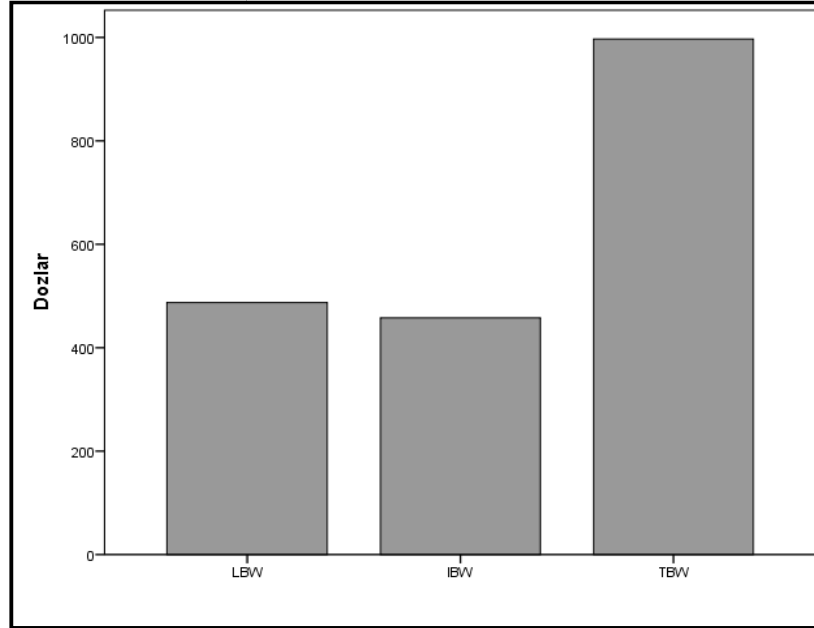


Fig. 3. The comparison of thiopental dose according to TBW, IBW and LBW

In these findings, induction doses calculated based on TBW will result in overdose in morbidly obese patient; drug doses made based on IBW will result in inadequate depth of anesthesia and insufficient muscle relaxation. To prevent this situation in the morbidly obese, induction should be made for sodium thiopental, rocuronium bromide and fentanyl on the basis of LBW calculated according to the Janmahasatian Formula. In addition, individual differences and altered drug clearance in obese morbidly should be considered, BIS and TOF monitoring should be done for adequate anesthetic depth, adequate muscle relaxation and secure extubation.

4. DISCUSSION

In our study, was made ASA I-II accompanied with BIS and TOF monitoring in patients undergoing elective bariatric surgery under general anesthesia by observing depth of anesthesia and muscle relaxation. Lean body weight of morbidly obese patients (LBW) was calculated according to Janmahasatian formula [9]. According to calculated LBW, 5 mg / kg thiopental sodium, 0.6 mg / kg rocuronium bromide and 2 mcg / kg fentanyl were given for induction. Time duration for falling of BIS value below 60 and TOF values below 0.2 were recorded with two separate stopwatch. The BIS value did not fall below 60 in any of the patients

who underwent induction using these doses and TOF value was not found to reach the 0.2. Dose changes were made to continue working. Based on calculated LBW value according to the same formula, 8 mg / kg thiopental sodium, 1 mg / kg rocuronium bromide and 2 mcg / kg made fentanyl were applied and recorded time with the stopwatch were compared statistically with the normal expected duration and intubation quality of patients was evaluated by the same anesthesiologist clinically. However, induction of drug doses were calculated based on LBW; were compared with the calculated dose based on IBW and TBW and were evaluated statistically.

Today obesity in both developed and developing countries are among the most significant health problems. According to 2008 data of The World Health Organization (WHO), 1.4 billion adults are overweight, over 200 million of them obese are men and up to 300 million are women, ie more than 10% of the world adult population has obesity status. According to data from the year 2011, more than 40 million children under age 5 are also overweight [1,2]. In Turkey Obesity Prevalence Study (TURDEP I), the prevalence of obesity was found as 22.3% [4]. TURDEP II study made in 2010 found that increased rates of obesity in Turkey to 32%. This remarkable rapid increase is quality of the alarm [5]. These patients need to receive anesthesia

due to bariatric surgery or other surgical procedure and more often than before in the operating room we will encounter morbidly obese patients [12].

For well-planned anesthesia process of morbidly obese patient who is scheduled surgery, it should be known that how morbid obesity effects the drug doses. Not only increased body weight and altered body composition, but physiological changes and comorbid conditions should be also evaluated for safe medication dosage. As a result of that, the wrong dose application increases the perioperative complications [10,11,13,14].

Kuipers et al. showed that according to ideal body weight to 1.2 mg / kg rocuronium provides intubation conditions 60 seconds after injection in morbidly obese people. They suggested the in morbidly obese TOF monitoring, because the maximum duration of drugs and drug disposal are highly variable for rocuronium and all other muscle relaxants. In our study, when patients were applied the rocuronium according to lbw's 0.6 mg / kg muscle relaxation was found to occur in much longer than the normal expected time. Since morbidly obese patients had longer muscle relaxation time than expected due to potential difficult a mask and/or difficult intubation and that is not desirable situation, study was gone on with changing in dose. According to LBW 1 mg/kg rocuronium was still used in induction. At this dose, reach time of TOF to 0.2 was found ($p < 0.98$) as meaningless when it was compared with the normal expected time of muscle relaxation which is 60 seconds, it was found as statistically significant ($p < 0.0001$) when it was compared with 90 seconds [15].

Shibutani et al. revealed a variable that is called pharmacokinetic mass as a new dose scale for the maintenance of fentanyl in obese [16]. Likewise LBW, pharmacokinetic mass recommends the maintenance dose of fentanyl which is LBW-based. Obesity increases the likelihood of preoperative respiratory depression. Therefore, they suggested to be carefully titrated according to the patient needs for the implementation of fentanyl and other opioids [16,17,18]. In our study, calculated fentanyl doses based on LBW, and IBW and TBW values were compared statistically and it was observed that the calculated dose based on TBW was significantly higher ($p < 0.0001$); the calculated

dose based on IBW was considerably lower ($p < 0.0001$).

Wada et al. have shown that arterial peak concentration of 250 mg dose of thiopental was 50% less compared to lean individuals in morbidly obese patients with high cardiac output by using physiologically based pharmacokinetic simulation. They have observed that thiopental dose was equal to the peak of a normal human plasma concentrations according to increased cardiac output or the lean body mass and they have recommended the use of LBW [19]. In our study, thiopental dose was calculated as 5 mg / kg with using LBW and it was injected in 30 seconds. BIS value was over 60 in 10 seconds after the end of the injection, this situation continued in this way without falling for 5 morbidly obese patients, and we increased the dose to 8 mg / kg and continued to study. After thiopental dose which was calculated as 8 mg/kg according to LBW and was injected within 30 seconds, fall period of BIS values below to the 60 were recorded and were found the statistically significant ($p < 0.0001$) when it was compared to 60 seconds. BIS scores of the patients continued to remain below the 60 until the end of intubation time. After intubation hypnosis was continued with volatile anesthetic.

In the study of Liu with 1380 patients, short-term and ambulatory cases were followed up with/without BIS monitoring. In BIS monitoring group, use of anesthetics decreased by 19%, postoperative nausea and vomiting decreased by 32%, the time spent in ASBÜ decreased by 45%. To prevent the commonly encountered opening of postoperative anastomosis lines in patients who underwent bariatric surgery BIS monitoring is important [20].

Myles et al. conducted the prospective and double-blind randomized study which is mediated with BIS about reduction of awareness during surgical anesthesia. 2463 patients were randomly divided into 2 groups which have more risk alertness. 1225 patients were included in the BIS group and 1238 patients were included in the routine follow-up group. The results showed that awareness was reported for 2 patients in the BIS group and for 11 patients in the routine follow-up group. BIS mediated anesthesia reduces the risk of alertness by 82% [21]. In addition, BIS monitoring should be done because morbidly obese patients are in the

group that is high risk of anesthesia awareness [21,22].

5. CONCLUSION

In our findings, induction doses calculated based on TBW will result in overdose in morbidly obese patient; drug doses made based on IBW will result in inadequate depth of anesthesia and insufficient muscle relaxation. As a result; induction drug doses should be calculated by LBW to reduce perioperative complications that we encounter more frequently every day in operating room for morbidly obese patients, it should be protected from the possibility of inadequate doses or high doses. Induction should be performed accompanied with BIS and TOF monitoring to morbidly obese patients, and it should still be extubated with TOF monitoring to protect from postoperative residual paralysis.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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