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REPORTS OF ORIGINAL INVESTIGATIONS

Optimal propofol induction dose in morbidly obese patients: A randomized controlled trial comparing the bispectral index and lean body weight scalar

Posologie optimale de propofol pour l'induction des patients obèses morbides: une étude randomisée contrôlée comparant l'indice bispectral et une échelle de poids idéal

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Abstract

Purpose *Propofol dosing based on total body weight (TBW) can lead to overdosing in morbidly obese (MO) patients. Our aim was to determine whether an induction dose of propofol based on a bispectral index (BIS) target is better for achieving loss of consciousness in MO patients than dosing based on lean body weight (LBW).*

Methods *Sixty MO patients with a body mass index (BMI) of ≥ 40 kg·m^{-2} were randomized to either BIS- or LBW-based propofol dosing groups. Anesthesia was induced with a propofol infusion of 100 mg·kg^{-1}·hr^{-1} to an initial target endpoint of a BIS of 50 (BIS group) or until a precalculated dose of 2.6 mg·kg^{-1} LBW based on the Janmahasatian equation was administered (LBW group). Induction was assessed using the observer's assessment alertness/sedation scale (OAA/S). If an OAA/S score of 0 was not achieved, infusions continued until it reached 0. The groups were compared for the primary outcome which was the difference in the propofol doses at the initial target endpoint.*

Results *The median [interquartile range] OAA/S score at the initial target endpoint was lower in the BIS group than in the LBW group (0 [0-0] vs 1 [0-3], respectively; median difference 1, 95% confidence interval [CI] 0 to 3; P = 0.001). The number of patients requiring additional propofol doses was also higher for the LBW group [1 vs 18 patients, respectively; relative risk of requiring additional propofol 18; 95% CI 3 to 126; P = 0.001]. The mean (SD) propofol dose at the target endpoint was significantly lower in the LBW group than in the BIS group [164 (36) mg vs 225 (44) mg, respectively; mean difference 61 mg; 95% CI 41 to 83 mg; P = 0.002]. There was no difference between the two groups, however, regarding the total induction dose of propofol needed for the OAA/S to reach 0 (P = 0.07).*

Conclusion *The induction dose of propofol based on the BIS index was different from the induction dose based on LBW in MO patients. Patients in the LBW group required additional propofol to achieve an OAA/S of 0.*

Résumé

Objectif *Le dosage du propofol en fonction du poids corporel total (PCT) peut entraîner un surdosage chez les patients obèses morbides. Notre objectif était de déterminer si une dose d'induction de propofol fondée sur une cible d'indice bispectral (BIS) était plus adaptée pour obtenir une perte de conscience chez les patients obèses morbides qu'une posologie fondée sur le poids idéal.*

Méthode *Soixante patients obèses morbides avec un indice de masse corporel (IMC) ≥ 40 kg·m^{-2} ont été*

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randomisés en groupes posologiques de propofol fondés sur le BIS ou le poids idéal. L'anesthésie a été induite à l'aide d'une perfusion de propofol de 100 mg·kg^{-1}·h^{-1} jusqu'à une cible initiale de BIS de 50 (groupe BIS) ou jusqu'à ce qu'une dose pré-calculée de 2,6 mg·kg^{-1} de poids idéal, fondée sur la formule de Janmahasatian, soit administrée (groupe poids idéal). L'induction a été évaluée selon l'échelle de sédation OAA/S (Observer's Assessment Alertness/Sedation Scale). Si un score de 0 sur l'échelle OAA/S n'était pas obtenu, les perfusions étaient poursuivies jusqu'à l'obtention de cette valeur. Les groupes ont été comparés par rapport au critère d'évaluation principal, soit la différence entre les doses de propofol au critère d'évaluation initial.

Résultats *Le score OAA/S médian [écart interquartile] au critère d'évaluation initial était plus bas dans le groupe BIS que dans le groupe poids idéal (0 [0-0] vs 1 [0-3], respectivement; différence médiane 1, intervalle de confiance [IC] 95 % 0 à 3; P = 0,001). Le nombre de patients nécessitant des doses supplémentaires de propofol était également plus élevé dans le groupe poids idéal [1 vs 18 patients, respectivement; risque relatif d'avoir besoin de propofol supplémentaire 18; IC 95 % 3 à 126; P = 0,001]. La dose moyenne (ÉT) de propofol au critère d'évaluation initial était significativement plus basse dans le groupe poids idéal que dans le groupe BIS [164 (36) mg vs 225 (44) mg, respectivement; différence moyenne 61 mg; IC 95 % 41 à 83 mg; P = 0,002]. Aucune différence n'a toutefois été observée entre les deux groupes quant à la dose d'induction totale de propofol nécessaire pour que l'échelle OAA/S atteigne 0 (P = 0,07).*

Conclusion *La dose d'induction de propofol fondée sur l'indice BIS était différente de celle fondée sur le poids idéal chez les patients obèses morbides. Les patients du groupe poids idéal ont eu besoin de plus de propofol pour atteindre un score de 0 sur l'échelle OAA/S.*

Obesity, a major public health problem, has long been recognized as a precursor of morbidity and premature mortality.[1] Consistent with global trends, an increasing number of morbidly obese (MO) patients [defined by the World Health Organization as having a body mass index (BMI) $\geq$ 40 kg·m^{-2}][2] are undergoing surgical procedures.[3] Surgery such as gastric bypass or laparoscopic adjustable gastric band insertion can be an integral part of the modalities for treating morbid obesity.[4]

Dosing recommendation of anesthetics is usually based on the total body weight (TBW). Dosing recommendations based on TBW are valid for normal-weight patients but not for MO patients as the fat mass and lean body weight (LBW) do not increase proportionately.[5] Although there are no clear data to guide the clinical decision regarding dose adjustments of intravenous anesthetics in the MO patient,[6,7] their dosing based on LBW has been suggested for MO patients.[8,9] LBW is the difference between the TBW and fat mass and can be calculated using the Janmahasatian equation.[5] The increase in LBW of MO patients has been estimated to be 20-40% that of normal-weight patients.[9] Furthermore, physiological changes associated with MO - e.g., increased cardiac output, changes in the regional blood flow, increased total blood volume, distribution volumes - affect the pharmacokinetics of anesthetics.[9,10] Derangements in respiratory functions - e.g., reduction of functional residual capacity, vital capacity, lung compliance; increased respiratory resistance - alter the pharmacodynamics and narrow the therapeutic window of anesthetics.[9]

Propofol is a highly lipophilic agent and is commonly used for anesthesia induction in obese and non-obese patients. A higher induction dose than required can have a detrimental effect in a vulnerable MO patient because these patients often have co-morbid conditions such as coronary artery disease, left ventricular hypertrophy, hypertension, stroke, obstructive sleep apnea, and/or pulmonary hypertension.[3,11-14] There is no consensus, however, as to the best weight scalar to be used to estimate LBW for administering propofol to MO patients.[8,15] The Janmahasatian equation has been suggested as an accurate means to calculate LBW and has favourable predictive properties when compared with LBW derived from dual-energy *x-ray* absorptiometry in MO individuals.[16]

The bispectral index (BIS) is a brain function monitor, based on the information on processed electroencephalograms, that is used to assess the depth of anesthesia.[17] Compared with traditional weight-based dosing, Gürses *et al.* recorded 43% reduction of the induction dose of propofol assessed using BIS analysis in non-obese patients.[18] In MO patients, utilization of the BIS monitor has been suggested to provide faster, more predictable recovery by preventing drug overdosing.[19]

The aim of this study was to determine, in MO patients, whether the induction dose of propofol based on the BIS is better for achieving loss of consciousness (LOC) than a dose based on the LBW scalar. We hypothesized that, as BIS provides an indication of propofol's targeted effect (i.e., level of hypnosis), it would be more useful than the LBW scalar for determining the optimal propofol induction dose.

Methods

After obtaining approval from the University Health Network Research Ethics Board (REB number 10-

0824AE, March 2012) and written informed patient consent, 60 MO (BMI $\geq$ 40 kg·m^{-2}) adult patients were recruited for this study from April 2012 to December 2012. All of the patients were scheduled for elective laparoscopic Roux-en-Y gastric bypass or vertical sleeve gastrectomy requiring endotracheal intubation. The exclusion criteria included a history of significant cardiac, pulmonary, liver, or renal disease; an anticipated difficult airway; patients scheduled for awake bronchoscopic intubation. Individuals with Alzheimer's disease, dementia, brain atrophy, previous cerebrovascular accident, and other neurological disorders and those on long-term drugs affecting the central nervous system, chronic benzodiazepines, and/or opioids were also excluded because of the possible effect on the BIS index.

All patients were weighed on the same scale in our preoperative clinic. The LBW was calculated from the recorded TBW using the Janmahasatian equation.[5]

LBW (kg) in men = (9270 · TBW)/6680 + (216 · BMI)

LBW (kg) in women = (9270 · TBW)/8780 + (244 · BMI)

Preoperative investigations, fasting guidelines, and preoperative preparations were performed as per the usual standard practice.[20] A statistician who was not otherwise directly involved with conducting the study randomly allocated the patients (1:1) into two groups (n = 30 each) according to a computer-generated randomization scheme. Patient assignments were placed in sequentially numbered, opaque, sealed envelopes that were opened just before the patient was brought into the operating room. The randomization scheme was kept inaccessible throughout the study period. Only the research staff member collecting the data was not blinded to the randomization.

On the day of the surgery, the patients received no premedication. After arrival in the operating room, patients were positioned on the Troop^{TM} elevation pillow (Goal Medical, Canada), aligning the suprasternal notch with the external auditory meatus to facilitate maximal endotracheal intubation by obtaining a head-elevated laryngoscopy position. Routine monitoring was applied to all patients. The BIS index (Medtronic, Canada) was additionally applied to the BIS group. These measurements, not performed in the LBW group, were performed before induction and recorded every 15 sec during induction in the BIS group. Pre-oxygenation was carried out for a minimum of three minutes to ensure adequate de-nitrogenation. Before induction, an intravenous cannula was inserted into a hand vein, normal saline was infused, and fentanyl 3 μg·kg^{-1} LBW was given to both groups. Anesthesia was induced with a propofol infusion of 100 mg·kg^{-1}·hr^{-1} until a BIS target of 50 was reached (BIS group) or until a pre-calculated total dose of 2.6 mg·kg^{-1} LBW was reached (LBW group).

The BIS target of 50 is based on studies by Gürses *et al.*[18] and Arya *et al.*,[21] which compared the clinical endpoint of the loss of verbal response with BIS for induction with propofol, using a BIS of 48 $\pm$ 2 as an endpoint for induction. The 2.6 mg·kg^{-1} dose of propofol was based on the results obtained in the study conducted by Ingrande *et al.*, which showed that the LBW scalar is appropriate for inducing MO patients with propofol.[8]

After the precalculated dose of propofol was administered to the LBW group or when the BIS index reached 50 in the BIS group, LOC was assessed using the responsiveness scores of the modified Observer's Assessment of Alertness/Sedation Scale (OAA/S).[22] A score of 0 (i.e., the patient does not respond to a painful trapezius squeeze) was used to confirm LOC (Table 1).[18] If a 0 score was achieved, the infusion was stopped. If the OAA/S score was $>$ 0, the infusion was continued for another 30 sec, and the scores were reassessed. This sequence was repeated until the OAA/S score reached 0.

The primary outcome measured was the difference in the propofol doses at the initial target endpoint in each group - i.e., when the BIS was 50 in the BIS group or the 2.6 mg·kg^{-1} dose was completed in the LBW group. The secondary outcomes measured were the OAA/S score at the target endpoint in each group, the number of patients requiring additional propofol, the total induction dose of propofol, and the time required for the OAA/S to reach 0. In addition, the heart rate and noninvasively measured mean arterial pressure (MAP) readings were recorded before induction and every minute for the first five minutes after the start of induction.

Neuromuscular blockade with rocuronium [0.6 mg·kg^{-1} of ideal body weight (IBW)] was administered when LOC was confirmed with OAA/S = 0. The IBW was calculated using the following formula.

Men: IBW = 50 kg + 2.3 kg for each inch $>$ 5 feet in height

Women: IBW = 45.5 kg + 2.3 kg for each inch $>$ 5 feet in height

Table 1 Responsiveness scores of the modified Observer's Assessment of Alertness/Sedation Scale (OAA/S)

Responsiveness	Score
Responds readily to name spoken in normal tone	5 (Alert)
Lethargic response to name spoken in normal tone	4
Responds only after name is called loudly and/or repeatedly	3
Responds only after mild prodding or shaking	2
Responds only after painful trapezius squeeze	1
Does not respond to painful trapezius squeeze	0

Patients were bag-and-mask ventilated after LOC and until laryngoscopy and intubation were performed after the disappearance of train-of-four in both groups.

Statistical analysis

The sample size was calculated used G*Power 3.1 software and was based on a study conducted by Gürses *et al.*[18] Those authors reported a 43% reduction of propofol dose from a mean (SD) of 147.4 (12.1) mg to 84.3 (11.4) mg when BIS was used as an endpoint for induction compared with a standard 2 $mg \cdot kg^{-1}$ propofol dose. Assuming a similar change in the mean dose of propofol consumption in the BIS group[18] with an alpha error of 0.05 and power of 0.80, a total of 30 patients were needed to be enrolled in each arm.

The results were analyzed using the Statistical Package for Social Sciences for Windows version 14 (SPSS Inc., Chicago, IL, USA). Continuous data with normal distribution are presented as means (SD). Data with skewed distribution are presented as medians [interquartile range (IQR)]. Categorical data are presented as frequencies and percentages. The primary outcome of the difference in propofol doses between the BIS and LBW groups at the initial propofol infusion target endpoint was analyzed using an unpaired, two-tailed *t* test. Continuous data for the different propofol doses were also analyzed with an unpaired, two-tailed *t* test. Categorical data on the number of patients requiring additional propofol were analyzed using the Chi-square test with confidence intervals (CI) on the relative risk (RR) of requiring additional propofol calculated based on the methods described by Gardner and Altman.[23] The hemodynamics data were analyzed using an independent samples *t* test. A value of $P < 0.05$ (two-sided) was considered to indicate statistical significance.

Results

Of the 1314 patients screened for inclusion, 86 met all the eligibility criteria. Patients were excluded if their BMI was < 40 $kg \cdot m^{-2}$, they did not give informed consent, or they were a part of another study. Of the 86 eligible patients, 26 patients were not enrolled because the research staff member was not available during the patient's surgery.

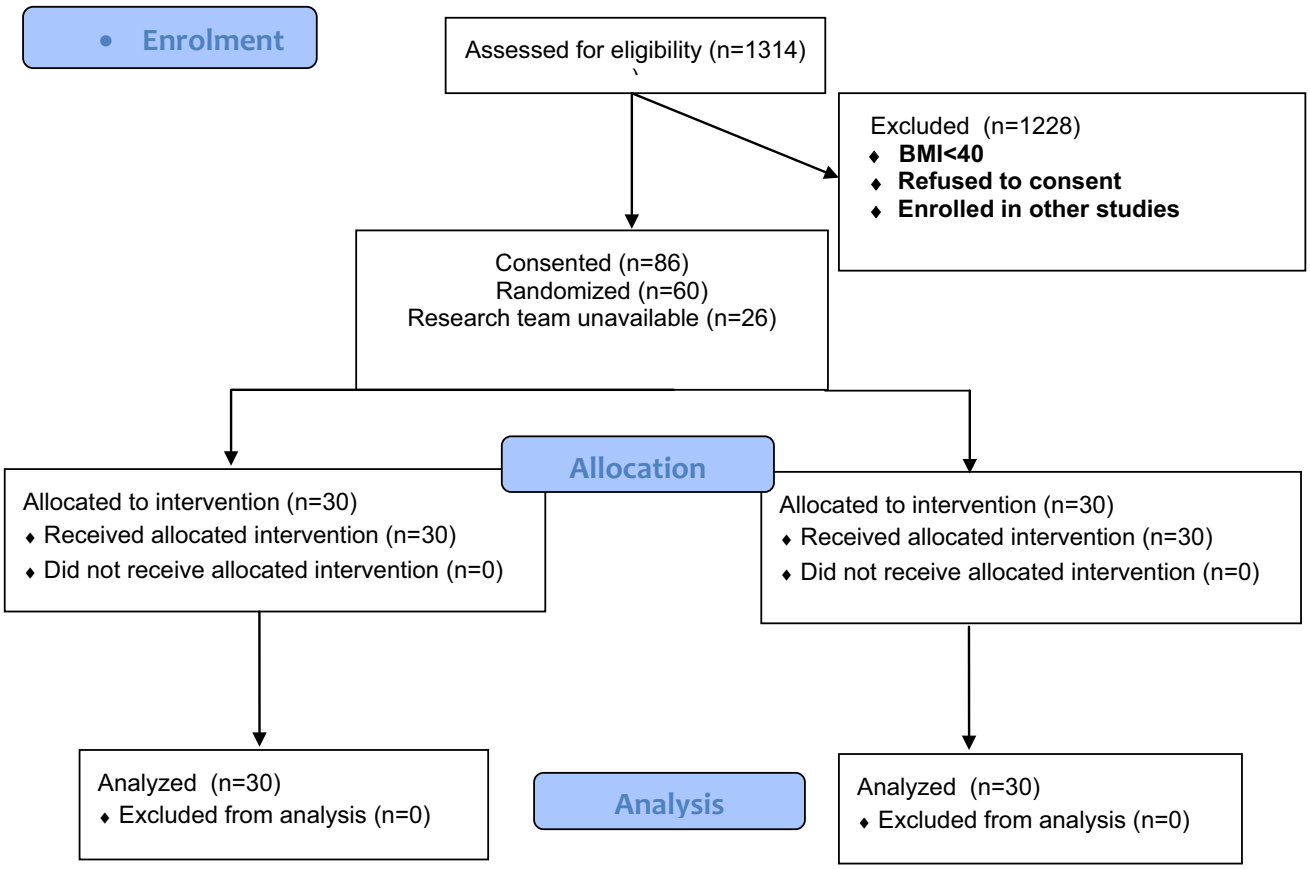

Fig. 1 Consort diagram. Flow diagram of participants included in the study

Table 2 Demographic and descriptive information

Characteristic	BIS group (n = 30)	LBW group (n = 30)
Age (yr)	45 (12)	39 (11)
Sex: Male/ female	2 (7%) / 28 (93%)	5(17%)/25 (83%)
BMI ($kg \cdot m^{-2}$)	48 (7)	50 (7)
Total body weight (kg)	129 (20)	136 (25)
Lean body weight (kg)	59 (7)	63 (14)
Associated medical co-morbidities		
OSA	15 (50%)	18 (60%)
Hypertension	19 (63%)	10 (33%)
DM	14 (47%)	7 (23%)
GERD	17(57%)	12 (40%)
CAD	2 (7%)	0 (0%)
COPD	1 (3%)	2 (28%)
Hypothyroidism	4 (13%)	1 (3%)

Data presented as mean (SD) or number (%)

BIS = bispectral index; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; GERD = gastroesophageal reflux disease; LBW = lean body weight; OSA = obstructive sleep apnea

Thus, 60 MO adult patients, 30 in each group, were enrolled and were randomly allocated to the LBW or BIS group (Fig. 1).

The baseline characteristics of the patients are shown in Table 2. Most of the demographic variables were comparable in the two groups, with the exceptions that the BIS group was somewhat older [45 (12) yr] than the LBW group [39 (11) yr], and 63% of patients in the BIS group had hypertension compared with 33% in the LBW group. All enrolled patients completed the study.

The propofol dose at the target endpoint was significantly lower in the LBW group than in the BIS group [164 (36) mg *vs* 225 (44) mg, respectively; mean difference 61, 95% CI 41 to 83; P = 0.001] (Table 3). The median [IQR] OAA/S score at the initial target endpoint was lower in the BIS group than in the LBW group (0 [0-0] *vs* 1 [0-3], respectively; median difference 1, 95% CI 0 to 3; P = 0.001), as were the number of patients requiring additional propofol doses (1 *vs* 18 patients, respectively; relative risk of requiring additional propofol 18; 95% CI 3 to 126; P = 0.001). Among the 30 patients in the LBW group, 18 (60%) required additional propofol to reach 0 on the OAA/S scale compared with only one of 30 patients (3%) in the BIS group (RR of requiring additional propofol in the LBW group 18, 95% CI 3 to 126; P = 0.001).

There were no differences in the total mean (SD) induction dose of propofol [3.9 (0.7) $mg \cdot kg^{-1}$ LBW in the BIS group *vs* 3.3 (0.7) $mg \cdot kg^{-1}$ LBW in the LBW group; mean difference 0.6, 95% CI 0.25 to 1.01 $mg \cdot kg^{-1}$; P = 0.07]. The mean (SD) time taken for OAA/S to reach 0 in the BIS group was 146 (24) sec *vs* 140 (39) sec in the LBW group (mean difference 6.4, 95% CI −10.4 to 23.2 sec; P = 0.452).

There was no difference in the mean (SD) heart rate. However, the mean (SD) arterial pressure (MAP) was significantly higher in the LBW group immediately after intubation and until the study ended [104 (23), 105 (19), and 98 (16) mmHg in the LBW group *vs* 92 (18), 94 (14), and 88 (14) mmHg in the BIS group at three, four, and five minutes, respectively; P = 0.032, 0.007, and 0.020, respectively] (Figs 2 and 3).

Discussion

In this study, the induction dose of propofol based on BIS was better for achieving a predictable LOC than the dosing based on the calculated LBW in MO patients. Our findings suggest that the LBW-based dose of propofol according to the Janmahasatian equation may be inadequate for inducing anesthesia in MO patients.

Sixty percent of patients in the LBW group required an amount of propofol that was above the predetermined dose for the OAA/S to reach 0, which was our target anesthesia LOC endpoint. We induced our patients with a propofol infusion up to a precalculated dose of 2.6 $mg \cdot kg^{-1}$ in the LBW group based on the results of the study conducted by Ingrande *et al.*[8] Those authors used a propofol infusion of 100 $mg \cdot kg^{-1} \cdot hr^{-1}$ until LOC and found that the mean dose requirement for propofol was 2.8 $mg \cdot kg^{-1}$ of the LBW. They suggested that LBW was the most appropriate weight-based scalar. In our study, the total propofol dose

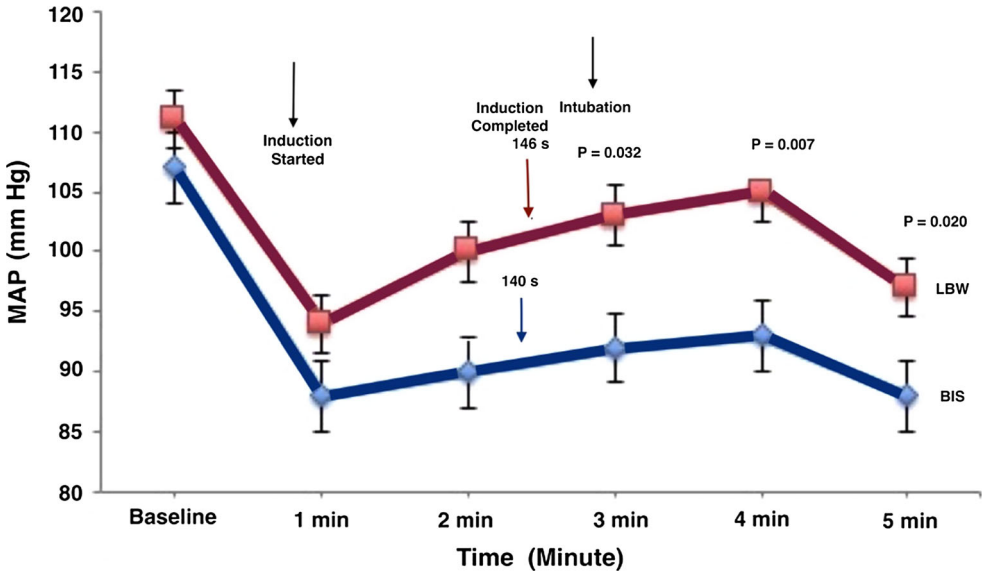

Fig. 2 Mean arterial pressure at various times during induction. Mean arterial pressure before induction and during the initial five minutes after induction in the BIS and LBW groups. Mean arterial pressure was significantly higher in the LBW group immediately after intubation and the elevation was sustained until the study ended compared to the BIS group. Data points and lines in red represent the LBW group. Data points and lines in blue represent the BIS group. *P* values were obtained by comparing the MAP between the LBW and BIS groups at three, four, and five minutes using one-way analysis of variance. Arrows indicate the time of induction and intubation in the LBW and BIS groups. BIS = bispectral index; LBW = lean body weight; MAP baseline = mean arterial pressure at baseline (before induction)

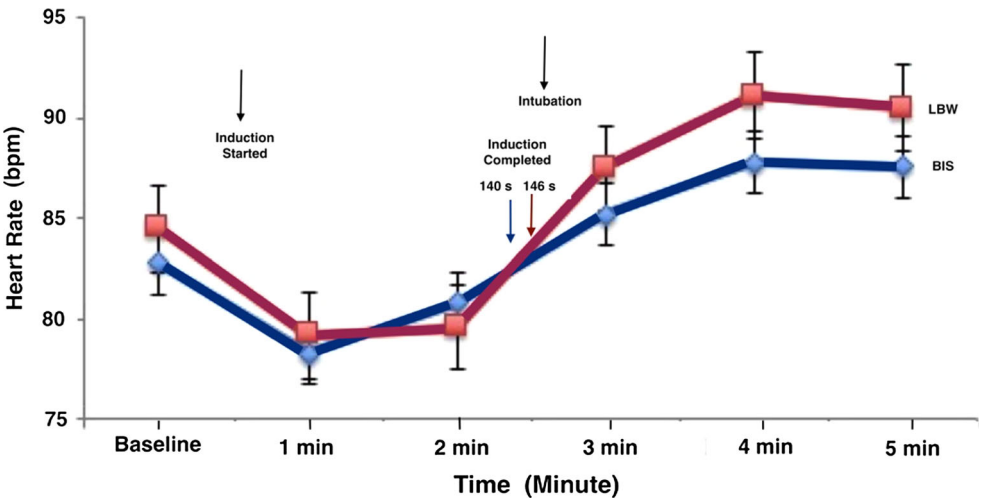

Fig. 3 Heart rate changes at various times during induction (before induction and during the initial five minutes after induction) in the BIS and LBW groups. Data points and lines in red represent the LBW group. Data points and lines in blue represent the BIS group. The arrows indicate the time of induction and intubation in both LBW and BIS groups. BIS = bispectral index; BPM = beats·min^{-1}; LBW = lean body weight

in the LBW group when OAA/S reached 0 was 3.3 (0.7) mg·kg^{-1} LBW compared to 2.8 mg·kg^{-1} LBW in the Ingrade *et al.* study. The patients in our LBW group had a higher mean (SD) BMI [49.8 (7.2) kg·m^{-2}] than Ingrande *et al.*'s patients, whose average BMI was 46.5 (6.5) kg·m^{-2}.[8] Despite receiving extra doses of propofol, patients in the LBW group had a significant increase in the blood pressure for a few minutes after intubation. The rise in heart rate and blood pressure is usually well tolerated by healthy individuals but may have serious consequences in MO patients with their possible co-morbidities of hypertension or coronary artery disease.

We noted a significant difference in the propofol dose between the two study groups at the target endpoint. This finding suggests that patients in the LBW group, who had been given a lower dose of propofol, could have been at increased risk for awareness during induction had neuromuscular blockade and laryngoscopy taken place at this initial target time. However, we did not collect data on awareness, and none of our patients explicitly reported it.

Table 3 Clinical data

Parameter	BIS group (n = 30)	LBW group (n = 30)	Mean Difference (95% CI)	Median Difference (95% CI)	P value	RR (95% CI)
OAA/S at the target point	0 (0-0)	1 (0-3)*		1 (0 to3)	0.001	
Time required for OAA/S to reach 0 (sec)	146 (24)	140 (39)	6 (−10 to 23)			
Propofol dose at target point (mg)	225 (44)*	164 (36)	61 (41 to 83)		0.001	
Propofol dose for LBW at target point ($mg{\cdot}kg^{-1}$)	3.8 (0.6)*	2.6 (0.05)	1.2 (1.0 to 1.5)		0.001	
Propofol dose for TBW at target point ($mg{\cdot}kg^{-1}$)	1.7 (0.3)*	1.20 (0.1)	0.6 (0.4 to 0.7)		0.001	
No. of patients who received additional propofol until OAA/S reached 0	1 (3.3%)	18 (60%)*			0.001	18 (3 to 126)
Total dose of propofol (mg)	228 (46)	204 (54)	23.9 (−1.9 to 49.8)			
Total propofol dose for LBW ($mg{\cdot}kg^{-1}$)	3.9 (0.7)*	3.3 (0.7)	0.6 (0.3 to 1.0)		0.001	
Total propofol dose for TBW ($mg{\cdot}kg^{-1}$)	1.8 (0.3)$^{\neq}$	1.5 (0.3)	0.3 (0.1 to 0.5)		0.003	

Data presented as mean (standard deviation), number (percentage), median (interquartile range) and mean difference (95% confidence interval of the difference)

BIS = bispectral index; CI = confidence interval; LBW = lean body weight; TBW = total body weight; OAA/S = modified Observer's Assessment of Alertness/Sedation Scale; RR = relative risk

*P = 0.001; $\neq P$ = 0.003

Morbidly obese patients are often excluded from clinical trials during the drug development process. Hence, the appropriate dose of drugs for MO patients is usually inferred from normal-weight patients.[9] Morbidly obese patients have unpredictable, high volumes of distribution, increased cardiac output and total blood volume, and changes in regional blood flow, thereby altering the pharmacokinetic properties of most drugs.[24-26] Dosing of drugs in MO patients should involve careful consideration of the above factors.

There is presently no consensus in the literature regarding the correct weight scalar for dosing propofol for induction in MO patients.[8] It has been reported that the propofol plasma concentration depends on TBW. Thus, the dose of propofol for both induction and maintenance in obese patients should be based on actual body weight.[19,27] Another study recommended the use of a fixed dose of 350 mg propofol for induction, which corresponds to 2.5 $mg{\cdot}kg^{-1}$ for a TBW of 140 kg.[28] La Colla *et al.* recommended an adjustment to the dosing weight by multiplying the difference between TBW and LBW by 0.4 then adding it to the LBW.[27] Lean body weight has a higher correlation with cardiac output than the fat tissue mass, thus making it ideal for determining loading and induction doses.[29]

Ingrande and Lemmens reported that, despite the actual increase in LBW in MO patients, a massive increase of body fat resulted in a reduction of the LBW/TBW ratio. Therefore, an LBW scalar should be used for dosing anesthetics to avoid medication overdose.[9] Servin *et al.* conducted one of the first studies examining propofol pharmacokinetics in the obese. They concluded that doses of drugs are determined by the drug's front-end kinetics during induction of anesthesia, which in turn is determined by the cardiac output.[30] As LBW strongly correlates with cardiac output, LBW appears to be the most appropriate weight-based scalar for calculating induction doses in MO patients. However, the use of LBW as a weight scalar has been limited by the relative inability to measure it accurately under normal clinical circumstances.[9]

Dual-energy *x-ray* absorptiometry is an excellent reference method for measuring LBW but is not readily utilizable in the clinical setting.[31] Also, there are no data available describing the relation between cardiac output and LBW in patients with obesity-related cardiomyopathy.[9] Friesen proposed another weight-based scalar, called the lean scaled weight (LSW). It is obtained by multiplying the Janmahasatian LBW equations[5] by a scale factor of 1.2332 for men and 1.5262 for women:

LSW for men (kg) = (11432 * TBW)/6680 + (216 * BMI)

LSW for women (kg) = (14148 * TBW)/8780 + (244 * BMI)].[32]

The author suggests that LBW cannot be used directly to calculate drug doses because it is always less than the TBW even in non-obese patients, and it must be scaled upward to avoid underdosing.[33]

Induction of anesthesia in MO patients can be complicated because of the reduction of a safe apneic time and the possibility of gastroesophageal reflux.[34] Relative overdosing of induction drugs predisposes to hypotension - in contrast to underdosing, which can result in the risk of awareness and hypertension.[35]

Recently, Nightingale *et al.* recommended incorporating some form of depth of anesthesia monitoring while using target-controlled infusion techniques to induce MO patients.[36] In our study, most of the patients in the BIS group did not require extra propofol for induction after reaching a BIS of 50, and they did not have a significant increase in MAP after intubation. Indeed, BIS monitoring has been shown to be an effective guide for dosing anesthetic drugs in both obese and non-obese individuals.[37-39] Bispectral index monitoring titrated to 60 was used to guide propofol infusions in obese patients undergoing open gastric bypass under thoracic epidural analgesia and provided hemodynamic stability and predictable recovery.[40] Monitoring the depth of anesthesia could be more useful in obese patients because of the difficulty associated with estimating the LBW in MO patients. The BIS index is known to correlate well with the plasma propofol concentration.[41-43] Although monitoring BIS is relatively simple, its use does add a small cost.

One of the limitations of our study relates to the potential shortcoming of the BIS monitor as there is a known latency between a change in the clinical situation and the corresponding change in the BIS reading.[44] Zanner *et al.* found that the time delay with BIS monitors is different for decreasing and increasing values of BIS. It also varies with the transition of different states of consciousness, with the latency ranging from 25 to 64 sec for the BIS monitor.[45] The computational algorithm of the equipment, however, was reported to be improved during the last decade such that the reported BIS values are much closer to the real-time values in newer models.[46] Other limitations were that we did not measure BIS in the LBW group, and the research staff member collecting the data was not blinded to the group allocation.

In conclusion, the LBW-based induction dose of propofol did not provide adequate LOC in the MO patients. The induction dose of propofol based on BIS was different from the induction dose based on LBW, and a majority of the patients in the LBW group required additional propofol to achieve adequate LOC.

Conflicts of interest None declared.

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