# Comparison of Sleep Dose of Propofol and Induction Time in Class 1 Obese and Normal Weight Patients

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## ABSTRACT

**Background:** Anaesthetic management of obese patients is challenging**.** Induction of anaesthesia with propofol is achieved by intravenous injection until loss of consciousness evidenced by loss of verbal response to command and loss of eyelash reflex. Physiological responses to dose of propofol may differ in class 1 obesity compared to normal weight patients. **Objectives**: We aim to compare the sleep dose of propofol and induction time in class 1 obese patients to normal weight patients. **Materials and Methods**: This is a prospective, single blinded, controlled study, conducted in patients aged 18 – 60 years with American Society of Anesthesiologist (ASA) physical status I or II, having body mass index (BMI) of 18.50-24.99 and 30.00-34.99, undergoing elective surgeries requiring general anaesthesia. Seventy patients were randomly recruited into 2 groups based on BMI. BMI was calculated for all the patients. Patients received intravenous propofol at 40mg every 10 seconds until loss of consciousness. The induction time and dose of propofol were recorded. **Results:** The mean induction dose of Propofol in the obese group was 132.71 ±19.30 mg compared to 128.57 ± 27.24 mg in the normal BMI patients (p=0.13). The mean induction time was 59.23 ± 17.88 seconds in the obese group compared to 65.34 ± 22.66 seconds in the normal BMI group (p=0.15). **Conclusion:** There was no significant difference in induction dose of propofol, induction time, heart rate and mean arterial pressure in patients with class 1 obesity compared to normal weight patients. Administration of sleep doses therefore should be encouraged.

**Keywords**: Induction, Obese, Patient, Propofol, Dose

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## INTRODUCTION

Obesity is the excess accumulation of adipose tissue or body fat. It is defined by a Body Mass Index (BMI) of 30kg/m$^2$ or more.[1] The prevalence of obesity has been on the increase over the years, the World Health Organization (WHO) estimates that the rate of obesity have nearly tripled since 1975.[2] In Nigeria, the prevalence of obesity has been reported as 14.5%.[3]

Obesity constitutes a source of morbidity under anaesthesia with an increased risk of awareness under general anaesthesia, reduction in functional residual capacity, atelectasis and shunting in the dependent parts of the lungs, increased resting metabolic rate, work of breathing and increased oxygen demand, hence, there is a rapid decrease in arterial oxygen levels during apnoea.[4-7] The influence of obesity on the pharmacokinetics and pharmacodynamics of drugs is a problem in the conduct of anaesthesia as the physiologic changes of obesity affect them.

In obese patients, propofol is commonly used for induction and maintenance of general anaesthesia, however, the selection of a size descriptor for dose calculation in the obese has remained controversial.[8,9]

Dosing of propofol using TBW may result in the administration of high doses and deep anaesthesia accompanied by deleterious systemic effects in the obese.[7,10]

Studies have reported dosing of propofol based on onset of loss of consciousness resulted in a satisfactory depth of anaesthesia, use of lower doses, and decreased occurrence of side effects.[11,12] Few studies have evaluated the outcome of the use of sleep doses of propofol in class I obesity.

The aim of this study is to compare the sleep dose of propofol in class I obesity to the sleep dose in normal weight patients, evaluate how obesity affects the induction dose of propofol and time to loss of consciousness in obese patients under general anaesthesia. This will be valuable in tailoring the drug requirements of patients to their exact needs.

## MATERIALS AND METHODS

After obtaining approval from the ethics review board of the Nnamdi Azikiwe University Teaching Hospital, 70 patients scheduled for surgical procedures requiring general anaesthesia were recruited into the study.

The patients were of both sexes aged 18-60 years of ASA Physical Status I and II with BMI 18.50-24.99 and 30.00-34.99. Exclusion criteria were cardiovascular disease, neurological conditions, pulmonary disease and known allergy to propofol. Written informed consent was obtained from all the study participants.

A preoperative evaluation was done for each patient, weights and heights of all patients were measured using the Su Hong RGZ-120/ZT-120, model 120 stadiometer (manufactured by Jiangsu Kangjian Medical Apparatus Co. Ltd China), recorded in kilograms and meters respectively and their BMI calculated. No sedative premedication was prescribed. Patients were allotted to either of two groups (35 per group) based on their BMI. Patients with BMI 18.50-24.99 were assigned to group N, while those with BMI 30.00-34.99 were assigned to group O. Each patient was given an identification number and the investigator was blinded to the patients' identity and group. Routine standard monitoring was applied to all the patients.

An intravenous (IV) access was secured with 18G cannula, intravenous fluid 0.9% Normal Saline was commenced for fluid management. All patients received IV paracetamol 900mg and morphine 6mg in 2mg aliquots with 0.2mg glycopyrolate. All patients were preoxygenated for three minutes with 100% oxygen. Induction of general anaesthesia was achieved using IV propofol given at 40mg (4ml) every ten seconds, until a clinical endpoint of loss of both verbal response to command and eyelash reflex were observed. Time to loss of consciousness was noted using a stopwatch. The total induction dose of propofol was documented for each patient.

The primary outcome measures were the mean induction dose of propofol and the time to loss of consciousness. The secondary outcome measures were the changes in heart rate (HR) and mean arterial pressure (MAP) at loss of consciousness and within ten minutes of induction of anaesthesia.

Neuromuscular blockade for laryngoscopy and endotracheal intubation was achieved using IV suxamethonium 100mg, administered at loss of consciousness. Following endotracheal intubation,

IV atracurium 0.25mg/kg was used for maintenance of muscle relaxation.

**Statistical analysis**

The IBM Statistical Package for the Social Sciences (IBM SPSS) Statistics software version 23 was used for data storage and analysis. All continuous variables (age, weight, height, BMI and hemodynamic responses and drug doses) were presented as mean ± standard deviation (SD). The Z – test (unpaired) was used to compare the mean age, weight, height, BMI, dose of propofol and time to loss of consciousness between the two groups. The Z- test (paired) was also used to compare data within the same group. Chi -square test was used to compare gender and ASA status. The level of statistical significance was set at P-value of <0.05.

## RESULTS

Complete data was obtained from all 70 patients. Group O had more females (26[74.29%]) than males (9 [25.71%]) (p=0.04), and group N also had more females (23[65.71%]) (p=0.05) than males (12 [34.29%]). All patients in group O were classified as ASA II, whereas group N had more patients of ASA II status (62.86%) than ASA I (37.14%). Table 1 shows the demographic characteristics of the patients.

The mean induction dose of propofol was higher in group O at 132.71 ± 19.30mg compared to 128.57 ± 27.24mg in group N (p= 0.13) (Table 2). The time to loss of consciousness was faster in group O at 59.23 ± 17.88secs, compared to 65.34 ± 22.66secs in group N (p= 0.15) (Table 2).

In group O, the mean HR increased from 85.34±13.72 at baseline to 92.89±20.13 at loss of consciousness (p=0.04), whereas this parameter increased in group N from a baseline value of 89.86±13.19 to 92.51±15.23 at loss of consciousness (p=0.14) (Table 3). Both groups had no significant difference between their mean baseline HR values (p= 0.14), nor the HR values at loss of consciousness (p= 0.13) (Table 4). In both groups, subsequent changes in HR were not statistically significant (Table 3) and the difference in mean HR between the groups over time were not statistically significant (Table 4).

There was an increase in mean MAP from 97.31±14.72 at baseline to 97.89±12.18 at loss of consciousness in group O (p=0.43). In group N, the mean MAP decreased from 101.91±10.80 at baseline to 96.20±15.28 at loss of consciousness (p=0.23). Both groups had no significant difference between their mean baseline MAP values (p= 0.88), nor the values at loss of consciousness (p= 0.14) (Table 4). In both groups, subsequent changes in MAP were not statistically significant and there was no difference in mean MAP between the groups over time.

Group O had a steady decline in mean MAP over a ten minute period, while in group N, there was an increase up to the second minute, and subsequent drop over the next four minutes. However, at the eighth minute after induction, there was an increase in mean MAP, followed by a decrease (Table 3).

**Table 1: Patient Demographic Characteristics**

| Variable | Group O | Group N | P-Value |
|---|---|---|---|
| Age (Years) | 38.37±8.57 | 43.31±12.48 | 0.14 |
| Weight (kg) | 84.37±6.23 | 61.57±11.16 | 0.22 |
| Height (m) | 1.62±0.07 | 1.66±0.07 | 0.19 |
| BMI (kg/m$^2$) | 32.09±1.31 | 23.11±2.04 | 0.32 |

*BMI: Body Mass Index, Kg: kilogram, m: meter*

**Table 2: Mean Induction Dose of Propofol And Time to Loss of Consciousness**

| Parameter | Group O (n=35) | Group N (n=35) | P-Value |
|---|---|---|---|
| **Mean induction dose of propofol (mg)** | 132.71±19.30 | 128.57±27.24 | 0.13 |
| **Time to loss of consciousness (seconds)** | 59.23±17.88 | 65.34±22.66 | 0.15 |

*Mg: milligram, n: number*

**Table 3: Comparison of Heart Rate and Mean Arterial Pressure Within Each Group**

| Parameter | Baseline | Loss of consciousness | P-Value |
|---|---|---|---|
| **Group O** | | | |
| HR (bpm) | 85.34±13.72 | 92.89±20.13 | 0.04 |
| MAP | 97.31±14.72 | 97.89±12.18 | 0.43 |
| **Group N** | | | |
| HR | 89.86±13.19 | 92.51±15.23 | 0.14 |
| MAP | 101.91±10.80 | 96.20±15.28 | 0.23 |
| **Parameter** | **Loss of consciousness** | **At 2 minutes** | **P value** |
| **Group O** | | | |
| HR (bpm) | 92.89±20.13 | 92.37±16.02 | 0.59 |
| MAP | 97.31±14.72 | 100.97±21.03 | 0.15 |
| **Group N** | | | |
| HR | 92.51±15.23 | 98.89±20.56 | 0.66 |
| MAP | 96.20±15.29 | 102.49±21.43 | 0.31 |
| **Parameter** | **2 minutes** | **4 minutes** | **P value** |
| **Group O** | | | |
| HR (bpm) | 92.37±16.02 | 91.29±16.27 | 0.85 |
| MAP | 100.97±21.03 | 96.26±20.51 | 0.51 |
| **Group N** | | | |
| HR | 98.89±20.56 | 98.00±20.00 | 0.68 |
| MAP | 102.49±21.43 | 97.17±13.18 | 0.21 |
| **Parameter** | **4 minutes** | **6 minutes** | **P value** |
| **Group O** | | | |
| HR (bpm) | 91.29±16.27 | 92.03±14.62 | 0.61 |
| MAP | 96.26±20.51 | 90.00±19.86 | 0.90 |
| **Group N** | | | |
| HR | 98.00±20.00 | 97.17±19.03 | 0.94 |
| MAP | 97.17±13.18 | 95.03±14.58 | 0.21 |
| **Parameter** | **6 minutes** | **8 minutes** | **P value** |
| **Group O** | | | |
| HR (bpm) | 92.03±14.62 | 89.96±12.78 | 0.92 |
| MAP | 90.00±19.86 | 89.20±15.44 | 0.15 |
| **Group N** | | | |
| HR | 97.17±19.03 | 96.20±9.21 | 0.76 |
| MAP | 95.03±14.58 | 96.51±18.14 | 0.78 |
| **Parameter** | **8 minutes** | **10 minutes** | **P value** |
| **Group O** | | | |
| HR (bpm) | 89.96±12.78 | 91.40±13.58 | 0.79 |
| MAP | 89.20±15.44 | 87.14±14.65 | 0.83 |
| **Group N** | | | |
| HR | 96.20±9.21 | 96.14±17.89 | 0.88 |
| MAP | 96.51±18.14 | 92.54±11.36 | 0.61 |

*bpm: beats per minute, HR: heart rate, MAP: mean arterial pressure,*

**Table 4: Comparison of Heart Rate and Mean Arterial Pressure Between Both Groups**

| Parameter | Group O (n=35) | Group N (n=35) | P-Value |
|---|---|---|---|
| **Preoperative** | | | |
| HR (bpm) | 78.17±11.29 | 80.69±11.44 | 0.25 |
| **AT BASELINE** | | | |
| HR | 85.34±13.72 | 89.86±13.19 | 0.14 |
| MAP | 97.29±12.18 | 101.91±10.81 | 0.88 |
| **At Loss Of Consciousness** | | | |
| HR | 92.89±20.13 | 92.51±15.23 | 0.13 |
| MAP | 97.31±14.72 | 96.20±15.28 | 0.14 |
| **At 2 Minutes Post Induction** | | | |
| HR | 92.37±16.02 | 98.89±20.56 | 0.06 |
| MAP | 100.97±21.03 | 102±21.43 | 0.09 |
| **At 4 Minutes Post Induction** | | | |
| HR | 91.29±16.27 | 98.00±20.00 | 0.02* |
| MAP | 96.26±20.51 | 97.17±13.18 | 0.02* |
| **At 6 Minutes Post Induction** | | | |
| HR | 92.03±14.62 | 97.17±19.03 | 0.13 |
| MAP | 90.00±19.86 | 95.03±14.58 | 0.20 |
| **At 8 Minutes Post Induction** | | | |
| HR | 89.96±12.78 | 96.20±9.21 | 0.16 |
| MAP | 89.20±15.44 | 96.51±18.14 | 0.18 |
| **At 10 Minutes Post Induction** | | | |
| HR | 91.40±13.58 | 96.14±17.89 | 0.04* |
| MAP | 87.14±14.65 | 92.54±11.36 | 0.12 |

*bpm: beats per minute, HR: heart rate, MAP: mean arterial pressure*

## DISCUSSION

In this study, we induced general anaesthesia in both groups of patients using sleep doses and found no significant different in mean induction dose of propofol between patients with class I obesity (132.71 ± 19.30mg) and normal weight patients (128.57 ± 27.24mg) (p=0.13). In obesity, lean body weight, body fat and of volume of distribution of propofol are increased and may play a role in the dose requirements of the drug.

Ismail *et al* [13], found the mean induction dose of propofol to be significantly higher in obese patients (10.2±2.3 mg/kg/hr) compared to normal weight patients (8.6±2.5mg/kg/hr). This has been suggested to be due to the increase in the volume of distribution and clearance of the highly lipophilic drug. The study by Ismail *et al* [13] is in concordance with the index study in parameters compared, however loss of consciousness was determined using the bispectral index (BIS) unlike the index study. Verbal response and loss of eyelash reflex are subjective and might account for the absence of significance differences in our study groups. Clinical methods of assessing loss of consciousness using loss of eyelash reflex and loss of verbal response to command may not indicate depth of anaesthesia as accurately as the BIS.

Garba *et al* [14] found that the mean propofol induction dose in non-obese patients was 175.75±19.20mg with a mean induction time of 83.50±18.88secs. Both values are higher than observations made in our study, where the mean induction dose of 128.57 ± 27.24mg and faster loss of consciousness of 65.34 ± 22.66secs were found in group N. The method of drug administration may account for these differences. Whereas Garba *et al* [14] used a syringe pump for drug administration at the rate of 70mg/minute, we administered the drug by bolus injection at the rate of 40mg in 10 seconds. Some authors have reported that the rate of drug administration may affect the onset of action of the drug.[15]

We found the time to loss of consciousness to be faster in group O at 59.23 ± 17.88secs, compared to 65.34 ± 22.66secs in group N, but this was not statistically significant (p=0.15). The obese group had a higher mean induction dose of propofol than the non-obese patients. Our findings in group N also contrasts with the results in the study by Edomwonyi *et al* [16] in which the mean induction time was 55.25±26.66secs. This difference may be because

Edomwonyi *et al* [16] used a calculated dose of propofol at 2-2.5mg/kg of TBW for induction, which may have resulted in higher total doses of the drug in their study.

The mean heart rate in the present study, increased at loss of consciousness from baseline values in both the obese and normal patients. This increase was not statistically significant and contrasts with the studies by Ismail *et al* [13] and Dutta *et al* [17] in which the HR was found to be significantly lower in the obese patients compared to the normal patients after induction. In Ismail's study [13], the mean induction dose of propofol in the obese group was 10.2 ± 2.3mg/kg/hr, and 8.6 ± 2.5mg/kg/hr in the non-obese group. This difference in the result of the HR in our study compared to the works by Ismail *et al* [13] and Dutta *et al* [17] may be due to the use of the premedicants midazolam and fentanyl respectively and calculated doses of propofol at 2mg/kg and 2.5mg/kg respectively by Ismail *et al* [13] and Dutta *et al* [17] unlike our study. Midazolam, fentanyl as well as large doses of propofol are known to decrease HR. Also, the bolus doses used in our study also may be contributory to the immediate hemodynamic response.

In contrast to our study, Belekar [20] found that the mean HR at induction was below baseline value after induction of anaesthesia with 2mg/kg of propofol. Patients in the study [20], however received premedication with midazolam, glycopyrolate and pentazocine and had a sustained drop in HR up to 5 minutes after induction.

The index study's finding in the non-obese is in concordance with findings by Belekar VR [20] and Rabadi *et al* [21], that at loss of consciousness, there is a decrease in the mean MAP. However, while the patients in Rabadi's study [21] received 2-2.5mg/kg of propofol over 30 seconds, those in Belekar's study [20] received the drug at 2mg/kg, but the rate of administration was not stated. This drop in MAP in their studies was also found to be statistically significant unlike our study. The difference in dose of drug and the rate of drug administration may account for this observation. .

As in the non-obese patients in our study, Dutta *et al* [17] also found a decrease in MAP following induction with propofol at 2.5mg/kg but found that the use of ringer's lactate and ephedrine resulted in less reduction of the MAP.

Group O was found to have an increase in SBP at loss of consciousness, the DBP and MAP were also increased at loss of consciousness, but this was not statistically significant. The increase in HR, SBP, DBP and MAP observed at induction in group O may be because of the sleep dose of Propofol used for induction.

In the index study, both groups had an increase in mean SBP, DBP and MAP 2 minutes after induction. This agrees with similar findings in Belekar's study.[20] Laryngoscopy and intubation may account for the observation of increased SBP, DBP and MAP at the immediate post induction time in the index study and Belekar.[20]

The strength of this work lies in the fact that no side effects of propofol were encountered in the patients, this may be attributed to the use of sleep doses of the drug instead of calculated doses. However, limitations were encountered in the study. Neurological monitors such as the bispectral index monitor were not used in confirming loss of consciousness during induction of general anaesthesia and the study did not include the use of syringe drive for administration of Propofol at induction. There was a limit to blinding in the study as patients that were obviously obese would have been known by the investigator.

In conclusion, there was no significant difference in induction dose of Propofol, induction time, heart rate and mean arterial pressure in patients with class 1 obesity compared to non-obese patients. The use of sleep doses of intravenous propofol in patients with class 1 obesity is safe and effective. We therefore recommend its use in general anaesthesia in this group of patients.

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**Authors contributions**

IOO conceptualized and designed the study. IOO, EON, CEN, ECE, KNO, PCO and BCO contributed to the implementation of the project and revision of the manuscript. All authors were involved in the writing and revision of the manuscript. The authors read, approved the final manuscript and agree to be accountable for all aspects of the work.

**Data availability**

The data used to support the findings of this study are available from the corresponding author upon request.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee of the Nnamdi Azikiwe University Teaching Hospital, Nnewi.

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