



Does anxious patients require more propofol at induction?

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ABSTRACT

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Background: Preoperative anxiety increases postoperative analgesic requirement, prolongs hospital stay and results in poor patient satisfaction. We investigated the correlation of preoperative state of anxiety on propofol requirement at induction of anesthesia and vital signs.

Methodology: This prospective study recruited 52 ASA I and II patients scheduled for surgery under general anesthesia. The Malay version of Generalized Anxiety Disorder-7 questionnaire was used to assess preoperative anxiety state. Anesthesia was induced with propofol infusion using the Schnider protocol to achieve target plasma concentration of 4 µg/ml. Baseline systolic blood pressure and heart rate (HR) prior to induction were recorded. The amount of propofol required until loss of consciousness, and bispectral index (BIS) values immediate post induction were recorded. Pearson's correlation coefficient was used to assess relationship.

Results: There was no correlation between the preoperative state of anxiety and propofol requirement at induction ($r = 0.07, p = 0.580$), and systolic blood pressure prior to induction ($r = 0.23, p = 0.101$). However, weak positive correlations were detected between preoperative state of anxiety and the HR prior to induction ($r = 0.27, p = 0.050$), and with BIS at loss of consciousness ($r = 0.32, p = 0.026$). However, no correlation was seen between propofol requirement for induction with HR prior to induction ($r = 0.13, p = 0.37$). Anxious patients were unable to sleep well pre-operatively ($p = 0.009$).

Conclusion: Preoperative state of anxiety does not influence propofol requirement for induction of anesthesia.

Key words: Anxiety; General anesthesia; Induction of anesthesia; Propofol; TIVA

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INTRODUCTION

Anxiety is an unpleasant state of uneasiness or tension which can be associated with abnormal hemodynamic responses resulting from sympathetic, parasympathetic and endocrine stimulation.¹ High pre-operative anxiety levels has been associated with increased postoperative analgesic requirement, prolonged hospital stay, adverse perioperative

outcome and poor patient satisfaction.²

In earlier studies, anxiety was assessed using validated self-reporting tools, the Spielberger's State Trait Anxiety Inventory form³ and the Hospital Anxiety and Depression scale (HAD)⁴ Millar et al⁵ compared both methods with 100 mm visual analogue score and concluded that all the three tools were comparable in their assessment of anxiety before surgery. Later,

anxiety and propofol induction

the seven items Generalized Anxiety Disorder scale (GAD-7) was developed for clinical practice.⁶This was a self-reporting questionnaire which had good reliability for diagnosing anxiety, with a sensitivity of 92% and specificity of 76%.Patients with scores of 8 and above were diagnosed as anxious. The GAD-7 was shown to be a good instrument in diagnosing generalized anxiety disorder, society anxiety disorder, panic disorder and post-traumatic stress disorder.⁷ The GAD-7 has also been translated into the local Malay language and validated.⁸

Preoperative anxiety has been shown to be associated with increased intraoperative anesthetic requirement.^{9,10} Maranets and Kain⁹ demonstrated that the propofol dose required for induction of anesthesia in the high trait anxiety group was significantly higher than that in the low trait anxiety group. However, Morley et al.¹¹ reported that anxiety score did not significantly affect propofol dose or cardiovascular end points.

This study aimed to assess the relationship between the preoperative state of anxiety using GAD-7 scores, and the amount of propofol required for induction of general anesthesia (GA), and to determine the relationship between GAD-7 scores and heart rate (HR), systolic blood pressure (SBP) and bispectral index(BIS) at induction of anesthesia.

METHODOLOGY

Following institutional ethics approval and informed consent from the patients, we recruited ASA I and II patients aged 18-65 years, scheduled for elective surgery requiring GA. Those excluded were patients with BMI more than 35 kg/m², or patients medicated with antihypertensive, anxiolytics, antidepressants or medications that affected their central nervous system. Those with communication difficulties, inability to answer the questionnaire, history of chronic alcoholism or substance abuse were also excluded.

At the preoperative assessment rounds, the patients' age, gender, weight and height were recorded, and they were given the GAD-7 questionnaire to complete in order to assess their anxiety state. This questionnaire was available in both English and Malay versions. The patients were regarded as having anxiety when the GAD-7 scored ≥ 8 . The attending anesthetists were blinded to the GAD-7 score. The patients were prepared as per protocol for general anesthesia but no oral sedation was given preoperatively. Patients were asked regarding their sleep on the night prior to surgery. The ability to sleep was assessed as able or unable to sleep well.

Prior to induction of anesthesia, electrocardiography (ECG), non-invasive blood pressure (NIBP), pulse oximetry and BIS monitoring were established and baseline values recorded. A 20G intravenous (IV) cannula was inserted and connected to a 3-way connector. Induction of anesthesia proceeded with propofol Lipuro® 10 mg/mL (1%) infused using the Schnider protocol, administered via the Injectomat® TIVA Agilia infusion pump to achieve a target plasma concentration of 4 $\mu\text{g}/\text{ml}$ until loss of consciousness (LOC).¹² Loss of consciousness was the clinical end point and defined as the point of loss of verbal response. Upon commencement of propofol infusion, the patients were repeatedly called by their first names in between fifteen seconds intervals, without any tactile stimulation. The patients were required to answer 'yes' each time their names were called and this continued until loss of verbal response. If LOC was not achieved, propofol infusion rate was adjusted according to the National Total Intravenous Guideline. The amount of propofol infused to attain LOC was recorded. The SBP, HR and BIS values immediately after induction of anesthesia were also recorded. Intravenous fentanyl 100mcg bolus was given to all patients after LOC. The conduct of anesthesia was then continued by the attending anesthetist as per requirement of the surgery.

Statistical analysis:

Sample size was calculated using the 'Power and Sample Size Calculations', alpha value was taken as 0.05 with the power of 0.8. Based on the study by Maranet et al.,⁹ propofol requirement for high anxiety group was 2.1 ± 0.4 mg/kg and low anxiety group was 1.7 ± 0.5 mg/kg, the difference in mean was 0.4 and standard deviation (SD) was taken as 0.5. Therefore, the calculated sample size was 52. Considering 10% drop out rate, a total of 58 patients was required.

Data analysis was performed using IBM SPSS version 22. Pearson correlation was used to analyze any correlation between GAD-7 scores with propofol requirement for loss of consciousness, pre-induction SBP and HR and BIS at LOC. A p-value of less than 0.05 was regarded as statistically significant. The Fisher exact test was used to analyze the relationship between the patients' state of anxiety and their ability to sleep well the night prior to surgery.

RESULTS

Fifty eight patients were recruited for this study but only 52 were analyzed. Surgery was postponed for three patients, and two patients breached the study protocol as one received midazolam in the ward and the other was given a subarachnoid block instead of

Table 1: Demographic data and type of surgery

Demographics n=52	n (%)
Gender	
Male	23 (44.2)
Female	29 (55.8)
Age(years)	41 ± 15*
Weight(kg)	67 ± 13*
Height(m)	160 ± 9*
Type of Surgery	
General surgery	15 (28.8)
Otorhinolaryngology	12 (23.1)
Orthopedics	11 (21.2)
Gynecology	9 (17.3)
Urology	4 (7.70)
Ophthalmology	1 (1.9)
Pre-induction systolic blood press (mmHg)	129.6 (± 17.3)
Pre-induction heart rate (bpm)	80.3 (± 14.3)

* Mean (SD)

Table 2: Correlation between GAD-7 scores and propofol requirement, hemodynamic parameters and BIS

Factors	GAD-7 score	
	r	p value
Propofol requirement	0.07	0.580
SBP	0.23	0.101
HR	0.27	0.050
BIS	0.32	0.026

There was significant correlation between GAD-7 scores and HR prior to induction of anesthesia, but no correlation between HR ($r = 0.13$, $p = 0.37$) or SBP ($r = 0.04$, $p = 0.78$), and propofol requirement for induction of GA.

Table 3: The GAD-7 scores and ability to sleep the night prior to surgery

GAD-7 scores	Slept well n (%)	Inability to sleep well n (%)
GAD ≥ 8	2 (33.3)	4 (66.7)
GAD < 8	40 (87.0)	6 (13.0)

Fisher exact test p value=0.009

general anesthesia. Demographic data is presented as Table 1.

Patients with GAD-7 score < 8 were considered as having no anxiety and the majority of our patients (88.5%) scored < 8. The GAD-7 scores showed weak positive correlation with heart rate just prior to

induction ($r = 0.27$, $p = 0.050$), and with BIS scores at the point of LOC ($r = 0.32$, $p = 0.026$), (Figures 1 & 2).

Propofol requirement at induction of anesthesia, and SBP prior to induction did not show significant correlation with the GAD-7 scores (Table 2).

Forty two patients reported that they slept well, but 10 patients with GAD-7 ≥ 8 claimed that they were unable to sleep well the night prior to surgery ($p = 0.009$) (Table 3).

DISCUSSION

There have been contrasting findings regarding patients' state of anxiety and propofol requirement during induction of anesthesia. Few researchers observed patients' state of anxiety influencing the propofol requirement at induction.^{9,10} However, some reported absence of any relationship between both factors.^{11,13} We found no association between the patients' preoperative state of anxiety and propofol requirement during induction of general anesthesia.

Those studies that ascertained correlation between the patients' preoperative state of anxiety and propofol requirement during induction of general anesthesia or sedation studied women going for gynecological procedures.^{9,10,14} Morley et al.¹¹ and Chung et al.¹³ whose study involved a mixed gender population (similar to ours) going for minor surgery under general anesthesia, found that anxiety did not affect the induction characteristic of propofol and cardiovascular end points. Evidence has shown that the clinical response to propofol is different between males and females¹⁵ and the prevalence of anxiety was 2-3 times higher in women compared to men.¹⁶ This could explain why Maranets and Kain,⁹ Kil et al.¹⁰ and Hong et al.¹⁴ found significant correlation between anxiety and propofol requirement in their studies amongst female patients which eliminated the confounding factor of gender bias.

Amongst our patients, only 11.5% of them were anxious preoperatively. This could explain why we were unable to demonstrate any correlation between anxiety and the propofol requirement for induction. Maranets and Kain⁹ on the other hand had equal numbers of anxious and non-anxious patients and thus able to demonstrate significant correlation between anxiety and propofol requirement for induction. Therefore, if our study had evenly distributed anxious and non-anxious patients preoperatively, we may have been able to demonstrate any influence of anxiety on propofol requirement at induction of anesthesia.

Anxiety is associated with increased heart rate.¹⁷ We found a weak correlation between heart rate and state of anxiety, however no correlation between increased heart rate and propofol requirement. Severine et al.¹⁸

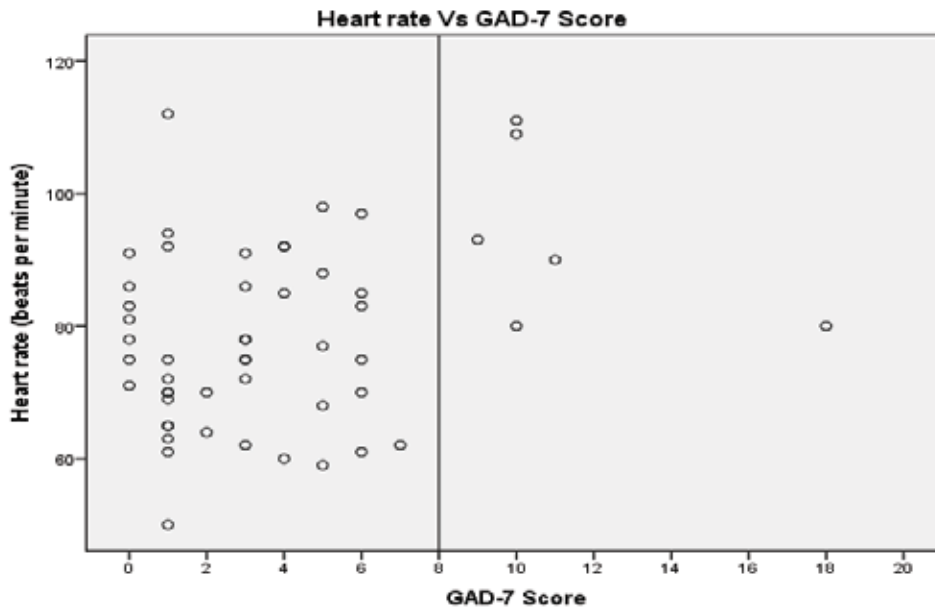


Figure 1: Correlation between GAD-7 scores and HR prior to induction

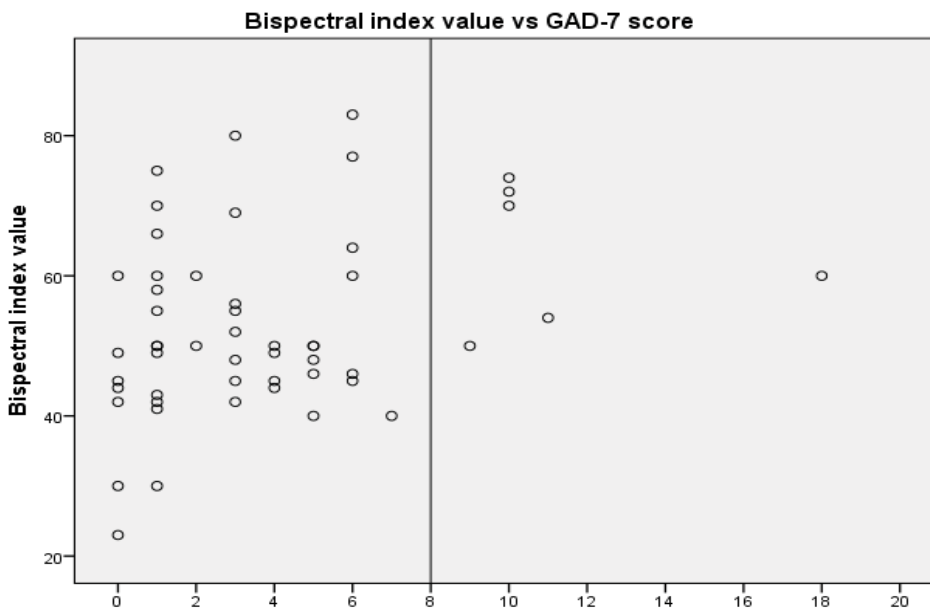


Figure 2: Correlation between GAD-7 scores with BIS value at loss of consciousness.

noted that there was a significant correlation between heart rate and anxiety. He further demonstrated that increased heart rate will significantly increase propofol requirement during anesthesia which was not demonstrated in our study.

The cause for sleep disturbances and insomnia can be multifactorial, however, anxiety is one of the main cause.¹⁹ We found that anxious patients were unable to sleep well the night prior to surgery.

Loss of verbal response, used to define the point of loss of consciousness in our patients, is a commonly accepted clinical end point when studying the effect of hypnotic drugs.²⁰ We monitored BIS, are commended monitoring tool of awareness during general anesthesia, and also useful to gauge depth of sedation and help anesthetist to titrate the drug for sedation and anesthesia.²¹ We found that BIS values at the point of loss of verbal response were significantly higher in patients with higher GAD-7 scores. In contrast, Morley et al.¹⁴ found that BIS at loss of verbal response decreased significantly with increasing anxiety trait. Our study may be confounded by this clinical end-point denoting the propofol requirement as BIS values are calculated from the raw electroencephalogram with a lag time of 30-45 secs.^{22,23} Therefore, the actual BIS value at point of loss of verbal response may be reflected later than the clinical sign of LOC. This may explain why BIS values at loss of verbal response were noted to be higher.

CONCLUSION

In conclusion, in our study population we found no correlation between preoperative state of anxiety and propofol requirement at induction of general anesthesia.

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