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"Observational Analysis of Pre Operative Anxiety on Dose of Propofol Required For Induction of General Anaesthesia"

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I. Introduction

Preoperative anxiety is described as an unpleasant state of uneasiness or tension that is secondary to a patient being concerned about a disease, hospitalization, anaesthesia and surgery, or the unknown[1].The reported incidence of preoperative anxiety in adults ranges from 11% to 80%, depending upon the assessment method. The highest incidence was noted by psychiatrists using a validated psychological questionnaire[2], whereas the lowest was reported in studies using clinical impression only[3]. Currently data exist with respect to the effects of anxiety and fear before surgery on preoperative outcomes, such as heart rate, blood pressure and neuroendocrinal changes [4].The neuroendocrine response is associated with characteristic hemodynamic and metabolic effects.[5]

Anxiety is also used in psychology to describe individual differences in anxiety proneness as a personality trait (trait anxiety).In contrast to the transitory nature of emotional states, personality traits are enduring differences among people in reacting or behaving in a certain way with predictable regularity.

State anxiety is defined as the subjective feelings of nervousness, apprehension and tension when one is subjected to an anxiety provoking stimulus. Trait anxiety of an individual implies differences between people in the disposition to respond to stressful situations with varying amounts of state anxiety[6].

There is a paucity of data, however, regarding the effects of preoperative anxiety on intraoperative outcomes. Nonetheless, it is assumed from clinical experience that larger doses of anaesthetics are required in the anxious patient to establish and maintain a clinically sufficient hypnotic component of the anaesthetic requirement.

Previous studies have yielded contradictory results on the relationship between anxiety and requirements for anaesthetics. This may be due to reasons like not using validated measures to assess anxiety or no controls for potentially confounding variables. Also, scale used was STAI (State Trait Anxiety Inventory) scale which was difficult to administer.

The present study was planned to assess the level of pre-operative anxiety using easy to administer scales namely –

(1) Modified Hospital Anxiety and Depression Scale. (MHADS)
(2) Amsterdam Preoperative Anxiety and Information Scale. (APAIS)

The present study was conducted to compare the level of preoperative "State" and "Trait" anxiety on dose of propofol used for induction of general anaesthesia in patients scheduled to undergo laparoscopic surgeries.

II. Aims And Objectives

- To evaluate the level of pre-operative anxiety.
- To evaluate the dose of propofol required for induction of general anaesthesia.
- To establish the correlation if any between level of pre-operative anxiety and requirement of propofol.

III. Review Of Literature

Charles Spielberger et al[7] in 1970 constructed STAI score based on the state-trait distinction proposed by Raymond Cattell in 1961. Their goal was to compile a set of items that could measure anxiety at both poles of the normal affect curve (state vs. trait). The STAI purports to measure one's conscious awareness at two extremes of anxiety affect, labeled state anxiety (A-state), and trait anxiety (A-trait), respectively. Higher STAI scores suggest higher levels of anxiety. The most recent version is the State-Trait Anxiety Inventory for

Adults™ (STAI-AD). The STAI was revised into its current form in 1983. It was used (along with other measures) in making diagnoses and distinguishing between anxiety and depression, in clinical settings, as well as in research.

M.A.E.Ramsay[1] in 1972 carried out a survey of preoperative fear. One hundred and eighty-three male and one ninety nine female patients were interviewed in the ward before they were premedicated and within twenty-four hours of proposed surgery. Two hundred and sixty-seven of the 382 patients interviewed admitted to having fears about the oncoming procedure. 70 % of the men had fears compared to 76 % of the females. This difference is not statistically significant ($p < 0.4$). Sixty-two per cent of the patients had anesthetic fears, 15 % surgical fears and 23 % miscellaneous fears. Fifty-nine per cent of the women had fears about the anesthetic compared to 67% of the men; 55 % of the 26 patients in the youngest age group (4 to12 years) had fears. In the middle age groups the percentages were: 13 to 21 years 61% of 31 patients, 22 to 41 years 84% of 147 and 42 to 61 years 81 % of 89. In the oldest group the rate was lower, 57 % of 89 cases between 62 and 82. There was thus less fear at both ends of the age scale. The comparison was statistically highly significant ($p < 0.001$). The main anxieties of the majority of the patients interviewed were associated with the prospect of the anesthetic and were related to the age and the previous anesthetic experience of the patient.

Hicks J.A. et al[8] in 1988,conducted study to assess Preoperative anxiety using the hospital anxiety and depression (HAD) scale, multiple affect adjective check list (MAACL) and linear analogue anxiety scale (LAAS) in 100 consecutive day case patients undergoing termination of pregnancy. The HAD scale, a self-assessment scale comprising 7 multiple choice questions, was readily accepted and easily understood by patients. There was a high degree of correlation between the HAD scale and both the MAACL (correlation coefficient 0.74) and the LAAS (correlation coefficient 0.67). There was only a moderate degree of correlation between the HAD scale and the anesthetist's assessment of anxiety (correlation coefficient 0.46). The HAD scale was easily understood and completed correctly by all the patients in the study. The same was not true of the MAACL or LAAS. The study had shown the HAD scale to be a useful subjective measure of preoperative anxiety.

Badner N.H.et al[9] in 1990 conducted a study to determine whether there is a correlation between anxiety the night before surgery and that existing immediately preoperatively, whether anesthetists can detect preoperative anxiety and to establish the presence of any factors that might assist in the determination of preoperative anxiety. Anxiety was measured objectively using the Spielberger State-Trait Anxiety Inventory (STAI and the Multiple Affect Adjective Check List (MAACL). Anxiety was found to be higher in females and those not having had a previous anesthetic, and to remain constant from the afternoon before surgery to the immediate preoperative period. Anesthetists were found to be poor assessors of anxiety unless they specifically questioned their patients about this.

Moerman N et al[10] in 1996 conducted a study to assess patients' anxiety level and information requirement in the preoperative phase. During routine preoperative screening, 320 patients were asked to assess their anxiety and information requirement on a six-item questionnaire, the Amsterdam Preoperative Anxiety and Information Scale (APAIS). Two hundred patients also completed Spielberger's State-Trait Anxiety Inventory (STAI State). Patients were able to complete the questionnaire in less than 2 min. On factor analysis, two factors emerged clearly: anxiety and the need for information. The anxiety scale correlated highly (0.74) with the STAI State. It emerged that 32% of the patients could be considered as "anxiety cases" and over 80% of patients have a positive attitude toward receiving information. Moreover, the results demonstrated that 1) women were more anxious than men; 2) patients with a high information requirement also had a high level of anxiety; 3) patients who had never undergone an operation had a higher information requirement than those who had. The APAIS can provide anesthesiologists with a valid, reliable, and easily applicable instrument for assessing the level of patients' preoperative anxiety and their need for information.

Marantes I and Kain Z.N.[11] in 1999 conducted cross sectional study to see whether larger doses of anesthetics are required in the anxious patient to establish and maintain a clinically sufficient hypnotic component of the anesthetic state. Fifty-seven women undergoing bilateral laparoscopic tubal ligation with a propofol-based anesthetic regimen were enrolled in this cross-sectional study. Trait (baseline) and state (situational) anxiety were assessed in all patients immediately before surgery, and the propofol doses required for the induction and maintenance of anesthesia were recorded. A bispectral index monitor was used to assure that the hypnotic component of the anesthetic state was the same in all patients. They found that patients with high trait anxiety required more propofol for both the induction (2.1 ± 0.4 vs. 1.8 ± 0.3 mg/kg; $p= 0.01$) and maintenance of anesthesia (170 ± 70 vs. 110 ± 20 mcg/ kg/ min; $p= 0.02$), compared with patients with low trait anxiety. State anxiety, however, was not found to affect the propofol doses required for the induction or maintenance of anesthesia. Multiple regression models confirmed that Trait anxiety is an independent predictor for intraoperative propofol requirements ($p=0.02$). They concluded that increased baseline (i.e., trait) anxiety is associated with increased intraoperative anesthetic requirements. They suggested that anesthesiologists should modify the initial induction dose based on the anxiety level exhibited by the patient.

Hong J.Y et al[12] in 2003 conducted a study to evaluate the correlation among the trial number of in vitro fertilization (IVF), preoperative anxiety, and propofol requirement for conscious sedation. One hundred and twenty six Korean women undergoing oocyte retrieval were enrolled. The target-controlled infusion by the anesthesiologist was conducted with initial target propofol concentration of 2.5 g/mL, which was manipulated until the sedation score 3 and desired clinical end point were achieved. A weak correlation was observed between visual analogue scale (VAS) anxiety and the dose of propofol required for the induction of conscious sedation (r=0.22, p=0.0192). A weak correlation was also found between VAS anxiety and the sedation time needed to reach the proper conscious sedation level for the procedure (r=0.181, p=0.0484). Multiple regression analysis showed that VAS anxiety, preoperative baseline prolactin level, and cortisol level had statistically significant effects on the propofol induction dose for target controlled conscious sedation. They concluded that the induction dose and time requirements for propofol in anesthesiologist-controlled conscious sedation be modified based on the preoperative anxiety level and the baseline blood concentration of stress hormone, cortisol and prolactin.

Osborn TM et al[13] in 2004 studied the effects of anxiety on 25 outpatients undergoing intravenous sedation for third molar extraction. Before the procedure, subjects completed the State-Trait Anxiety Inventory, and intraoperative patient movement was assessed using a subjective scale. They found that patients with a high level of preoperative anxiety had a greater degree of average intraoperative movement ($p = 0.037$) and also required a greater amount of propofol to maintain a clinically acceptable level of sedation ($p = 0.0273$) when compared with patients with less preoperative anxiety. Increased state anxiety and trait anxiety serve as predictors for an increased total dose requirement of propofol to maintain an acceptable level of sedation ($r^2 = 0.285$, $p = 0.0060$, and $r^2= 0.233$, $p = 0.0146$, respectively). An increased level of trait anxiety was also a predictor of an increased degree of average intraoperative movement ($r^2 = 0.342$, $p = 0.0022$). Patients who exhibit a high level of preoperative anxiety require agreater total dose of propofol to achieve and maintain a clinically acceptable level of sedation and are more prone to unwanted movement while under sedation.

Gras S.et al[14] in 2007 conducted a study to address the effect of perioperative HR on propofol dose required for LOC and, second, the effect of perioperative anxiety on HR. Forty-five ASA physical status I–II female patients undergoing gynecological surgery were studied. Anxiety was assessed in the operating room with the State-Trait Anxiety Inventory (STAI)-state Spielberger scale (situational anxiety). After HR recording, anesthesia was induced with a 200-mL/h 1% propofol infusion with the Base Primea pump (Fresenius-Vial, Brezins, France) until LOC. The propofol dose was recorded at the time of LOC. Relationships between STAI-state and HR versus propofol dose at LOC were tested with the Spearman test with a P value of 0.01.A significant relationship was observed between HR and propofol dose at LOC (=0.487, P = 0.0012) but not between STAI-state and propofol dose (=0.330, P = 0.0306). However, a significant relationship was observed between STAI-state and HR (= 0.462 and P = 0.0054).They concluded that Increased perioperative HR is associated with increased propofol dose required for LOC. Perioperative anxiety accounts for increased HR.

Morley A.P. et al[15] in 2008 conducted a prospective study to investigate the effects of anxiety on the induction dose of propofol and subsequent cardiovascular changes in 197 patients. Pre-operative state and trait anxiety scores were measured using the State Trait Anxiety Inventory. Propofol was administered at 40 mg x $kg^{(-1)}$ x $h^{(-1)}$. Propofol dose was recorded at loss of verbal response and when EEG Bispectral Index decreased to 50. Thereafter, propofol infusion rate was reduced to 8 mg x $kg^{(-1)}$ x $h^{(-1)}$. Cardiovascular data were collected for 15 min after starting induction. Maximum percentage decreases in heart rate and mean arterial pressure, and the point at which the latter occurred, were recorded. On multivariate analysis, anxiety scores did not significantly affect propofol dose or cardiovascular end-points, although Bispectral Index at loss of verbal response decreased with increasing trait anxiety ($p = 0.02$). Anxiety, measured using State Trait Anxiety Inventory, does not appear independently to affect the induction characteristics of propofol.

Kil H.K. et al[16] in 2012 conducted a cross sectional study investigated whether preoperative psychological factors can predict anesthetic requirements and postoperative pain. Before total thyroidectomy, 100 consecutive women completed the Spielberger's State–Trait Anxiety Inventory (STAI) and the pain sensitivity questionnaire (PSQ).Controlled propofol was administered for induction of anesthesia, and sevoflurane–oxygen–air was given to maintain equal depths of anesthesia, as determined by bispectral index (BIS) monitoring. They found that patients with higher anxiety scores (state and trait) required greater amounts of propofol to reach light (BIS=85) and moderate (BIS=75) levels of sedation, but only trait anxiety was significantly associated with propofol requirements in reaching a deep level of sedation (BIS=65). The MAC-hour of sevoflurane was significantly correlated only with PSQ scores. The postoperative pain intensity was significantly correlated with both STAI and PSQ. They concluded that Preoperative anxiety and pain sensitivity are independent predictors of propofol and sevoflurane requirements in general anesthesia. Anesthetic and analgesic doses could be modified based on the patient's preoperative anxiety and pain sensitivity.

Hernández-palazón J, et al [17] conducted prospective longitudinal study in 2015 aimed to analyze the incidence and level of preoperative anxiety in the patients scheduled for cardiac surgery by using a Visual

Analogue Scale for Anxiety (VAS-A) and Amsterdam Preoperative Anxiety and Information Scale (APAIS) and to identify the influencing clinical factors. This prospective, longitudinal study was performed on 300 cardiac surgery patients in a single university hospital. The patients were assessed regarding their preoperative anxiety level using VAS-A, APAIS, and a set of specific anxiety-related questions. Their demographic features as well as their anesthetic and surgical characteristics (ASA physical status, EuroSCORE, preoperative Length of Stay (LoS), and surgical history) were recorded, as well. Then, one-way ANOVA and t-test were applied along with odds ratio for risk assessment. According to the results, 94% of the patients presented preoperative anxiety, with 37% developing high anxiety (VAS-A $\geq$ 7). Preoperative LoS > 2 days was the only significant risk factor for preoperative anxiety (odds ratio = 2.5, CI 95%, 1.3 - 5.1, P = 0.009). Besides, a positive correlation was found between anxiety level (APAISa) and requirement of knowledge (APAISk). APAISa and APAISk scores were greater for surgery than for anesthesia. Moreover, the results showed that the most common anxieties resulted from the operation, waiting for surgery, not knowing what is happening, postoperative pain and awareness during anesthesia, and not awakening from anesthesia. APAIS and VAS-A provided a quantitative assessment of anxiety and a specific qualitative questionnaire for preoperative anxiety in cardiac surgery. According to the results, preoperative LoS > 2 days and lack of information related to surgery were the risk factors for high anxiety levels.

Manjunatha SM et al[18] in 2016, conducted a correlation study to see the effect of pre-anesthetic anxiety and heart rate on propofol dose requirement for induction. The aim of the study was to delineate the correlation between pre-anesthetic anxiety and heart rate on propofol requirement for induction. Total 42 patients of ASA (American Society of Anesthesiologists) physical status I and II, 13 male and 29 female, aged between 18 to 50 years and scheduled for elective surgery under general anesthesia, were enrolled in this study. Trait anxiety in the waiting room and state anxiety both in the waiting room and operating room were assessed using Spielberger's revised State-Trait Anxiety Inventory (STAI) scale. After heart rate (HR) recording, anesthesia was induced with 200 ml/hr 1% propofol infusion till loss of verbal contact. Pre-anesthetic trait anxiety and HR had strong positive correlation with propofol requirement (ρ>0.6, P<0.05) while state anxiety had not. But pre-anesthetic state anxiety measured just before induction is strongly associated with increase in HR (ρ>0.6, P<0.05).They concluded that pre-operative anxiety should be considered and the dose of propofol should be titrated for induction accordingly.

SCALES OF ANXIETY

1.Modified Hospital Anxiety and Depression Scale (MHADS)

Hospital Anxiety and Depression Scale (HADS) was originally developed by Zigmond and Snaith (1983)[19] .As originally described the HAD scale had 14 questions, 7 scoring anxiety and 7 scoring depression. We omitted those questions relating to depression. Hence the name Modified Hospital Anxiety and Depression Scale (MHADS).

Description [20]

- **Purpose:** In general the MHADS was developed as a brief measure of generalized symptoms of anxiety and fear. The purpose of the HADS was to screen for clinically significant anxiety and depressive symptoms in medically ill patients.
- **Content:** The MHADS includes specific items that assess generalized anxiety including tension, worry, fear, panic, difficulties in relaxing, and restlessness.
- **Number of items:** The MHADS has 7 items.
- **Recall period/response items:** Respondents indicate how they currently feel. Responses are rated on a 4-point Likert scale and range from 0 to 3. Anchor points for the Likert items vary depending on the item (e.g., "I can sit still and feel relaxed" scores as 0 for definitely to 3 for not at all; and "I get sudden feelings of panic" scores as 0 for not at all to 3 for very much indeed).
- **Examples of use**: This measure evaluates common dimensions of anxiety. This measure can be used to detect and quantify magnitude of symptoms of anxiety. The target population patients' age in this study was 18 – 50 yrs. undergoing laparoscopic surgeries.

Practical Application:

- **Method of administration:** Paper and pencil administered.

This is an individually administered questionnaire and can be given via self-report or by interviewer.

- **Score interpretation**: Scoring is easily accomplished by summing scores for items, with special attention to reversed items. The total score for the MHADS can range from 0 to 21. The following guidelines are recommended for the interpretation of scores:

- 0 –6 mild anxiety,
- 7-13 moderate anxiety,
- 14–21 for severe anxiety.

- **Respondent burden**: For adults, this measure typically requires 5 minutes to complete.
- **Translations/adaptations**: Translations are available in Hindi, Marathi and English. (Appendix 1,2,3 respectively)

The MHAD scale was easily understood and completed correctly by all the patients in the study.[8] It is a simple, reproducible method of measuring preoperative anxiety. The scale has high specificity and sensitivity.[21]

Questionnaire

Q.1.	**I feel tense or 'Wound up'**
A	Most of the time ……..…[ ] (3)
B	A lot of the time ……..….[ ] (2)
C	Time to time, occasionally……...[ ] (1)
D	Not at all …… . [ ] (0)
Q.2.	**I get a sort of frightened feeling as if something awful is about to happen:**
A	Very definitely and quite badly ……..….[ ] (3)
B	Yes, but not too badly ……..….[ ] (2)
C	A little, but it doesn't worry me……... [ ] (1)
D	Not at all ……..……..[ ] (0)
Q.3.	**Worrying thoughts go through my mind**
A	A great deal of the time ……..…… [ ] (3)
B	A lot of the time ……..…… [ ] (2)
C	From time to time but not too often……...[ ] (1)
D	Only occasionally …… .. [ ] (0)
Q.4	**I can sit at ease and feel relaxed**
A	Definitely ……..…[ ] (0)
B	Usually ……..….[ ] (1)
C	Not often……...…..[ ] (2)
D	Not at all …… ..[ ] (3)
Q.5.	**I get a sort of frightened feeling like 'butterflies' in my stomach :**
A	Not at all ……..…..[ ] (0)
B	Occasionally ……..…... [ ] (1)
C	Quite often…….[ ] (2)
D	Very often ……....[ ] (3)
Q.6.	**I feel restless as if I have to be on the move :**
A	Very much indeed ……..…[ ] (3)
B	Quite a lot ……..…..[ ] (2)
C	Not very much……... [ ] (1)
D	Not at all ……..…... [ ] (0)
Q.7.	**I get sudden feelings of panic :**
A	Very often indeed ……..…[ ] (3)
B	Quite often ……..…. [ ] (2)
C	Not very often……... [ ] (1)
D	Not at all ……..…... [ ] (0)

Amsterdam Pre-Operative Anxiety and Information Scale (APAIS)

The APAIS score was developed by Moerman N.et al [22] in 1994 to distinguish anxious from nonanxious patients and patients who want information from those who don't. APAIS was developed as a screening instrument for use in the preoperative period.

Comment: Description:

- **Purpose:** The APAIS score was developed to assess the State component of anxiety[23] and patient's need for information about anaesthesia and surgical procedure.
- **Content:** It has two components:

1. Anxiety Scale: Consists of four items (questions 1, 2, 4, 5) related to anaesthesia (question 1, 2) and surgical procedure (question 4, 5) .It measures State anxiety i.e. situation related anxiety.
2. Need for information scale: Consists of 2 items (questions 3, 6) .
It covers both "Monitor" and "Blunting" aspect.

- **Number Of items:** APAIS has 6 items.
- **Response options / Scale:** Respondents indicate how they feel in preoperative period. Responses are rated on a 5-point Likert scale and range from 0 to 5. Anchor points for the Likert items vary depending on the item, from 1= Not at all to 5= Extremely.
- **Examples of use:** The APAIS was easily and very quickly completed by patients. Two clear factors emerged: anxiety and information requirements. The anxiety scale correlated highly with the standard questionnaire for measuring anxiety: Spielberger's STAI-State(r=0.74).Both the anxiety and the need-for-information scale showed good psychometric properties and were feasible in clinical practice and for research purpose. The target population in this study was patients of age 18 – 50 yrs. posted for laparoscopic surgeries.

Practical Application

- **Method of administration:** Paper and pencil administered. This is an individually administered questionnaire and can be given via self-report or by interviewer.
- **Scoring:** The rating of the items bases of a five- point Likert Scale with the extreme poles "not at all" (1) to "Highest" (5)
- **Score Interpretation:** Scoring is easily accomplished by summing scores for items

1) Anxiety scale: It is assessed from Question No.1, 2, 4, 5. The scores are classified as:
i) Low Anxiety: 4-8
ii) Moderate Anxiety: 9-15
iii) High Anxiety: 16-20
2) Need for Information Scale: It is assessed from Question No. 3 and 6. The scores are classified as:
i) No or Little Information Requirement (Blunters): 2-4
ii) Average Information Requirement: 5-7
iii) High Information Requirement (Monitors): 8-10

- **Respondent Burden:** For adults, this measure typically requires 2 minutes to complete.
- **Translations/adaptations:** Translations are available in Hindi, Marathi and English.(Appendix 4,5,6)

Amsterdam Pre-Operative Anxiety and Information Scale (APAIS)

Comment : The rating of the items bases of a five- point Likert Scale with the extreme poles "not at all" (1) to "Highest" (5)

-

1. I am worried about the anaesthetic.

1	2	3	4	5
Not at all	Less Degree	More Degree	A Lot More	Highest

2. The anaesthetic is on my mind continually.

1	2	3	4	5
Not at all	Less Degree	More Degree	A Lot More	Highest

3. I would like to know as much as possible about the anaesthetic.

1	2	3	4	5
Not at all	Less Degree	More Degree	A Lot More	Highest

4. I am worried about the procedure.

1	2	3	4	5
Not at all	Less Degree	More Degree	A Lot More	Highest

5. The procedure is on my mind continually.

1	2	3	4	5
Not at all	Less Degree	More Degree	A Lot More	Highest

6. I would like to know as much as possible about the procedure.

1	2	3	4	5
Not at all	Less Degree	More Degree	A Lot More	Highest

PHARMACOLOGY

PROPOFOL

HISTORY: Since its introduction in the 1970s, propofol has become the most widely used IV hypnotic today. Building on work on the sedative properties of phenol derivatives in mice, propofol was developed in the United Kingdom by Imperial Chemical Industries as ICI 35868. The initial solution of propofol was released in 1977 in Cremophor EL.[24] It was withdrawn because of anaphylactic reactions and was replaced and reformulated as an emulsion of a soybean oil–propofol mixture in water and relaunched in 1986.

CHEMICAL NAME: 2, 6-diisopropylphenol

CONTENT:

- 1% solution in Aqueous solution of 10% Soyabean Oil(Oil phase)
- 2.25% glycerol as a tonicity-adjusting agent,
- 1.2% purified egg phosphatide(emulsifying agent).[25-27]
- Sodium hydroxide to change the pH.

PHYSICOCHEMICAL PROPERTIES:

Propofol is highly lipid soluble and insoluble in aqueous solutions[28] .It has a pH of 7 and appears as a slightly viscous, milky white substance, a result of small lipid droplets in solution. All formulations commercially available are stable at room temperature, are not light sensitive, and may be diluted with 5% dextrose in water.

MECHANISM OF ACTION:

1. Relatively selective modulator of γ-amino-butyric acid ($GABA_A$) receptors although it also has activity at glycine receptors. Propofol is presumed to exert its sedative hypnotic effects through a $GABA_A$ receptor interaction [29].

2.The interaction of propofol with specific components of $GABA_A$ receptors appears to decrease the rate of dissociation of the inhibitory neurotransmitter ,GABA from the receptor ,thereby increasing the duration of the GABA – activated opening of the chloride channel with resulting hyperpolarization of cell membranes.

PHARMACOKINETICS:

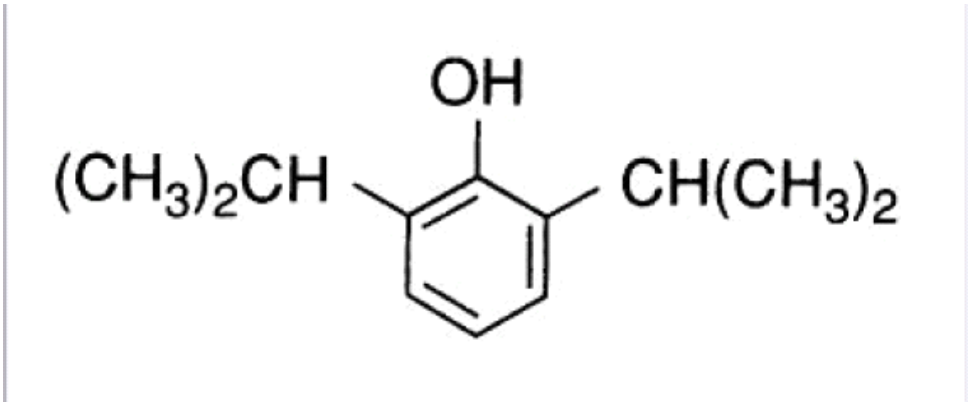
Metabolism:

1. Hepatic: Oxidative metabolism by cytochrome p50 .Propofol is oxidized to 1, 4-diisopropyl quinol in the liver. Propofol and 1,4-diisopropyl quinol are conjugated with glucuronic acid to propofol-1-glucuronide and quinol-1-glucuronide and quinol-4-glucuronide, which then may be excreted by the kidneys [30-31].

2. Extrahepatic: The most important extrahepatic site of propofol metabolism is the kidney [32-33] .Renal metabolism of propofol accounts for up to 30% of propofol clearance, and this explains the rapid clearance of propofol, which exceeds liver blood flow. The lungs also may play a role in extrahepatic propofol metabolism.[34-35]

- Initial Distribution half-life= 2 to 8 minutes
- Elimination half-life= 4 to 23.5 hr.
- Context sensitive half-life for propofol infusion up to 8hrs =less than 40 min.
- Volume of distribution of the central compartment has been calculated at between 6 and 40 L, and the volume of distribution at steady state has been calculated as 150 to 700 L.
- The clearance of propofol =1.5 to 2.2 L/minute.

STRUCTURE OF PROPOFOL



PHARMACODYNAMICS:

- **EFFECTS ON CNS**:
- The hypnotic action of propofol is mostly mediated by enhancing γ-amino butyric acid (GABA)-induced chloride current through its binding to the β subunit of the $GABA_A$ receptor.
- **SITE OF ACTION**:

1. Brainstem - Thalamocortical arousal circuits.
2. Frontoparietal association cortex.
3. Through its action on $GABA_A$ receptors in the hippocampus, propofol inhibits acetylcholine release in the hippocampus and prefrontal cortex.[36]
4. The α2-adrenoreceptor system also seems to play an indirect role in the sedative effects of propofol.[37]
5. Propofol results also in widespread inhibition of the N-methyl-d-aspartate (NMDA) subtype of glutamate receptor through modulation of sodium channel gating, an action that also may contribute to the drug's CNS effects.[38-39]
6. The sense of well-being in patients with propofol is related to the increase in dopamine concentrations in the nucleus accumbens (a phenomenon noted with drugs of abuse and pleasure-seeking behavior).[40]
7. Propofol's antiemetic action may be explained by the decrease in serotonin levels it produces in the area postrema, probably through its action on GABA receptors.[41]

- The onset of hypnosis after a dose of 2.5 mg/kg is rapid (one arm–brain circulation), with a peak effect seen at 90 to 100 seconds.
- The median effective dose (ED50) of propofol for loss of consciousness is 1 to 1.5 mg/kg after a bolus.
- The duration of hypnosis is dose dependent and is 5 to 10 minutes after 2 to 2.5 mg/kg.
- Age markedly affects the induction dose, which is highest at younger than 2 years (95% effective dose [ED95], 2.88 mg/kg) and decreases with increasing age.
- Propofol may suppress seizure activity through GABA agonism, inhibition of NMDA receptors (NMDARs), and modulation of slow calcium ion channels. However, the same GABA agonism and glycine antagonism may also induce clinical seizures and EEG epileptiform changes[42], especially during induction of and emergence from anesthesia.
- Propofol decreases intracranial pressure (ICP) in patients with either normal or increased ICP by 30% to 50% which is associated with significant decreases in cerebral perfusion pressure (CPP).[43]
- The propofol is neuroprotective because it reduces the metabolic oxygen use.
- Propofol has no direct preconditioning effect but may attenuate glutamate-mediated excitotoxicity.[44-46]
- Propofol acutely reduces intraocular pressure by 30% to 40%. It is more effective in preventing an increase in intraocular pressure secondary to succinylcholine and endotracheal intubation.
- Normal cerebral reactivity to carbon dioxide and autoregulation are maintained during a propofol infusion.

Effects on the Respiratory System:

- Apnea occurs after administration of an induction dose of propofol; the incidence and duration of apnea depend on dose, speed of injection, and concomitant premedication.[47]
- A maintenance infusion of propofol (100 μg/kg/minute) results in a 40% decrease in tidal volume and a 20% increase in respiratory frequency, with an unpredictable change in minute ventilation. Doubling the infusion rate from 100 to 200 μg/kg/minute causes a further moderate decrease in tidal volume but no change in respiratory frequency.[48]

- Propofol (50 to 120 μg/kg/minute) also depresses the ventilatory response to hypoxia, presumably by a direct action on carotid body chemoreceptors.[49]
- Propofol induces bronchodilation in patients with chronic obstructive pulmonary disease.
- Propofol potentiates hypoxic pulmonary vasoconstriction, an effect caused by inhibition of potassium–adenosine triphosphate (ATP)–mediated pulmonary vasodilatation.

Effects on the Cardiovascular System:

- Induction dose of 2 to 2.5 mg/kg produces a 25% to 40% reduction of systolic blood pressure. Similar changes are seen in mean and diastolic blood pressure.
- The decrease in arterial blood pressure is associated with a decrease in cardiac output and cardiac index (± 15%), stroke volume index (± 20%), and systemic vascular resistance (15% to 25%). Left ventricular stroke work index also is decreased (± 30%).
- The decrease in systemic pressure after an induction dose of propofol is caused by vasodilation. The decrease in cardiac output after propofol administration may result from its action on sympathetic drive to the heart.
- The myocardial depressant effect and the vasodilation depend on the dose and on the plasma concentration.[50]
- Propofol either may reset or may inhibit the baroreflex, thus reducing the tachycardic response to hypotension.
- An infusion of propofol reduces myocardial blood flow and oxygen consumption. Thus, global myocardial oxygen supply-to-demand ratio is likely preserved.

Other Effects:

- Propofol, similar to thiopental, does not enhance neuromuscular blockade produced by neuromuscular blocking drugs.
- Propofol does not trigger malignant hyperthermia and is an appropriate choice in patients with this condition.[51-53]
- After a single dose or a prolonged infusion, propofol does not affect corticosteroid synthesis or alter the normal response to adrenocorticotropic hormone stimulation.
- Propofol in the emulsion formulation does not alter hepatic, hematologic, or fibrinolytic function.
- Propofol alone in intralipid does not trigger histamine release.
- Propofol also possesses significant antiemetic activity with small (subhypnotic) doses (i.e., 10 mg in adults).
- Propofol decreases polymorphonuclear leukocyte chemotaxis, but not adherence phagocytosis and killing.
- The intralipid that acts as the solvent for propofol is an excellent culture medium. Disodium edetate or metabisulfite has been added to the formulation of propofol in an attempt to retard such bacterial growth.
- The administration of propofol is associated with the development of pancreatitis,[54] which may be related to hypertriglyceridemia.

USES:

- Induction of general anesthesia=1-2.5 mg/kg IV, dose reduced with increasing age
- Maintenance of general anesthesia=50-150 μg/kg/min IV combined with N2O or an opiate
- Sedation=25-75 μg/kg/min IV
- Antiemetic action=10-20 mg IV, can repeat every 5-10 min or start infusion of 10 μg/kg/min

SIDE EFFECTS AND CONTRAINDICATIONS:

- Induction of anesthesia with propofol is often associated with pain on injection, apnea, hypotension, and rarely, thrombophlebitis of the vein into which propofol is injected.[55] Pain on injection is reduced by using a large vein, avoiding veins in the dorsum of the hand, and adding lidocaine to the propofol solution or changing the propofol formulation.
- **Propofol Infusion Syndrome**: It is associated with infusion of propofol at 4 mg/kg/hour or more for 48 hours or longer.[56] This syndrome was first described in children but subsequently has been observed in critically ill adults [57-58] .The clinical features of propofol infusion syndrome are acute refractory bradycardia leading to asystole in the presence of one or more of the following: metabolic acidosis (base deficit >10 mmol/L), rhabdomyolysis, hyperlipidemia, and enlarged or fatty liver. Other features include cardiomyopathy with acute cardiac failure, skeletal myopathy, hyperkalemia, hepatomegaly, and lipemia. The symptoms and signs are the result of muscle injury and the release of intracellular toxic contents. The major risk factors are poor oxygen delivery, sepsis, serious cerebral injury, and large propofol dosage. Predisposing factors are likely genetic disorders impairing fatty acid metabolism, such as medium-chain acyl coenzyme A (MCAD) deficiency and low

carbohydrate supply. Because lipemia has been noted, a failure of hepatic lipid regulation, possibly related to poor oxygenation or a lack of glucose, may be the cause. In some cases, increasing lipemia was the first indication of impending propofol infusion syndrome onset; therefore, lipemia is a sign.

IV. Materials And Methods

After institutional ethics committee approval, this Prospective Observational Study was carried out over a period of 18 months in various operation theatres in a tertiary care center. The patients were assessed for below mentioned inclusion and exclusion criteria, were explained about the study and invited to participate in the study after taking informed consent.

The study was conducted in the 60 consecutive patients presenting for elective laparoscopic surgeries using the following standard protocol.

- **INCLUSION CRITERIA:**

1. Age: 18 to 50 years
2. Patients scheduled to undergo elective laparoscopic surgeries under general anaesthesia.
3. ASA Grade I/II

- **EXCLUSION CRITERIA:**

1. Psychiatric illness.
2. Patients on psychotropic medications.
3. Pregnancy.
4. Known or Expected allergy to propofol.
5. Patients unable to understand Hindi, Marathi or English.

V. Methodology:

On the pre-operative visit, the patient's anxiety trait was assessed using Modified Hospital Anxiety and Depression Scale. English, Hindi or Marathi versions (Appendix 1, 2, 3 respectively) were made available to patient for marking of the self-assessment scale. In case of language/ literacy barrier, investigator read out/ translated the questions. This scale was considered the patient's existing anxiety trait.

On the morning of surgery, the same patient underwent a complete pre-operative assessment with all relevant investigations and adequate starvation was checked. The patient was assessed for state and level of anxiety and coping strategy using Amsterdam Pre-operative Anxiety and Information Scale. English, Hindi or Marathi versions (Appendix 4, 5, 6 respectively) were made available to patient for marking of the self-assessment scale. In case of language/ literacy barrier, investigator read out/ translated the questions. This scale was considered the patient's baseline anxiety state, level and coping strategy.

No sedative premedication was given. Patient was taken on O.T. table and pulse oximeter, cardioscope and noninvasive BP monitor were connected. Patient's heart rate, blood pressure and oxygen saturation were checked and noted.

Premedication given as Inj. Glycopyrrolate 0.004mg/kg iv +Inj. Midazolam 0.02mg/kg iv + Inj. Fentanyl 2mcg/kg iv. Patient Pre-oxygenated with 100% O_2 for 3 min.

The anaesthesia was induced with Inj. Propofol 2mg/kg iv slowly as bolus dose followed by 0.5 mg/kg increments as required every 30 sec. till loss of response to verbal command, onset of unconsciousness and centralization of eyeball.

Total dose of Propofol required for induction was noted.

Statistical Methods: Descriptive and inferential statistical analysis had been carried out in the present study. Results on continuous measurements were presented on Mean SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5 % level of significance. The following assumptions on data were made, Assumptions: 1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent.

Analysis of variance (ANOVA) had been used to find the significance of study parameters between three or more groups of patients , Student t test (two tailed, independent) had been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

VI. Observation And Results

The present study was conducted on sixty patients presented for elective laparoscopic surgeries for observational analysis of preoperative anxiety on dose of propofol required for induction of general anaesthesia.

Study design: An observational clinical study

Table 1: Age distribution of patients studied

Age in years	No. of patients	%
21-30	15	25.0
31-40	19	31.7
41-50	26	43.3
Total	60	100.0

Mean ± SD: 38.48±9.42

Table 1 shows demographic distribution of patients studied.
Mean age of patients studied was 38.48 yrs with standard deviation of 9.42
No. of patients in age group 21-30 yrs. =15(25%)
No. of patients in age group 31-40yrs =19(31.7%)
No. of patients in age group 41-50yrs =26(43.3%)

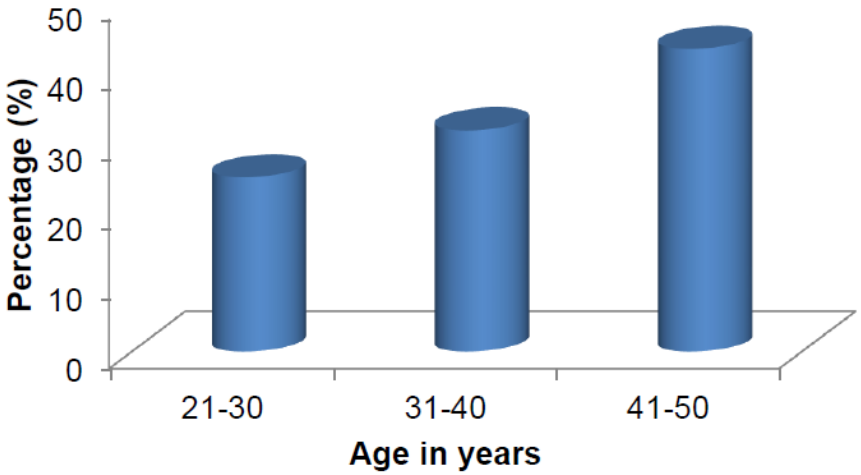


Figure 1: Age distribution

Table 2: Gender distribution of patients studied

Gender	No. of patients	%
Female	41	68.3
Male	19	31.7
Total	60	100.0

Table 2 shows gender distribution of patients studied.
Total no. of females participated= 41 (68.3%)
Total no. of males participated=19 (31.7%)

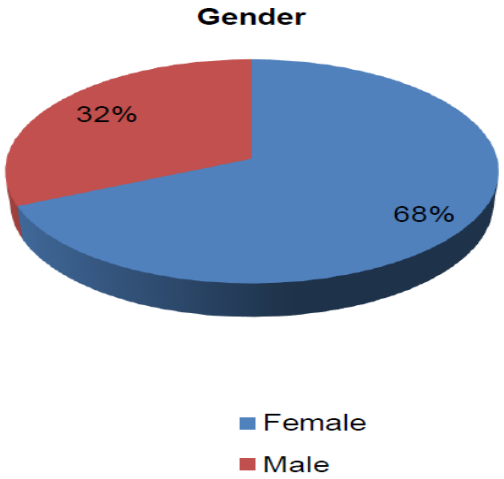


Figure 2: Gender distribution

Table 3: Surgery distribution of patients studied

Types of Surgeries	No. of patients	%
Lap. Cholecystectomy	47	78.33
Diagnostic laparoscopy	8	13.3
Lap. hydatid cystectomy	1	1.7
Lap. myomectomy	1	1.7
Lap. ovarian cystectomy	3	5
Total	60	100

Table 3 shows distribution of number of patients for different types of surgeries.
No. of patients undergoing laparoscopic cholecystectomy=47(78.33%)
No. of patients undergoing diagnostic laparoscopy=8(13.3%)
No. of patient undergoing laparoscopic hydatid cystectomy=1(1.7%)
No. of patient undergoing laparoscopic myomectomy =1(1.7%)
No. of patients undergoing laparoscopic ovarian cystectomy=3(5%)

Table 4: Weight (kg) distribution of patients studied

Weight (kg)	No. of patients	%
31-40	3	5.0
41-50	12	20.0
51-60	25	41.7
61-70	14	23.3
>70	6	10.0
Total	60	100.0

Mean ± SD: 57.95±10.55

Table 4 shows weight distribution (in kg) of patients undergoing laparoscopic surgeries.
Mean weight was 57.95 kg with standard deviation of 10.55

Table 5: MHADS: Trait anxiety distribution of patients studied

MHADS	No. of patients	%
0-6 {low}	24	40.0
7-13 {moderate}	25	41.7
14-21 {high}	11	18.3
Total	60	100.0

Mean ± SD: 8.18±4.67

Table 5 shows Trait anxiety score distribution of patients studied by Modified Hospital Anxiety and Depression Scale.
Score 0-6 represented low anxiety score which consisted of 24 patients (40%) of total patients studied.
Score 7-13 represented moderate anxiety score which consisted of 25 patients (41.7%) of total patients studied.
Score 14-21 represented high anxiety score which consisted of 11 patients (18.3%) of total patients studied.
Mean score was 8.18 with standard deviation of 4.67

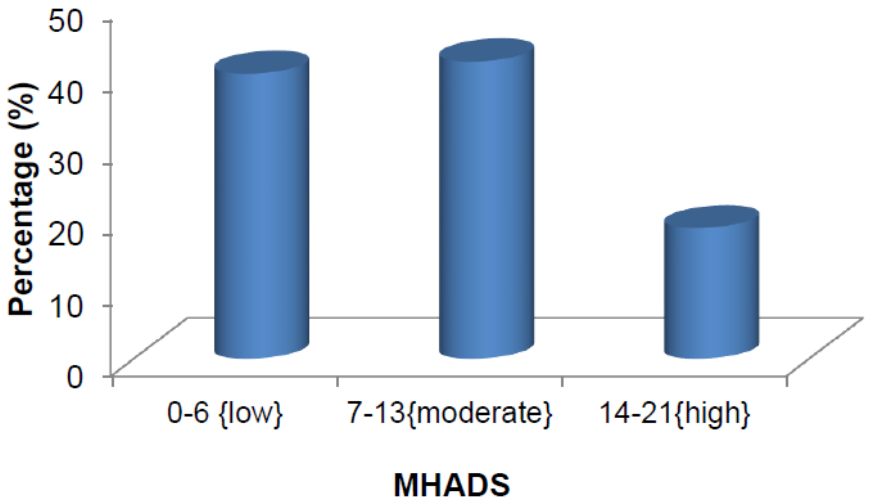


Figure 3: Classification of Trait Anxiety by MHADS

Table 6: APAIS: State Anxiety Score distribution of patients studied

	No. of patients	%
Anaesthesia		
• 2-4	43	71.7
• 5-7	16	26.7
• 8-10	1	1.7
Surgery		
• 2-4	39	65.0
• 5-7	18	30.0
• 8-10	3	5.0
Total		

• 4-8 {low}	38	63.3
• 9-15 {moderate}	21	35.0
• 16-20 {high}	1	1.7

Mean ± SD: 8.12±3.43

Table 6 shows State anxiety score distribution by Amsterdam Preoperative Anxiety and Information Scale. It was divided into Anxiety score related to anaesthesia, Anxiety score related to surgical procedure and total anxiety score.

Total anxiety score was divided into Low anxiety score: 4-8 which consisted of 38 (63.3%) of patients.

Moderate anxiety score: 9-15 which consisted of 21(35%) of patients.

High anxiety score: 16-20 which consisted of 1(1.7%) of patients.

Mean anxiety score was 8.12 with standard deviation of 3.43

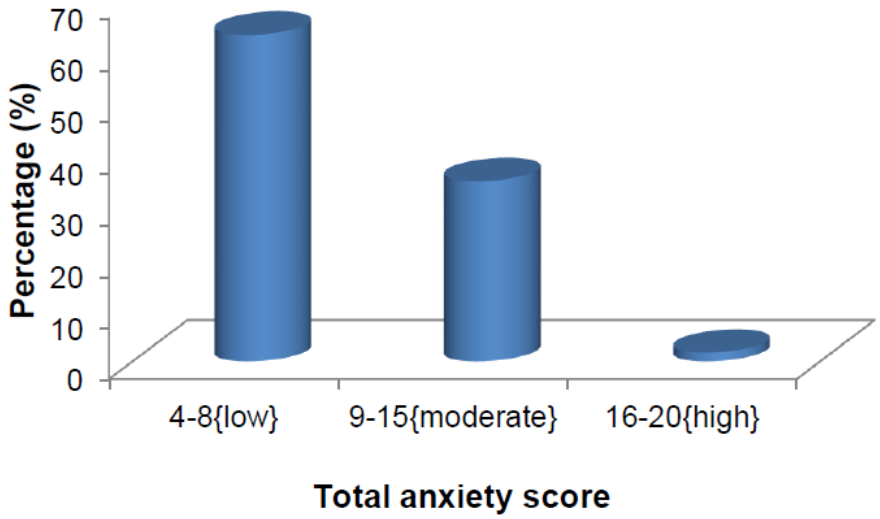


Figure 4: Classification of State anxiety by APAIS

Table 7: APAIS: Need for information of score distribution of patients studied

Need information of score	No. of patients	%
2-4 {Blunters}	25	41.7
5-7 {Average need for information}	23	38.3
8-10 {Monitors}	12	20.0
Total	60	100.0

Mean ± SD: 5.40±2.45

Table 7 shows Need for information score distribution of patients studied by Amsterdam Preoperative Anxiety and Information Scale. It consisted of little or no information requirement (Blunters) with score of 2-4 which comprised of 25(41.7%) of patients.

Average information requirement with score of 5-7 which comprised of 23(38.3%) of patients.

High information requirement (Monitors) with score of 8-10 which comprised of 12(20%) of patients

Mean for Need for information score was 5.4 with standard deviation of 2.45

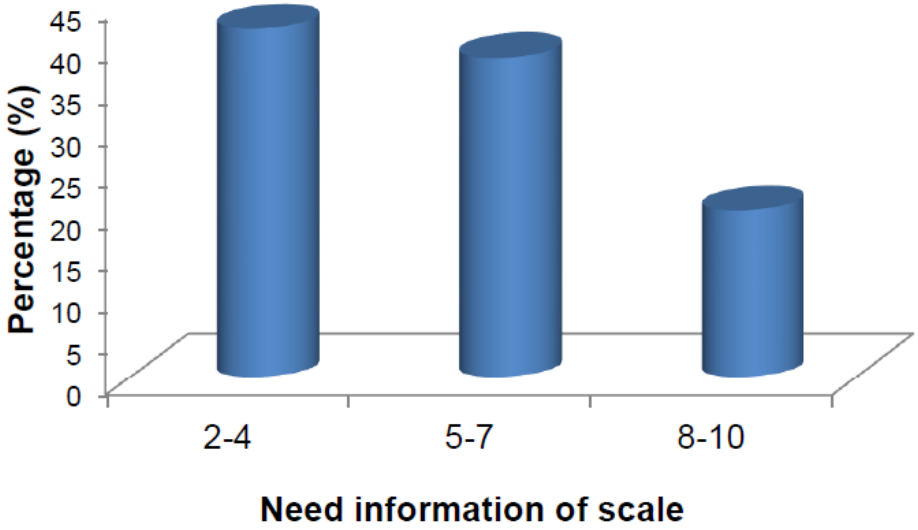


Figure 5: Classification of need for information by APAIS

Table 8: Baseline Pulse Rate of the patients studied.

Baseline Pulse rate (bpm)	No. of patients	%
<80	18	30
80-110	41	68.3
>110	1	1.7
Total	60	100
Mean ± SD	85.55±10.09	

Table 8 shows baseline Pulse rate of the patients studied.
Mean for baseline pulse rate was 85.55 with standard deviation of 10.09

Table 9: Baseline Systolic Blood Pressure of the patients studied.

Baseline SBP (mm Hg)	No. of patients	%
<120	9	15
120-140	35	58.3
>140	16	26.7
Total	60	100
Mean ± SD	134.98±13.50	

Mean baseline systolic blood pressure was 134.98 with standard deviation of 13.5

Table 10: Baseline Diastolic Blood Pressure of the patients studied.

Baseline DBP (mm Hg)	No. of patients	%
<80	14	23.3
80-100	45	75

>100	1	1.7
Total	60	100
Mean ± SD	84.87±8.30	

Mean baseline diastolic blood pressure was 84.87 with standard deviation of 8.3

Table 12: Comparison of Total dose and dose per kg in relation to surgery

	Surgery					**Total**	**'p'value**
	Lap Cholecystectomy	**Diagnostic lap**	**Lap ovarian cystectomy**	**Lap hydatid cystectomy**	**Lap Myomectomy**		
Total Dose(mg)	137.02±37.00	133.75±22	126.67±35.12	130.00±0.00	160.00±0.00	136.33±34.39	0.942
Dose per kg(mg/kg)	2.34±0.50	2.29±0.44	2.77±0.15	2.16±0.00	2.90±0.00	2.36±0.49	0.454

Table 12 shows Comparison of Total dose of propofol and dose per kg in relation to different types of surgeries. The 'p'values for total dose of propofol required for different surgeries were nonsignificant (>0.05), so all groups were comparable in this aspect.

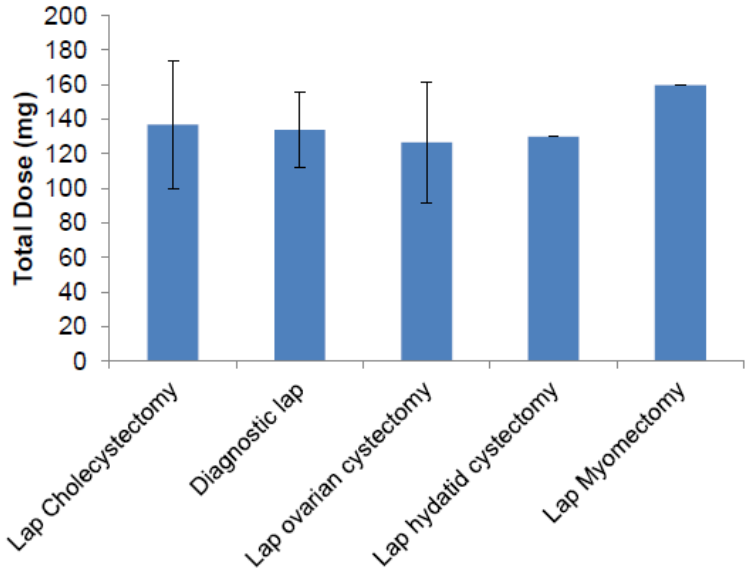


Figure 6: Total dose of propofol for different types of surgeries.

Table 13: Comparison of Total dose and dose per kg in relation to age in years

	Age in years			**Total**	**'p' value**
	21-30	**31-40**	**41-50**		
Total Dose(mg)	124.67±30.67	137.37±37.39	142.31±33.74	136.33±34.39	0.287
Dose per kg(mg/kg)	2.44±0.56	2.25±0.52	2.40±0.42	2.36±0.49	0.471

Table 13 shows Comparison of Total dose of propofol and dose per kg in relation to age in years. The 'p' values for total dose of propofol were nonsignificant (>0.05), so all groups were comparable in this aspect.

Table 14: Comparison of Total dose and dose per kg in relation to gender

	Gender		Total	'p' value
	Male	Female		
Total Dose(mg)	145.79±36.71	131.95±32.80	136.33±34.39	0.149
Dose per kg(mg/kg)	2.39±0.48	2.35±0.50	2.36±0.49	0.741

Table 14 shows Comparison of Total dose of propofol and dose per kg in relation to gender. The 'p' value for total dose of propofol was nonsignificant (>0.05), so no significant difference observed for induction dose of propofol with respect to gender factor.

Table 15: Comparison of Total dose and dose per kg in relation to MHADS

	Anxiety score by MHADS			Total	'p' value
	0-6 {Low}	7-13 {Moderate}	14-21 {High}		
Total Dose(mg)	123.75±33.08	131.20±25.71	175.45±27.34	136.33±34.39	<0.001**
Dose per kg(mg/kg)	2.10±0.35	2.27±0.28	3.13±0.31	2.36±0.49	<0.001**

Table 15 shows comparison of total dose of propofol and dose per kg in relation to Modified Hospital Anxiety and Depression Scale.
Total dose of propofol for Low anxiety score was 123.75mg with standard deviation of 33.08
Total dose of propofol for Moderate anxiety score was 131.20mg with standard deviation of 25.71
Total dose of propofol for High anxiety score was 175.45mg with standard deviation of 27.34

'p' value for this comparison is <0.01 which was strongly significant. The patients with low trait anxiety score required less dose of propofol for induction of anaesthesia as compared to patients with high trait anxiety score.

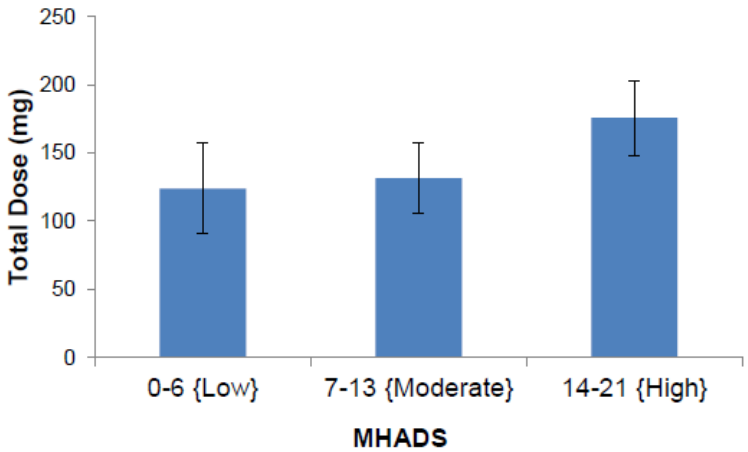


Figure 7: Comparison of total dose of propofol and MHADS anxiety score

Table 16: Comparison of Total dose and dose per kg in relation to Anxiety score by APAIS

	Anxiety Score by APAIS			Total	'p' value
	4-8 {Low}	9-15 {Moderate}	16-20 {High}		
Total Dose(mg)	126.58±31.30	153.00±33.42	155.00±49.50	136.33±34.39	0.013*
Dose per kg(mg/kg)	2.19±0.35	2.64±0.54	2.75±1.06	2.36±0.49	0.001**

Table 16 shows comparison of Total dose of propofol and dose per kg in relation to Anxiety score by Amsterdam Preoperative Anxiety and Information Scale.
Total dose of propofol for low anxiety score was 126.58mg with standard deviation of 31.30
Total dose of propofol for moderate anxiety score was 153mg with standard deviation of 33.42
Total dose of propofol for high anxiety score was 155mg with standard deviation of 49.50
'p' value for comparison of Total dose of propofol and anxiety score was 0.013 which was moderately significant.
This showed that the patients with low state anxiety score required less dose of propofol for induction of anaesthesia as compared to patients with high state anxiety score.

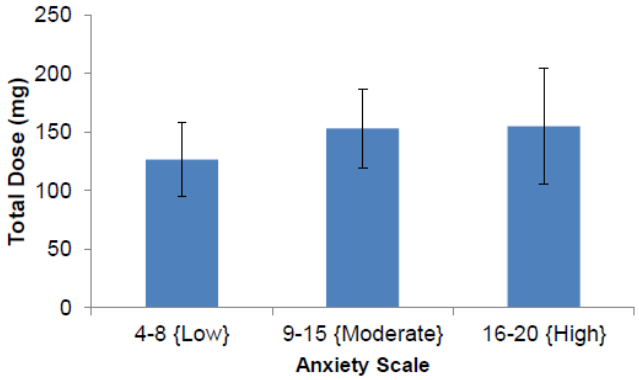


Figure 8: Comparison of total dose of propofol and APAIS anxiety score

Table17: Comparison of Total dose and dose per kg in relation to anxiety score for Anaesthesia by APAIS.

	Anxiety score for Anaesthesia			Total	'p' value
	2-4	5-7	8-10		
Total Dose(mg)	126.74±30.37	161.43±30.60	156.67±49.33	136.33±34.39	0.002**
Dose per kg(mg/kg)	2.19±0.34	2.78±0.48	2.93±0.81	2.36±0.49	<0.001**

Table 17 shows comparison of total dose of propofol and dose per kg in relation to anxiety scale for anaesthesia.
Total dose of propofol for anxiety score of 2-4 was 126.74mg with standard deviation of 30.37
Total dose of propofol for anxiety score of 5-7 was 161.43mg with standard deviation of 30.60
Total dose of propofol for anxiety score of 8-10 was 156.67mg with standard deviation of 49.33
'p' value for Total dose of propofol and anxiety score for anaesthesia was <0.01 which was strongly significant.
This showed that patients with low anxiety score for anaesthesia required less dose of propofol and patients with high anxiety score for anaesthesia required higher dose of propofol.

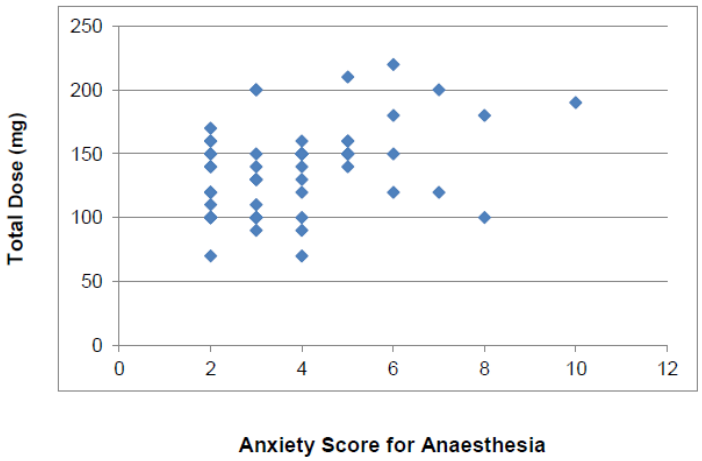


Figure 9: Correlation between total dose of propofol and Anxiety score for Anaesthesia

Figure 9 shows scatter diagram for correlation between Total dose of propofol and Anxiety score for anaesthesia. The Pearson correlation coefficient was 0.41 which showed moderate correlation between them.

Table 18: Comparison of Total dose and dose per kg in relation to anxiety score for Surgery by APAIS

	Anxiety score for Surgery			Total	'p' value
	2-4	5-7	8-10		
Total Dose(mg)	127.95±33.34	154.00±33.76	146.67±26.58	136.33±34.39	0.030*
Dose per kg(mg/kg)	2.21±0.36	2.61±0.59	2.69±0.60	2.36±0.49	0.004**

Table 18 shows comparison of total dose of propofol and dose per kg in relation to anxiety scale for surgery by APAIS.
Total dose of propofol for anxiety score of 2-4 was 127.95mg with standard deviation of 33.34
Total dose of propofol for anxiety score of 5-7 was 154mg with standard deviation of 33.76
Total dose of propofol for anxiety score of 8-10 was 146.67mg with standard deviation of 26.58
'p' value for above comparison was 0.03 which was moderately significant. This showed that patients with low anxiety score for surgery required less dose of propofol and patients with high anxiety score for surgery required higher dose of propofol.

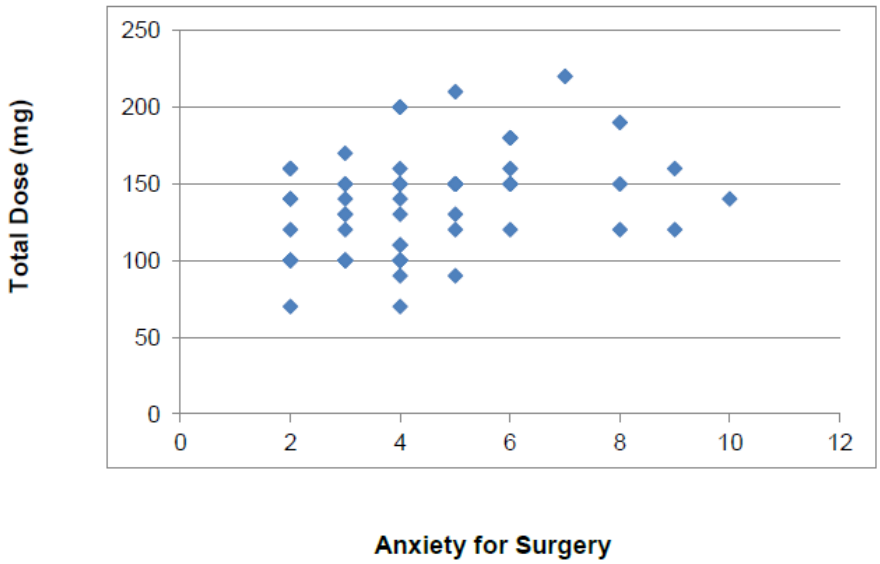


Figure 10: Correlation between total dose of propofol and anxiety score for surgery

Figure 10 shows scatter diagram for correlation between total dose of propofol and anxiety score for surgery. The Pearson correlation coefficient was 0.325 which showed moderate correlation.

Table 19: Comparison of Total dose and dose per kg in relation to need for Information score

	Need for Information Score			Total	'p' value
	2-4	5-7	8-10		
Total Dose(mg)	137.20±36.80	136.52±32.70	134.17±35.28	136.33±34.39	0.969
Dose per kg(mg/kg)	2.37±0.53	2.28±0.39	2.51±0.57	2.36±0.49	0.430

Table 19 shows comparison of total dose of propofol and dose per kg in relation to need for information score.
Total dose for No or little information requirement (Blunters) with score 2-4, was 137.2 mg with standard deviation of 36.8
Total dose for moderate information requirement with score 5-7, was 136.52 mg with standard deviation of 32.7

Total dose for high information requirement (Monitors) with score 8-10, was 134.17mg with standard deviation of 35.28
'p' value for above comparison was >0.01 which was nonsignificant. This showed that need for information did not affect dose of propofol required for induction of general anaesthesia.

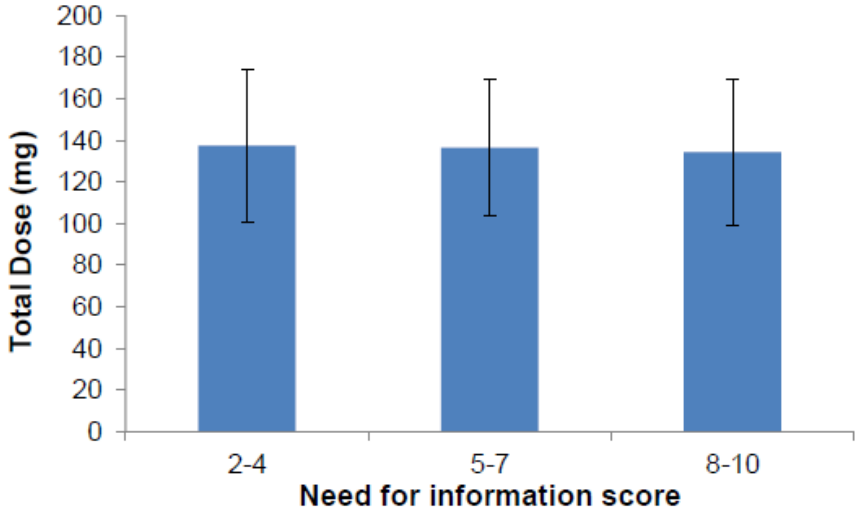


Figure 11: Comparison of total dose of propofol and need for information score

Table 20: Comparison of total dose and dose per kg in relation to baseline pulse rate (bpm)

	Pulse rate (bpm)			Total	'p' value
	<80	80-110	>110		
Total Dose(mg)	126.36±26.47	142.16±37.87	140.00±0.00	136.33±34.39	0.017**
Dose per kg(mg/kg)	2.25±0.36	2.40±0.53	3.20±0.00	2.36±0.49	0.002

Table 20 shows comparison of total dose of propofol and dose per kg in relation to baseline pulse rate.
Total dose of propofol for baseline pulse rate of <80 bpm was 126.36mg with standard deviation of 26.47
Total dose of propofol for baseline pulse rate of 80-110 bpm was 142.16mg with standard deviation of 37.87
Total dose of propofol for baseline pulse rate of >110 bpm was 140mg with standard deviation of 0.
'p' value for above comparison was 0.017 which was moderately significant.
This showed that in baseline pulse rate had moderately significant effect on dose of propofol required for induction of general anaesthesia.

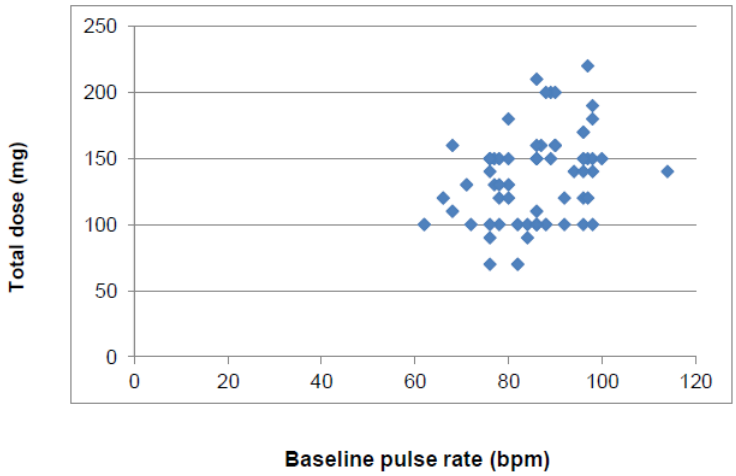


Figure 12: Correlation between Total dose of propofol and baseline pulse rate

Figure 12 shows scatter diagram for correlation between total dose of propofol and baseline pulse rate. The Pearson correlation coefficient was 0.306 which showed moderate correlation.

Table 21: Comparison of Total dose and dose per kg in relation to baseline SBP (mm Hg)

	SBP (mm Hg)			Total	'p' value
	<120	120-140	>140		
Total Dose(mg)	106.67±21.88	141.25±32.20	148.75±35.19	136.33±34.39	<0.001**
Dose per kg(mg/kg)	2.17±0.36	2.38±0.51	2.46±0.52	2.36±0.49	0.300

Table 21 shows comparison of total dose of propfol and dose per kg with baseline Systolic Blood pressure (mm Hg).
Total dose of propofol for baseline systolic blood pressure of less than 120 mm Hg was 106.67mg with standard deviation of 21.88
Total dose of propofol for baseline systolic blood pressure of 120-140 mm Hg was 141.25mg with standard deviation of 32.2
Total dose of propofol for baseline systolic blood pressure of more than 140mm Hg was 148.75 with standard deviation of 35.19
'p' value for above comparison was <0.01 which was strongly significant.
This showed that baseline systolic blood pressure had significant effect on dose of propofol required for induction of general anaesthesia.

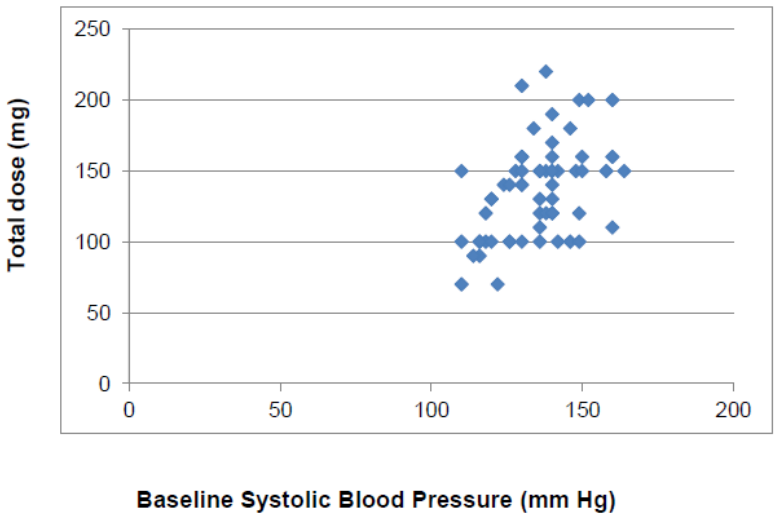


Figure 13: Correlation between total dose of propofol and baseline systolic blood pressure

Figure 13 shows scatter diagram for correlation between total dose of propofol and baseline systolic blood pressure. The Pearson correlation coefficient was 0.463 which showed moderate correlation.

Table 23: Comparison of Total dose and dose per kg in relation to baseline DBP (mm Hg)

	DBP (mm Hg)			Total	'p' value
	<80	80-100	>100		
Total Dose(mg)	123.81±33.83	141.58±32.26	200.00±0.00	136.33±34.39	0.002*
Dose per kg(mg/kg)	2.27±0.41	2.41±0.53	2.66±0.00	2.36±0.49	0.142

Table 23 shows comparison of total dose of propofol and dose per kg in relation to baseline diastolic blood pressure (mm Hg).

Total dose of propofol for baseline diastolic blood pressure of less than 80 mm Hg was 123.81mg with standard deviation of 33.83
Total dose of propofol for baseline diastolic blood pressure of 80-100 mm Hg was 141.58mg with standard deviation of 32.26
Total dose of propofol for baseline diastolic blood pressure of more than 100 mm Hg was 200 with standard deviation of 0.
'p' value for above comparison was 0.002 which was strongly significant
This showed that baseline diastolic blood pressure had significant effect on dose of propofol required for induction of general anaesthesia.

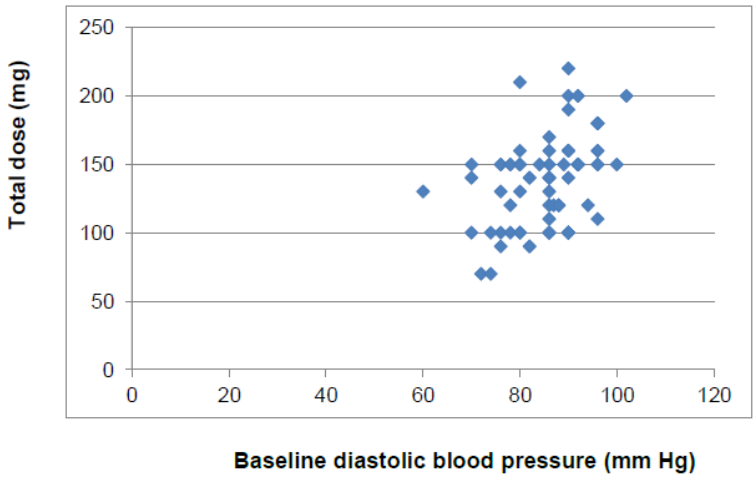


Figure 14: Correlation between total dose of propofol and baseline diastolic blood pressure

Figure 14 shows scatter diagram for correlation between total dose of propofol and baseline diastolic blood pressure. The Pearson correlation coefficient was 0.394 which showed moderate correlation.

Table 24: PEARSON CORRELATION COEFFICIENT (r) and 'p'value.

	PAIR	'r' value	'p' value
•	Total dose(mg) vs. Age(yrs.)	0.178	0.287
•	Total dose (mg) vs. MHADS Anxiety score	0.533	<0.001***
•	Total dose(mg) vs. APAIS Anxiety score	0.398	0.013*
•	Total dose (mg) vs. APAIS Anxiety score related to anaesthesia	0.410	0.002**
•	Total dose (mg) vs. APAIS Anxiety score related to surgery	0.325	0.030*
•	Total dose (mg) vs. APAIS score for Need for information	0.0197	0.969
•	Total dose (mg) vs. Baseline Pulse Rate(bpm)	0.306	0.017*
•	Total dose (mg) vs. Baseline Systolic Blood Pressure (mm Hg)	0.463	<0.001***
•	Total dose (mg) vs. Baseline Diastolic Blood Pressure (mm Hg)	0.394	0.002**

To summarize our results,

- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and age distribution was 0.178 (small correlation) and 'p'value was 0.287 (non-significant).
- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and MHADS trait anxiety score was 0.533 (large correlation) and 'p'value was <0.001 (strongly significant).
- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and APAIS state anxiety score was 0.398 (moderate correlation) and 'p'value was 0.013 (moderately significant).
- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and APAIS state anxiety score related to anaesthesia was 0.410 (moderate correlation) and 'p'value was 0.002 (strongly significant).
- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and APAIS state anxiety score related to surgery was 0.325 (moderate correlation) and 'p'value was 0.03 (moderately significant).
- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and APAIS score for need for information was 0.0197 (trivial correlation) and 'p'value was 0.969 (non-significant).
- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and baseline pulse rate was 0.306 (moderate correlation) and 'p'value was 0.017 (moderately significant).

- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and baseline systolic blood pressure was 0.463 (moderate correlation) and <0.001 (strongly significant).
- The Pearson coefficient of correlation (r) for the comparison of Total dose of propofol and baseline diastolic blood pressure was 0.394 (moderate correlation) and 'p'value was 0.002 (strongly significant).

Pearson correlation between study variables was performed to find the degree of relationship, Pearson correlation co-efficient ranging between -1 to 1

- **Classification of Correlation Co-efficient (r)**

Up to 0.1 Trivial Correlations
0.1-0.3 Small Correlation
0.3-0.5 Moderate Correlation
0.5-0.7 Large Correlation
0.7-0.9 V.Large Correlation
0.9- 1.0 Nearly Perfect correlation
1 Perfect correlation

Significant figures

+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P 0.05)
** Strongly significant (P value: P0.01)

Statistical software: The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel had been used to generate graphs, tables etc**.** [59-62]

VII. Discussion

Anxiety is an emotional state characterized by apprehension and fear resulting from anticipation of threatening event. It has been shown that the majority of patients admitted to hospital for elective surgery experience anxiety preoperatively.[63] Anxiety and stress are unpleasant sensations and can also adversely influence the surgical procedure as well as affect the patient's recovery [64].

State anxiety (situational anxiety) is defined as subjective feelings of apprehension, nervousness, tension, and worry when subjected to an anxiety-provoking stimulus, whereas trait anxiety (baseline anxiety) is defined as individual differences in the disposition of responses to stressful situations.

The degree to which each patient manifests anxiety related to future experiences depends on many factors. These include, but are not limited to, age, gender, cultural and physiological status, personality development, education, diseases, drug treatment and interactions, type and extent of the proposed surgery, familiarity with and preparedness for the procedures, previous surgical experience, and personal susceptibility to stressful situations (trait-anxiety).[9,65] Some degree of anxiety is a natural reaction to the unpredictable and potentially threatening circumstances typical of the preoperative period, especially for the patient's first few surgical experiences. However, excessive degrees of preoperative anxiety can lead to pathophysiological responses. These include tachycardia, hypertension, arrhythmias, and higher levels of pain that may persist into the postoperative period.[66-67]

Traditionally the patients were admitted to hospital the day before surgery. Anaesthesiologists used the inpatient preoperative visit to assess the patient's clinical and psychological state, and to establish rapport. These encounters were also used to address and alleviate patients' concerns regarding their upcoming procedure. Despite the apparent benefits of the in-patient preoperative visit and pre-anaesthetic clinics (PAC), there is still a need for the anaesthesiologist to address the patients' medical and psychological concerns. New tools are needed to assist the anaesthesiologist in this task. One such needed tool is a quantitative scale of preoperative anxiety. Such a scale could provide an opportunity for patients to express their feelings. Also, the ability to quantify anxiety objectively in the preoperative period has other advantages. The information could be used to screen for highly anxious patients who might benefit from preoperative anaesthetic consultation or anxiolytic medications. An anxiety scale could be further utilized to assess adequacy of preoperative patient preparation, and to measure the effectiveness of preoperative communication. In our study, we used simple and brief quantitative tests for measurement of anxiety.

Our study included the patients undergoing Laparoscopic cholecystectomy, diagnostic laparoscopy, laparoscopic ovarian cystectomy, laparoscopic myomectomy, and laparoscopic hydatid cystectomy under general anaesthesia. Patients undergoing same type of surgeries have comparable level of anxiety. Furthermore laparoscopic surgeries have small port incisions so, lesser postoperative pain, early recovery from surgery and cosmetically better scars. These factors are important while considering anxiety of patients.

Our study included the patients of age group 18 to 50 yrs. Younger patients might not understand the questionnaires of anxiety scales. Adolescent age group is known to have more anxiety and elderly patients are more anxious about their health, dependency after surgery, coexisting diseases, so these age groups were

excluded. We included ASA grade I and II patients as the patients with higher ASA grade with uncontrolled systemic disease or associated comorbid condition can have higher anxiety.

We excluded the patients with existing psychiatric illness, patients on psychotropic medications as such patients could have higher anxiety than the other patients. We excluded the pregnant patients as the laparoscopy in pregnant patients is risky; also pregnancy itself increases the anxiety of women. We excluded the patients with history of known or expected allergy to propofol. We excluded the patients who were unable to understand Hindi, Marathi or English as they could not understand the questionnaire.

Our study was carried out to observe the correlation between preoperative anxiety on dose of propofol required for induction of general anaesthesia in laparoscopic surgeries. Preoperative anxiety was studied under two components of anxiety i.e. 'Trait' anxiety using 'Modified Hospital Anxiety and Depression Scale' and 'State' anxiety using 'Amsterdam Preoperative Anxiety and Information Scale'. We studied the effect of trait and state anxiety on propofol requirement separately.

We used Modified Hospital Anxiety and Depression Scale for measurement of Trait anxiety on the preoperative visit. It consisted of 7 multiple choice questions each with 4 possible answers. It was a reliable instrument for screening of clinically significant anxiety. It was also shown to be free from item bias by gender, age or location. Multiple choice questions are a familiar part of modern life and our questionnaire was easily understood, readily accepted and completed correctly by all the patients in study. The total scores of MHADS were classified as low, moderate and high anxiety trait. Total dose of propofol required for each of these groups were compared.

We used Amsterdam Preoperative Anxiety and Information Scale for measurement of State anxiety on the morning of surgery. It was a 6 item questionnaire. It was easily and very quickly completed by patients. It reproduced 2 components i.e. anxiety and need for information. Some patients require more than basic information given prior to surgery, known as "Monitors", while some patients like to shut themselves off from the information, known as "Blunters"[68-69]. It is important to realize that anxious patients might derive great benefit from more attention and information. However, extensive information is not always useful and may even induce anxiety. Particularly patients with a "blunting" coping style may become anxious when confronted with extensive information. By contrast, patients with a "monitoring" coping style become anxious when they are not provided with as much information as they want. The APAIS scale is beneficial in clinical practice for anaesthesiologists to know whether they are dealing with a patient who wanted more than basic information which is routinely given, or a patient who would rather not be given any extra information.

On the morning of surgery, no sedative premedication was given to the patient. The premedication was given just before induction of anaesthesia to prevent intubation response. After giving induction dose of propofol, loss of response to verbal command, onset of unconsciousness and centralization of eyeball were our clinical end point, because they are the commonly accepted terminal point in clinical practice.

So, in this study we studied the correlation between preoperative Trait as well as State anxiety separately with the total dose of propofol required for induction of general anaesthesia in laparoscopic surgeries.

We observed that there was no significant difference for induction dose of propofol with respect to different types of surgeries like laparoscopic cholecystectomy, diagnostic laparoscopy, laparoscopic ovarian cystectomy, laparoscopic hydatid cystectomy, laparoscopic myomectomy.($p=0.94$).In other words, anxiety level from these types of surgeries did not differ much. This could be because of the advantages of laparoscopic surgeries like short postoperative stay, cosmetic incisions and lesser pain. Moerman N[10] in his study of APAIS found that there was no statistically significant relationship between type of operation and scores on the anxiety scale. However, Hernández-palazón J. et al[17] in his study of measurement of preoperative anxiety in cardiac surgery found that most of the anxiety resulted from the operation. In those cases, cardiac surgery itself was one of the anxiety provoking factors.

We observed that there was no significant difference for induction dose of propofol with respect to different age groups ($p=0.287$). MAE Ramsay[1] in his study of preoperative fear found that there was less preoperative fear at the ends of age scale i.e. 55% in age group of 4-12yrs, 61% in age group of 13-21yrs, 84% in age group of 42-61yrs, 57% in age group of 62-82yrs ($p<0.001$).Ebirim L[70] in his study of factors responsible for preoperative anxiety in elective surgical patients found that the percentage of participants with significant anxiety in various age groups decreased with increasing age, however the difference was not clinically significant ($p>0.05$). In our study, we excluded the extremes of age group. We included the patients of age group 18-50 yrs i.e. predominantly middle age adults, so we didn't get significant difference for induction dose of propofol.

We observed that there was no significant difference for induction dose of propofol with respect to gender ($p=0.149$). Ebirim L[70] in his study of factors responsible for preoperative anxiety in elective surgical patients found that gender difference was not statistically significant for preoperative anxiety ($p>0.05$).Moerman N.[10] in his study of APAIS found that women were more anxious than men. Badner N.H.[9] in his study of preoperative anxiety found that anxiety was higher in females ($p< 0.05$).

We observed that preoperative trait anxiety, measured on the preoperative visit by using MHADS, independently affected the propofol dose required for induction of anaesthesia (Figure 7). 'p' value for this comparison was <0.01 which was highly significant. The Pearson correlation coefficient for this comparison was 0.762 which showed very large correlation.

We also observed that preoperative state anxiety, measured by using APAIS, independently affected the propofol dose required for induction of anaesthesia. (Figure 8). 'p' value for this comparison was 0.013 which was moderately significant. The Pearson correlation coefficient was 0.398 which showed moderate correlation.

Osborn TM et al[13] in 2004 showed that increased state anxiety and trait anxiety serve as predictors for an increased total dose requirement of propofol to maintain an acceptable level of sedation.

Marantes et al[11] in 1999 showed that patients with high trait anxiety required more propofol for both induction and maintenance of anaesthesia but the state anxiety was not found to affect the propofol doses required for induction or maintenance of anaesthesia.

Kil H.K. et al[16] in 2012 found that patients with higher anxiety scores (state and trait) required greater amounts of propofol to reach light (BIS=85) and moderate (BIS=75) levels of sedation, but only trait anxiety was significantly associated with propofol requirements in reaching a deep level of sedation (BIS=65)

Manjunatha SM et al[18] in 2016 showed that pre-anesthetic trait anxiety and HR had strong positive correlation with propofol requirement while state anxiety had not.

On the contrary, Morley[15] et al. did not observe any influence of the STAI-T or STAI-S with propofol dose administered to achieve a BIS of 50. Gras S[14] et al. found no strong correlation between state and trait anxiety with propofol dose requirement for loss of consciousness (LOC).

We observed that need for information measured by APAIS has no effect on dose of propofol required for induction of anaesthesia. 'p' value for this comparison was 0.969 which was nonsignificant. The coefficient of correlation for this comparison was 0.0197 which showed trivial correlation. The reason behind this observation can be explained as follows. Our study was carried out in tertiary care center where most of the patients were from lower socio economic status and lower educational status. So they might not seek for information regarding their details of anaesthetic or surgical procedures they had to undergo. They just relied on the treating doctor to administer optimum treatment for them.

We observed that the Pearson correlation coefficient for comparison of total dose of propofol and anxiety related to anaesthesia was 0.41 whereas the Pearson correlation coefficient for comparison of total dose of propofol and anxiety related to surgery was 0.325 .This showed that higher induction dose of propofol was required when anxiety for anaesthesia was more than anxiety for surgery. Ramsay MAE[1] in his survey of preoperative fear found that 62% of total patients had anaesthetic fears and 15% of patients had surgical fears. However, Hernández-palazón J[17] in his study found that APAIS score for anxiety ($APAIS_a$) and knowledge ($APAIS_k$) were significantly higher for surgery than for anaesthesia.

We observed that baseline pulse rate independently affected dose of propofol required for induction of anaesthesia. 'p' value for above comparison is 0.017 which is moderately significant. The Pearson correlation coefficient for this comparison was 0.306 which showed moderate correlation. Manjunatha SM[18] et al showed that operating room heart rate had strong positive correlation with the propofol dose for induction of anesthesia. Gras S[14] et al. found significant positive correlation between HR (heart rate) in the operating room and propofol dose and also between STAI-S in the operating room and HR, thereby supporting an indirect effect of pre-anesthetic anxiety through changes in the HR. However, Kil HK et al[16] showed that preoperative HR did not correlate with anxiety.

We observed that baseline systolic blood pressure independently affected dose of propofol required for induction of anaesthesia. 'p' value for above comparison was <0.001 which was strongly significant. The Pearson correlation coefficient for above comparison was 0.463 which showed moderate correlation. The baseline diastolic blood pressure also independently affected dose of propofol required for induction of anaesthesia. 'p' value for above comparison was 0.002 which was highly significant. The Pearson correlation coefficient for above comparison was 0.394 which showed moderate correlation. Morley AP [15] in his study of preoperative anxiety on induction of anaesthesia with propofol, found that propofol dose required for loss of verbal response increased significantly with baseline mean arterial pressure. Kil H.K.[16] in his study of psychological factors and anaesthetic requirements found that systolic blood pressure correlated significantly with state and trait anxieties whereas diastolic blood pressure correlated significantly with trait anxiety.

It has been proven long back that anxiety is associated with a raise in both heart rate (HR) and cardiac output (CO).[71-73] Fell [74] et al. suggested that anxiety and stress-induced adrenaline release may account for the preoperative increase in HR and CO. Anxiety causes increase in catecholamine levels through sympathetic surge. The catecholamines affect CO by increasing contractility and HR. Hence propofol dose requirement is increased in anxiety as there is increase in CO by increase in both HR and contractility.

We had chosen loss of response to verbal command, onset of unconsciousness and centralization of eyeball as our clinical end point, because it is the commonly accepted terminal point used in many studies of the effects of hypnotic drugs.[72,75]

However, there were several limitations of this study.

1. Anxiety measurement was based on subjective scorings of anxiety rather than objective physical indicators. Hence, self-reporting bias might present.
2. It would have been more accurate if we had used propofol arterial concentrations.
3. Use of BIS or any other EEG (electroencephalogram) analog/depth indicators would have been helpful in confirming the level of depth of anaesthesia. This was merely a correlation study and from the present data we cannot conclude that increase in propofol requirement is related to pharmacodynamic or pharmacokinetic changes.
4. Another aspect was the inclusion of nearly 68% female subjects as study population. There are studies both supporting and opposing female preponderance of pre-operative anxiety.
5. Among other limitations were single-center design and selected study population (pediatric, elderly and ASA III-IV patients were excluded).

VIII. Summary And Conclusion

Pre - Operative anxiety is described as an unpleasant state of uneasiness or tension in a patient posted for surgery. The common concerns are fear of disease, hospitalization, anaesthesia and surgery, or the unknown.

The present study was planned to assess the level of pre-operative anxiety using easy to administer scales namely –

(1) Modified Hospital Anxiety and Depression Scale. (MHADS)
(2) Amsterdam Preoperative Anxiety and Information Scale. (APAIS)

In this prospective observational study, we compared this level of anxiety with the dose of propofol required for induction of general anaesthesia in 60 patients of either sex of age group 18 to 50 years, scheduled to undergo elective laparoscopic surgeries and willing to participate in the study using consecutive sampling method.

After obtaining informed consent, on the pre-operative visit, the patient's anxiety trait was assessed using Modified Hospital Anxiety and Depression Scale. On the morning of surgery, the same patient underwent a complete pre-operative assessment with all relevant investigations and adequate starvation was checked. The patient was assessed for state and level of anxiety and coping strategy using Amsterdam Pre-operative Anxiety and Information Scale.

No sedative premedication was given. Patient taken on O.T. table and pulse oximeter, cardioscope and noninvasive BP monitor connected. Patient's heart rate, blood pressure and oxygen saturation were checked and noted.

Premedication was given as Inj. Glycopyrrolate 0.004 mg/kg iv+ Inj. Midazolam 0.02mg/kg iv+ Inj. Fentanyl 2mcg/kg iv. Patient Pre-oxygenated with 100% O_2 for 3 min. Anaesthesia was induced with Inj. Propofol 2mg/kg iv slowly as bolus dose followed by 0.5 mg/kg increments as required every 30 sec. till loss of response to verbal command, onset of unconsciousness and centralization of eyeball. Total dose of propofol required for induction was noted.

Descriptive and inferential statistical analysis was carried out in this study. Analysis of variance (ANOVA) had been used to find the significance of study parameters between three or more groups of patients , Student t test (two tailed, independent) had been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

We observed that there was no significant difference for induction dose of propofol with respect to different types of surgeries like laparoscopic cholecystectomy, diagnostic laparoscopy, laparoscopic ovarian cystectomy, laparoscopic hydatid cystectomy, laparoscopic myomectomy.($p=0.94$)

We observed that there was no significant difference for induction dose of propofol with respect to different age groups ($p=0.287$) and gender ($p=0.149$).

We observed that preoperative trait anxiety, measured on the preoperative visit by using MHADS, independently affected the propofol dose required for induction of anaesthesia (Figure 7). 'p' value for this comparison was <0.01 which was highly significant. Pearson correlation coefficient for this comparison was 0.762 which showed very large correlation.

We also observed that preoperative state anxiety, measured by using APAIS, independently affected the propofol dose required for induction of anaesthesia. (Figure 8). 'p' value for this comparison was 0.013 which was moderately significant. Pearson correlation coefficient was 0.398 which shows moderate correlation.

We observed that need for information measured by APAIS has no effect on dose of propofol required for induction of anaesthesia. 'p' value for this comparison was 0.969 which is nonsignificant. Coefficient of correlation for this comparison was 0.0197 which showed trivial correlation.

We observed that Pearson correlation coefficient for comparison of total dose of propofol and anxiety related to anaesthesia was 0.41 whereas Pearson correlation coefficient for comparison of total dose of propofol and anxiety related to surgery was 0.325 .This showed that higher induction dose of propofol was required when anxiety for anaesthesia was more than anxiety for surgery.

We observed that baseline heart rate independently affected dose of propofol required for induction of anaesthesia. 'p' value for above comparison was 0.017 which was moderately significant. The Pearson correlation coefficient for this comparison was 0.306 which showed moderate correlation.

We observed that baseline systolic blood pressure independently affected dose of propofol required for induction of anaesthesia. 'p' value for above comparison was <0.001 which was strongly significant. The Pearson correlation coefficient for above comparison was 0.463 which showed moderate correlation. The baseline diastolic blood pressure also independently affected dose of propofol required for induction of anaesthesia. 'p' value for above comparison was 0.002 which was highly significant. The Pearson correlation coefficient for above comparison was 0.394 which showed moderate correlation.

IX. Conclusion:

It can thus be concluded that preoperative trait as well as state anxiety significantly affected dose of propofol required for induction of general anaesthesia. Also, baseline pulse rate, systolic blood pressure and diastolic blood pressure significantly affected dose of propofol required for induction of general anaesthesia in laparoscopic surgeries. The need for information did not correlate with total induction dose of propofol.

On the positive side, this study was performed under well controlled environment, we used easy to administer scales of anxiety, we studied surrogate parameters like baseline pulse rate, systolic blood pressure, diastolic blood pressure along with main parameters i.e. State and trait anxiety, we used clinically accepted terminal point for depth of anaesthesia.

Our study was however limited by possibility of self-reporting bias while solving questionnaire, inability to measure arterial concentration of propofol and depth of anaesthesia, female predominance in sample population and selected study population.

Bibliography

[1]. Ramsay MAE. A survey of pre-operative fear. Anaesthesia 1972; 27:396–402.
[2]. Corman H, Hornick E, Kritchman M, Terestman N. Emotional reactions of surgical patients to hospitalization, anesthesia and surgery. Am J Surg 1958; 96:646 – 53.
[3]. Wallace LM. Psychological preparation as a method of reducing the stress of surgery. J Human Stress 1984; 10:62–77.
[4]. Czeisler CA, Ede MC, Regestein QR, et al. Episodic 24-hour cortisol secretory patterns in patients awaiting elective cardiac surgery. J Clin Endocrinol Metab 1976; 42:273– 83.
[5]. Weissman C, Biebuyck J, Phil D. The metabolic response to stress: an overview and update. Anesthesiology.1990; 73:308-27.
[6]. Speilberger C. State-Trait Anxiety Inventory for Adults. Redwood City, Calif: Mind Garden; 1983:4-12.
[7]. Spielberger CD, Gorsuch RL, Lushene RE. State trait anxiety inventory manual. Palo Alto, CA: Consulting PsychologistsPress, 1970.
[8]. Hicks J.A., Jenkins J.G., The measurement of preoperative anxiety,Journal of the Royal Society of Medicine.1988;81:517-19.
[9]. Badner N.H.,Nielson W. R.,Munk S.,Gelb A.W., Preoperative anxiety:detection and contributing factors,CAN J ANAESTH 1990;37(4):444-7.
[10]. Webber GC. Patient education: a review of the issues. Med Care 1990; 28:1089-1103.
[11]. Maranets I and Kain Z.N., Preoperative Anxiety and Intraoperative Anesthetic Requirments. , ANAESTH ANALG 1999, 89:1346-51.
[12]. Hong JY, Kang IS, Koong MK, Yoon HJ, Jee YS, Park JW,et al. Preoperative anxiety and propofol requirement in conscious sedation for ovum retrieval. J Korean Med Sci 2003; 18(6):863-68.
[13]. Osborn TM, Sandler NA. The effects of preoperative anxiety on intravenous sedation. Anesth Prog 2004; 51: 46–51.
[14]. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. J Pers Sot Psycho1 1987;52:345-53.
[15]. Morley AP, Papageorgiou CH, Marinaki AM, Cooper DJ and Lewis CM. The effect of pre-operative anxiety on induction of anaesthesia with propofol. Anaesthesia 2008; 63(5):467-73.
[16]. Kil HK, Kim WO, Chung WY, Kim GH, Seo H, Hong JY. Preoperative anxiety and pain sensitivity are independent predictors of propofol and sevoflurane requirements in general anaesthesia. Br J Anaesth. 2012; 108(1):119–25.
[17]. Hernández-palazón J, Fuentes-garcía D, Falcón-araña L, Rodríguez- A, García-palenciano C, Roca-calvo MJ. Visual Analogue Scale for Anxiety and Amsterdam Preoperative Anxiety Scale Provide a Simple and Reliable Measurement of Preoperative Anxiety in Patients Undergoing Cardiac Surgery. Int Cardiovasc Res J. 2015;9(1):1–6.
[18]. Manjunatha S.M.,Hazra R,Das A,Chakraborty S,Bose R,Garain S,Purkait D. Effect of pre-anesthetic anxiety and heart rate on propofol dose requirement for induction:A correlation study, Asian Journal of Medical Sciences 2017; 8(2):64-8.
[19]. Zigmond AS, Snaith RP. "The hospital anxiety and depression scale". Acta Psychiatrica Scandinavica. 1983.67 (6): 361–70.
[20]. Julian L.J. Measures of Anxiety. Arthritis Care & Research.2011; 63(11): 467–72.
[21]. Goldberg D. Identifying psychiatric illness among general medical patients. Br Med J 1985; 291:161-2.
[22]. Moerman N, Dam van F, Boulogne-Abraham T, Hooff van M. The patient's need for information in the preoperative period. Proceedings of the 9th European Congress of Anaesthesiology. Jerusalem, Israel, 1994:257.

[23]. Boker A, Brownell L, Donen N. The Amsterdam preoperative anxiety and information scale provides a simple and reliable measure of preoperative anxiety. Can J Anaesth. 2002; 49(8):792–8.
[24]. Glen JB, Hunter SC, Thomson DS: The role of Cremophor EL in anaphylactoid reactions to i.v. anesthetics, Br J Anaesth1982; 54:231-2.
[25]. Bryson HM, Fulton BR, Faulds D.Propofol: an update of its use in anaesthesia and conscious sedation.Drugs.1995; 50:513-59
[26]. Fulton B, Sorkin EM.Propofol: an overview of its pharmacology and a review of its clinical efficacy in intensive care sedation.Drugs.1995; 50:636-57.
[27]. Yamakura T, Bertaccini E, Trudell JR, et al.Anesthetics and ion channels: molecular models and sites of action.Annu Rev Pharmacol Toxicol.2001;41:23-51.
[28]. James R, Glen JB: Synthesis, biological evaluation, and preliminary structure-activity considerations of a series of alkylphenols as intravenous anesthetic agents, J Med Chem. 1980; 23:1350-7.
[29]. Smith I, White PF, Nathanson M,et al.Propofol:an update on its clinical use.Anesthesiology.1994;81:1005-43.
[30]. Vree TB, Lagerwerf AJ, Bleeker CP, de Grood PM: Direct high performance liquid chromatography determination of propofol and its metabolite quinol with their glucuronide conjugates and preliminary pharmacokinetics in plasma and urine of man, J Chromatogr B Biomed Sci Appl.1999; 721:217-28.
[31]. Bleeker C, Vree T, Lagerwerf A, Bree EW: Recovery and long-term renal excretion of propofol, its glucuronide, and two di-isopropylquinol glucuronides after propofol infusion during surgery, Br J Anaesth.2008;101:207-12.
[32]. Takizawa D, Hiraoka H, Nakamura K, et al: Propofol concentrations during the anhepatic phase of living-related donor liver transplantation, Clin Pharmacol Ther. 2004; 76:648-69.
[33]. Takizawa D, Hiraoka H, Goto F, et al: Human kidneys play an important role in the elimination of propofol, Anesthesiology.2005; 102:327-30.
[34]. Kuipers JA, Boer F, Olieman W, et al: First-pass lung uptake and pulmonary clearance of propofol: assessment with a recirculatory indocyanine green pharmacokinetic model, Anesthesiology.1999; 91:1780-87.
[35]. Reekers M, Boer F, Vuyk J: Basic concepts of recirculatory pharmacokinetic modelling, Adv Exp Med Biol.2003; 523:19-26.
[36]. Franks NP: General anaesthesia: from molecular targets to neuronal pathways of sleep and arousal, Nat Rev Neurosci.2008; 9:370-86.
[37]. Kushikata T, Hirota K, Yoshida H, et al: Alpha-2 adrenoceptor activity affects propofol-induced sleep time, Anesth Analg.2002; 94:1201-06.
[38]. Lingamaneni R, Birch ML, Hemmings HC: Widespread inhibition of sodium channel–dependent glutamate release from isolated nerve terminals by isoflurane and propofol, Anesthesiology.2001; 95:1460-66.
[39]. Lingamaneni R, Hemmings HC: Differential interaction of anaesthetics and antiepileptic drugs with neuronal Na+ channels, Ca2+ channels, and GABA(A) receptors, Br J Anaesth.2003; 90:199-211.
[40]. Pain L, Gobaille S, Schleef C, et al: In vivo dopamine measurements in the nucleus accumbens after nonanesthetic and anesthetic doses of propofol in rats, Anesth Analg.2002; 95:915-9.
[41]. Gelb AW, Diab T, Cechetto DF: Effects of propofol on neuronal activity in the area postrema of the rat, Anesthesiology.1995; 83:A752.
[42]. San-Juan D, Chiappa KH, Cole AJ: Propofol and the electroencephalogram, Clin Neurophysiol.2010; 121:998-1006.
[43]. Noterman J, Berre J, Vandesteene A, Brotchi J: Intracranial-pressure monitoring in the postoperative period of cerebral aneurysms, Neurochirurgie.1988; 34:161-3.
[44]. Adembri C, Venturi L, De Gaudio RA: Propofol is neuroprotective in a rat model of focal cerebral ischemia when administered after the insult, Crit Care Med.2002; 30:A24.
[45]. Adembri C, Venturi L, Tani A, et al: Neuroprotective effects of propofol in models of cerebral ischemia: inhibition of mitochondrial swelling as a possible mechanism, Anesthesiology.2006; 104:80-9.
[46]. Adembri C, Venturi L, Pellegrini-Giampietro DE: Neuroprotective effects of propofol in acute cerebral injury, CNS Drug Rev.2007; 13:333-51.
[47]. Dahan A, Nieuwenhuijs DJ, Olofsen E: Influence of propofol on the control of breathing, Adv Exp Med Biol.2003; 523:81-92.
[48]. Goodman NW, Black AMS, Carter JA: Some ventilatory effects of propofol as sole anesthetic agent, Br J Anaesth.1987; 59:1497-1503.
[49]. Jonsson MM, Lindahl SG, Eriksson LI: Effect of propofol on carotid body chemosensitivity and cholinergic chemotransduction, Anesthesiology.2005; 102:110-6.
[50]. Pagel PS, Warltier DC: Negative inotropic effects of propofol as evaluated by the regional preload recruitable stroke work relationship in chronically instrumented dogs, Anesthesiology.1993; 78:100-8.
[51]. Denborough M, Hopkinson KC: Propofol and malignant hyperpyrexia, Lancet 1988; 1:191-3.
[52]. Denborough MA: Malignant hyperthermia, Anesthesiology.2008; 108:156-7.
[53]. Foster PS, Hopkinson KC, Denborough MA: Propofol anesthesia in malignant hyperpyrexia susceptible swine, Clin Exp Pharmacol Physiol.1992; 19:183-6.
[54]. Devlin JW, Lau AK, Tanios MA: Propofol-associated hypertriglyceridemia and pancreatitis in the intensive care unit: an analysis of frequency and risk factors, Pharmacotherapy.2005; 25:1348-52.
[55]. Jalota L, Kalira V, George E, et al: Prevention of pain on injection of propofol: systematic review and meta-analysis, BMJ 2011; 342:d1110,
[56]. Roberts R, Devlin JW, Schutnaker G, et al: Incidence of the propofol infusion syndrome in critically ill adults, Crit Care Med.2008; 36:A180.
[57]. Otterspoor LC, Kalkman CJ, Cremer OL: Update on the propofol infusion syndrome in ICU management of patients with head injury, Curr Opin Anaesthesiol .2008; 21:544-51.
[58]. Fudickar A, Bein B: Propofol infusion syndrome: update of clinical manifestation and pathophysiology, Minerva Anestesiol.2009; 75:339-44.
[59]. Bernard Rosner (2000). Fundamentals of Biostatistics, 5th Edition, Duxbury:80-240
[60]. Riffenburg RH (2005). Statistics in Medicine. Second edition. Academic press: 85–125.
[61]. Sunder Rao P S S, Richard J (2006). An Introduction to Biostatistics, A manual for students in health sciences , New Delhi: Prentice hall of India. 4th edition: 86-160
[62]. Suresh K.P. and Chandrasekhar S (2012). Sample Size estimation and Power analysis for Clinical research studies. Journal Human Reproduction Science, 5(1), 7-13.
[63]. Norris W, Baird WLM. Preoperative anxiety - a study of the incidence and aetiology. Br J Anaesth 1967; 39: 503-9.

[64]. Jamison RN, Parris WLV, Maxson WS. Psychological factors influencing recovery from outpatient surgery. Behav Res Ther 1987; 25: 31-3.
[65]. Millar K, Jelicic M, Bonke B, Asbury AJ. Assessment of preoperative anxiety: comparison of measures in patients awaiting surgery for breast cancer. Br J Anaesth 1995; 74 :180–3.
[66]. Williams JGL, Jones JR. Psychophysiological responses to anesthesia and operation. JAMA 1968; 203: 415–7.
[67]. Nelson F V, Zimmerman L, Barnason S, Nieveen J, Schmaderer M. The relationship and influence of anxiety on postoperative pain in the coronary artery bypass graft patient. J Pain Symptom Manage 1998; 15(2): 102-9.
[68]. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. J Pers Sot Psycho1 1987; 52:345-53.
[69]. Moerman N, Dam van F, Boulogne-Abraham T, Hooff van M. The patient's need for information in the preoperative period. Proceedings of the 9th European Congress of Anaesthesiology. Jerusalem, Israel, 1994:257.
[70]. Ebirim LN, Tobin M. Factors Responsible For Pre-Operative Anxiety In Elective Surgical Patients At A University Teaching Hospital: A Pilot Study. Internet J Anesthesiol.2010;29(2):2–7.
[71]. Piccirillo G, Elvira S, Bucca C, Viola E, Cacciafesta M and Marigliano V. Abnormal passive head-up tilt test in subjects with symptoms of anxiety power spectral analysis study of heart rate and blood pressure. Int J Cardiol 1997; 60(2):121-131.
[72]. Tenenbaum G and Milgram RM. Trait and state anxiety in Israeli student athletes. J Clin Psychol 1978; 34 (3):691-3.
[73]. Bergamaschi M and Longoni AM. Cardiovascular events in anxiety: Experimental studies in the conscious dog. Am Heart J 1973; 86:385-94.
[74]. Fell D, Derbyshire DR, Maile CJD, Larsson IM, Ellis R, Achola KJ,et al. Measurement of plasma catecholamine concentrations: An assessment of anxiety. Br J Anaesth 1985; 57(8):770-4.
[75]. Adachi YU, Watanabe K, Higuchi H and Satoh T. The determinants of propofol induction of anesthesia dose. Anesth Analg 2001; 92(3):656-61.