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Original Research Article

A comparative study of intravenous lignocaine, dexamethasone and combination of lignocaine-dexamethasone in attenuating propofol induced pain

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ABSTRACT

Background: General anesthesia is preferred during surgeries to reduce the pain stimuli in patients and to increase the precision of surgical procedure. Propofol is amongst the most widely used general anesthetic agent with limitation of induced pain during administration. Current study was conducted to compare the effect of intravenous pre-administration of various drugs in attenuating propofol induced pain.
Methods: A comparative observational study was conducted on patients of either sex and aged between 18-60 years. Patients were divided in three groups, who received intravenous lignocaine, dexamethasone and combination of lignocaine-dexamethasone respectively to attenuate propofol induced pain. Different variables like HR, SBP, DBP, MAP, RR SpO_2 and any adverse events were monitored in all the patients.
Results: The 46.66% and 53.33% patients who received lignocaine and dexamethasone alone perceived propofol induced mild to moderate pain; while only 23.33% patients who received lignocaine and dexamethasone in combination perceived mild propofol induced pain. The propofol induced pain event was persistent in only 2 out of 30 patients after a time lapse of 30 seconds for the group receiving lignocaine and dexamethasone in combination. Whereas, the pain event was present even after time lapse of 30 seconds in 08 and 07 out of 30 patients of groups receiving lignocaine and dexamethasone alone.
Conclusions: Pre-administration of lignocaine and dexamethasone in combination attenuated the propofol induced pain more significantly in comparison to single administration of mentioned drugs. No significant adverse events except perianal irritation were observed in some patients who received combination of lignocaine and dexamethasone intravenously.

Keywords: Propofol induced pain, Lignocaine, Dexamethasone, General anesthesia, Surgery

INTRODUCTION

General anaesthesia is a term used to describe a condition wherein a patient is rendered to medically induced loss of consciousness in order to alleviate pain during surgery.[1,2] Currently the application of anaesthesia is not only restricted towards alleviation of pain by inducing unconsciousness, but has evolved towards palliative, perioperative and critical care also.[3,4] General anaesthesia not only relieves the patient from pain stimuli during surgery but it also aids the health care providers or surgeons by rendering benefits of immobilizing patients which is desired to improve precision of surgery.[5,6]

Propofol is one of the most widely used intravenous anaesthetic agents which is commonly known as milk of anaesthesia.[7] Chemically propofol is 2,6-diisopropyl-phenol with an empirical formula of $C_{12}H_{18}O$ and molecular weight of 178027.[7,8] Propofol is highly lipophilic in nature with a very slight water solubility; because of this reason current marketed formulation of propofol are in the form of oil-in-water emulsion usually

consisting of 1 or 2% (w/v) of propofol, 10% soya bean oil, 2.% glycerol, around 1% egg phosphatide and 0.005% EDTA.[7-9] Propofol is considered to be a potent intravenous anaesthetic drug substance that was first launched in Europe in 1986.[10] Propofol exerts its hypnotic and sedative action by acting as γ-aminobutyric acid (GABA) receptor agonist.[10] Propofol over other anaesthetic agents renders advantages like fast and smooth induction of anaesthesia with no excitation events, rapid onset of action and rapid terminal half-life with least possibilities of postoperative adverse events of nausea and vomiting.[11] Propofol is used in almost all the types of surgeries ranging from cardiac and neurosurgery to diagnostic or invasive procedures.[12] Despite of numerous advantages offered by propofol; the adverse effects of propofol are also well established and reported the most common adverse effect of propofol as a general anaesthetic is pain on injection.[13] In order to combat the limitations of pain induced by using propofol as a general anaesthetic it is either co-administered with drugs or patients are given pretreatment with drugs like lignocaine, dexamethasone and others to reduce the incidence of pain and any other adverse events.[14]

Lignocaine is a widely used local anaesthetic that belongs to amino amide class. Lignocaine works by blocking the nerve impulse conduction and generation.[15] Pre-treatment of patients receiving intravenous propofol with lignocaine is reported to reduce the incidence of pain caused due to propofol administration.[16] Dexamethasone is a corticosteroid with a well-established and reported anti-inflammatory and immunosuppressive effects.[17] Dexamethasone works by inhibiting the inflammatory cells and suppressing the inflammatory mediators.[18] Dexamethasone as established from its mechanism of action can also be a potential agent to reduce the impact of pain caused due to propofol administration.[19] Thus the current study was aimed towards comparing the pain attenuating properties of lignocaine and dexamethasone when given alone or in combination to patients before administering propofol intravenously.

Aim and objectives

Current investigation was carried out with an aim and objective of comparing the effect of intravenous lignocaine, dexamethasone and combination of lignocaine-dexamethasone to attenuate propofol induced pain and to determine the side effects of propofol and other drugs used in current study.

METHODS

Study design, population location and duration

Current study was a comparative observational study conducted on patients of either sex aged between 18 to 60 years who were scheduled and consented for elective surgery under general anaesthesia and who exhibited physical status I and II according to American society of anaesthesiologist (ASA). The study was conducted from August 2021 to November 2021 at department of anaesthesia, government TD medical college, Alappuzha.

Sample size and sampling method

In current study sample size was calculated through N-master software developed by CMC Vellore using the formula:

$$N = (Z\alpha + Z\beta)2 \times [P1\,(1 - P1) + P2\,(1 - P2)] \div (P1 - P2)2$$

Where, Zα at 95% confidence interval=1.96, Zβ at 80% power=0.84, on substituting P1=0.6 and P2=0.26 as indicated in previous published reports the sample size for each group was calculated to be 29 which was rounded up to 30. Total 90 patients were divided into three groups in a turn wise manner: patients of group A received 40 mg lignocaine, group B received 0.2 mg/kg dexamethasone and group C received 40 mg lgnocaine and 0.2 mg/kg dexamethasone.

Inclusion criteria

All patients of age between 18 to 60 years who belonged to either ASA grade I or II (ASA I: healthy patients and ASA II: patients with mild to moderate systemic disease caused by the surgical condition or by other pathological processes, and medically well controlled) were included.

Exclusion criteria

Patients with allergy to any of the component of propofol: egg, soyabean or allergy to any of the study drugs, patients with cardiac, respiratory, renal or hepatic disease, patients with history of chronic pain, gastrointestinal ulcer, patients on sedatives and analgesics and diabetic patients were excluded from the study.

Study variables

Variables that were observed and investigated in current study were; heart rates, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, oxygen saturation, and respiratory rate. The variables were monitored and recorded every 5 minutes till the surgery started. Hypotension (decrease in systolic blood pressure <90 mmHg or a decrease in mean arterial pressure more than 20% from baseline), bradycardia (heart rate <50 beats/min), respiratory depression (respiratory rate <8/min or SpO_2<95%) were observed and documented during induction. Assessment of pain was done using verbal rating scale after giving study drug: scale 0; was considered as no pain, scale 1; was considered as mild pain (pain reported only in response to questioning without any behavioural signs), scale 2; was considered as moderate pain (pain reported in response to questioning and accompanied by behavioural signs or

pain reported spontaneously without questioning) and scale 3; was considered as severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears).

Procedure

Subjects were selected based on inclusion and exclusion criteria as mentioned above. Demographic details like age, gender, height and weight of participating patients were recorded. Detailed pre-anaesthetic checkup was done and written informed consent was obtained from all the participating patients. All participating patients were given pantoprazole 40 mg tablet, ondansetron 4 mg tablet and alprazolam 0.25 mg tablet on preoperative day and on the day of surgery. Vital baseline parameters systolic blood pressure, diastolic blood pressure and heart rate were determined after overnight fasting and were recorded preoperatively in pre-anaesthesia room. In the operation room intravenous line was established on dorsum of hand using an 18G cannula. Intravenous fluid Ringer lactate was started and standard monitors such as ECG, pulse oximeter, noninvasive blood pressure were attached. Preoperative heart rate, SpO_2, blood pressure was determined and recorded. All the three groups of patients were administered drug solution prepared by investigators in turn wise manner. No other drugs were administered through the IV cannula prior to administration of the study drugs. Venous drainage at mid-forearm was occluded with a rubber tourniquet, following which study drugs were given in all the three groups over a period of 5 seconds. One minute later, the occlusion of venous drainage was released and 1% propofol injection was drawn immediately before use. One fourth of the calculated dose of propofol was injected over 5 seconds. After the propofol injection at time intervals of 15 and 30 seconds the patients were assessed for pain. Patients in group A, received standard pre-treatment drug; lignocaine usually given in regular practice. Patients in group B received pretreatment with dexamethasone and patients in group C received pretreatment with dexamethasone and lignocaine. Pain was evaluated using verbal rating scale (0-3). After induction, patients were intubated and maintained with vecuronium (loading dose 0.1 mg/kg and maintenance dose 0.02 mg/kg) and isoflurane. At the end of surgery, residual neuro-muscular blockade was antagonized with 0.05 mg/kg of neostigmine and 0.01 mg/kg of glycopyrolate. Extubation was done when the patients were fully conscious and followed all directions.

Data collection tool

A predetermined proforma was used to collect the data which included patient's particulars, indication for surgery, study group and study drug that was given, anaesthetic details, pain score, intra-operative monitoring, side effects of propofol and study drugs.

Data analysis

Data was entered in Microsoft excel sheet and was analysed using appropriate statistical test. Qualitative variables were expressed as percentage or proportions with 95% confidence interval (CI). Quantitative variables were summarized using mean with standard deviation. Test of significance such as Student's t test for quantitative variables and Chi square test for qualitative variables were done and data was analysed using SPSS statistical software.

RESULTS

Results of the demographic investigations of participating patients revealed that age of participating patients in the current study ranged from 18 years to 60 years, mean age of patients in each group is depicted in (Table 1). It was observed that there was no significant variation in the mean age of participating patients of each group. Weight of the participating patients in the current study ranged between 35 kg to 95 kg, no significant difference was observed in the mean weight of participating patients of all the three groups (Table 1). Height of all the current study participants ranged between 142 to 178 cm; no significant difference was observed in the mean height of participants of all study groups. Average BMI of study participants of all the three groups did not exhibit significant variation (Table 1). Total 61 out of 90 participating subjects were females and remaining i.e., 29 were males (Figure 1). Total 52 out of 90 participating patients exhibited ASA status I, while remaining 38 exhibited ASA status II.

It was observed that 53.33% of group A patients exhibited no pain perception, while 13 (43.33%) reported mild pain feeling with pain score of 1 and 1 patient (3.33%) reported moderate pain with pain score of 2. Among 14 group A patients who initially reported mild to moderate pain feeling; 7 (50%) patients reported absence of pain feeling within a time span of 15 to 30 seconds (Table 2 and 3). In group B total 46.66% of study participants reported no pain feeling with pain score of 0; while 15 patients (50%) and 1 patient (3.33%) reported mild to moderate pain feeling with pains scores of 1 and 2 respectively. Among the 16 patients of group B who reported mild to moderate pain initially, 9 patients (56.25%) reported absence of pain feeling within a time span of 15 to 30 seconds (Table 2 and 3). In group C total 76.66% of study participants reported no pain feeling with pain score of 0; while 07 patients (23.33%) reported mild pain feeling with pains score of 1. Among the 07 patients of group C who reported mild pain initially, 5 patients (71.42%) reported absence of pain feeling within a time span of 15 to 30 seconds (Table 2 and 3).

It was observed through current investigational findings that no significant variation was observed in the parameters like heart rate, systolic blood pressure,

diastolic blood pressure, mean arterial blood pressure, respiratory rate, and oxygen saturation (Table 4 and 6).

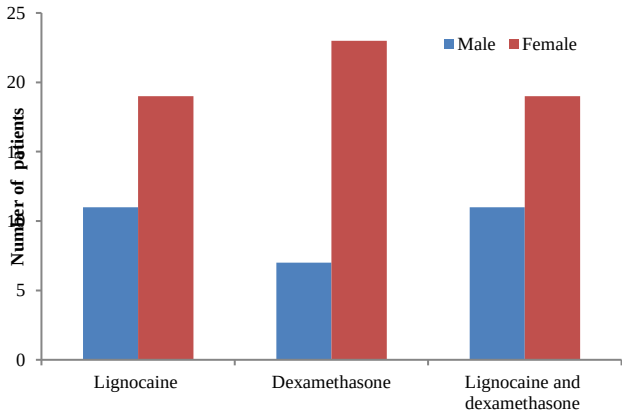

Figure 1: Gender based distribution of patients.

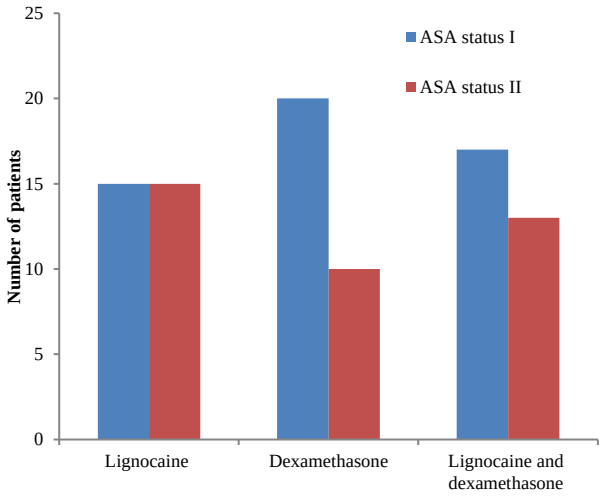

Figure 2: Distribution of patients on the basis of their ASA status.

Table 1: Demographic details of participating subjects, (n=30).

Parameters	Lignocaine	Dexamethasone	Lignocaine and dexamethasone
Mean age (years)	43.46±15.28	41.8±12.65	39.13±13.24
Height (centimetres)	158.16±8.44	156.40±8.74	155.86±9.28
Weight (kg)	61.8±12.55	61.16±13.68	61.76±12.38
BMI (kg/m^2)	24.7±2.0	25.0±2.3	25.4±1.8

Table 2: Distribution of patients on the basis of pain score.

Pain	Lignocaine		Dexamethasone		Lignocaine-dexamethasone	
	N	%	N	%	N	%
No pain	16	53.33	14	46.66	23	76.66
Mild pain	13	43.33	15	50	07	23.33
Moderate pain	01	03.33	01	03.33		-
Severe pain	-	-	-			-

Table 3: Distribution of patients on the basis of persistence of pain feeling.

Treatment group	Pain feeling post 15 seconds, n (%)		Pain feeling post 30 seconds, n (%)	
	Present	Absent	Present	Absent
Lignocaine	13 (92.85)	01 (7.14)	08 (57.14)	06 (42.85)
Dexamethasone	16 (100)	--	07 (43.75)	09 (56.25)
Lignocaine-dexamethasone	06 (85.71)	01 (14.28)	02 (28.57)	05 (71.42)

Table 4: Observations of various variables measured at baseline and during drug administration.

Variables	Baseline			During study drug administration		
	Lignocaine	Dexamethasone	Lignocaine-dexamethasone	Lignocaine	Dexamethasone	Lignocaine-dexamethasone
Heart rate (beats/ minute)	84.16±14.07	88.66±16.81	87.23±17.70	83.13±13.9	85.9±14.05	85.9±17.05
Systolic blood pressure (mmHg)	140±19.25	142.1±20.85	138.83±15.33	137.86±19.4	139.03±19.28	135.2±16.37

Continued.

Variables	Baseline			During study drug administration		
	Lignocaine	Dexamethasone	Lignocaine-dexamethasone	Lignocaine	Dexamethasone	Lignocaine-dexamethasone
Diastolic blood pressure (mmHg)	84.83±10.89	87.46±9.06	84.33±7.03	84.5±8.53	86.46±10.35	83.83±9.08
Mean arterial pressure (mmHg)	100.53±13.6	107.23±14.79	101.83±11.18	101.9±16.38	103.36±11.58	99.93±12.84
Respiratory rate (breaths/ minute)	16.4±3.74	17.3±4.35	16.76±12.77	16.06±9.46	15.7±9.81	15.83±3.08
SpO_2 (%)	99.73±0.62	99.83±0.2	99.63±0.69	99.4±0.8	99.56±0.64	99.5±0.88

Table 5: Observations of various variables measured during administration of one-fourth of propofol dose.

Variables	During administration of one-fourth of propofol dose.		
	Lignocaine	Dexamethasone	Lignocaine-dexamethasone
Heart rate (beats/ minute)	82±13.33	85.63±13.22	84.96±15.58
Systolic blood pressure (mmHg)	132.93±13.12	134±20.23	130.8±12.81
Diastolic blood pressure (mmHg)	81.5±6.93	81.83±9.91	79.86±8.19
Mean arterial pressure (mmHg)	97.5±8.98	97.66±11.75	95.13±11.12
Respiratory rate (breaths/ minute)	15.76±3.87	15.03±2.60	14.63±2.61
SpO_2 (%)	99.63±0.54	99.66±0.47	99.46±0.84

Table 6: Observations of various variables measured during and after induction of anaesthesia.

Variables	During induction of anesthesia			After induction of anesthesia		
	Lignocaine	Dexamethasone	Lignocaine-dexamethasone	Lignocaine	Dexamethasone	Lignocaine-dexamethasone
Heart rate (beats/ minute)	80.86±13.26	83.03±12.69	82.26±14.77	86.3±12.96	88.93±11.72	89±12.85
Systolic blood pressure (mmHg)	122.6±15.34	117.86±15.13	117.5±15.96	121.36±16.82	127.9±21.82	126.33±17.21
Diastolic blood pressure (mmHg)	76.96±10.87	76.26±14.93	76.4±10.52	78.9±12.79	83.1±16.7	81.66±16.42
Mean arterial pressure (mmHg)	92.8±14.92	88.73±14.50	88.06±11.78	94.36±16.61	93.5±18.48	93.4±14.4
Respiratory rate (breaths/ minute)	14±3.61	14.23±3.04	14.8±3.68	13±1.65	12.56±0.88	12.76±1.26
SpO_2 (%)	99.4±0.88	99.46±0.61	99.43±0.803	99.53±0.58	99.83±0.37	99.73±0.51

It was also observed from the current study findings that no significant adverse effects were observed in group A patients who received lignocaine treatment, whereas 04 out of 30 group B patients who received dexamethasone treatment reported perianal irritation and 06 out of 30 group C patients also exhibited perianal irritation. No other adverse events like dizziness, weakness or any other allergic reactions were observed in any participant of either of the current study groups (Figure 3).

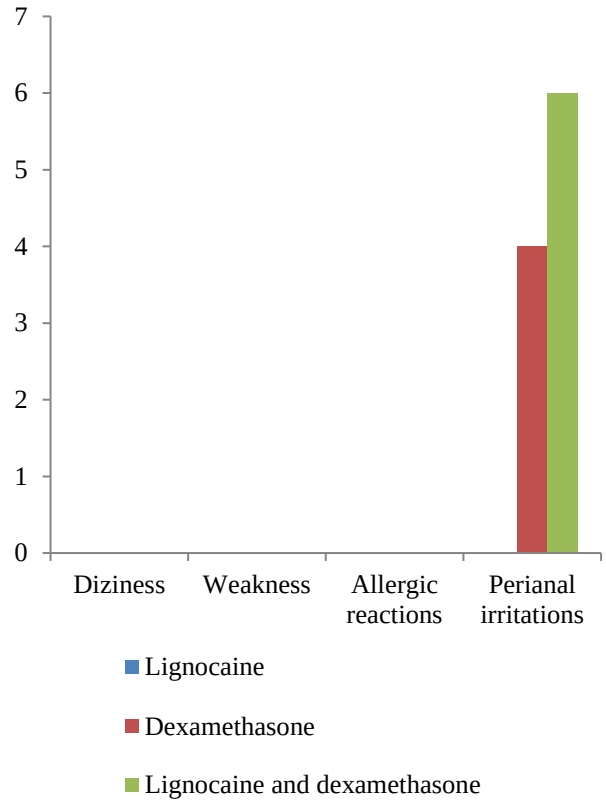

Figure 3: Adverse effects observed amongst study groups.

DISCUSSION

Results of the current investigation indicated that mean age of the participating patients in the current study was around 41 years and average BMI of the study participants was observed to be around 25 kg/m^2. It was also observed in the current investigation that female participants outnumbered the male participants. The majority of the participating patients belonged to ASA status I followed by patients of ASA status II. The observations of the current investigation pertaining to demographic details or ASA status were in close resemblance to earlier reports published by Euasobhon et al, Kaya et al, Sumalatha et al and Mecklem.[20-23]

Results of pain score analysis at different time span after co-administration of propofol with drugs like lignocaine, dexamethasone and combination of lignocaine and dexamethasone revealed that majority of patients (76.66%) who received a combination of lignocaine and dexamethasone did not perceive any pain and exhibited the pain score of 0. Only 7 (23.33%) of patients who received combination of lignocaine and dexamethasone reported mild pain with a pain score of 1 initially; 5 out of these 7 patients reported no pain feeling post 30 seconds of time interval. It was also observed in the current investigation that 14 (46.66%) of patients who received lignocaine reported mild to moderate pain initially; out of these 14 patients 6 patients reported no pain post 30 seconds while 08 of remaining patients perceived pain even after a time phase of 30 seconds. Total 16 (53.33%) out of 30 patients who received dexamethasone revealed mild to moderate pain perception initially; 7 out of these 16 patients reported the perception of pain even after a time phase of 30 seconds. The results of the study closely resembled to earlier reports published by Ahmad et al, Kim et al and Xing et al.[24-26]

Results of various variables like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR) and oxygen saturation (SpO_2) measured at baseline and different time phase of during study drug administration, during one-fourth propofol dose administration and during and after induction of anesthesia revealed that heart rate of patients of all the group was non-significantly suppressed during induction of anesthesia but it almost normalized after the induction of anesthesia. Similarly systolic, diastolic and mean arterial pressure of patients of all the three groups were also observed to be reduced during administration of one fourth dose of propofol or induction of anesthesia but the values of all these variables again increased after induction of anesthesia. The rate of respiration was also observed to be reduced during administration of one fourth dose of propofol or induction of anesthesia. It was also observed through current investigational findings that there was no significant difference observed in the oxygen saturation value when compared to base line, either during drug administration or during one fourth propofol drug administration or during and after induction of anesthesia. Results of the current investigation were in close resemblance and in accordance to the earlier reports published by Matchett et al, Zheng et al, Momota et al, Wiorek et al, Mascha et al, Ball et al and Hempenstall et al.[27-34] Current study findings revealed that there was no significant adverse event observed due to administration of lignocaine for the purpose of reducing the propofol induced pain in group A participants, while effects of perianal irritation were observed in group B and C participants who received either dexamethasone alone or in combination with lignocaine for reducing the propofol induced pain. This, results were in accordance to the studies published by Baharav et al and Klygis.[35,36] Thus it was inferred through current study findings that co-administration of lignocaine and dexamethasone in combination significantly reduced the pain induced during propofol induced anesthesia, in comparison to

reduction in pain observed due to administration of lignocaine or dexamethasone alone.

Limitations

Limitations of the current study were; the sample size of the investigated study groups was small; more concrete results and recommendations could have been made with a larger sample size.

CONCLUSION

It was concluded from current study findings that pre-administration of intravenous combination of lignocaine and dexamethasone would attenuate the propofol induced pain significantly more in comparison to intravenous administration of lignocaine or dexamethasone alone. It was also concluded that intravenous pre-administration of combination of lignocaine and dexamethasone would not lead to any significant adverse event except of perianal irritation in few cases. Thus, lignocaine and dexamethasone combination can be given to attenuate propofol induced pain during general anaesthesia for surgery.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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