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Role of propofol with total intravenous anesthesia in intra-abdominal surgeries: A prospective study

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Abstract

Background: Postoperative pain can be severe post multiple abdominal surgeries due to the upper abdominal incision and pain management can be difficult for this group of patients, therefore total intravenous anaesthesia is a technique involving infusion and maintenance of anaesthetic state with intravenous drugs alone. But no agent has all the characteristics of ideal TIVA agent. Propofol has three important characteristics of ideal TIVA agent, i.e. rapid induction, rapid metabolism and rapid recovery. In this communication we studied the characteristics of propofol in total intravenous anaesthesia in various intra-abdominal surgeries.

Methods: Here our sample size was 52 patients aged 18 to 60 years belonging to ASA gr 1 and gr 11 undergoing various elective intra-abdominal surgery took part in this prospective study. All patients were induced with 2mg/kg body weight 1% propofol after premedication 0.03 mg midazolam and pentazocine. Anaesthesia maintained with 0.1% propofol at rate of 100Ug/kg/min with 100% oxygen and incremental dose muscle relaxant. Based on haemodynamic sings and sympathetic over activity dose of propofol was adjusted in intraoperative period. At skin closure infusion was discontinued and neuromuscular blockade reversed.

Result: In our results, TIVA with propofol enabled smooth and rapid induction in all patients with induction time of 29.7 seconds. In maintenance phase propofol provides adequate depth of anaesthesia assessed by haemodynamic changes and sympathetic over activity in 47 (92%) of the patients. Five patients (8%) needed higher dose of infusion to maintain adequate depth of anaesthesia. Recovery was good with short response time of 10.3 minutes and orientation time of 14.54 minutes.

Conclusion: Our study concludes like others, Propofol based TIVA provides smooth and rapid induction and acceptable haemodynamic status during maintenance period in most of the patients. All patients were alert and clear headed with smooth recovery from anaesthesia effect.

Keywords: abdominal surgeries, propofol, total intravenous anaesthesia (TIVA), haemodynamic stability, anaesthesia quality

Introduction

Intravenous anesthetic propofol, according to its pharmacokinetic profile, is the mainstay for total intravenous anesthesia (TIVA); it has rapid onset and offset with fewer side effects, particularly postoperative nausea and vomiting (PONV) [1]. In our previous study, we found that patients recovered quicker after TIVA via a target-controlled infusion (TCI) system, than with volatile anesthesia in lumbar spine surgery [2]. Propofol has long been considered a non-analgesic intravenous hypnotic. However, studies have been conducted to explore the possible anti-nociceptive mechanisms of propofol and its potential role as an analgesic. In animal studies, propofol has been shown to directly depress dorsal horn neurons in the spinal cord [3]. To overcome the side effects of inhalational anaesthetic agents and nitrous oxide; an alternative technique was thought of. One such alternative technique is total intravenous anaesthesia (TIVA) where in there is total avoidance of nitrous oxide and inhalational anaesthetic agent and operative anaesthetic depth was maintained by continuous infusion of intravenous anaesthetic agent [4]. The introduction of propofol has revolutionized the practice TIVA. Propofol because of its rapid onset of action and rapid clearance behaves like inhalational agent but without its side effect [5]. The depth of anaesthesia can be varied quickly by employing propofol because of its above-mentioned properties. In view of this, the present study was undertaken to evaluate the safety and efficacy of propofol for TIVA [6].

Material and Methods

None of the patients in this study received premedication. Patients in the TIVA group had

anesthesia induced and maintained with propofol. The present prospective study entitled "TIVA with propofol for intra-abdominal surgeries" was undertaken for 18 months, in the department of anaesthesiology, P K DAS Institute of Medical Sciences, Vaniamkulam, Ottapalam Kerala, 52 adult patients aged between 18 to 60 years of either sex scheduled for various elective intra-abdominal surgeries belonging to ASA Grade-I and Grade-II physical status were included in the study. Patients with associated cardiovascular or respiratory comorbid disease, diabetes mellitus, bronchial asthma and history of drug allergy were excluded from the study. Patients with previous unexpected adverse experience with intravenous or general anaesthesia and patients with ASA Grade III, IV and V were excluded from the study. Preparation Patients were nil oral for 12 hours and were advised to take oral alprazolam 0.5 mg, ranitidine 150 mg the previous night. In the operation room 18 gauge intravenous cannula was cannulated to a large vein in the dorsum of hand or fore arm and dextrose normal saline was started. Multi-channel monitor which records ECG, pulseoximeter and non-invasive blood pressure (NIBP) was connected. Baseline, systolic blood pressure, diastolic blood pressure and mean arterial pressure, heart rate and oxygen saturation were recorded. All patients received 0.03 mg kg⁻¹ midazolam and pentazocine 0.5 mg kg⁻¹ intravenous 5 minutes prior to induction of anaesthesia. Meanwhile a second intravenous line was taken in the other hand with 20 gauge cannula for propofol infusion. Patients were preoxygenated with 100% O₂ for 3 minutes and received 1% propofol as an induction agent in the dose of 2 mg kg⁻¹. Propofol was given as a bolus over 20 sec. Meanwhile patient was asked to start counting one, two, three onwards. Time taken from the administration of the drug to loss of counting, loss of verbal response and loss of eyelash reflexes were noted. Induction time was taken as the time in seconds from the start of injection to disappearance of eyelash reflex. When eyelash reflex disappeared mask was applied over the face and patients received 100% oxygen via face mask connected to a Bain circuit. During this period, patients were observed for pain on injection, apnoea, abnormal or excitatory movements of the limb cough and hiccough. During this period haemodynamic response for induction and intubation were recorded. For patients who developed apnoea, gentle mask ventilation was done with 100% Oxygen In all patients after induction (loss of eye lash reflex) tracheal intubation was facilitated using vecuronium bromide in dose of 0.1 mg kg⁻¹ body weight. After 3 minutes of mask ventilation, laryngoscopy was done and trachea was intubated with an appropriate size cuffed endotracheal tube. Ventilation was done with 100% Oxygen with Bain Circuit. Maintenance Phase of TIVA Immediately after intubation through the second line (20 gauge cannula) propofol infusion was started. For maintenance of anaesthesia 0.1% of propofol was used, which was prepared by taking 360 ml of 5% dextrose into which 40 ml of 1% propofol was added. Hence 400 ml of 5% dextrose contains 400 mgs of propofol. The resulting concentration of propofol is 1 mg ml⁻¹ (i.e., 0.1% solution). Infusion of propofol was given by using Infusomat FM infusion pump of B. Braun Company During maintenance period continuous propofol infusion was started at the rate of 100 µg kg⁻¹ min⁻¹. Ventilation was continued with 100% oxygen with adequate oxygen flow of 8 litres to maintain minute ventilation. Nitrous oxide was omitted altogether. In

intra operative period increments with muscle relaxant vecuronium bromide was administered whenever required. Patients were observed for sympathetic over activity like tachycardia, increase in blood pressure, sweating and lacrimation to assess the adequacy of depth of anaesthesia. When mean arterial pressure (MAP) increased by 20% above the baseline or increase in heart rate of 20% above the base line, associated with other signs of increased sympathetic activity like lacrimation and sweating, indicating inadequate depth of anaesthesia⁷ the propofol infusion was increased by 20 to 30 µg kg⁻¹ min⁻¹ and observed for subsiding of these signs. Infusion was stopped at the time of skin closure. At the end of surgery neuromuscular blockade is reversed with injection, neostigmine. 0.5 mg kg⁻¹ along with injection atropine 0.02 mg kg⁻¹ in all patients. The total duration of anaesthesia, total dose of infusion and total duration of surgery were noted. The response time is the time taken in minutes from the cessation of infusion to; response to verbal commands after reversal was noted. After ensuring adequate spontaneous respiration and muscle power, extubation was done. Following extubation patients were tested for orientation to time, place and asked to tell his/her name, native place. The time interval between cessation of infusion to recall his/her name or native place, after extubation was taken as orientation time. Cardiovascular parameters like heart rate (HR), mean arterial pressure (MAP), were studied at the following intervals:

1. Preoperative (baseline)
2. Immediately after induction
3. Just before intubation
4. Just before intubation
5. 1 minute
6. 5 minutes
7. 15 minutes after intubation and

There after every 15 minutes till the end of surgery and in the immediate post-operative period. Patients were observed for one hour after extubation in postoperative care unit. Post-operative events like pain at operating site, nausea, vomiting, restlessness, cough, vision problem and slurred speech were noted.²⁸ Intraoperative awareness was assessed in all patients in the postoperative period.

Results

There were no significant differences between groups with respect to age weight, height and gender distribution. Loss of eyelash reflex time was taken as induction time (i.e. time taken from the commencement of injection to loss of eyelash reflex). The mean induction time were 29.77 ± 1.6 seconds. In the present study involuntary movement observed in 2 patients, 16 patients complained of pain on injection, hiccough was seen in 2 patients and apnoea was seen in 18 patients. The infusion dose employed in the present study was 100 µg kg⁻¹ min⁻¹. Mean duration of infusion was 54.22 ± 12.8 minutes, the mean dose of propofol infused was 279.89 ± 91.10 mg. Forty-six patients had stable haemodynamics during maintenance of anaesthesia at the infusion dose of 100 µg kg⁻¹ min⁻¹. In two cases there was rise of heart rate above 20% of baseline and MAP rise was less than 20% of the baseline. In the remaining two cases, there was rise of both HR and MAP by more than 20% above the baseline values. All the four cases were associated with sweating and lacrimation indicating

lighter plane of anaesthesia. The above signs subsided on increasing the infusion rate of propofol from 100 to 120 μg

$\text{kg}^{-1} \text{min}^{-1}$ in these four patients.

Table 1: Mean total dose of the drug given.

Loading dose (mg)	Mean dose infused (mg)	Mean total dose given (loading dose + dose infused)
100.88 \pm 16.7	279.89 \pm 91	380.77 \pm 70.18

Table 1, shows the mean total dose of the drug given, i.e. the sum of the loading bolus dose during induction and the

mean dose infused during maintenance phase of TIVA.

Table 2: Recovery characteristics

Response time Time from cessation of infusion to respond to command after reversal	1-Average Time	10.59 Minutes
	2-Maximum Time	12.66 Minutes
	3-Minimum Time	8.0 Minutes
Orientation time Time taken from cessation of infusion to recall of name after extubation	1-Average Time	14.32 Minutes
	2-Maximum Time	16.0 Minutes
	3-Minimum Time	13.0 Minutes

Table 3: Cardiovascular changes while TIVA.

	Hr	SBP	DBP	MAP
Pre-induction values	89.02 \pm 9.8	132.24 \pm 10.1	80.7 \pm 7.7	98.5 \pm 9.5
10minute after induction	87.5 \pm 13.2	122.5 \pm 12.0	74 \pm 8.0	90.52 \pm 7.8
Just before intubation	83.9 \pm 10.7	118.5 \pm 15.6	72.74 \pm 12.1	87.04 \pm 12.8
1minute after	100.2 \pm 9.1	143.02 \pm 11.9	97.22 \pm 10.23	112.14 \pm 9.8
5minute after intubation	95.88 \pm 9.4	136.8 \pm 11.3	86.62 \pm 11.9	103.1 \pm 9.7
15minutes after intubation	92.72 \pm 10.1	131.96 \pm 13.5	83.64 \pm 11.0	99.44 \pm 10.5
30minutes after intubation	87.38 \pm 9.7	128.2 \pm 10.7	80.74 \pm 9.4	96.34 \pm 8.6
45minutes after intubation	86.9 \pm 8.4	127.2 \pm 9.8	80.5 \pm 7.3	95.9 \pm 6.4
60minutes after intubation	86.13 \pm 9.27	126.52 \pm 12.4	80.39 \pm 7.5	95.4 \pm 7.3
75minutes after intubation	85.3 \pm 5.4	126.3 \pm 8.35	80.2 \pm 5.56	93.8 \pm 6.9
From the discontinuation of the infusion to recovery	86.6 \pm 6.18	130 \pm 8.9	82.5 \pm 6.0	97.3 \pm 5.6
recovery	89.82 \pm 3.6	130.46 \pm 8.9	83.6 \pm 6.2	98.24 \pm 5.9
Recovery post-operative	88.12 \pm 5.5	131.9 \pm 6.6	83.52 \pm 6.5	100.0 \pm 6.4

* Statistically significant ($p < 0.001$)

Discussion

Propofol was reported to significantly decrease pain scores by 40% and areas of hyperalgesia and allodynia in human volunteers. Propofol's preferential binding to the HCN1 pacemaker channels further reinforces its anti-hyperalgesic effect. Moreover, the anti-inflammatory effects of propofol have been shown both *in vitro* and in human studies, and they may be responsible for propofol role in postoperative analgesia. Development of TIVA gained momentum with synthesis of short acting hypnotic barbiturates in 1930. Recently TIVA has regained popularity as understanding of pharmacokinetics and pharmacodynamic principles have improved and drugs more suited to TIVA have been developed. Ideal TIVA agent should be water soluble, stable in solution and on exposure to light over a long period of time, produce sleep in one arm brain circulation time, have a short duration of action due to rapid metabolism with no cumulative properties should not cause venous damage or hepatotoxicity when used in large doses and should have analgesic properties. Induction process involves inducing hypnosis with deep sleep to facilitate for intubation with depolarizing or nondepolarizing muscle relaxant. Induction should be smooth, should enable stable haemodynamic conditions with less side effects like hiccough, pain during injection, involuntary movements, signs of histamine release and apnoea [6, 7]. In the present study with propofol induction, the mean time to loss of counting was 26.6 \pm 1.7 secs (Range 22-30 secs). This could be due to use of opioid pre medication in the present study 27.68 \pm 1.8 secs (Range

23 to 31 secs) which was almost similar to the time observed by Lal A. *et al.* (1995). In the present study the time for loss of eyelash reflex (induction time) was 29.7 \pm 1.6 seconds (Range 27 to 33 secs). In the present study apnoea was observed in 18 patients i.e, an incidence of 36%. In present study, small vein on the dorsum of hand were employed, pain on injection with was observed in 16 patients, an incidence of 32%. In the present study, involuntary movements incidence was observed in 2 patients (4%). In this study no signs of histamine release were observed. Many authors used different doses for maintenance of TIVA with propofol along with or without opioid infusion. A few authors used fixed dose of propofol infusion, while some employed variable dose of propofol. In the present study the propofol infusion rate of 100 $\mu\text{g} \text{kg}^{-1} \text{min}^{-1}$ was used during maintenance phase of TIVA for various intra-abdominal surgeries [8, 9, 10]. The present study dose correlates with dose employed by Coates David P (1987) which is equivalent to ED95 dose of propofol (112 $\mu\text{g} \text{kg}^{-1} \text{min}^{-1}$), with this dose of infusion the blood level of propofol is maintained at 3.38 $\mu\text{g} \text{ml}^{-1}$ which is sufficient to maintain the depth of anaesthesia intra-operatively In the present study out of 50 patients, in 46 patients with the dose of 100 $\mu\text{g} \text{kg}^{-1} \text{min}^{-1}$ of propofol, the depth of anaesthesia was maintained excellently in the intraoperative period as assessed by haemodynamic values and sympathetic over activity [11]. In present study signs of lighter plane of anaesthesia were noticed in 4 patients (8%). In two cases there was rise of heart rate above 20% of baseline and MAP

rise was less than 20%. In the remaining two cases there was rise of both HR and MAP by more than 20% above the baseline values. All the four cases were associated with sweating and lacrimation indicating lighter plane of anaesthesia. Increasing the infusion rate of propofol to 120 µg kg⁻¹ resulted in amelioration of haemodynamic and autonomic signs within 30 minutes. However one case took 45 minutes with increased infusion rate for settling of haemodynamic and autonomic variables [12]. Lack of analgesia for increased MAP and HR as not a cause can be assumed as all these patients had received pentazocine as analgesic at the beginning of the surgery in the dose of 0.5 mg kg⁻¹. Therefore, this rise was primarily attributed to lighter plane of anaesthesia and this is further substantiated by the fact that all signs settled by increasing the infusion rate of propofol. The speed, reliability and quality of recovery from anaesthesia is of paramount importance in TIVA. In the present study the mean response time was 10.59 mins (range 8-12.46 minutes) and the mean orientation time i.e., recovery time was 14.13 mins (range 13-15.3 minutes) which similar to that observed by Watson and Shah and Jestrup *et al.* In the present study demand for post-operative analgesia was observed in 32 patient (64%) which is similar to that of Watson K.R. and Shah M.V. study.^[9,13] Restlessness was noticed in 2 patients in the present study (4%) which is comparable with Mackenzie N and Grant I.S. (1988) who observed restlessness in 1 patient (5%) in their study. Cardiovascular Changes Induction with propofol causes decrease in systemic pressure due to vasodilatation and myocardial depression [10, 14]. The reduction in blood pressure without tachycardia associated with use of propofol is said to offer advantage at the time of laryngoscopy and intubation. In the present study, atropine premedication was not employed. Following 3 minutes after induction with propofol, MAP fell from 98.5 to 87.04 mmHg, representing a fall of 11.2% which was statistically significant ($p < 0.001$). The mean heart rate fell from 89.02 to 83.9 BPM, representing a fall of 5.9% which was statistically significant ($p < 0.001$). These changes concur with the study of Lindgren *et al.* (1993) [15]. In the present study, we observed that in patients who were induced with propofol, one minute after intubation, facilitated by vecuronium bromide the MAP increased from 98.5 to 112.1 mmHg representing rise of 13.8% which is statistically significant ($p < 0.001$) [15]. The mean HR increases from 89.02 BPM to 100.2 BPM representing a rise of 12.5% which is statistically significant ($p < 0.001$). These changes concur with the study of Dose Van A. In the present study at five minutes after intubation, MAP was 5% above the baseline and mean heart rate was 6% above the baseline.

Conclusion

Patients anesthetized with propofol TIVA reported less pain during coughing and consumed less daily, however in our study it is concluded that Propofol because of smooth and rapid induction with good haemodynamic stability and faster recovery can be said to be an ideal agent for the technique of TIVA. Propofol based TIVA avoids problem of awareness under anaesthesia. Propofol does not have analgesic properties, so there will be need for analgesic in the immediate postoperative period of TIVA with propofol. TIVA with propofol play great help for short surgical procedures and day care surgeries.

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