International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 9; Issue 04 (B); April 2020; Page No.21914-21918
DOI: http://dx.doi.org/10.24327/ijcar.2020.21918.4314

Research Article

COMPARISON OF HAEMO DYNAMIC CHANGES AND RECOVERY FROM ANAESTHESIA IN TWO PROTOCOL OF SUFENTANIL INFUSION USING PROPOFOL INFUSION FOR TOTAL INTRAVENOUS ANAESTHESIA (TIVA) IN DAY CARE SURGERY

Dr Rajeev Nair[1], Dr Satish Kumar Mishra[2] and Dr Deeparani [3]

[1]MD Anesthesiology HOD Department of Anesthesiology and Critical Care Command Hospital Airforce Bangalore
[2]MD DM Cardiac Anesthesia Department of Anesthesiology and Critical care Command Hospital Airforce Bangalore
[3]DA DNB Anesthesiology Department of Anesthesiology and Critical care Command Hospital Airforce Bangalore

A R T I C L E I N F O

Article History:
Received 12th January, 2020
Received in revised form 23rd February, 2020
Accepted 7th March, 2020
Published online 28th April, 2020

Key words:

Sufentanil, Propofol, Day care Surgery, TIVA.

A B S T R A C T

Background and Objectives; Sufentanil is a potent opioid that offers favorable pharmacological properties for use in total Intavenous Anaesthesia (TIVA). Numerous protocols of delivery of sufentanil infusion have been described but each shows different hemodynamic response as well as recovery time. It is a short acting opioid with high hepatic clearence and has synergistic activity with propofol. This study was done to evolve an infusion protocol that bpermits adequate anaesthetic depth along with rapid recovery, while avoiding or minimizing the side effects of this potent drug in day care surgery. **Materials and methods:** The study was a prospective, randomized, controlled study carried out at command Hospital Air Force, Bangalore after hospital ethical committee approval, 60 adult patients were studied. These patients were then allocated randomly into a group A and group B of 30 each by picking up chits labeled A and B. All the patients received general anaesthesia. The patients were monitored at pre-induction, post induction, 1 minute after intubation and every three minute there after. Anesthesia was induced by propofol infusion with a bolus of 1.5 mg/kg followed by an infusion @140 mcg/kg/min for 10 minutes and @ 50mcg/kg/min there after. Six minutes after propofol infusion (@140mcg/kg/min), sufentanil was started. In group A,a bolus of 0.1 mcg/kg of sufentanil was administered and followed by an infusion of 0.3 mcg/kg/h of sufentanil. In group B Patients were given a bolus of 0.25 mcg/kg of sufentanil followed by an infusion of 0.1 mcg/kg/h of sufentanil as per protocol. Orotracheal intubation in both groups was facilitated by Inj succinylcholine 1.5 mg/kg IV. After confirmation of endotracheal tube placement, vecuronium (0.05 mg/kg) was administered to provide muscle relaxation during surgical procedure. Patients lungs were ventilated with 30% of oxygen in nitrous oxide.
patients were reversed with Injection Neostigmine 50 mcg/kg and Inj Glycopyrolate 10 mcg/kg IV. Patients were observed for recovery time from anaesthesia and were assessed on the basis of modified post anaesthesia discharge scoring system (MPDSS). The time taken to satisfy discharge criteria was considered as recovery time and was compared with two groups. **Result:** Our result showed that the haemodynamic changes were better controled in group B patient compare to Group A patients and are highly significant with p<
0.001. the recovery from anaesthesia was better in-Group B compare to Group A and is highly significant ($p<0.0001$) Conclusion: Our study concluded that sufentanil 0.25 mcg/kg/ IV as a bolus after induction with propofol effectively controls responses to tracheal intubation. After tracheal intubation in the subsequent perioperative period, sufentanil either as0.1 mcg/kg/hr infusion or as a0.3 mcg/kg/hr infusion IV with propofol infusion @ 50mcg/kg/min was equally effective to control intraoperative responses. Emergence from anaesthesia was however more rapid when an infusion rate of 0.1 mcg/kg/hr infusion was used when compare to an infusion rate of 0.3 mcg/kg/hr

Copyright©2020 ***Dr Rajeev Nair, Dr Satish Kumar Mishra and Dr Deeparani .*** *This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited*

INTRODUCTION

Anaesthesia is a complex state , involving unconsciousness, amnesia,and loss of response to noxious stimulation[1] . The first two components can be controlled by hypnotics and the third by opioids. A synergistic interaction has been demonstrated between these two drugs classes,each of them having a dose-dependent sparing effect on the requirements of the other. Synergism is more pronounced for blocking reaction to noxious stimuli than for loss of consciousness (LOC)[2]. Thus different dose combinations of hypnotics and opioids may be suitable for maintaining adequate anaesthesia. The optimal combination could be based on maximal synergism and minimal side effects [3], the fastest recovery[4], or the combination associated with the lowest cost.

Propofol-opioid combination for total IV anaesthesia (TIVA) have been extensively studied [5-7] . How ever,most of the published data were extrapolated to sufentanil from clinical studies using other opioids,assuming a fixed potency ratio (e.g., sufentanil/alfentanil=630)[4]

Corresponding author:* **DR Satish kumar mishra
MD DM Cardiac Anesthesia Department of Anesthesiology and Critical Care Command Hospital Airforce Bangalore

Sufentanil is apotent opioid that offers favorable pharmacological properties for use in total intravenous anaesthesia (TIVA). It is ashort acting opioid with high hepatic clearence and has synergistic anaesthetic activity with propofol[8-9]. In day care surgery, it is important to evolve infusion protocol that permits adequate anaesthetic depth along with rapid recovery, while avoiding or minimizing the side effects of this potent drug. The drug has been explored in a variety of settings, finding favourable application in obstetrics, paediatric and cardiac sugery during fast tracking.

Numerous protocols of delivery of sufentanil infusion have been described but each shows different hemodynamic response as well as recovery time. In day care surgery the data is lacking and this study will offer additional insight.

MATERIAL AND METHODOLOGY

Source of Data: After hospital ethical committee approval. 60 adult patients were studied after written informed consent from the patients. These patients were then allocated randomly into group A and group B of 30each by picking up chits labeled A and B. This was done by an individual not involved in the study.

Inclusion criteria

1. Adult patients aged between 18-60 years.
2. ASA-1 and 2 physical status.
3. study included only day care surgical patients.
4. Scheduled for elective surgeries requiring endotracheal general anaesthesia.

Exclusion Criteria

1. Patients with significant coronary artery disease and cardiac arrythmia.
2. Patients with respiratory depression and decreased respiratory reserve.
3. Renal failure
4. Hepatic dysfunction
5. Morbid obesity
6. Haematocrit less than 25%
7. Uncontrolled Hypothyroidism
8. Alcoholism

METHOD OF COLLECTION OF DATA

The patients were reviewed one day prior to surgery and preoperative advice was given. All patients received oral premedication with diazepam 5 mg the night before surgery and on the morning of surgery. All the patients received general anaesthesia. In the operation theatre, intravenous access was established and monitors attached. The patients were monitored at pre-induction, post-induction, 1 minute after intubation and every three minutes there after for the following parameteres.

1. Heart Rate
2. Blood pressure (SBP,DBP,and MAP) by automated NIBP monitor,
3. ECG for arrhythmia or other abnormality
4. SpO2 by pulse oximetry.

Base line BP and Heart rate were defined as the average of the two lowest measurements: obtained the day before surgery, reading recorded within the two hrs preceding surgery and before induction of anaesthesia.Inj Propofol 10 mg/ml in 20ml vials (Rapifol 1%) and Inj Sufentanyl 0.050 mg/ml (Claris life SCIENCES limited) was used in all patients. Electronic Syringe Infusion pump (Infusor 850- EMCO Ltd) was used for the delivery of these drugs using extension tubing's and two three way stopcocks with a flushing solution through a dedicated IV cannula.

After pre oxygenation for three minutes, anaesthesia was indused by propofol infusion with a bolus of 1.5 mg/kg followed by an infusion @140 mcg/kg/min for 10 minutes and @ 50mcg/kg/min there after. After 06 minutes of propofol infusion (@ 140 mcg/kg/min), sufentanil infusions was started. In Group A,a bolus of 0.1 mcg/kg of sufentanil was administered followed by an infusion of 0.3mcg/kg/hr of sufentanil. In group B patient were given a bolus of 0.25 mcg/kg of sufentanil followed by an infusion of 0.1 mcg/kg/hr of sufentanil as per protocol.

Orotracheal intubation in both groups was facilitated by Inj succcinylcoline 1.5mg/kg IV. After confirmation of endotracheal tube placement , vecuronium (0.05mg/kg)was administerd to provide muscle relaxation during surgical procedure. Patients's lungs were ventilated with 30% oxygen in nitrus oxide. Supplementary vecuronium was given as required. Patients were ventilated with Drager RA 2S ventilator with a tidal volume of 10ml/kg and at afrequency of 12/min.

The primary efficency end point was adequacy of anaesthesia for Endo-tracheal intubation.Secondary end points included patients responses to skin incision and intraoperative surgical stimuliuntil the end of surgery. Inadequate anaesthesia was defined as an increase in SBP of greater than 15mm of Hg from baseline for 1 min or longer, HR greater than 90/min lasting for more than 1 min, movement of patient, eye opening or grimacing, lacrimation, or sweating,When evidence of inadequate anaesthesia was observed a bolus of Propofol 20 mg IV were given (propofol rescue). If episodes of inadequate anaesthesia persisted even after the IV bolus of propofol the propofol Infusion was increased to 140 mcg/kg/min until adequate anaesthesia was present for 5 min.Thereafter the propofol infusion was decreased to 50 mcg/kg/min

Hypotension was defined as SBP of less than 80 mm of Hg or MAP of less than 60 mm of Hg. Hypotension was treated with an increased in the IV infusion rate. Bradycardia (HR less than 60 bpm with hypo tension or HR less than 40 bpm lasting more than >1 min) was treated with injection atropine 0.6 mg intravenously.Ten minutes before the anticipated end of surgery, the propofol infusion rate was decreased by 50% and discontinued at the end of the surgery. Sufentanil infusion was discontinued at the completion of the surgery.

Reversal

Patients were reversed with injection neostigmine 50mcg/kg and Inj Glycopyrolate 10mcg/kg IV at the end of skin closure with maximum of 2.5 mg Neostigmine and 0.4 mg of glycopyrolate.

Recovery Time from Anaesthesia

Patients were assessed for recovery from anaesthesia based on modified post anaesthesia discarge scoring system(MPDSS). In MPDSS the following were recorded and scored

Vital signs	Pain
2=within 20% of preoperative value	2=minimal
1=20-40% of preoperative value	1=moderate
0=>40% of preoperative value	0= severe

Nausea and vomiting	Surgical bleeding
2=minimal	2=minimal
1=moderate	1=moderate
0= severe	0= severe

Following Were recorded

Total anaesthesia time – from administration of induction agent to stopping of sufentanil infusion.

Total surgical duration – from skin incision to placement of last suture.

Time to extubation- from discontinuation of sufentanil infusion.

Early recovery

a. Time to awakening - Eye opening
b. Time to verbal command - Squeeze Finger
c. Time to orientation - Place, time, date

Time to discharge from operating room MPDSS more than 6

Patients were observed for recovery time from anaesthesia and were assessed on the basis MPDSS. The time taken to satisfy the discharge criteria was considered as recovery time and was compared between the two group. All satical tests were two sided with significance considered for values of P< 0.05.

RESULT

Comparison at 3 mins after intubation of Group A vs Group B

Parameters	Mean		Probability
	Group A	Group B	
Systolic	119	110	<0.0001
Diastolic	77	68	<0.0001
Heart Rate	71	65	0.02663
SPO2	99	99	0.01922

Mean changes is haemodynamic parameters (HR and BP) 1 minutes after intubation as compared to base line

Parameters	Difference in Mean		Probability
	Group A	Group B	
Systolic	Increase by 3.2 (mm of Hg)	Decrease by 8.2 (mm of Hg)	<0.0001
Diastolic	Increase by 5.1 (mm of Hg)	Decrease by 8.2 (mm of Hg)	<0.0001
Heart Rate	Increase by 3 Bpm	Decrease by 8.4 Bpm	<0.0001

Mean changes is haemodynamic parameters (HR and BP) 3 minutes after intubation as compared to base line

Parameters	Difference in Mean		Probability
	Group A	Group B	
Systolic	Decrease by 6.1 (mm of Hg)	Decrease by 12 (mm of Hg)	<0.0001
Diastolic	Decrease by 4.8 (mm of Hg)	Decrease by 11.9 (mm of Hg)	<0.0001
Heart Rate	Decrease by 5.5 Bpm	Decrease by 11.5 Bpm	0.02663

Recovery Parameters

(All values in minutes)

Measures	Group A			
	Time to extubated	Time of awakening	Time of verbal command	Time of orientation
Mean	4.967	2.800	2.133	4.867
SD	1.217	1.126	0.900	0.629
SE	0.042	0.039	0.031	0.022
95%CI – Upper limit	5.049	2.876	2.073	4.824
95%CI – Lower limit	4.884	2.724	2.073	4.824

Measures	Group B			
	Time to extubated	Time of awakening	Time of verbal command	Time of orientation
Mean	3.900	1.700	1.367	3.500
SD	1.029	0.750	0.556	0.682
SE	0.035	0.026	0.019	0.024
95%CI – Upper limit	3.970	1.751	1.404	3.546
95%CI – Lower limit	3.830	1.649	1.329	3.454

Group A vs. Group B Recovery

Parameter	Mean Time (min)		Probability
	Group A	Group B	
Time to Extubated	4.97	3.90	0.0005
Time of Awakening	2.80	1.70	<0.0001
Time of Verbal Command	2.13	1.37	0.0002
Time of Orientation	4.87	3.50	<0.0001

Analysis of results: The results were analyzed using student's t – test. The critical value of student'st – test for a significance level (or p- value) is 0.05. A 'p' value of more than 0.05 meant that the difference between the groups was not significant, A 'p' value of less than 0.05 was taken to be stastistically significant and a value less than 0.001 were highly significant. The results were also analyzed using odds ratio. A odds ratio of more than 1 meant that the difference between the groups was significant. A odds ratio of less than 1 was considered stastistically insignificant.

Demographic Charecteristics: like age, sex, weight and ASA physical status were compared between the two groups and weere similar.

Haemodynamic Parameters

Systolic Blood Pressure

Group A responded to Tracheal Intubation with an increase in systolic BP with a mean rise from 125.40 mm Hg base line to 128.66 mm Hg one minute after intubations, whereas Group B responded to Tracheal Intubation with a decrease in systolic BP with a mean 1.22.86 mm Hg base line to 114.60 mm Hg one minute after intubation which was highly significant. ($P \leq 0.001$).

Diastolic blood pressure

Group A responded to Tracheal Intubation with an increase in DBP with a mean of 82.13 mm Hg Baseline to 87.23 mm Hg one minute after intubation, where as Group B responded to Tracheal Intubation with a decrease in DBP from a mean of 80.00 mm Hg Baseline to 72.00 mm Hg one minute after intubation, which is highly significant ($P \leq 0.001$).

Heart rate response

Group A responded to Tracheal Intubation with an increase in HR from a mean of 77.26 BPM at base line to 80.23 BPM one minute after intubation where as Group B responded to Tracheal Intubation with a decrease in HR from a mean of 77.33 BPM baseline to 68.93 BPM one minute after intubation which was significant (P = 0.02663).

Propofol rescue doses

The mean infusion rate of Sufentanil at tracheal intubation and skin incision were different between groups as defined by the protocol. A comparable number of patients in both groups required propofol rescue doses for pre-defined responses. In-group A four patients (13%) required propofol rescue dose

compared to eight patients in-group B (27%) with no significant correlation (Odds ratio = 0.4231). The total dose of propofol, duration of infusion and the infusion rate from skin incision to completion of surgery of propofol was no different between groups.

The Haemodynamic changes were better controlled in group B patients compared to group A patients and are significant with p≤ 0.001.

Recovery charecteristics

Time to extubation: In-group A the time to extubation (mean ± SD) was (4.96± 1.217) mins compared to Group B, which was (3.90± 1.029) mins, which was sinificant (p = 0.0005).

Time to awakening: The time of awakening (mean + SD) mins in- group A was (2.800± 1.123) compared to Gruop B, which was (1.700± 0.750) mins, which was highly significant (P≤ 0.0001).

Time to verbal command: The time to verbal command (mean± SD) mind in-group A was (2.133± 0.900) mins compared to Group B, which was (1.367± 0.556) mins, which was highly significant (P= 0.0002).

Time to orientation: The time to orientatio (mean± SD) in-group A was (4.867± 0.629) mins compared to Group B, which was (3.500± 0.682) mins, which was highly significant (P≤ 0.0001). The recovery from anaesthesia was better in-group B comparedto group A and is highly significant (P≤ 0.0001).

DISCUSSION

Our results show that sufentanil 0.1 – 0.3 microgram/kg/hr administered in a TIVA technique with propofol is an effective anaesthetic regimen, allowing for rapid control of intraoperative stress in a variety of Day care surgical procedures. The attenuation of haemodynamic responses to tracheal intubation was better achived with 0.25 microgram /kg bolus followed by 0.1 microgram /kg/hr was similar to that reported by Bowdle TA *et al*.[9] and Cork *et al* [10]

Twenty-seven percent of patients receiving the small-dose infusion of sufentanil required propofol rescue compared with thirteen percent of patients recieving the larger dose of sufentanil. Regardless the duration of the sufentanile infusion, emergence from anaesthesia was rapid (three to seven minutes) across a diverse surgical population. How ever emergence from anaesthesis was rapid when an infusion rate of 0.1 microgram/kg/hr. Rapid emergence from anaesthesia using low dose infusion rate correlated with the study conducted by Cork *et al*[10]

The short elimination half-life of sufentanile is independent of the duration of infusion and appears to make sufentanile well suited for rapid emergence from TIVA compared with opioid/ propofol combinations. The infusion rate of propofol used in this study, 50 micrograms/kg/min, was less than that normally used for maintanance of anaesthesia with nitrous oxide, and when combined with other opioids for a TIVA (100-150 microgram/kg/min) as reported by Bailey PL *et Al* [11].

A concern with the use of smaller propofol doses is the potential for intraoperative recall. One patient in this study reported intraoperative recall without pain when queried afterv surgery. This frequency of recall (1%) is similar that reported by Ghoneim MM *et al* (1.4%)[12]. An IV infussion device malfunction resulted in interruption of sufentanile administration for 5-10 minutes during surgery in this patient. Thos patient's recall can be explained by the mechanical failure, although the temporal relationship between recall and interuption of drug delivery cannot be ascertained. Becase the use of potent opioids reduses the amount of propofol required for TIVA, caution is required to maintain adequate propofol infusion rates to ensure hypnosis and amnesia. These results suggest tha the propofol infusion rate during TIVA should be at least 50 microgram/kg/min which is similar to that reported by vuyk *et al* [13].

The most frequent drug-related adverse events in this study were transient hypotension and bradycardia. Decreses in arterial blood pressure and bradycardia have also been observed with other opioids as reported by Moldenhauer CC *et al*[14]. Sufentanile has no effects on myocardial contractility and does not cause histamine release. Propofol has many cardiovascular effects including hypotension. Other intraoperative adverse events, such as muscle rigidity observed in the current study, are similar to those reported for other opioids as reported by Bailey PL *et al* [11].

CONCLUSION

Our study concluded that sufentanile 0.25 microgram/kg IV as a bolus after induction with propofol (1.5 mg/kg bolus followed by 140 microgram/kg/min for 10 minutes followed by 50microgram/kg/min) effectively controls responses to tracheal intubation.After tracheal intubation in the subsequent perioperative period, sufentanile either as 0.1 microgram/kg/hr infusion or as 0.3 microgram/kg/hr infusion IV with propofol infusion @ 50 microgram/kg/min was equally effective to control intraoperative responses.

Emergence from anaesthesis was however more rapid when an infusion rate of 0.1 microgram/kg/hr infusion was when compared to an infusion rete of 0.3microgram/kg/hr.

References

1. Kissin I. General anesthic action: an obselete notion [editorial]? Anesth Analg 1993; 7: 215-8.
2. Kazama T, Ikeda K, morita K, Reduction by fentanyl of the Cp50 values of propofol and hemodynamic responses to various noxious stimuli. Anesthesiology 1997; 87: 213-7.
3. Stanski DR, Shafer SL. Quantifying anesthetic drug interaction. Anesthesiology 1995; 83; 1-5.
4. Vuyk J, Mertens MJ, Olofsen E, *et al*. Propofol anesthesia and rational opioid selection: determination of optimal EC50-EC95 propofol-opioid concentrations that assure adequate anesthesia and a rapid return of consciousness. Anesthesiology 1997; 87: 1549-62.
5. Vuyk J, Lim T, Enbergs FHM, *et al*. The pharmacodynamic interaction of propofol and alfentanil during lower abdominal surgery in women. Anesthesiology 1995; 83: 8-22.
6. Kazama T, Ikeda K, Morita K. The pharmacodynamic interaction between propofol and fentanyl with respect to the suppresssion of somatic or hemodynamic responses to skin incision, peritonium incision, and abdomial wall retraction. Anesthesiology 1998; 89: 894-906.

7. Han T, Kim D, Kil H, Inagaki Y. The effects of plasma fentanyl concentrations on propofol requirement, emergence from anesthesia, and post operative analgesia in propofol-nitrous oxide anesthesia. Anesth Analg 2000; 90: 1365-71.
8. J.W Sear, Recent advances and developments in the clinical use of i.v. Opioids during the perioperative period. Br. J. Anaesth,1998: 81: 38-50.
9. Bowdle TA, Rooke GA: Postoperative myoclonus and rigidity after anesthesiawith opioids. Anesth Analg, 1994; 78: 783.
10. Cork RC, Gallo JA, Weiss LB *et al*: Sufentanil infusion: Pharmacokinetics compared to bolus (abstract). Anesth Analg, 1988;67:S1.
11. Bailey PL, Stanley Th. Intravenous opioid anesthetics. In: Miller RD, ed. Anesthesia. 5Th Ed. New York: Churchill Livingstone, 1994:337-8.
12. Ghoneim MM, Block RI. Learning and consciousness during general anesthesia. Anesthesiology 1992; 76:279-305.
13. Vuyk J, Lim T, Enberga FHM, *et al*. The pharmacodynamic interaction of propofol and alfentanil during lower abdominal surgery in women. Anesthesiology 1995;83: 8-22.
14. Moldenhauer CC, Griesemer RW, Hug CC, Holbrook GW. Hemodynamic changes during rapid induction of anesthesia with alfentanil [abstract] Anesth Analg 1983;62:276.

How to cite this article:

Dr Rajeev Nair, Dr Satish Kumar Mishra and Dr Deeparani (2020) 'Comparison of Haemo Dynamic Changes and Recovery from Anaesthesia in two Protocol of Sufentanil Infusion Using Propofol Infusion for Total Intravenous Anaesthesia (TIVA) in Day Care Surgery', *International Journal of Current Advanced Research,* 09(04), pp. 21914-21918. DOI: http://dx.doi.org/10.24327/ijcar.2020.21918.4314

****