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Dose sparing of induction dose of propofol by fentanyl and butorphanol: A comparison based on entropy analysis

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Abstract
Many studies portend the use of Butorphanol and Fentanyl as pre-medication agents, but as there is no firm conclusion derived as yet, especially on dose sparing of induction dose of propofol by butorphanol and fentanyl and its effect on entropy. This study would help to throw some light in this regard. Written informed consent was obtained. All patients were kept nil per oral for 8 hours prior to surgery. All patients on arrival to the operation theatre, intra venous line was secured with 18G cannula and intra venous fluid was on flow. Average requirement of propofol was found to be 1.272 ± 0.133(mg/kg) in Group F and 1.238± 0.122(mg/kg) in Group B with P value of 0.117.The results of our study shows that the reduction in the induction dose of propofol with 20 µg/kg of butorphanol was comparable to fentanyl 2 µg/kg.

Keywords: propofol, fentanyl, entropy analysis

Introduction
Among the various induction agents, propofol has become increasingly popular in last two decades for induction of anesthesia. Major drawbacks of propofol are a greater degree of hypotension [25-40%], compared with other hypnotic agents and inadequate attenuation of hypertensive response to intubation, respiratory depression, apnoea & blunts hypoxic-hypercapnic drive, allergic reactions, pain & thrombophlebitis of the vein into which propofol is injected [1].

Opioids are given as a pre-medication agent during induction of anesthesia to provide analgesia in various surgical procedures. It is also known to potentiate hypnotic effect of propofol, thus reducing the requirement of propofol and subsequent hypotension due to propofol. It is also known to reduce the hypertensive response to intubation, unwanted vagal reflexes & stress response to surgery [2].

Fentanyl is a synthetic opioid, phenylpiperidine series acting on the *u* receptors. Fentanyl is approximately 100 times more potent than morphine. Peak analgesic effect after intravenous administration is being reached in about 5minutes, short acting [30-50min], elimination $t^{1/2}$~4hrs. Nausea, vomiting and itching can be observed after the administration of Fentanyl [3].

Butorphanol is a synthetic opioid, morphinan series has mixed agonistic antagonistic properties. It is a *k* opioid receptor agonist and antagonist at *u* opioid receptor. The analgesic effect of 2-3 mg Butorphanol is approximately equal to 10mg of morphine. Plasma $t^{1/2}$~3hrs. The most prominent side effect is sedation, nausea and sweating.

There is abundant literature on the analgesic properties of butorphanol and fentanyl and its efficacy as an adjuvant to epidural and intra-thecal local anaesthetics is well documented. However, few studies are present on the sparing effect of fentanyl and butorphanol on induction dose of propofol and regarding the effect of fentanyl and butorphanol on Entropy [4, 5].

Many studies portend the use of Butorphanol and Fentanyl as pre-medication agents, but as there is no firm conclusion derived as yet, especially on dose sparing of induction dose of propofol by butorphanol and fentanyl and its effect on entropy. This study would help to throw some light in this regard [6].

Methodology

Following approval of institutional ethical committee, 140 patients was taken up for the study. A routine pre anaesthetic checkup was done in the evening before the surgery assessing for:

- History and general condition of the patient.
- Airway assessment by Mallampati grading.
- Nutritional status, height and weight of the patient.
- A detailed examination of the cardiovascular system, Respiratory system and Central nervous system & other systems.
- Examination of the spine.

The following investigations were done in all patients

- Complete blood count
- Urine examination for albumin, sugar and microscopy.
- Random blood sugar
- Blood urea and Serum creatinine.
- S. Electrolytes
- Standard 12-lead electrocardiogram.
- Chest X-ray

Written informed consent was obtained

All patients were kept nil per oral for 8 hours prior to surgery. All patients on arrival to the operation theatre, intra venous line was secured with 18G cannula and intra venous fluid was on flow.

Pulse oximeter, Non-invasive blood pressure and ECG monitors, Entropy was connected.

Base line heart rate, blood pressure, SpO_2, Respiratory rate and Entropy values was recorded.

Patients were randomly allocated into two groups of 70 each using sealed envelope technique.

Premedicated with Inj. Glycopyrrolate 0.2mg plus

Group F: Inj.Fentanyl 2mcg/ kg

Group B: Inj.Butorphanol 20mcg/ kg

Study drug dose was calculated per kg body weight and diluted to 5ml with normal saline and given as pre-medication 5minute before the procedure.

Heart rate, blood pressure, SpO_2, Respiratory rate and Entropy values was recorded @ 1 & 5 minutes after pre-medication

Sedation level was assessed by OAA/S scale @ 1 & 5 minute after pre-medication.

Patient was pre-oxygenated with 100% oxygen for 3minutes prior to induction of anaesthesia

Inj. Lignocaine 40 mg with proximal vein occlusion to alleviate pain and then induced with Inj. Propofol 30mg/10seconds till loss of response to verbal commands and loss of response to eyelash reflex and

Heart rate, blood pressure, SpO2, Respiratory rate and entropy values was recorded for 2 minutes after induction.

Inj. Succinyl choline 2 mg/ kg was given. After adequate relaxation, endotracheal intubation was performed.

Results

Table 1: Comparison of RE in two groups of patients studied

RE	Group F	Group B	Total	P value
Baseline	94.43±2.99	94.53±2.99	94.48±2.98	0.843
1 Minute after Premedication	94.39±3.01	94.09±2.94	94.24±2.97	0.552
5 Minute after premedication	83.24±2.94	83.31±3.03	82.78±3.02	0.889
At Induction	80.60±5.62	81.69±3.42	81.14±4.66	0.169
1 Minute after induction	60.46±6.16	59.49±6.10	59.97±6.13	0.350
2 Minute after induction	52.83±4.79	52.29±5.09	52.56±4.93	0.516
1 Minute after intubation	55.13±5.23	56.59±4.90	56.86±5.34	0.090
2 Minute after intubation	52.96±4.93	54.49±4.51	56.22±5.73	0.057
3 Minute after intubation	52.00±5.05	53.37±4.20	56.19±6.25	0.083
4 Minute after intubation	52.64±4.70	54.00±4.62	57.44±6.68	0.086
5 Minute after intubation	52.49±4.74	53.70±4.38	57.59±6.85	0.119

Student t test

Response Entropy is comparable between group F and Group B without significant difference

Table 2: Comparison of SE in two groups of patients studied

SE	Group F	Group B	Total	P value
Baseline	84.83±2.95	84.79±2.97	84.81±2.95	0.932
1 Minute after Premedication	84.66±3.01	84.51±3.08	84.59±3.03	0.782
5 Minute after premedication	74.07±3.08	74.30±2.77	74.69±2.98	0.643
At Induction	72.97±4.40	73.84±3.04	73.91±3.88	0.175
1 Minute after induction	55.47±5.85	53.7±6.34	54.59±6.14	0.088+
2 Minute after induction	50.94±4.82	49.94±5.25	49.94±5.12	0.242
1 Minute after intubation	51.16±4.94	52.06±3.67	52.11±4.44	0.223
2 Minute after intubation	50.36±4.94	51.03±3.58	52.19±4.68	0.359
3 Minute after intubation	50.44±4.84	51.67±3.73	52.56±4.8	0.094
4 Minute after intubation	50.41±4.84	51.8±4.27	53.11±5.29	0.073
5 Minute after intubation	50.39±4.85	51.11±4.08	53.25±5.31	0.343

Student t test

State Entropy is comparable between group F and Group B without significant difference

Table 3: Comparison of OAA/S in two groups of patients studied

OAA/S	Group F	Group B	Total	P value
Baseline	5.00±0.00	5.00±0.00	5.00±0.00	-
1 Minute after Premedication	4.94±0.23	4.93±0.26	4.94±0.25	0.733
5 Minute after premedication	4.40±0.55	4.31±0.53	4.36±0.54	0.347

Student t test

Sedation score is comparable between group F and Group B without significant difference

Table 4: Comparison of Propofol (mg) in two groups of patients studied

Propofol (mg)	Group F	Group B	Total
<70	13(18.6%)	20(28.6%)	33(23.6%)
70-100	56(80%)	49(70%)	105(75%)
>100	1(1.4%)	1(1.4%)	2(1.4%)
Total	70(100%)	70(100%)	140(100%)
Mean ± SD	74.14±10.56	70.86±10.18	72.50±10.47

P=0.063+, Significant, student t test

Propofol requirement is comparable between group F and Group B without significant difference

Table 5: Nature of Surgery in two groups of patients studied

Nature of Surgery	Group F	Group B	Total
Laparoscopic Mesh repair	19(27.1%)	19(27.1%)	38(27.1%)
Laparoscopic Cholecystectomy	12(17.1%)	12(17.1%)	24(17.1%)
Excision	9(12.9%)	9(12.9%)	18(12.9%)
Hemithyroidectomy	8(11.4%)	10(14.3%)	18(12.9%)
Laparoscopic Appendectomy	8(11.4%)	8(11.4%)	16(11.4%)
Laparoscopic Tubectomy	6(8.6%)	4(5.7%)	10(7.1%)
Septoplasty	4(5.7%)	4(5.7%)	8(5.7%)
Contracture release	2(2.9%)	2(2.9%)	4(2.9%)
SSG	1(1.4%)	1(1.4%)	2(1.4%)
Tympanoplasty	1(1.4%)	1(1.4%)	2(1.4%)
Total	70(100%)	70(100%)	140(100%)

Table 6: Propofol

Propofol	Group F	Group B	Total	P value
Propofol mg/kg	1.272±0.133	1.238±0.122	1.26±0.10	0.117

Propofol requirement in Group F & Group B is comparable between two groups without significant difference between the two groups

Discussion

Clinical end point for induction of anaesthesia with propofol was considered as loss of response to verbal commands and entropy values was noted at that time.

Average requirement of propofol was found to be 1.272 ± 0.133(mg/kg) in Group F and

1.238± 0.122(mg/kg) in Group B with P value of 0.117

The results of our study shows that the reduction in the induction dose of propofol with 20 µg/kg of butorphanol was comparable to fentanyl 2 µg/kg.

The loss of response to verbal commands occurred at normal entropy values [40-60] in both fentanyl and butorphanol groups.

Two studies in dogs reported that butorphanol, along with other premedicants, significantly reduced the dose requirement of propofol at induction [7, 8].

In another study in cats, premedication with butorphanol or morphine, combined with acepromazine, significantly reduced the propofol dose for induction [9].

Jasleen Kaur *et al.* [9] [2013] studied dose sparing of induction dose of propofol by fentanyl(2mcg/kg) and butorphanol (20mcg/kg and 40mcg/kg) on 120patients three groups of 40 each & the induction dose of propofol (mg/kg) was observed to be 1.1±0.50 in Group F, 1.05±0.35 in Group B 20 and 1.18±0.41 in Group B40.

The results obtained in our study is in consistent with the previous study of Jasleen Kaur *et al.* Where the requirement of propofol with butorphanol 20mcg/kg as pre-medicant is comparable to fentanyl 2mcg/kg.

In 2004, W. Riad *et al.* [6] studied the effect of electroencephalographic entropy on propofol requirement and haemodynamic parameters during induction of anaesthesia in 72 elderly patients. Standard monitoring was performed for all patients together with entropy monitor. Total dose of propofol and the dose kg-1 were significantly reduced by 37.1% and 31.8%, respectively, in the entropy group (P value < 0.01)

The requirement of propofol in our study was found to be 1.272±0. 133(mg/kg) in Group F and 1.238± 0.122(mg/kg) in Group B. Considering 2mg/kg as the conventional dose, total dose of propofol was reduced by 36.4% in group F and 38.1% in group B.

The results obtained in our study is in consistent with the previous study of W. Riad *et al*. Where there is reduction in the requirement of propofol by more than 30% by using simultaneous entropy monitoring and clinical end point and the requirement of propofol with butorphanol 20mcg/kg as pre-medicant is comparable to fentanyl 2mcg/kg.

SE/RE indices have been widely used to estimate the depth of anesthesia and sedation. The administration of opioids together with anesthetics may substantially change the predictive value of these EEG monitors.

In our study, we found that the entropy values was between 50-60 which is within normal range [40-60], when the patients had become unresponsive to verbal commands in both the group.

In Jasleen kaur *et al.* [9] study, Response entropy and State entropy was higher than 60 at induction in all three groups. But, in our study RE and SE at induction was between 50-60 in both fentanyl 2mcg/kg and butorphanol 20mcg/kg group.

This is in contrast to the study of Jasleen kaur *et al*. Study who had obtained an entropy values of higher than 60 in fentanyl 2mcg/kg and butorphanol 20mcg/kg and butorphanol 40mcg/kg

Butorphanol 20mcg/kg had lower sedation scores compared to fentanyl 2mcg/kg at 1minute and 5 minute after pre-medication but there was no statistically significant difference in sedation scores in the fentanyl and butorphanol group at doses 2mcg/kg and 20mcg/kg respectively.

This difference could be explained due to the difference in the opioid receptor spectra. Butorphanol is a kappa-receptor partial agonist as well as a mu-receptor antagonist, whereas fentanyl is predominantly a mu-receptor agonist. Butorphanol is therefore associated with more sedation than fentanyl. In Jasleen kaur *et al.* [9] study higher sedation was observed in the butorphanol groups especially with 40mcg/kg [4.1+/-0.64] of butorphanol than 20mcg/kg of

butorphanol [4.3+/-0.60] as compared with Group F [4.57+/-0.54] Butorphanol at higher doses [40mcg/kg] increases the depth of sedation without much reduction in the consumption of propofol. So, at the dose used in our study [20mcg/kg butorphanol] sedation scores are similar to the previous study of Jasleen kaur *et al*. Without significant increase in depth of sedation [10].

Conclusion

- Butorphanol due to its lack of euphoric effects may be useful for clinical populations prone to drug-seeking behavior [21].
- Butorphanol is not a controlled substance, its use can reduce administrative liability for abuse and can lower the number of distribution records associated with Schedule II narcotics. It is also economical than fentanyl.
- So, Butorphanol 20mcg/kg is an acceptable alternative to fentanyl as an adjuvant to balanced general anaesthesia.

References

1. Jaap Vuyk, Elske Sitsen, Marije Reekers. Intra-venous Anesthetics. In: Miller RD. Millers anesthesia, 8th edition. Philadelphia: Elsevier 2015, 822-832.
2. Pandit SK, Kothary SP, Pandit UA, Mathai MK. Comparison of fentanyl and buturphanol for outpatient anesthesia. Can J Anesthesia 1987;34:130-4.
3. Philip BK, Scott DA, Freiberger D, Gibbs RR, Hunt C, Murray E. Butorphanol compared with fentanyl in general anaesthesia for ambulatory laparoscopy. Can J Anaesth 1991;38:183-6.
4. MI WD, Sakai T, Singh H, Kudo T, Kudo M, Matsuki A. Hypnotic endpoints vs the bispectral index, 95% spectral edge frequency during propofol infusion with or without fentanyl. Eur J Anaesthesiol 1999;16:47-52.
5. Lysakowski C, Dumont L, Pellegrini M, Clergue F, Tassonyi E. Effects of fentanyl, alfentanyl, remifentanil and sufentanil on loss of consciousness and bispectral index during propofol induction of anesthesia. Br J Anaesth 2001;86:523-7.
6. Riad W, Schreiber M, Saeed AB. Monitoring with EEG entropy decreases propofol requirement and maintains cardiovascular stability during induction of anaesthesia in elderly patients. European Journal of Anaesthesiology 2007;24(8):684-688.
7. Verma R *et al*., Total intravenous anesthesia in laparoscopic cholecystectomy: comparison of butorphanol and fentanyl: The Internet Journal of Anesthesiology 2007, 14(1).
8. Vikramjeet Arora, Sukhmindar Jit Singh Bajwa, Sarajit Kaur. Comparitive evaluation of recovery charateristeics of fentanyl and butorphanol when used as a supplement to propofol anaesthesia. Int J Appl Bsic Med Res 2012;2(2):97-101.
9. Kaur J, Srilata M, Padmaja D, Gopinath R, Bajwa SJ, Kenneth DJ *et al*. Dose sparing of induction dose of propofol and fentanyl: A comparison based on entropy analysis. Saudi J Anaesth 2013;7:128-33.
10. Robert SK. Opioid agonists and antagonists. Chapter 3. In: Pharmacology and physiology in anaesthesia practice. 3rd edition. Lipincott Raven publishers 1999, 77-112.