# A COMPARITIVE STUDY OF INTRA OPERATIVE FENTANYL REQUIREMENT BETWEEN SPI AND HEMODYNAMIC GUIDANCE IN MASTECTOMIES

**Author 1 - Dr.Kaluvala Prasad Rao**, Associate Professor,Department of Anaesthesiology & Critical Care,Nizam's Institute of Medical Sciences,Panjagutta,Hyderabad,Telangana,India.

**Author 2 - Dr.SingamGeetha**,Associate Professor,Department of Anaesthesiology & Critical Care,Nizam's Institute of Medical Sciences,Panjagutta,Hyderabad,Telangana,India.

**Author 3 - Dr. Krishna Rao Maremanda**,Assistant Professor,Department of Anaesthesiology & Critical Care,Nizam's Institute of Medical Sciences,Panjagutta,Hyderabad,Telangana, India.

**Author 4 - Dr.Thandu Priyanka**,Senior Resident,Department of Anaesthesiology & Critical Care,Nizam's Institute of Medical Sciences,Panjagutta,Hyderabad,Telangana, India.

**Author 5 - Dr.PadmajaDurga**,Professor & Head Department of Anaesthesiology & Critical Care,Nizam's Institute of Medical Sciences,Panjagutta,Hyderabad,Telangana, India.

**Corresponding Author - Dr.Kaluvala Prasad Rao,** Associate Professor,Department of Anaesthesiology & Critical Care,Nizam's Institute of Medical Sciences,Panjagutta,Hyderabad,Telangana,India.

## ABSTRACT

**Background and objectives:** To perform comparative investigation of intra-operative Fentanyl dose administered between the study group and the control group of the population selected for study. To distinguish the intra-operative dose requirement of Fentanyl administered between the study group and the control group. Evaluation of the degree of post operative pain in the study and the control group. Estimation of the rescue analgesic required in Post Operative Care Unit in the study group and the control group. To report the peri-

operative adverse events in the study and the control group. To approximate the time required for extubation in the study group and the control group.

**Methods:** A Prospective comparative randomized study was conducted after obtaining Institutional Ethical Committee approval with no EC/NIMS/2736/2021 and Informed Consent of the patients was conducted in Department of Anaesthesia at Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad, Telangana, India from December 2020 – November 2021 which included females of 18-60 years age undergoing mastectomy Surgery under General Anaesthesia.

**Results:**The study statistically evaluated impression of intra operative fentanyl dose guided by hemodynamic and SPI parameters. Correlation of different fentanyl doses to the parameters like age, BMI, cardiological health, Spectral entropy, intraoperative and post operative events and symptoms, mean extubation time was estimated during mastectomy.

**Conclusion:** The study derives inference from mastectomy performed under general anaesthesia that SPI guided group will distinguish by better hemodynamic stability which will probably result into lower intraoperative fentanyl requirement. Also, apositive postoperative analgesic property andlesser chance of postoperative nausea and vomiting reported when compared with study conducted using conventional hemodynamic guidance.

**Keywords:**BMI, extubation time, hemodynamic parameter, mastectomy.

## INTRODUCTION

During surgery, anaesthesia shields patients from discomfort and different anaesthetic types are combined, general, and regional/local anaesthesia. The drug-induced unconsciousness and insensitivity to pain is known as general anaesthesia [1,2]. "Utilizing lesser doses of diverse medications to amplify their desirable benefits and lessen their negative side effects" is the definition of balanced anaesthesia. General anaesthetics and muscle relaxants are used to induce hypnosis and immobility, respectively. One technique for analysing EEG signals is spectral entropy [2,3]. The monitors measure and analyse the irregularities in the EEG signals, and then they display two numerical values that represent the depth of anaesthesia. The two spectral entropy indicators known as State Entropy (SE) and Response Entropy (RE) are frequently used to gauge the degree of sedation and anaesthesia [3, 4,5]. It has been demonstrated that the signal's entropy decreases when a patient drifts off to sleep and rises

once again when the patient awakens. Analgesia is the "absence of pain in response to stimulus that would normally be painful [5,6]." In-operatively, adequate analgesia balanced by nociception and anti-nociception will assist prevent certain side effects, such as over- or underdosing and associated adverse responses. Additionally, it is linked to a better post-operative result in terms of healing, mobility, and patient satisfaction. There are currently no gold standards for measuring the balance of nociception and antinociception during anaesthesia [6,7,8]. The anaesthesiologist's experience continues to be the foundation for how analgesics are administered. Post-operative pain control is just as crucial to post-anaesthesia care as intraoperative pain control.The monitoring of postoperative pain is done using a variety of scales. After a six-surgery, post-operative pain is assessed using instruments such the Visual Analogue Scale (VAS), Numeric Rating Scale (NRS), Verbal Rating Scale (VRS), and McGill Pain Questionnaire. The most popular medications used to treat post-operative pain were NSAIDS, followed by opioid analgesics [8,9].

## MATERIAL AND METHODS

A randomized study was held that included females of 18-60 years age undergoing mastectomy. The mean fentanyl consumption during the surgery was 108.30 ± 21.84 µg and 125.70 ± 24.87µg in SPI guided group and Conventional group respectively [9,10]. Thirty patients undergoing breast surgery were randomly placed to Study group (SPI guided analgesia group, n=15) or control group (Conventional analgesia group, n = 15). Anaesthesia was maintained with 34 Sevoflurane 0.8 – 1 MAC and oxygen. Intra operative fentanyl 0.5µg/kg was administered for the event persisting for 5 min [11,12]. The study participants were randomly allocated to study group and control group by chits' method.Instructed about the surgery timings and the surgical procedure. Then the patient was explained about the procedure. The SPI sensor enabled on the monitor to the patients in the study group i.e SPI guided group. IV cannula was secured in the peripheral vein of upper limb further premedication of Inj. Fentanyl 2 µg/kg was given to all the patients undergoing breast surgery under GA over 3 min. During the surgical procedure cardiac functioning, hemodynamic parameters, spectral entropy, PONV, mean extubation was monitored for further statistical data evaluation for deriving outcomes [12,13,14].

### Inclusion criteria:

1. 18 – 65 years

2. ASA grade I and II

3. Females

4. Scheduled for elective mastectomy

**Exclusion criteria:**

1. Patient Refusal

2. Known allergy to Fentanyl drug

3. Hypertension & those on beta blockers

4. Cardiovascular disease, Cardiac arrhythmias, drugs influencing HR, Pacemakers

5. Previous Sympathectomy, Vagotomy

6. Respiratory disorder like asthma

7. Neurologic disorders like Seizures

8. Renal disease

9. Patients on chronic medication like analgesics or psychiatric medication.

**RESULTS**

The study involved 15 to 30 participants to be in each group i.e., Study group and control group. Population only included all female participants aged between 18-65 year undergoing mastectomy surgery for breast cancer.

**Table No. 1 Age wise distribution of the study participants**

| **Age Group** | **< 45 years** | **≥ 45 years** | **Total**<br>**Number (%)** |
|---|---|---|---|
| **SG** | 3 (20) | 12 (80) | 15 |
| **CG** | 1 (6.67) | 14 (93.33) | 15 |
| **Total** | 4 (13.33) | 15 (86.67) | 30 (100) |

P = 0.2 (not significant)

**Table no.2 Distribution of the study population based on BMI classification**

| BMI Classification for Asians (kg/m$^2$) | Study Group n (%) | Control Group n (%) | Total n (%) |
|---|---|---|---|
| **Underweight (<18.5)** | 1 (100) | 0 (0) | 1 (100) |
| **Normal (18.5 – 22.9)** | 5 (45) | 6 (55) | 11 (100) |
| **Overweight (23-24.9)** | 2 (50) | 2 (50) | 4 (100) |
| **Obese (≥ 25)** | 7 (50) | 7 (50) | 14 (100) |
| **Total** | 15 (50) | 15 (50) | 30 (100) |

P = 0.7 (not significant); n = frequency

**Table No.3 Table showing the distribution of study participants according to ASA grading in study and control group**

| Parameter | Study Participants | | Total (%) |
|---|---|---|---|
| | Study Group (n) | Control Group (n) | |
| **ASA 1** | 7 | 8 | 15 (50) |
| **ASA II** | 8 | 7 | 15 (50) |
| **Total (%)** | 15 (50) | 15 (50) | 30 (100) |

P = 0.7 (not significant) n= frequency

**Table No. 4 Table showing the Mean arterial pressure values at different time intervals intra-operatively**

| Time of readings | Mean MAP Mean (SD) mmHg | | P value (t test) |
|---|---|---|---|
| | Study Group | Control Group | |
| **Baseline Readings** | 94.35 (9.82) | 92.04 (3.55) | 0.3 |
| **1 min after intubation** | 94.68 (12.37) | 101.82 (11.69) | 0.1 |
| **5 min after intubation** | 90.02 (10.57) | 96.75 (8.11) | 0.06 |

| | | | |
|---|---|---|---|
| **1 min after Incision** | 101.02 (11.51) | 107.6 (9.24) | 0.09 |
| **5 min after incision** | 91.33 (9.43) | 97.78 (9.55) | 0.07 |
| **10 min after incision** | 87.06 (8.52) | 92.04 (6.9) | 0.08 |
| **20 min after incision** | 91.73 (13.5) | 100.04 (10.94) | 0.07 |
| **30 min after incision** | 91.08 (8.54) | 98.53 (13.07) | 0.07 |
| **60 min after incision** | 89.26 (7.52) | 90.53 (6.48) | 0.62 |
| **End of surgery** | 90.53 (9.18) | 87.28 (4.71) | 0.2 |
| **At extubation** | 94.62 (10.57) | 94.26 (5.82) | 0.9 |

P<0.05 - significant

**Table no. 5 Table showing the Heart rate values at different time intervals intra-operatively**

| **Time interval** | **Mean HR (SD)** | | **P Value** |
|---|---|---|---|
| | **SG beats/min** | CG **beats/min** | |
| **Baseline Readings** | 81.2 (14.31) | 78.8 (10.93) | 0.6 |
| **1 min after intubation** | 85.73 (12.84) | 86.93 (13.38) | 0.8 |
| **5 min after intubation** | 77.8 (9.03) | 84.33 (8.59) | 0.052 |
| **1 min after Incision** | 84.2 (9.44) | 93.73 (17.01) | 0.06 |
| **5 min after incision** | 78.13 (9.16) | 85.46 (13.87) | 0.1 |
| **10 min after incision** | 76.13 (8.08) | 82.6 (11.76) | 0.08 |
| **20 min after incision** | 79.8 (8.45) | 88.13 (15.62) | 0.08 |
| **30 min after incision** | 78.2 (11) | 85.73 (12.09) | 0.08 |
| **60 min after incision** | 72.2 (3.09) | 78.67(12.96) | 0.07 |
| **End of surgery** | 75.47 (10.06) | 77 (10.81) | 0.6 |
| **At extubation** | 85 (14.04) | 79.6 (14) | 0.3 |

P<0.05 - significant

**Table no.6 Table showing the Mean values of Spectral entropy indicators**

| **Time of readings** | **State Entropy (mean ± SD)** | **Response Entropy (mean ± SD)** |
|---|---|---|

| | Study Group | Control group | P value | Study Group | Control group | P value |
|---|---|---|---|---|---|---|
| **Baseline Readings** | 86.73 ± 5.64 | 84.53 ± 12.59 | 0.54 | 92.13 ± 7.15 | 87.93 ± 12.33 | 0.2 |
| **1 min after intubation** | 49.93 ± 11.8 | 50.40 ± 10.07 | 0.9 | 54.40 ± 8.97 | 54.80 ± 7.63 | 0.8 |
| **5 min after intubation** | 49.13 ± 9.12 | 51.40 ± 9.39 | 0.51 | 52.93 ± 7.93 | 57.13 ± 10.11 | 0.2 |
| **1 min after Incision** | 49.47 ± 10.74 | 52.67 ± 7.09 | 0.3 | 51.93 ± 11.66 | 58.07 ± 9.65 | 0.1 |
| **5 min after incision** | 50.13 ± 9.69 | 51.87 ± 8.33 | 0.6 | 53.53 ± 9.8 | 57.40 ± 7.13 | 0.2 |
| **10 min after incision** | 54.27 ± 7.56 | 50.13 ± 3.48 | 0.06 | 56.67 ± 9.33 | 51.73 ± 3.17 | 0.06 |
| **20 min after incision** | 51.67 ± 8.4 | 53.00 ± 6.71 | 0.6 | 54.60 ± 8.72 | 56.60 ± 6.95 | 0.4 |
| **30 min after incision** | 50.33 ± 7.51 | 50.67 ± 7.65 | 0.9 | 54.27 ± 8.72 | 56.07 ± 5.43 | 0.5 |
| **60 min after incision** | 55.93 ± 3.75 | 51.93 ± 4.59 | **0.01** | 57.20 ± 3.93 | 55.53 ± 5.46 | 0.3 |
| **End of surgery** | 61.73 ± 7.52 | 57.00 ± 5.76 | 0.06 | 63.27 ± 8.36 | 60.47 ± 6.16 | 0.3 |
| **At extubation** | 86.47 ± 4.05 | 86.80 ± 5.27 | 0.8 | 92.07 ± 3.35 | 91.67 ± 3.96 | 0.7 |

**Table no.7 The Mean values of the difference of SE and RE in Study group and Control group**

| Time of readings | SE-RE | | P value (t test) |
|---|---|---|---|
| | Study Group | Control Group | |
| **Baseline Readings** | -5.4 (3.98) | -3.40 (4.19) | 0.1 |
| **1 min after intubation** | -4.47 (4.56) | -4.40 (5.79) | 0.9 |
| **5 min after intubation** | -3.80 (5.4) | -5.73 (4.79) | 0.3 |
| **1 min after Incision** | -2.47 (4.42) | -5.40 (5.04) | 0.1 |
| **5 min after incision** | -3.40 (4.29) | -5.53 (4.44) | 0.2 |

| | | | |
|---|---|---|---|
| **10 min after incision** | -2.40 (4.78) | -1.60 (2.87) | 0.5 |
| **20 min after incision** | -2.93 (4.01) | -3.60 (4.45) | 0.6 |
| **30 min after incision** | -3.93 (6.02) | -5.40 (7.34) | 0.5 |
| **60 min after incision** | -1.27 (3.20) | -3.60 (3.40) | 0.06 |
| **End of surgery** | -1.53 (3.64) | -3.47 (6.29) | 0.3 |
| **At extubation** | -5.60 (3.40) | -4.87 (5.04) | 0.6 |

**Table no. 8 Table showing the mean dose of fentanyl drug in both study and control groups**

| **Fentanyl requirement** | **Group (Mean ± SD)** | | **P value** |
|---|---|---|---|
| | **Study Group** | **Control group** | |
| **Loading dose (µg)** | 116.4 ± 14.67 | 113.33 ± 15.58 | 0.5 |
| **Intra operative dose (µg)** | 36.47 ± 20.18 | 73.53 ± 34.21 | 0.001 |
| **Total (µg)** | 152.8 ± 33.14 | 186.87 ± 45.79 | 0.02 |

P< 0.05 = significant

**Table No. 9 The Mean No. of Fentanyl doses given intra-operatively in the study participants in Study group and Control group**

| **No. of Fentanyl bolus** | **Study Group** | **Control Group** | **P value** |
|---|---|---|---|
| **Mean** | 1.2 | 2.53 | < 0.001 |
| **Standard deviation** | 0.56 | 1.06 | |

P < 0.05 significant

**Table No. 10The requirement of fentanyl dose in study group and control group after giving the loading dose of fentanyl drug**

| **Time interval** | **Mean Fentanyl administered (µg/kg)** | **P value** |
|---|---|---|

| | SG | CG | |
|---|---|---|---|
| **Baseline Readings** | 0 | 0 | 0 |
| **1 min after intubation** | 8 (2.06) | 8 (2.06) | > 0.99 |
| **5 min after intubation** | 1.33 (0.34) | 1.33 (0.34) | > 0.99 |
| **1 min after Incision** | 9.33 (2.4) | 16 (4.13) | 0.1 |
| **5 min after incision** | 2.67 (0.68) | 5.33 (1.37) | 0.09 |
| **10 min after incision** | 0 | 1.33 (0.34) | 0.001 |
| **20 min after incision** | 0 | 10.67 (2.75) | 0.001 |
| **30 min after incision** | 2.67 (0.68) | 8 (2.06) | 0.02 |
| **60 min after incision** | 0 | 0 | 0 |
| **End of surgery** | 0 | 0 | 0 |
| **At extubation** | 0 | 0 | 0 |

**Table No. 11 Table showing the Mean Extubation time in the study participants**

| Extubation time | Study Group (min) | Control Group (min) | P value |
|---|---|---|---|
| **Mean** | 6.26 | 10.33 | < 0.001 |
| **Standard Deviation** | 2.49 | 3.47 | |

P< 0.05 - significant

**Table No. 12 The post operative details of the study participants while in** PACU

| Parameter | Category | Frequency (Percentage) | | Chi square value<br>P value |
|---|---|---|---|---|
| | | Study group | Control group | |

| | | | | |
|---|---|---|---|---|
| **Post operative Nausea** | None (8) | 7 (87.5) | 1 (12.5) | 9.05<br>0.02 |
| | Mild (11) | 6 (54.5) | 5 (45.5) | |
| | Moderate (6) | 1 (16.7) | 5 (83.3) | |
| | Severe (5) | 1 (20) | 4 (80) | |
| **Post operative Vomiting** | Yes (10) | 2 (20) | 8 (80) | 5.4<br>0.02 |
| | No (20) | 13 (65) | 7 (35) | |
| **Total (%)** | 30 (100) | 15 (50) | 15 (50) | |

* $p<0.05$ was considered as significant

**Table no.13 Post operative requirement of Analgesic medication in the study participants**

| **Analgesia in PACU** | **Study Group (mg)** | **Control Group (mg)** | **P value** |
|---|---|---|---|
| **Mean Rescue Ketorolac Requirement*** | 12 | 25 | < 0.001 |
| **Standard Deviation** | 8.41 | 7.32 | |

* The analgesic used in the present study was Inj. ketorolac 15mg

**Table no. 14 Post operative requirement of Medication for PONV in the study and control group**

| **Anti-emetic in PACU** | **Study Group** | **Control Group** | **P value** |
|---|---|---|---|
| **Mean Rescue Ondansetron Requirement** | 0.53 | 2.13 | 0.01 |
| **Standard Error** | 0.13 | 0.55 | |

P< 0.05 – significant

**DISCUSSION:**

The recent study aims to compare the intra operative dose requirement of fentanyl administered between the study group and the control group of the study population [14,15]. Induction and intraoperative maintenance of anaesthesia was with propofol titrated with Fentanyl which was most commonly used in our department. The base line hemodynamic parameters were comparable in SPI guided group and Conventional monitoring group in our study [15,16]. Intra operative hemodynamic changes like rise of parameters in response to noxious stimuli after intubation and incision is observed in the present study in both the groups.

Increase in SPI values are also observed in response to noxious stimuli and is inconsistent with hemodynamic changes corresponding to it [17]. Surgical Pleth Index (SPI) monitoring during General Anaesthesia reflects the sympathetic changes better than the hemodynamic changes. The mean fentanyl administration was lower in SPI guided group but the mean post operative analgesic requirement that observed to be higher in SPI guided group which was explained by the presence of blood vessel distensibility and increased baseline heart rate in children [17,18]. The study needed lower dosing of fentanyl when compared to control group. The mean volume of fluid infusion and blood loss is significantly less in SPI guided group in our study. This can be explained by better hemodynamic stability in SPI guided group as the analgesic and anesthetic titrations are made on changes in SPI values and not on hemodynamic changes [18].

The lesser mean duration of surgery in study group in the present study can be explained as a chance effect or due to better hemodynamic stability in terms of lesser events and less

amount of blood loss in the SPI guided group. In our study,the mean extubation time was significantly low in SPI guided group when compared to conventional group which may be proved by sedative effect of higher fentanyl dose in control group [18,19]. Also, there was an increase in SPI values in response to painful stimulus like intubation or incision and this change was inconsistent with a change in 63 hemodynamic parameters. The mean post operative pain scores as measured by NRS scale in post PACU and mean rescue analgesic requirement for about an hour is less in our study group than control group that is due to lesser intra operative stress in SPI guided group than control group which affects the post operative recovery. The post operative frequency of Nausea & vomiting and mean rescue Ondansetron requirement was significantly more in Control group than study group due to higher dose of fentanyl used intra operatively. Rise in the blood pressure and HR during the surgery is believed to be due to high surgical stress and this is evident with most of the cases undergoing surgery [19]. Truly speaking, these hemodynamic changes were the late signs of sympathetic activation in response to noxious stimuli [19,20]. ANS modulation may be the better index of nociceptive stress during the surgery which can be monitored by Heart rate variability & Pulse plethysmographic analysis i.e SPI [20]. Thus SPI 64 guidance will give the better analgesic and hypnotic drug titrations during General Anaesthesia than conventional method of monitoring. SPI guidance in monitoring general anaesthesia is an important area for further research in the field of Anaesthesia.

## Conclusion

We discovered that the SPI advised group patients had a lower mean intraoperative fentanyl requirement in our trial, which also included 30 patients undergoing mastectomy under general anaesthesia. The SPI led group also experienced fewer hemodynamic events, intravenous fluids, intraoperative blood losses, and longer surgical times. Early extubation was facilitated by a lower fentanyl dose, and the need for ondansetron was reduced due to less nausea and vomiting. With lower NRS values, SPI guiding also improved postoperative analgesia, lowering the demand for rescue analgesics. Therefore, we come to the conclusion that mastectomy performed under general anaesthesia using SPI guidance will result in better hemodynamic stability, less need for intraoperative fentanyl, better postoperative analgesia, and a lower incidence of postoperative nausea and vomiting than when conducted using conventional hemodynamic guidance.

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