SPECTRAL ENTROPY FOR ASSESSING THE PATIENT RESPONSIVENESS DURING PROPOFOL/FENTANYL SEDATION IN DAY CARE SURGERIES

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Abstract

Background: For day care surgery under monitored anesthetic care, precise monitoring of sedation depth facilitates optimization of dosage and prevents adverse complications from over sedation. Conventionally subjective sedation scales, such as the Modified observer’s assessment of alertness/ sedation scale (MOAA/S) have been widely utilized for sedation monitoring. The newer monitoring called entropy is considered to be beneficial for objective assessment with combined use of opioids and hypnotics if applied. The primary objective is to determine measurement of entropy as a marker for measuring depth of anaesthesia.

Methods: Two groups P and PF (with 25 patients each) received either propofol 1mg/kg followed by maintenance infusion of 250 mic/ kg/hr whereas “PF” group received additional single dose of fentanyl 2 mic/kg respectively. The values of response entropy (RE) and state entropy (SE) corresponding to each MOAA/S (5 to 0) were determined.

Results: The patient’s demographic profile and clinical characteristics were comparable in both the groups. No difference observed in duration of anaesthesia and surgery in both groups. No difference observed in MOAA/S in both groups. The results shows a highly significant differences in the observed means of SE, RE, MAP and HR with considerably higher mean values in group P (p<0.0001). However other parameter such as SPO2, ETCO2 and RR were almost comparable in both groups.

Conclusion: The mean value of SE and RE in group P and PF indicates that deeper plane of anaesthesia is observed in PF group. It is concluded that in assessing the level of hypnosis during intra-operative sedation in MAC, entropy corresponds to MOAA/S and increases or decreases proportionately depending upon increase or decrease level of sedation. Hence from these results it is proposed that entropy monitoring is a reliable monitoring index of anaesthesia depth in MAC.

Keywords: Entropy, Propofol, Sedation, Day care surgery, Observer’s assessment of alertness/ sedation scale, Monitored anaesthesia Care

INTRODUCTION

Even after a century, assessment of anaesthetic depth remains evasive. Despite realizing that awareness under anaesthesia is frantic for patients and the treating physician, the general notion of anaesthesia awareness remains unclear. There have been several thoughtful discussions of the monitoring of depth of anesthesia and of the problem of awareness. The precise monitoring of sedation depth to titrate the proper dosage to prevent adverse complications is still to be discovered. The newer monitoring called entropy monitoring consists of spectral entropy (SE) is considered to be beneficial for depth monitoring during use of opioids and hypnotics if applied. ¹ Its work with overall depth of sedation synergistically via the extra cortical pathway. The primary objective is to determine measurement of entropy as a marker for measuring depth of anesthesia.

Materials and method

This study was conducted in a tertiary care super specialty hospital in India. After approval from the Institutional ethics committee, written informed consent was obtained from the patients. A total of 50
patients of ASA physical status I and II in the age group of 17 years to 60 years, of either sex, posted for elective day care surgery under GA were enrolled for this prospective, randomized double blind study. Exclusion criteria included over weight, underweight, neurological disorder patients and recent use of psychoactive medication, including alcohol. According to a computer-generated randomization chart, the patients were assigned to one of the treatment groups. To ensure blinding, premedication was given by an anaesthesiologist who not involve in the study. An 18 G intracath was placed in each patient and IV fluid RL/NS started at 10 ml/kg/hrs. Patient was premedicated with Inj. Midazolam 0.06 mg/kg and Inj. Atropine 0.01 mg/kg injected IV 10 mins before the procedure. Patients in group “P” received bolus dose of propofol IV 1 mg/kg, followed by maintenance infusion of 250 mcg/ kg/hr and patients in group “PF” group received additional single dose of fentanyl 2 mcg/kg after 05 mins of sedation. Vitals were recorded by blinded treating clinician.

The entropy electrodes were placed on the forehead of each patient and monitoring of mean arterial pressure (MAP), heart rate (HR) and saturation of peripheral oxygen (SPO2), respiratory rate was done. Entropy (Both SE and RE) was monitored using a Datex ohmeda S/5™ monitor. Modified observer’s assessment of alertness/ sedation scale (MOAA/S) (5-

| 5- Responds readily to name spoken in normal tone, 4-Lethargic response to name spoken in normal tone, 3- Response only after name is called loudly and/or repeatedly, 2- Response only after mild prodding or shaking, 1- Response only after painful trapezius squeeze, 0- No response after painful trapezius squeeze) was used to evaluate the level of sedation, during and after surgery. The basic aim was to keep the intra operative level of sedation at MOAA/S < 3. Prior to surgery, each patient was explained in the PAC clinic about 0 – 10 verbal rating scale (VRS), in which 0 corresponds to no pain and 10 corresponds to excessive pain. Patient was given a reminder about the scale in the preoperative room. After measuring the control (i.e. Before initiation of sedation), values of entropy (RE and SE), MAP, HR, SPO2 and RR, MOAA/S for pain scores, corresponding measurements were made for 45 mins after initiation of sedation for every 5 mins intervals. After ending of surgery and anaesthesia, entropy (SE and RE) MOAA/S were measured for 15 mins at 5 mins intervals. In most of the cases the surgery/anaesthesia lasted for 45-50 mins. The surgery was initiated when MOAA/S < 3 was achieved. Accordingly anaesthesia doses were adjusted to keep MOAA/S < 3. During maintenance of anaesthesia, all patients were assessed for signs of inadequate anaesthesia, hypotension or bradycardia. Inadequate anaesthesia was defined as hypertension, tachycardia or patient movement, eye opening, swallowing, grimacing, lacrimation or sweating. Respiratory depression was predefined as RR < 10 breaths/min during surgery or post – operatively, SPO2 < 92 for > 30 s or apnea > 20 s. In case of patients with respiratory depression, patients were given verbal/tactile stimulation and in case of persistent respiratory depression the patients were given respiratory support. Hypotension was predefined as an intra-operative or post-operative decrease in systolic BP of > 25% of control value or to < 70 mmHg. It was treated with IV fluids (Colloids in case required) and mephedrine 06 mg. Bradycardia was predefined as HR < 50 beats/min and was treated with Inj. Atropine 0.6 mg IV.

Data were analyzed using statistical package for social sciences (SPSS). Student’s t-test was used to compare the results for parametric data at each point. Results are expressed as mean ± SD and P values < 0.05 were considered statistically significant.

Results

A total of 25 patients in each group were included in this study. The patient’s demographic profile including age, weight and height were comparable in both the groups (Table 1). No difference observed in duration of anaesthesia and surgery in both groups. No difference observed in MOAA/S in both groups. The results shows a highly significant differences in the observed means of SE, RE, MAP and HR with considerably higher mean values in group P (p<0.0001). (Table 2 and 3) However other parameter such as SPO2, ETCO2 and RR were almost comparable in both groups (p>0.05). The mean value of SE and RE in group P and PF indicates that at deeper plane of anaesthesia observed in PF group.
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Table 1: Demographic profile and baseline clinical characteristics of patients in both the group

| Parameter               | Group P          | Group PF         | p-value |
|-------------------------|------------------|------------------|---------|
| Age in years            | 47.8±5.1         | 48.1±8.8         | 0.88    |
| Male/female             | 13/12            | 15/10            |         |
| Weight(Kg)              | 54.7±4.3         | 56.3±3.6         | 0.16    |
| Height (Cm)             | 162.9±3.9        | 161.7±4.4        | 0.31    |
| Duration of surgery(min)| 46.3±10.2        | 50.1±11          | 0.21    |
| Duration of Anesthesia (min)| 45.2±10.4    | 49.6±9.9         |         |
| Total Dosage of Propofol(mg) | 259.8±25.4   | 278.5±28.4       | 0.01    |
| Total dose of Fentanyl(mcg)| NA              | 82.1±10.5        |         |

#all values expressed as mean ± SD or as expressed otherwise

Table 2: MOAA/S and RE/SE Entropy at different time interval

| Time (min) | MOAA/S | Entropy | MOAA/S | Entropy |
|------------|--------|---------|--------|---------|
| 0 (control)| 5      | 98+ 0.03| 5      | 97.0 +0.02 |
| 5          | 3.5 +0.4| 93 + 0.05| 3.5 +0.4| 97 +0.1 |
| 10         | 3 + 0.2 | 74.2 + 7.5| 3 + 0.2 | 86.2 +2.2 |
| 15         | 3      | 73.1 + 6.5| 3      | 75.3 +4.6 |
| 20         | 3      | 72.1 + 7.5| 3      | 62.6+6.2 |
| 25         | 3.01   | 72.2 + 7.5| 3      | 55.3+7.6 |
| 30         | 3      | 72.2 + 8.5| 3      | 51.2+7.6 |
| 35         | 3      | 72.2 + 8.5| 3      | 49.2+8.1 |
| 40         | 3      | 72.7 + 8.5| 3      | 47.8+9.4 |
| 45         | 3      | 72.8 + 9.8| 3      | 47.5+9.8 |
| 50         | 3.4+0.1 | 98.4 + 0.1| 3.4 +0.1 | 89.4+2.1 |
| 55         | 4+0.4  | 98 + 0.03| 4 +0.4 | 94.2+0.3 |
| 60         | 4.00 +0.55| 99.10 + 0.02| 4.00 +0.55| 96.8+0.1 |

# MOAA/S- Modified observer’s assessment of alertness/ sedation scale, SE-spectral entropy, RE- Response entropy

Table 3: SE/RE Entropy and haemodynamics between two groups at different time interval

| Group                  | PROPOFOL | PROPOFOL + FENTANYL |
|------------------------|----------|---------------------|
|                        | Mean±SD  | Mean±SD             | T    | P     |
| SE                     | 76.5±8.8 | 57.2±9.8            | 10.3 | 0.0001|
| RE                     | 72.8±9.8 | 47.5±9.8            | 12.8 | 0.0001|
| MAP                    | 80.1±7.8 | 73±5.3              | 5.2  | 0.0001|
| HR                     | 88±9.06  | 67.9±9.3            | 10.8 | 0.0001|
| SPO2                   | 98.4±0.6 | 98.5±0.6            | -1.11| 0.267 |
| ETCO2                  | 36.6±3.5 | 36.5±4.4            | 0.1  | 0.92  |
| RR                     | 12.9±0.7 | 12.8±0.6            | 0.742| 0.46  |

# MAP-mean arterial Pressure, HR-Heart rate, ETCO2-End tidal carbon dioxide, RR-respiratory rate, SE-spectral entropy, RE- Response entropy

Discussion

Monitoring the level of sedation in a spontaneously breathing patient undergoing surgery is an important determinant for safety of the patient. In addition this allows the anaesthesiologist to adjust the drug doses for sufficient sedation, during procedure under monitored anaesthesia care (MAC).This is largely required because during intraoperative sedation, anaesthesia should be followed more closely during spontaneous breathing as insufficient sedation may cause patient to move, where as deep sedation may lead to respiratory depression. We determined entropy (RE and SE) at equivalent sedation scores in both P and PF group. Entropy decreased
proportionately at increased sedation level, thereby enabling the anaesthesiologist to titrate the sedation accordingly. In the measurement of entropy, a single sensor receives signals and this provides for relatively easy utilization. The EEG signal is converted to two sets of numerical data, SE and RE. The lower frequency of EEG band is used to derive the SE value and reflow control activity. Since SE is resistant to the abrupt reaction of facial muscles and is therefore acceptable as an index of the effects of hypnotics on the brain during general anaesthesia. On the other hand, RE index is used as an indicator of analgesia. The SE and RE value in P group is 76.56 + 8.85 and 72.80 + 9.86 respectively. The SE and RE value in PF group is 57.26 + 9.84 and 47.52 + 9.80 respectively. The infusion of Propofol and Fentanyl administration in the present study was adjusted by the same anesthesiologist or the resident working with him and conversant with the protocol, in response to clinical signs and VRS scores. It has been noted that entropy decreased proportionately with increased level of sedation and more so in case of PF group. On the other hand it increased proportionately in the recovery period in both the groups but more rapidly in case P group. This rapid decrease and increase of entropy with increasing or decreasing level of sedation indicated it to be a more sensitive indicator of the level of hypnosis. There have been some studies comparing BIS and entropy as an indicator of hypnosis. But all of them have corroborated (except study by Soto et al where only one patient was studied) that BIS decreases or increases more slowly than Entropy, thereby indicating Entropy as a more sensitive indicator of hypnosis.

Schmidt at al compared the monitoring of entropy and BIS during propofol and remifentanil anaesthesia and reported that both could be used to follow the depth of anaesthesia. Ellerkmark at al compared BIS and entropy (RE and SE) during sevoflurane anaesthesia and reported that entropy (RE and SE) may also be used to follow the depth of anaesthesia and that both BIS and entropy decreased with increasing Sevoflurane concentration. Thus they concluded that RE and SE is useful in assessment of the effects of sevoflurane. Anderson et al studied entropy at different levels of alertness during propofol hypnosis and concluded that monitoring entropy would be appropriate in grading clinical hypnotic effects. The present study showed that entropy corresponded to the level of sedation and based on this, we propose that entropy may be used to monitor the hypnotic level induced by sedation agents. In the present study, propofol infusion was suspended at the end of surgical procedure. The effects of short acting propofol and fentanyl were followed in the recovery room and it was found that entropy increased proportionately with decreased level of sedation.

**Conclusion**

Hence it is concluded that in assessing the level of hypnosis during intra-operative sedation in MAC, entropy corresponds to MOAA/S and increases or decreases proportionately depending upon increase or decrease in level of sedation. Hence from these results it is proposed that monitoring entropy is a reliable monitoring index of anaesthesia depth in MAC.

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