

Evaluation of Benefits of Monitoring Entropy while using Isoflurane in General Anaesthesia and Recovery from Anaesthesia

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Abstract:

Introduction: Maintaining adequate anaesthetic depth is essential for preventing excessive anaesthetic exposure and delayed recovery. Conventional clinical indicators may inadequately reflect hypnosis. Entropy monitoring provides continuous assessment of cerebral electrical activity and may facilitate individualized isoflurane titration, reduce anaesthetic consumption and improve postoperative recovery.

Aim: To compare entropy-guided and conventional clinically guided isoflurane anaesthesia regarding recovery characteristics, anaesthetic consumption, postoperative recovery scores, adverse events, and intraoperative recall.

Methods: This prospective, quasi-experimental study was conducted over 18 months at a tertiary care teaching hospital. Consecutive sampling recruited 150 patients aged 18–65 years, with American Society of Anesthesiologists physical status I–II, undergoing elective general surgery or otorhinolaryngological procedures. Patients were allocated to entropy monitoring (Group E) or conventional clinical monitoring (Group C), with 75 participants each. Anaesthesia was induced using propofol and vecuronium and maintained with isoflurane in oxygen and air. Isoflurane was titrated to maintain response entropy between 40 and 60 in Group E; Group C received titration according to clinical parameters and minimum alveolar concentration targets. A blinded observer recorded recovery outcomes following anaesthetic discontinuation. Anaesthetic consumption, modified Aldrete scores, postoperative adverse events, and recall on the first postoperative day were assessed. Statistical significance was defined as $p < 0.05$.

Results: Compared with Group C, Group E demonstrated significantly shorter times to eye opening (6.2 ± 2.1 versus 8.7 ± 2.8 minutes), obeying verbal commands (7.4 ± 2.3 versus 10.1 ± 3.0 minutes), extubation (8.9 ± 2.5 versus 11.8 ± 3.1 minutes), orientation (12.8 ± 4.2 versus 16.5 ± 5.1 minutes), and readiness for post-anaesthesia care unit discharge (38.6 ± 9.8 versus 47.4 ± 12.5 minutes); all $p < 0.001$. Total isoflurane consumption (13.9 ± 3.8 versus 17.2 ± 4.5 mL), hourly consumption (9.7 ± 2.4 versus 11.8 ± 2.9 mL/hour), and mean end-tidal concentration ($0.86 \pm 0.16\%$ versus $1.03 \pm 0.19\%$) were significantly lower with entropy monitoring (all $p < 0.001$). Modified Aldrete scores were significantly higher at all assessed intervals. Discharge delayed beyond 60 minutes occurred less frequently in Group E (5.3% versus 17.3%; $p = 0.020$). Postoperative nausea, vomiting, shivering, respiratory depression, and rescue analgesia requirements did not differ significantly. Definite recall occurred in no Group E patients and 1.3% of Group C; recall differences were not statistically significant.

Conclusion: Entropy-guided isoflurane anaesthesia was associated with reduced anaesthetic consumption, faster emergence, and improved early postoperative recovery compared with conventional monitoring. A reduction in intraoperative awareness was not established. Entropy monitoring may serve as an adjunct to routine clinical assessment; larger randomized studies are needed to confirm these findings and establish their applicability across broader surgical populations.

Keywords: Entropy Monitoring; Isoflurane; General Anaesthesia; Postoperative Recovery; Intraoperative Awareness.

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Introduction

General anaesthesia is an essential component of modern surgical practice. It produces a reversible

state of unconsciousness, amnesia, analgesia, and immobility, allowing surgical procedures to be

performed safely and comfortably. One of the primary responsibilities of the anaesthesiologist is to maintain an adequate depth of anaesthesia throughout surgery. Both inadequate and excessive anaesthesia can have adverse consequences. While inadequate anaesthesia may result in awareness and stress responses during surgery, excessive anaesthesia may lead to haemodynamic instability, delayed recovery, and prolonged hospital stay. [1,2]

Although uncommon, intraoperative awareness remains a matter of concern in anaesthetic practice. Patients who experience awareness under anaesthesia may later develop anxiety, sleep disturbances, or even post-traumatic stress disorder. For many years, anaesthesiologists have relied on clinical signs such as heart rate, blood pressure, lacrimation, sweating, and patient movement to judge the depth of anaesthesia. However, these indicators are indirect and may not always accurately reflect the patient's level of consciousness. Their usefulness becomes even more limited when neuromuscular blocking agents are used, as patient movement is abolished and autonomic responses can be influenced by several factors unrelated to anaesthetic depth. [3]

Advances in monitoring technology have led to the development of electroencephalogram (EEG)-based methods for assessing brain activity during anaesthesia. These techniques provide a more objective assessment of the hypnotic component of anaesthesia than traditional clinical signs. Among them, entropy monitoring has gained increasing attention because it offers continuous information about the patient's cerebral state during surgery. [4]

Entropy is a mathematical measure of the irregularity and complexity of EEG signals. During wakefulness, brain activity is relatively complex and irregular, resulting in higher entropy values. As the depth of anaesthesia increases, EEG activity becomes more organized and predictable, leading to lower entropy values. [5,6]

The entropy monitor provides two parameters: State Entropy (SE) and Response Entropy (RE). State Entropy mainly reflects cortical EEG activity and is considered an indicator of the hypnotic state of the patient. Response Entropy includes both EEG and frontal electromyographic activity and therefore responds more rapidly to external stimulation. In routine clinical practice, maintaining entropy values between 40 and 60 is generally considered appropriate for surgical anaesthesia. [7]

In recent years, several studies have reported favourable outcomes with entropy guided anaesthesia. By providing real-time information regarding anaesthetic depth, entropy monitoring allows more precise titration of anaesthetic agents and helps avoid unnecessarily deep levels of

anaesthesia. A recent meta-analysis reported improved postoperative recovery and reduced anaesthetic consumption in patients managed with entropy-guided anaesthesia. [8] Other studies have shown reductions in volatile anaesthetic requirements as well as shorter times to awakening and extubation when entropy monitoring is used. [9,10]

Isoflurane continues to be widely used for maintenance of general anaesthesia, particularly in many teaching hospitals and resource-limited settings because of its affordability and availability. However, achieving the correct balance between adequate anaesthesia and rapid recovery can sometimes be challenging with isoflurane. Excessive administration may prolong emergence from anaesthesia and delay recovery, whereas inadequate administration may increase the risk of awareness and haemodynamic responses to surgical stimulation. [11]

Entropy-guided administration of isoflurane may help overcome these challenges. By allowing anaesthetic delivery to be adjusted according to the patient's brain activity rather than relying solely on clinical signs, entropy monitoring may reduce unnecessary anaesthetic exposure while maintaining adequate depth of anaesthesia. Previous studies have demonstrated lower isoflurane consumption, better haemodynamic stability, faster eye opening, earlier extubation, and shorter recovery room stay in patients managed using entropy monitoring. [12]

Another useful feature of entropy monitoring is its ability to detect responses to surgical stimulation. Changes in Response Entropy may indicate inadequate analgesia before significant haemodynamic changes become evident, enabling timely intervention by the anaesthesiologist. This may contribute to smoother intraoperative management and improved patient recovery. [13]

Despite these potential advantages, entropy monitoring is not routinely used in all centres. Factors such as equipment cost, limited availability, and varying institutional practices continue to influence its adoption. In addition, although a number of studies have evaluated entropy-guided anaesthesia, data specifically focusing on Isoflurane based anaesthesia remain relatively limited.

Therefore, the present study was undertaken to evaluate the role of entropy monitoring during isoflurane anaesthesia. The study aims to assess its effect on anaesthetic consumption, recovery characteristics, and intraoperative awareness. The findings may help determine whether entropy-guided anaesthesia offers meaningful clinical benefits over conventional monitoring in patients undergoing surgery under general anaesthesia.

Material and Methods

The present study prospective, quasi-experimental was conducted to evaluate the benefits of entropy monitoring during Isoflurane based general anaesthesia in comparison with conventional clinical monitoring by the department of Anaesthesiology at a tertiary care teaching hospital for a duration of 18 months. The study population comprised patients from the Surgery and ENT departments who were scheduled to undergo elective procedures under general anaesthesia. The sample size was calculated using standard statistical formulae based on expected mean differences between groups. The calculated minimum sample size was 75 patients per group, resulting in a total sample size of 150 patients. Patients were recruited using a consecutive sampling technique, and were allocated into two groups.

The enrolled patients were divided into two groups:

i) Group E (Entropy Group): Patients in whom anaesthesia was guided using entropy monitoring and ii) Group C (Clinical Practice Group): Patients in whom anaesthesia was guided using conventional clinical parameters.

Inclusion Criteria: Patients were included in the study if they met the following criteria: age between 18 and 65 years, patients undergoing elective surgery under general anaesthesia and patients belonging to American Society of Anesthesiologists (ASA) Class I and II.

Exclusion Criteria: Patients were excluded if they had: Age <18 years or >65 years, ASA Class III and IV, history of psychiatric illness or use of antipsychotic medications, pregnant patient, undergoing intracranial surgery, known allergy to inhalational anaesthetic agents, refusal to participate in the study.

Preoperative Assessment: All patients underwent a detailed pre-anaesthetic evaluation, including history, physical examination, and relevant investigations. Written informed consent was obtained prior to enrolment.

Anaesthetic Technique: Upon arrival in the operating room, standard monitors including electrocardiography (ECG), non-invasive blood pressure (NIBP), and pulse oximetry (SpO₂) were attached. In patients allocated to the entropy group, the forehead skin was cleaned with alcohol swab, and a self-adhesive EEG electrode strip was applied for entropy monitoring.

Induction of Anaesthesia: All patients were induced with: Propofol (1.5–2 mg/kg) and Vecuronium (0.1 mg/kg) for neuromuscular blockade. Following

induction, patients were ventilated with 2% isoflurane in 6 L/min oxygen.

Maintenance of Anaesthesia: Anaesthesia was maintained using a mixture of oxygen and air in a 1:1 ratio along with isoflurane. In Group E (Entropy Group): Isoflurane concentration was titrated to maintain response entropy (RE) between 40–60, and the anaesthesiologist was blinded to MAC values. And, in Group C (Clinical Group): Isoflurane was titrated based on clinical parameters such as heart rate and blood pressure, maintaining MAC between 1.0–1.3, with a minimum of 0.6 even in hemodynamically unstable patients. Anaesthesia was continued until closure of the surgical incision in both groups.

Reversal and Extubation: Neuromuscular blockade was reversed using: Neostigmine (50 µg/kg) and Glycopyrrolate (10 µg/kg). Patients were extubated after fulfilling standard extubation criteria.

Outcome Assessment: From the time of discontinuation of inhalational anaesthesia, the following parameters were recorded by a blinded observer:

Primary Outcome Measures: Time to eye opening on verbal command, time to extubation, time to readiness for discharge from PACU.

Secondary Outcome Measures: Total isoflurane consumption during surgery, postoperative recall of intraoperative events (assessed on the following day) and incidence of dreams or nightmares.

Postoperative Monitoring: All patients were transferred to the Post Anaesthesia Care Unit (PACU), where: Oxygen was administered at 2 L/min via face mask, pain was assessed using a Visual Analog Scale (VAS), sedation was assessed using a 4-point sedation scale at: o Admission o 30 minutes o 1 hour o 2 hours postoperatively. Patients were interviewed on the first postoperative day for recall of intraoperative events.

Statistical Analysis: The collected data were entered into Microsoft Excel and analyzed using GraphPad Prism version 5. Quantitative data were expressed as mean ± standard deviation, non-normally distributed data were expressed as median and interquartile range and qualitative data were expressed as frequency and percentage.

Statistical Tests Used- Z-test for comparison of hemodynamic variables and Mann–Whitney U test for non-parametric data. A p-value < 0.05 was considered statistically significant.

Results

Table 1: Comparison of total intraoperative isoflurane consumption between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

Anaesthetic-use variable	Group E, n=75	Group C, n=75	Difference	p-value
Total Isoflurane consumption, mL	13.9 +/- 3.8	17.2 +/- 4.5	3.3 mL lower in Group E	<0.001

Table 1 presents the comparison of total intraoperative isoflurane consumption between the entropy-monitored group and the conventional clinical monitoring group. The total isoflurane

consumption was 13.9 ± 3.8 mL in Group E and 17.2 ± 4.5 mL in Group C. The table presents a difference of 3.3 mL between the two groups and provides the corresponding p-value.

Table 2: Comparison of hourly isoflurane consumption during maintenance of anaesthesia between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

Anaesthetic-use variable	Group E, n=75	Group C, n=75	Difference	P - value
Isoflurane consumption, mL/hour	9.7 +/- 2.4	11.8 +/- 2.9	2.1 mL/hour lower in Group E	<0.001

Table 2 presents the comparison of hourly isoflurane consumption during maintenance of anaesthesia between the entropy-monitored group and the conventional clinical monitoring group. The hourly

isoflurane consumption was 9.7 ± 2.4 mL/hour in Group E and 11.8 ± 2.9 mL/hour in Group C. The table shows a difference of 2.1 mL/hour between the two groups and includes the corresponding p-value.

Table 3: Comparison of mean end-tidal isoflurane concentration during maintenance of anaesthesia between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

Anaesthetic-use variable	Group E, n=75	Group C, n=75	Difference	pvalue
Mean end-tidal isoflurane, %	0.86 +/- 0.16	1.03 +/- 0.19	0.17% lower in Group E	<0.001

Table 3 presents the comparison of mean end-tidal isoflurane concentration during maintenance of anaesthesia between the entropy-monitored group and the conventional clinical monitoring group. The

mean end-tidal isoflurane concentration was $0.86 \pm 0.16\%$ in Group E and $1.03 \pm 0.19\%$ in Group C. The table reports a difference of 0.17% between the groups and provides the corresponding p-value.

Table 4: Comparison of isoflurane titration events during maintenance of anaesthesia between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

Titration event	Group E, n=75	Group C, n=75	Risk difference	pvalue
Any increase in isoflurane concentration	18 (24.0%)	31 (41.3%)	-17.3%	0.024
Any reduction in isoflurane concentration	39 (52.0%)	21 (28.0%)	+24.0%	0.003
No change after maintenance target achieved	18 (24.0%)	23 (30.7%)	-6.7%	0.366

Table 4 presents the comparison of isoflurane titration events during maintenance of anaesthesia between the entropy-monitored group and the conventional clinical monitoring group. An increase in isoflurane concentration was recorded in 18 participants (24.0%) in Group E and 31 participants (41.3%) in Group C. A reduction in isoflurane

concentration was recorded in 39 participants (52.0%) in Group E and 21 participants (28.0%) in Group C. No change after achieving the maintenance target was recorded in 18 participants (24.0%) in Group E and 23 participants (30.7%) in Group C. The table also provides risk differences and p-values for each titration event.

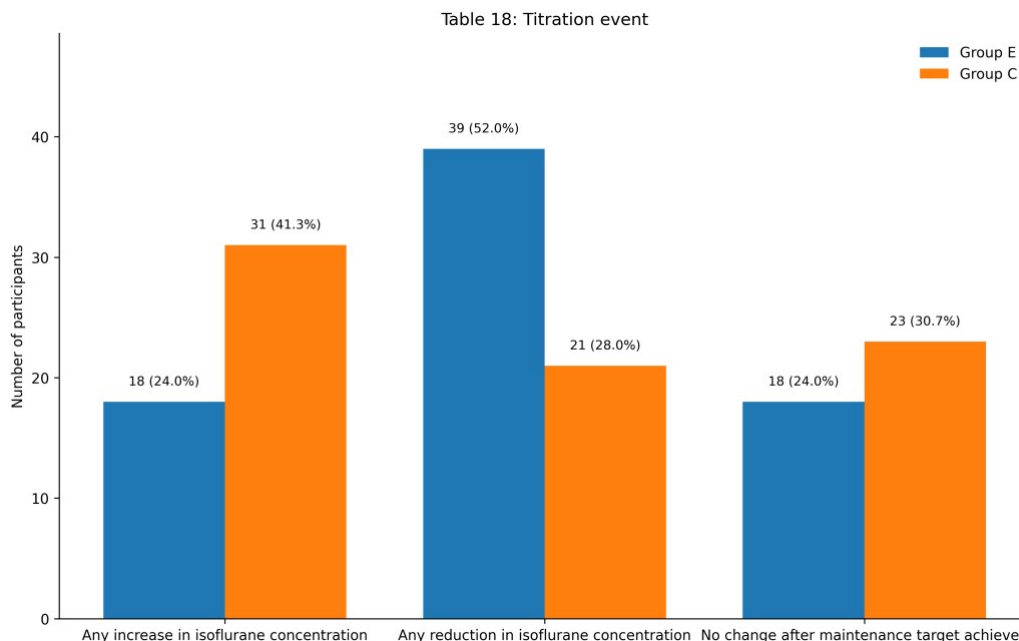


Figure 1: Comparison of isoflurane titration events during maintenance of anaesthesia between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

Table 5: Intraoperative response entropy and state entropy values at predefined time points in the entropy-monitored group (Group E, n=75)

Time point	Response Entropy, mean +/- SD	State Entropy, mean +/- SD	Target interpretation
After induction	42.8 +/- 5.6	39.5 +/- 4.9	Within adequate hypnotic range
15 min after incision	48.6 +/- 6.2	44.1 +/- 5.7	Maintained within RE 40-60
30 min after incision	47.9 +/- 5.8	43.7 +/- 5.4	Maintained within RE 40-60
60 min after incision	49.2 +/- 6.5	45.2 +/- 5.9	Maintained within RE 40-60
At skin closure	55.8 +/- 7.1	51.6 +/- 6.4	Expected lighter plane before emergence

Table 5 presents intraoperative Response Entropy and State Entropy values at predefined time points in the entropy-monitored group. After induction, the mean Response Entropy was 42.8 ± 5.6 and the mean State Entropy was 39.5 ± 4.9 . At 15 minutes after incision, the values were 48.6 ± 6.2 and 44.1 ± 5.7 , respectively. At 30 minutes after incision, the

values were 47.9 ± 5.8 and 43.7 ± 5.4 , while at 60 minutes after incision, the values were 49.2 ± 6.5 and 45.2 ± 5.9 . At skin closure, the Response Entropy was 55.8 ± 7.1 and State Entropy was 51.6 ± 6.4 . The table also provides the target interpretation for each intraoperative time point.

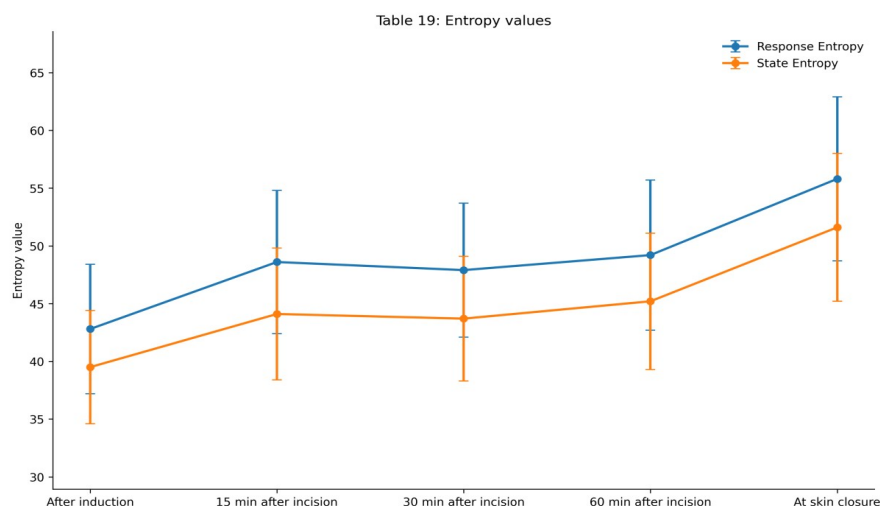


Figure 2: Intraoperative response entropy and state entropy values at predefined time points in the entropy-monitored group (Group E, n=75)

Table 6: Comparison of modified Aldrete scores at predefined post-anaesthesia care unit time points between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

PACU time point	Group E, n=75	Group C, n=75	Mean difference	pvalue
PACU admission	8.1 +/- 0.8	7.5 +/- 0.9	0.6 higher in Group E	<0.001
30 min	9.2 +/- 0.6	8.6 +/- 0.8	0.6 higher in Group E	<0.001
1 hour	9.8 +/- 0.4	9.5 +/- 0.6	0.3 higher in Group E	0.001
2 hours	10.0 +/- 0.2	9.9 +/- 0.3	0.1 higher in Group E	0.018

Table 6 presents the comparison of modified Aldrete scores at predefined post-anaesthesia care unit time points between the entropy-monitored group and the conventional clinical monitoring group. At PACU admission, the modified Aldrete score was 8.1 ± 0.8 in Group E and 7.5 ± 0.9 in Group C. At 30 minutes,

the scores were 9.2 ± 0.6 and 8.6 ± 0.8 , respectively. At 1 hour, the scores were 9.8 ± 0.4 in Group E and 9.5 ± 0.6 in Group C. At 2 hours, the scores were 10.0 ± 0.2 in Group E and 9.9 ± 0.3 in Group C. The table also provides mean differences and p-values at each PACU time point.

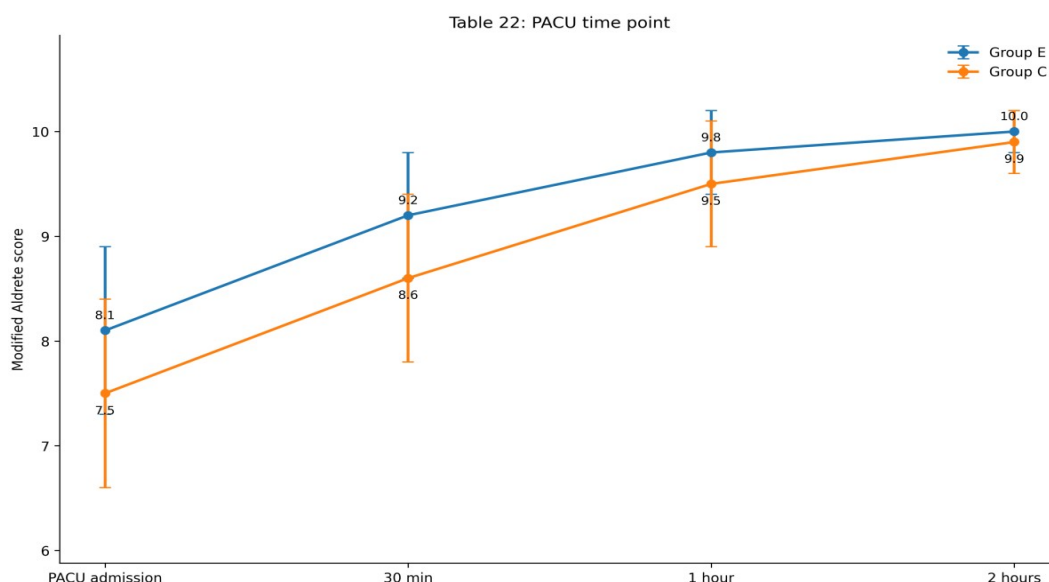


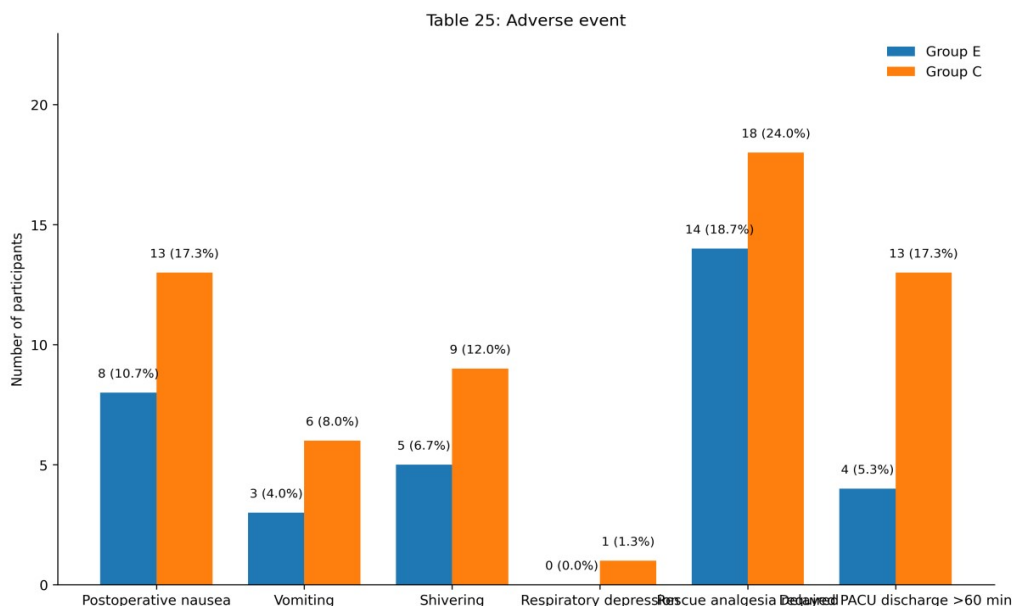
Figure 3: Comparison of modified Aldrete scores at predefined post-anaesthesia care unit time points between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

Table 7: Comparison of post-anaesthesia care unit adverse events between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)

Adverse event	Group E, n=75	Group C, n=75	Total, n=150	pvalue
Postoperative nausea	8 (10.7%)	13 (17.3%)	21 (14.0%)	0.239
Vomiting	3 (4.0%)	6 (8.0%)	9 (6.0%)	0.303
Shivering	5 (6.7%)	9 (12.0%)	14 (9.3%)	0.265
Respiratory depression	0 (0.0%)	1 (1.3%)	1 (0.7%)	0.316
Rescue analgesia required	14 (18.7%)	18 (24.0%)	32 (21.3%)	0.427
Delayed PACU discharge >60 min	4 (5.3%)	13 (17.3%)	17 (11.3%)	0.020

Table 7 presents the comparison of post-anaesthesia care unit adverse events between the entropy-monitored group and the conventional clinical monitoring group. Postoperative nausea was recorded in 8 participants (10.7%) in Group E and 13 participants (17.3%) in Group C. Vomiting was recorded in 3 participants (4.0%) in Group E and 6 participants (8.0%) in Group C. Shivering was recorded in 5 participants (6.7%) in Group E and 9 participants (12.0%) in Group C. Respiratory

depression was recorded in 0 participants (0.0%) in Group E and 1 participant (1.3%) in Group C. Rescue analgesia was required in 14 participants (18.7%) in Group E and 18 participants (24.0%) in Group C. Delayed PACU discharge of more than 60 minutes was recorded in 4 participants (5.3%) in Group E and 13 participants (17.3%) in Group C. The table also provides the total frequency and p-value for each adverse event.

**Figure 4: Comparison of post-anaesthesia care unit adverse events between the entropy-monitored group (Group E, n=75) and the conventional clinical monitoring group (Group C, n=75)**

Discussion

The present prospective quasi-experimental comparative study evaluated the benefits of entropy monitoring during isoflurane-based general anaesthesia, with particular emphasis on recovery profile, isoflurane consumption, intraoperative titration, postoperative recall, and PACU recovery outcomes. The study compared 75 patients managed with entropy-guided anaesthesia with 75 patients managed using conventional clinical monitoring.

The baseline characteristics of the two groups were comparable, which strengthens the internal validity of the study findings. Mean age, sex distribution, BMI, ASA physical status, surgical specialty, procedure-duration categories, duration of surgery,

duration of anaesthesia, and baseline haemodynamic variables did not differ significantly between Group E and Group C.

The most clinically important finding of the present study was the significantly faster recovery observed in the entropy-monitored group. Time to eye opening was 6.2 ± 2.1 minutes in Group E compared with 8.7 ± 2.8 minutes in Group C, showing a mean reduction of 2.5 minutes. Time to obey verbal command was also significantly shorter in Group E, with patients obeying command at 7.4 ± 2.3 minutes compared with 10.1 ± 3.0 minutes in Group C. Similarly, time to extubation was 8.9 ± 2.5 minutes in Group E compared with 11.8 ± 3.1 minutes in Group C, representing a clinically meaningful

reduction of 2.9 minutes. Time to orientation was 12.8 ± 4.2 minutes in Group E compared with 16.5 ± 5.1 minutes in Group C, and readiness for PACU discharge occurred at 38.6 ± 9.8 minutes in Group E compared with 47.4 ± 12.5 minutes in Group C. All these differences were statistically significant with p values <0.001 .

Miller et al. [14] and Eger et al. [15] have described the pharmacological properties of isoflurane that contribute to slower emergence when higher concentrations are administered or when tissue accumulation occurs. Brown et al. [16] also emphasized that recovery after general anaesthesia depends not only on discontinuation of the anaesthetic agent but also on the degree and duration of brain exposure to hypnotic drugs. In the present study, entropy-guided titration likely prevented unnecessarily deep anaesthesia during maintenance, thereby reducing residual hypnotic effects at the end of surgery.

He et al. [8] reported in a meta-analysis that entropy-assisted general anaesthesia improved postoperative recovery quality and reduced recovery-related endpoints. Hassanien et al. [9] similarly observed improved recovery characteristics and reduced isoflurane consumption when entropy monitoring was used. Trivedi et al. [10] also reported that entropy monitoring reduced anaesthetic consumption and shortened recovery parameters. Chen et al. [17] demonstrated improved emergence and recovery with entropy monitoring during sevoflurane anaesthesia, but the pharmacological behaviour of sevoflurane differs from isoflurane. Goyal et al. [18] evaluated entropy monitoring in isoflurane anaesthesia and reported improvements in recovery and extubation parameters, although the effect on total consumption varied.

The reduction in isoflurane consumption in the entropy group was another major finding. Total intraoperative isoflurane consumption was 13.9 ± 3.8 mL in Group E compared with 17.2 ± 4.5 mL in Group C, showing a reduction of 3.3 mL. Hourly consumption was also significantly lower in Group E, at 9.7 ± 2.4 mL/hour compared with 11.8 ± 2.9 mL/hour in Group C. Mean end-tidal isoflurane concentration was $0.86 \pm 0.16\%$ in Group E compared with $1.03 \pm 0.19\%$ in Group C, and mean MAC during maintenance was 0.87 ± 0.13 in Group E compared with 1.06 ± 0.17 in Group C. All these differences were statistically significant. These results indicate that entropy monitoring allowed adequate anaesthesia to be maintained at lower volatile anaesthetic exposure.

Any increase in isoflurane concentration was required in only 24.0% of patients in Group E compared with 41.3% in Group C, whereas reduction in isoflurane concentration occurred in 52.0% of Group E compared with only 28.0% of

Group C. This is consistent with the mechanism described by Viertiö-Oja et al. [19] who explained that entropy monitoring reflects EEG signal irregularity and allows titration of anaesthetic agents according to brain-state changes rather than indirect autonomic variables alone. Chhabra et al. [20] also reported that spectral entropy monitoring may reduce inhalational agent use compared with standard monitoring, although the magnitude of reduction varies between studies.

After induction, mean Response Entropy was 42.8 ± 5.6 and mean State Entropy was 39.5 ± 4.9 , indicating adequate hypnosis. At 15, 30, and 60 minutes after incision, Response Entropy remained between 47.9 and 49.2, while State Entropy remained between 43.7 and 45.2. At skin closure, Response Entropy increased to 55.8 ± 7.1 and State Entropy to 51.6 ± 6.4 , reflecting a lighter but still acceptable plane of anaesthesia before emergence. This controlled transition likely contributed to earlier eye opening, command response, extubation, and orientation in Group E.

Response Entropy incorporates both EEG and frontal EMG activity, while State Entropy mainly reflects cortical EEG activity. Laferrière-Langlois et al. [1], Roche et al. [2], and Viertiö-Oja et al. [19] have emphasized that objective depth-of-anaesthesia monitoring can help bridge the limitations of conventional clinical signs. Conventional signs such as heart rate and blood pressure are influenced by pain, hypovolaemia, medications, autonomic tone, and surgical stimulation, and they may not reliably indicate cortical consciousness. Avidan et al. [21] similarly highlighted that processed EEG monitoring should be used as an adjunct because clinical signs alone may fail to detect inadequate or excessive hypnotic depth, especially in patients receiving neuromuscular blocking agents. In the present study, all patients received vecuronium, making movement an unreliable indicator of anaesthetic adequacy.

The postoperative recall findings require careful interpretation. No recall was reported in 98.7% of Group E and 94.7% of Group C. Possible recall or vague auditory memory was reported in 1.3% of Group E compared with 4.0% of Group C, while definite recall occurred in 0% of Group E and 1.3% of Group C. Although the numerical trend favoured entropy monitoring, the differences were not statistically significant. Mashour et al. [22] and Avidan et al. [21] have noted that very large sample sizes are required to demonstrate statistically significant reductions in awareness because the baseline incidence is low.

The dream and nightmare outcomes also showed a favourable but statistically non-significant trend in the entropy group. No dream or nightmare was reported in 96.0% of Group E compared with 89.3%

of Group C. Pleasant or neutral dreams occurred in 4.0% of Group E and 8.0% of Group C, while nightmares occurred in 0% of Group E compared with 2.7% of Group C. Therefore, while the numerical trend is reassuring, these outcomes should be interpreted as secondary exploratory findings rather than definitive evidence of awareness prevention.

Modified Aldrete scores were significantly higher in Group E at PACU admission, 30 minutes, 1 hour, and 2 hours. At PACU admission, the score was 8.1 ± 0.8 in Group E compared with 7.5 ± 0.9 in Group C, and at 30 minutes it was 9.2 ± 0.6 compared with 8.6 ± 0.8 . Although both groups approached near-complete recovery by 2 hours, the entropy group achieved better early recovery. He et al. [8] reported that entropy-guided anaesthesia improves recovery endpoints, while Wu et al. [7] and Lipp et al. [11] similarly emphasized the role of EEG-based monitoring in improving recovery profiles.

Postoperative sedation scores were significantly lower in the entropy group at all PACU time points. At PACU admission, sedation score was 2.1 ± 0.6 in Group E compared with 2.5 ± 0.7 in Group C, and at 30 minutes it was 1.5 ± 0.5 compared with 1.9 ± 0.6 . Lower sedation in the entropy group is consistent with reduced isoflurane exposure and faster elimination of hypnotic effect. Brown et al. [16] described anaesthesia as a brain-state intervention in which excessive drug exposure may delay return of cognition and responsiveness.

Postoperative pain scores were slightly lower in the entropy group at all PACU time points, but the differences were not statistically significant. VAS scores at PACU admission were 3.1 ± 1.2 in Group E and 3.3 ± 1.3 in Group C, and at 2 hours were 1.6 ± 0.8 and 1.8 ± 0.9 , respectively. Ajayan et al. [23] showed that entropy indices may respond to noxious stimuli such as laryngoscopy, intubation, and surgical stimulation, but Avidan et al. [21] cautioned that processed EEG indices cannot independently quantify analgesic adequacy. Rather, it reinforces that entropy monitoring should be viewed mainly as a hypnotic-depth and titration tool, while postoperative pain control continues to require multimodal analgesic assessment and management.

Autonomic changes during surgery may reflect nociception, fluid status, vasoactive responses, or surgical stimulation rather than inadequate hypnosis. Roche et al. [2], Avidan et al. [21], and Laferrière-Langlois et al. [1] have emphasized that depth of anaesthesia and nociception are related but distinct dimensions of anaesthetic care.

Traditional anaesthetic practice often relies on population-based MAC values, but anaesthetic requirement varies according to age, comorbidities, drug interactions, surgical stimulation, and

individual neurophysiology. Obert et al. [3] and Jin et al. [5] have discussed variability in EEG-based anaesthesia indices and the need for more precise monitoring approaches. Nilsen et al. [6] and Weyer et al. [12] described anaesthetic-induced EEG changes and their relationship with brain complexity. The present study demonstrates that using entropy values as real-time feedback permits titration according to the patient's actual brain response rather than relying only on fixed MAC ranges.

However, entropy monitoring should not be interpreted as a replacement for clinical judgement. Its values may be affected by EMG activity, neuromuscular blockade, artefacts, electrode positioning, age-related EEG differences, and other physiological variables. Ebensperger et al. [24] reported that the reliability of GE Entropy module values may be affected during maintenance anaesthesia, particularly in older patients. Therefore, entropy should be integrated with haemodynamic monitoring, clinical assessment, end-tidal agent concentration, neuromuscular monitoring, and surgical context.

The study was quasi-experimental rather than fully randomized, and although the groups were comparable at baseline, allocation bias cannot be completely excluded. The study included only ASA I and II patients aged 18–65 years, which limits generalizability to elderly, paediatric, high-risk, obstetric, emergency, or critically ill populations. The study was conducted in elective general surgery and ENT procedures, and findings may differ in longer operations or procedures with intense nociceptive stimulation. Postoperative recall was assessed on the first postoperative day, but awareness detection may require structured repeated interviews over several days. The study was also not powered to detect rare events such as definite intraoperative awareness.

Future randomized controlled trials should include larger sample sizes, multicentre designs, standardized analgesic protocols, objective neuromuscular monitoring, cost effectiveness analysis, environmental impact assessment, and longer postoperative cognitive outcomes. Studies in elderly patients, ASA III–IV patients, emergency surgery, and high-risk awareness populations would also help define the broader applicability of entropy monitoring. Additionally, future research should investigate whether combining entropy monitoring with nociception monitoring provides better titration of both hypnotic and analgesic components of anaesthesia.

Entropy monitoring should therefore be considered a useful adjunct in routine isoflurane anaesthesia, particularly where faster recovery, optimized

volatile agent use, and improved perioperative efficiency are desired.

Conclusion:

This study evaluated entropy monitoring during isoflurane-based general anaesthesia compared with conventional clinical monitoring. Entropy monitoring provides continuous assessment of brain activity, enabling more precise titration of anaesthetic depth than indirect parameters such as heart rate and blood pressure. Patients receiving entropy-guided anaesthesia demonstrated significantly earlier eye opening, faster response to verbal commands, shorter extubation time and earlier readiness for post-anaesthesia care unit discharge. Isoflurane consumption was also reduced through individualized administration, avoiding unnecessary anaesthetic exposure while maintaining adequate surgical anaesthesia. Although entropy monitoring provides additional information about hypnotic depth, a reduction in intraoperative awareness was not established. Entropy values can be influenced by muscle activity, age-related EEG changes and neuromuscular blockade; therefore, monitoring should supplement clinical judgement and routine assessment. Overall, entropy-guided isoflurane anaesthesia improved recovery and optimized anaesthetic consumption, supporting its usefulness as an adjunct in perioperative care.

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