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Measurement of Entropy Level in Comparison between Remifentanil and Propofol in Open Heart Surgery

***Dr. Marwa Adel Kareem*[1], *Dr. Samara Awad Kadhim*[1], *Dr. Sarah Dakhil Miri*[1] *and Dr. Marwan AlMashhadani*[2]**

[1]*MBChB, FICA, Anesthesia and intensive care specialist, Medical City, Baghdad, Iraq*

[2]*MBChB, DA, CABA&IC, Medical City, Baghdad, Iraq*

Abstract: **Background:** There is a high rate of awareness during open heart surgery, which causes severe complications that endanger the patient's life and potentially lead posttraumatic stress disorder. Various techniques have been employed to measure the depth of anesthesia and awareness by Entropy (EEG, EMG monitoring) autonomic response (H.R, B.P), Bispectral index (EEG monitoring) skin conductance (change in sweat production), lower esophageal contractility. **Aims:** In our study we try to compare the incidence of awareness by measuring the difference in level of entropy) EEG) in these two groups of anesthetic drugs ,1st group Remifentanil, 2nd group propofol. **Patients and methods:** A randomized prospective comparative clinical trial, of 44 adult patients were undergone open heart surgery,22 of them received Remifentanil, the other 22 patients received propofol both as maintenance of anesthesia. Before induction of anesthesia, we apply three forehead entropy leads to measure the depth of anesthesia in the pre cardiopulmonary bypass period. **Results:** There was significant decrease in awareness (state entropy) in R group, P value 0. 016m.The H. R significantly decrease in P Group P value 0. 046.While there is no significant difference in blood pressure in both groups. **Conclusion:** The use of Remifentanil for maintenance of anesthesia in open heart surgery is more suitable than propofol maintenance because it has shown less awareness and more hemodynamic stability.

Keywords: Awareness, Entropy, Remifentanil, Propofol.

INTRODUCTION

One of the most common concerns expressed by patients who are about to undergo anesthesia is that they will remember intraoperative event, It is the unexpected and explicit recall by patients of events that occurred during anesthesia (Orser, B.A. *et al*., 2008). Awareness with recall after general anesthesia is an infrequent, but well described phenomenon that may result in posttraumatic stress disorder (Sebel, P. S. *et al*., 2004). The use of neuromuscular blocking agents is associated with a higher intraoperative awareness incidence, as well as with implicit memory (Nunes, R. R. *et al*., 2007). Most frequently they remember an auditory perception (voices 66%, noises 17%), the feeling of motor function lost (not being able to breath 48%, sensation of paralysis 17%), pain (38%), feelings of helplessness, anxiety, panic, impending death, or catastrophe (34%). Depending of what part of the operation they remember, the pain can come from intubation, incision or the following surgical procedure (Radovanovic, D. *et al*., 2011). Motor responses and sympathetic activation can indicate light levels of anesthesia. Increased respiratory effort, accessory muscle use, swallowing, grimacing, and extremity motion are signs of insufficient anesthesia. Use of neuromuscular blockade eliminates the information that motor signs can provide regarding anesthetic depth. Sympathetic effects of light anesthesia include hypertension, tachycardia, mydriasis, tearing, and sweating. Such findings are nonspecific; thus, their absence or presence may be unreliable indicators of awareness. Indeed, concomitant medications such as β blockers and sympathetic blockade may diminish changes in heart rate and blood pressure(Duke, J. C. *et al*.,) ,Therefore, a more direct and reliable method of measuring anesthetic drug effects on the brain is highly desirable and has been the object of research for many years. Electro- encephalography (EEG) is an obvious brain monitoring modality because it is non-invasive and continuous. Many anesthetic drugs produce characteristic effects on the EEG, and these have been extensively studied (Andrew, T. *et al*., 2006).

The concept of entropy, originally derived from thermodynamics, has been successfully applied to EEG analysis. Various entropy algorithms have been used in clinical studies, but until now a commercially available monitor exists only for spectral entropy (Bruhn, J. *et al*., 2000).

PATIENTS AND METHODS

a randomized comparable prospective clinical trial in Iraqi center for heart disease started from April 2017 to January 2018, 44 adult patients underwent elective open-heart surgery divided into two groups, group (R) 22 patients were receiving 0.3 mcg/kg/min Remifentanil infusion and Group (P) 22 patients were receiving propofol infusion

***Corresponding Author:** Dr. Marwa Adel Kareem

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50mcg/kg/min both for maintenance of anesthesia after induction and both before starting heart lung machine (HLM) i.e., pre bypass period. Patients in both groups were receiving same induction agent and technique.

Regarding entropy monitoring data were collected for HR, MAP, EEG (State entropy) levels on three occasions first data were recorded immediately after induction, second data were recorded after one hour, third one immediately before (HLM) started (bypass time).

Inclusive Criteria

1. Patients underwent CABG with
2. Cardiopulmonary bypass.
3. Adult group was selected.
4. Randomized sex group.
5. ASA III, IV.

Exclusive Criteria

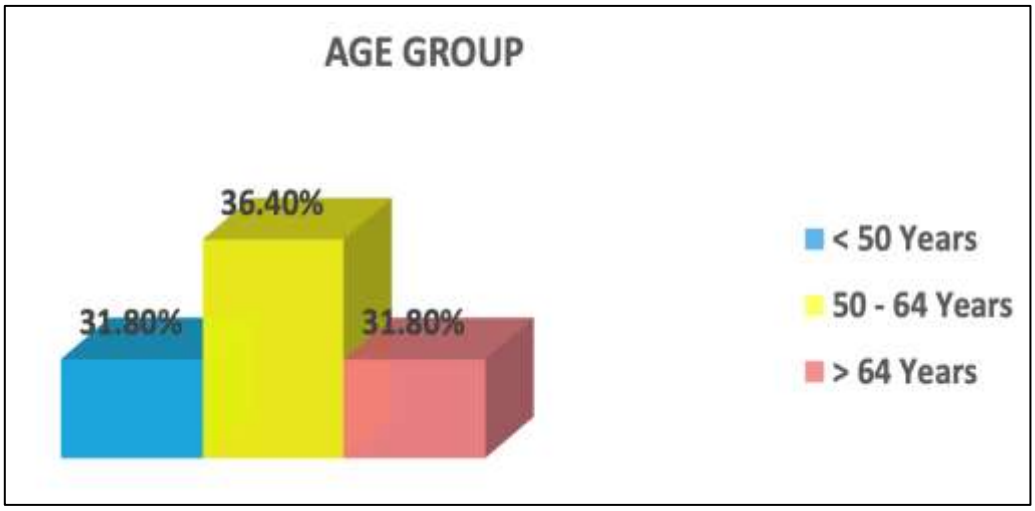
1. Pediatric group.
2. Congenital heart disease.
3. Patients on chronic anti-psychiatric therapy.
4. Patients with history of neurological deficit or head injury.
5. Emergency operation.
6. Pt. On vasoactive agents.
7. When above pt. with some degree of heart block.

Statistical analysis was performed using SPSS windows version 23 software. Suitable tables and graphs were used to describe the data. Student's t test was used for comparison between continuous variables. P value < 0.05 was considered significant.

RESULTS

The distribution of study patients by age and weight is shown in table and figure (3.1). Study patient's age was ranging from 36 to 81 years with a mean of 56.36 years and standard deviation (SD) of ± 12.08 years. The highest proportion of study patients was found in age group 50 – 64 (36.4%).

Regarding weight, it was ranging from 60 to 125 kgs with a mean of 81.86kgs and standard deviation (SD) of ± 14.78kgs.



We noticed that the mean of EEG measure was higher in propofol group of patients than the mean of EEG measure in Remifentanil group of patients after induction, 1st hour pre by pass, and 2nd hour pre by pass.

There was a statistically significant difference (P=0.016) between mean of EEG measures of the two groups in the 2nd hour pre by pass, while the differences were not statistically significant after induction and 1st hour pre by pass.

The highest mean of EEG measure in the two groups was after induction (66.72 in propofol group of patients and 59 in Remifentanil group of patients).

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Mean of EEG measure in study patients groups

Time	SE Entropy (EEG Measure)		P-Value
	Propofol group Mean ± SD	Remifentanil group Mean ± SD	
After induction	66.72 ± 13.73	59.0 ± 20.17	0.145
1st hour pre by pass	49.81 ± 18.48	43.4 ± 14.03	0.216
2nd hour pre by pass	55.18 ± 11.67	45.81 ± 12.96	0.016

The mean of MAP in study patients' groups is shown in table (3.3). The mean of MAP was higher among Remifentanil group of patients than the mean of MAP in propofol group of patients after induction and 2nd hour pre by pass, while the means of MAP were the same in the two groups 1st hour pre by pass, but the differences in means of MAP in the two groups were statistically not significant ($P \geq 0.05$). The highest mean of MAP in Remifentanil group of patients was after induction (89.75), while the highest mean of MAP in propofol group of patients was 1st hour pre by pass (84.81).

Mean of MAP in study patients' groups

Time	Mean Arterial Pressure (MAP)		P-Value
	Propofol group Mean ± SD	Remifentanil group Mean ± SD	
After induction	83.36 ± 16.37	89.75 ± 19.63	0.248
1st hour pre by pass	84.81 ± 20.39	84.18 ± 13.95	0.904
2nd hour pre by pass	77.13 ± 18.22	82.0 ± 13.64	0.322

The mean of heart rate was higher in Remifentanil group of patients than in propofol group of patients after induction, 1st hour pre by pass, and 2nd hour pre by pass.

There was a statistically significant difference (P=0.046) between means of heart rate of the two groups in the 2nd hour pre by pass, while the differences were not statistically significant after induction and 1st hour pre by pass.

The highest mean of heart rate in the two groups was after induction (79 in propofol group of patients and 83 in Remifentanil group of patients).

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Mean of heart rate in study patients' groups

Time	Heart Rate		P-Value
	Propofol group Mean ± SD	Remifentanil group Mean ± SD	
After induction	79 ± 13.01	83 ± 16.76	0.382
1st hour pre by pass	75.05 ± 10.65	78.27 ± 14	0.401
2nd hour pre by pass	71 ± 8.5	78 ± 13.53	0.046

DISCUSSION

Regarding awareness during open heart surgery Serfontein L found in his study the intraoperative awareness during cardiac surgery may be the result of fluctuations in hypnotic state, so that conclude the recognition of high-risk patients, the use of balanced anesthesia techniques and increased attentiveness on the part of the anesthetist will go a long way in preventing intraoperative awareness There is evidence that using processed EEG monitors reduces the incidence of awareness (Serfontein, L. *et al*., 2010).

Inour study we use state entropy and vital signs as indicators for awareness in two groups, group R (Remifentanil) and group P (Propofol), we found that there is significant reduction in EEG with R group & HR with P group after 2hrs of induction, were the EEG P value 0.016, HR 0.046. There are nonsignificant results immediate after induction and after one hour in all parameters in both P group and R group, and there is no significant difference in MAP throughout this period. GunterN. Schmidt, M.D; *et al* found SE entropy change superior to MAP and HR to distinguish between different steps of anesthesia with propofol and Remifentanil during five minutes, SE significance started at fourth minute while MAP and HR significance started from the second minutes (Schmidt, G. N. *et al*., 2004), As we found that Remifentanil significantly decrease the level of awareness which was measured by state entropy, Amorin P, *et al*. found in their study that increase Remifentanil dose decrease EEG(Coste, C. *et al*., 2004), also Ferreira DA, Nunes CS, Antunes LM, *et al*. Show that Remifentanil boluses significantly reduces spectral and response entropy value especially in female (Eur, J. *et al*., 2016). While Munchaster AR, *et al* study shown that EEG decreased paradoxically in six pts. From 21 patients was studied when the Remifentanil concentration decrease(Muncaster, A. R. *et al*., 2003), Guignard, Bruno MD; *et al* in their study show the relationships between Remifentanil effect-site concentrations and Changes in EEG, MAP, and HR ,were negatively correlated with Remifentanil effect-site concentration (Guignard, B. *et al*., 2000)Groesdonk HV, Pietzner J, Borger MA *et al*, when they studied The incidence of awareness during cardiac surgery ,they conclude that, with respect to intraoperative awareness, the use of ultra-short-acting opioid should be considered as a safe method of management of patients undergoing a wide variety of cardiac operations(Groesdonk, H. V̈. *et al*., 2010). Elliott, Peter MD: *et al* study investigates the effect of Remifentanil of various rates of administration on H.R and MAP in patients with coronary artery disease The results show that Remifentanil should be given by slow infusion to such patients because of severe hemodynamic instability i.e. sever hypotension, bradycardia with a reduction in systemic vascular resistance after Remifentanil boluses administration (Elliott, P. *et al*., 2000).

R.E. Anderson, J.G. Jakobsson found During propofol anaesthesia both entropy parameters decreased with increasing sedation,SE 34(17-70) Compared with nitrous oxide when the loss of consciousness with nitrous oxide is not associated with change in entropy indices SE 88 (85_91) (Anderson, J. G. *et al*., 2004), the propofol decrease H.R according to our results that agree

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with Hamzeh Hosseinzadeh, *et al* in their study of Hemodynamic Changes following Anesthesia Induction and LMA Insertion in comparison between Propofol, Etomidate, and Propofol & Etomidate they reported propofol use could be associated with significant decreased blood pressure, bradycardia, and prolonged apnea(Hosseinzadeh, H. *et al*., 2013).

Yağan, Ö. *et al*., in their study to investigate the effect of propofol on hemodynamic response in comparison with etomidate and Etomidate-Propofol Combination in Anaesthesia Induction, they found a significant decrease in MAP values with propofol group (Yağan, Ö. *et al*., 2015). Also, Masoudifar M, Beheshtian E. Their study showed that propofol significantly decrease the systolic, diastolic blood pressure and MAP in comparison with etomidate, while there were no significant differences in terms of H.R in both group (Masoudifar, M. *et al*., 2013).

CONCLUSION

Regarding awareness measured by entropy, we found that Remifentanil group statically significantly in second hour better than propofol in decreasing the awareness in open heart surgery. Negatively affect HR more statically significant with the propofol group than with Remifentanil. Effect on MAP not statically significant in both groups.

RECOMMENDATION

We recommended Remifentanil for maintenance of anesthesia in open heart surgery to decrease the risk of awareness and to maintain hemodynamic stability.

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