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Evaluation of the Effect of BIS Monitoring in Patients Undergoing Renal Transplant.

Debadas Biswal[1], Bidhu Bhusan Mohanty[2], Trishna Sahoo[3], Smruti ranjan Muduli[3]

[1]Asst. Professor, Dept. of anaesthesiology, SCB Medical College, Cuttack.
[2]Associate Professor, Dept of Anaesthesiology, SLN Medical College, Koraput.
[3]PG student, Dept of Anaesthesiology, SCB Medical College, Cuttack.

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ABSTRACT

Background: Awareness during general anaesthesia can lead to anxiety, irritability, sleep disturbances and many more. Bispectral index monitored administration of general anaesthesia help in maintenance of proper plane of anaesthesia, faster wake up or recovery, more cost effective use of drugs and fewer unwanted intraoperative responses. **Methods:** Thirty adult patients of age 20 to 65 years scheduled for renal transplant were divided into two groups of fifteen each. Patient in Group I (Haemodynamic group) anaesthesia was maintained based upon haemodynamic variables. Patients in Group II (BIS group) anaesthesia was maintained by monitoring BIS value of 40-60. **Results:** In the BIS group BIS values were within acceptable (40-60) range, except two values that were high, because anaesthesia was titrated to maintain the normal BIS values for surgery. Whereas in Haemodynamic group BIS values were high on many occasions. No patients developed awareness in our study group. In our study intraoperative haemodynamic variability is less with BIS group. Hypertension developed in 4 patients in haemodynamic group and tachycardia in 5 patients. In BIS group none developed hypertension and 1 patient developed tachycardia. Similarly, 6 patients developed bradycardia and hypertension in haemodynamic group but only 1 patient had hypotension in BIS group. The time to eye opening was prolonged in the haemodynamic group (BIS group 14.3 ± 3.18 minutes and Haemodynamic group 17.9 ± 3.76 minutes). **Conclusion**: It demonstrates that anaesthesia was maintained at a deeper level in haemodynamic group resulting in delay in recovery.

Keywords: Awareness, BIS monitoring, Renal transplant.

INTRODUCTION

Awareness during general anaesthesia is the undesired, unanticipated patient wakefulness during surgery or recall afterward. Patient may present with anxiety, irritability, nightmares, sleep disturbances, panic and depression post-traumatic stress syndrome. Clinical signs of somatic or autonomic responsiveness have always been the mainstay of anaesthetic depth monitoring, but they lack proven utility in detecting awareness. Recently, sophisticated pattern recognition systems that assess multiple features of EEG have been developed, one such monitor is bispectral index (BIS). The BIS index is obtained by performing a multivariate analysis of the EEG and is the weighted sum of different sub-parameters such as a special frequency measure (β-ratio), a bispectral measure (Synch Fast Slow) and a measure of burst suppression (QUAZI), combined in a non-linear fashion. The advantage being maintenance of proper plane of anaesthesia, faster wake up or recovery, more cost effective use of drugs and fewer unwanted intraoperative responses. In Renal Transplant there is chance of awareness during anaesthesia as the anaesthetic drugs administered in renal transplant surgery are titrated according to effect-site concentration and half-life, there is an increased chance of haemodynamic perturbations, metabolic derangements and late recovery. This study is being conducted to monitor depth of anaesthesia by bispectral index in patients undergoing renal transplant.

Name & Address of Corresponding Author
Dr Debadas Biswal,
Asst. Professor,
Dept of Anaesthesiology,
SCB Medical college, cuttack-7

MATERIALS AND METHODS

Thirty adult patients of age 20 to 65 years scheduled for renal transplant were taken in randomised single blind manner. They were divided into two groups of fifteen each. Patient in Group I (Haemodynamic group) anaesthesia was maintained based upon haemodynamic variables. Patients in Group II (BIS group) anaesthesia was maintained by monitoring BIS value of 40-60. Exclusion Criteria- patients

having any neurological impairment like head injury, stroke, psychiatric disease, epilepsy, hepatic failure, patients receiving long term opioids, alcohol abuse.

All patients were pre-medicated with oral diazepam 0.1mg/kg night before surgery and were instructed to remain fasting from midnight. An epidural catheter was inserted in the upper lumbar region. Patients were premedicated with inj. glycopyrolate 0.2mg, nalbuphine 20mg and midazolam 0.05mg/kg. Anaesthesia was induced with propofol 2.5mg/kg and muscle relaxation was achieved with atracurium 0.5mg/kg. The trachea was intubated with appropriately sized cuffed endotracheal tube. Arterial canulation and central venous canulation were performed after intubation. Anaesthesia was maintained with oxygen, nitrous oxide, isoflurane, atracurium and incremental nalbuphine.

In group I patients the isoflurane concentration was adjusted to maintain the MAP and HR within 20% of the pre-operative baseline. Other signs of inadequate anaesthesia were noted (sweating, lacrimation etc.) and isoflurane concentration adjusted accordingly. The anaesthesiologist was blinded to the BIS readings.

In group II patients the isoflurane concentration was adjusted to maintain a BIS value of 40-60. BIS monitoring was continuously available to the anaesthesiologist administering anaesthesia.

Volume replacement was done with crystalloids adequately throughout the surgery after appropriate calculation of requirements. At the end of surgery residual neuromuscular paralysis was reversed with neostigmine 50 µg/kg and glycopyrolate 10 µg/kg. Intraoperative monitoring were heart rate, non-invasive blood pressure (MAP), invasive blood pressure, bispectral index, $ETCO_2$, dial setting concentration of isoflurane, temperature, urine output, CVP, neuromuscular monitoring.

Along with the haemodynamic variables the BIS values were recorded before induction, after induction, during surgery every 15min and at the end of surgery. The eye opening time was recorded in all patients after the surgery which was defined as the time interval from switching off the anaesthetic vaporiser till the patient opened his or her eyes and obeyed verbal commands. All the patients were interviewed on the first and third post-operative day to determine occurrence of awareness. Post-operative analgesia was maintained with intermittent boluses of epidural 10ml ropivacaine 0.2% with butorphanol 0.5mg.

To assess awareness the patients were interviewed with the following questions on first and third post-operative day.

1. What was the last thing you remembered happening before you went to sleep?
2. What is the first thing you remember after your operation?
3. Can you remember anything in between?
4. Can you remember if you had any dreams during your operation?
   What was the worst thing about your operation?

RESULTS

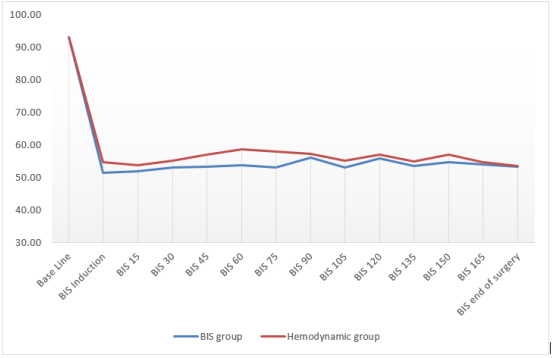
Table 1: Baseline characteristics of study participants

Variables	BIS group (Mean ± SD)	Hemodynamic group (Mean ± SD)	P value
Age	42.73 ± 9.95	41.27 ± 7.25	0.648
Weight	59.33 ± 11.26	60.13 ± 13.79	0.863
Duration of surgery	185.73 ± 17.42	190.87 ± 18.85	0.445

Fifteen patients were enrolled in the study in each group. Patient characteristics distribution in each group is shown in [Table 1]. There was no significant difference between the two groups.

Table 2: Comparison of BIS values among the groups at different time

BIS values in different time of Surgery	BIS group (Mean ± SD)	Hemodynamic group (Mean ± SD)	P value
Baseline	93.06 ± 4.10	92.92 ± 3.45	0.919
At induction	51.39 ± 6.25	54.71±3.88	0.092
15 mins	51.93± 3.26	53.67± 3.17	0.152
30 mins	52.93 ± 2.31	55.20±2.65	0.019
45 mins	53.27± 6.23	57.00±2.47	0.041
60 mins	53.67 ± 4.38	58.67±5.43	0.010
75 mins	53.00± 3.33	58.00±3.22	<0.001
90 mins	56.07±3.01	57.13± 4.24	0.434
105 mins	53.00± 3.54	55.13± 3.11	0.091
120 mins	55.80± 2.65	57.00±3.68	0.315
135 mins	53.53± 2.82	55.00±3.44	0.213
150 mins	54.60± 3.46	57.00± 4.08	0.094
165 mins	53.93± 3.43	54.60± 5.36	0.688
At the end of surgery	53.33± 3.79	53.53± 4.17	0.892



The mean BIS values were comparable between the two groups except at four occasions where there was significant difference between the two.

Interview was done on the first and third post-operative day and none of the patients developed awareness in both groups.

Table 3: Incidence of awareness in different group

Group	BIS Group	Hemodynamic group
First postoperative day Present Absent	0 15	0 15
Third postoperative day Present Absent	0 15	0 15

Heart rate and Blood pressure

In haemodynamic group six patients developed hypotension and bradycardia but only one patient developed hypotension in the BIS group and none developed bradycardia in BIS group. This is both clinically as well as statistically significant.

Table 4: Incidence of Hypertension in different group.

Hypertension	BIS Group N (%)	Hemodynamic group N (%)	Total N (%)	P value
Yes	0 (0)	4 (26.67)	5 (16.67)	0.099
No	15 (100)	11 (76.66)	25 (73.33)	

Table 5: Incidence of Hypotension in different group.

Hypotension	BIS Group N (%)	Hemodynamic group N (%)	Total N (%)	P value
Yes	1 (6.67)	6 (40.0)	7 (23.34)	0.031
No	14 (93.33)	9 (60.0)	23(76.66)	

Table 6: Incidence of tachycardia in different group.

Tachycardia	BIS Group N (%)	Hemodynamic group N (%)	Total N (%)	P value
Yes	1 (6.7)	5 (40.0)	6 (20.00)	0.168
No	14 (93.3)	10 (60.0)	24(80.00)	

Table 6: Incidence of bradycardia in different group.

Bradycardia	BIS Group N (%)	Hemodynamic group N (%)	Total N (%)	P value
Yes	0 (0)	6 (40.0)	6 (20.0)	0.017
No	15 (100)	9 (60.0)	24(80.0)	

BIS values correlated with the haemodynamic variability. In the BIS group none of the patients developed hypertension, one developed tachycardia whereas in haemodynamic group four patients developed hypertension and five developed tachycardia. This was clinically significant but not of statistical significance.

Eye opening time and extubation time

There was significant difference in the time to reach the defined recovery end point or the time to tracheal extubation between the two groups. Eye opening time was 14.34±3.18 and 17.95±3.76 minutes in BIS and Haemodynamic groups respectively (p value < 0.05). Time to tracheal extubation was 15.45±4.09 and 20.41±5.96 minutes in BIS and Haemodynamic groups respectively. Eye opening times and extubation times are given in [Table 7 & 8].

The MAC values and the end tidal isoflurane concentration, amount of isoflurane used were high in the Haemodynamic group. This is statistically significant.

Table 7: Comparison of eye opening time between two groups.

Groups	Mean	Standard deviation	P value
BIS group	14.34	3.18	**0.008**
Hemodynamic group	17.95	3.76	

Table 8: Comparison of extubation time between two groups.

Groups	Mean	Standard deviation	P value
BIS group	15.45	4.09	**0.013**
Hemodynamic group	20.41	5.96	

Table 9: Comparison of MAC between two groups.

Groups	Mean	Standard deviation	P value
BIS group	0.665	0.192	0.005
Hemodynamic group	0.836	0.105	

Table 10: Comparison of end tidal isoflurane between two groups.

Groups	Mean	Standard deviation	P value
BIS group	0.603	0.129	0.003
Hemodynamic group	0.787	0.180	

DISCUSSION

During renal transplant there is a need to titrate anaesthetic drugs according to duration of action to achieve stable haemodynamics, adequate urine output. With unclamping of vessels there may occur a surge in catecholamine levels leading to awareness during anaesthesia. Intraoperative awareness can be a horrifying experience resulting in psychological trauma. There are no studies to assess the depth of anaesthesia during renal transplant. The main aim of anaesthetic depth monitoring is to tailor the amounts of anaesthetic to the needs of the individual patient, thus avoiding either unnecessary deep anaesthesia or awareness. Clinical signs of somatic or autonomic responsiveness have always been the mainstay of anaesthetic depth monitoring, but they lack proven utility. Ideally, the safe approach would be to titrate the drugs according to their presumed effect-site concentrations or any measure that reflects this effect. In clinical practice it would be easier to rely upon a monitor that reflects effect-site changes produced by drugs rather than on complex mathematics involved in calculating effect-site concentrations. Differences in drug sensitivity between individuals can also occur despite identical effect-site concentrations. This can be caused by different receptor subtypes.

This is one of the reasons why a monitor of anaesthetic depth, e.g. the BIS monitor, may improve anaesthesia. The Bispectral Index monitor processes a modified EEG to assess the hypnotic effects of sedative and anaesthetics, replacing the reliance on physiological variables for determining the depth of anaesthesia. The advantages are faster wake up and recovery, cost effective use of drugs and fewer unwanted intraoperative responses.

In the BIS group BIS values were within acceptable (40-60) range, except two values that were high, because anaesthesia was titrated to maintain the normal BIS values for surgery. Whereas in Haemodynamic group BIS values were high on many occasions, here anaesthesia was maintained with haemodynamic parameters without considering the BIS values. During the transplant period patients might have gone into lighter plane of anaesthesia in the haemodynamic group because anaesthetists were unable to directly monitor the balance between need and delivery. Alternatively, insufficient anaesthesia could have been delivered as a result of technical errors or equipment failure. Additionally, some patients might have unpredictably high anaesthetic requirements, on the other hand, anaesthetic delivery might be constrained by concern about haemodynamic side effects of the anaesthetic drugs and extubation. Some evidence suggested that anaesthetists treated patients differently if they were allocated to haemodynamic group. This study failed to demonstrate any incidence of awareness in the intraoperative period when the BIS was used to titrate the anaesthetic administration.

Awareness was assessed by the use of Brice structured questionnaire on first and third post-operative day. We could not find awareness in our study and a large number of patients need to be studied to generalise this to all surgical patients. In contrast to our study, PS Myeles et al in a randomised multicentric study in 2463 general surgical patients, found BIS guided anaesthesia reduced the risk of awareness by 82% (n=1227, 2 patients) in comparison to the control group (n=1238, 11 patients). In this study awareness was studied in 2463 patients (large group of population) and patients were assessed for awareness at 2 to 6 hours, 24 to 36 hours, and 30 days.

In SAFE-II study the use of BIS monitoring was associated with significantly reduced incidence of awareness (78% reduction) when compared with historical controls from the same hospitals and investigators. Recruitment of fewer patients may also be the reason for the differences being insignificant. Following up patients for longer periods after operation is more desirable to determine the true incidence of recall.

The BIS has been demonstrated to be safe and efficient as a pharmacodynamic measure of the central effects of anaesthetics during short surgical procedures. It is desirable to ascertain how the index performs during the long surgical procedures as well as during renal transplant. In our study intraoperative haemodynamic variability is less with BIS group. Hypertension developed in 4 patients in haemodynamic group and tachycardia in 5 patients. In BIS group none developed hypertension and 1 patient developed tachycardia. Similarly, 6 patients developed bradycardia and hypertension in haemodynamic group but only 1 patient had hypotension in BIS group. There is a significant correlation between MAP and BIS. A decreased incidence of haemodynamic variability in the BIS controlled group may be due to the improvements in the titration of drugs in the intraoperative period. As the BIS provides additional information of the hypnotic state, the anaesthesiologist should be able to react before such haemodynamic changes occur.

G D Puri et al used BIS controlled anaesthesia during cardiopulmonary bypass and found BIS controlled group had significantly less tachycardia and hypertension. BIS is a useful monitor to adjust the anaesthetic dosages with decreased incidence of haemodynamic disturbances and improved recovery. This demonstrates that the anaesthesiologist was mainly reacting to the haemodynamic variables and

trying to restore them to normal while unknowingly accepting a lightly anaesthetised patient.

The time to eye opening was prolonged in the haemodynamic group (BIS group 14.3 ± 3.18 minutes and Haemodynamic group 17.9 ± 3.76 minutes). It demonstrates that anaesthesia was maintained at a deeper level in haemodynamic group resulting in delay in recovery. Anaesthetists may differ in the way they reduce anaesthetic drug administration towards the end of surgery; some discontinue administration before or during wound dressing, while others wait until wound dressing is complete. But a reduction in recovery times with BIS-guided anaesthesia has been shown previously. However, Pavlin and colleagues also reported that BIS monitoring did not influence the duration of recovery. As BIS patients had less haemodynamic variability and BIS values within acceptable range, this could be a possible reason for early awakening in this group of patients.

Time to tracheal extubation was higher in haemodynamic group (15.45±4.09 and 20.41±5.96 minutes in BIS and Haemodynamic groups respectively). Consciousness cannot be the sole predictor of successful tracheal extubation as it includes many other factors such as adequate respiratory parameters, haemodynamics, body temperature, adequate neuromuscular blockade recovery. In our study we have monitored neuromuscular blockade in all patients. Patients were monitored until recovery of all four switches following the train-of-four stimuli and all the patients recovered before extubation. Anaesthesia was maintained at deeper levels in the haemodynamic group, which resulted in delay in recovery.

The MAC values and the end-tidal isoflurane concentration, amount of isoflurane used were high in the Haemodynamic group. This indicates that anaesthesia was maintained at deeper levels in the Haemodynamic group.

Epidural catheter was placed in lower lumbar space in all patients. Epidural 10ml ropivacaine 0.2% with butorphanol 0.5mg were given for post op pain relief in both groups. Epidural anaesthesia intraoperatively reduces the hypnotic anaesthetic requirement. Hodgson et al used general anaesthesia with epidural and intravenous analgesia, epidural group patients required less sevoflurane than intravenous group.

In general technology assessment studies, it is known that, the technology influences those practitioners who use it for a small number of their patients thereby improving the outcome for all. No measures were taken in this study to address the influence of learning, so it is not biased against new technology. Moreover, the BIS by itself is shown to be an effective teaching tool.

CONCLUSION

It demonstrates that anaesthesia was maintained at a deeper level in haemodynamic group resulting in delay in recovery.

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