Bispectral Index Monitoring Improves the Cognitive Function After Desflurane –Anaesthesia in Elderly Patients Undergoing Spine Surgery

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Abstract: Postoperative cognitive dysfunction is a common complication in the elderly patients receiving desflurane anaesthesia. The bispectral index score (BIS) -targeted desflurane anaesthesia may hasten the recovery and cognitive function in the elderly patients after spine surgery. Forty patients aged >60 yr., scheduled for elective spine surgery were randomly allocated to BIS targeted (n=20) and MAC targeted (n=20) groups. Perioperative changes in the end-tidal (ET) concentrations of desflurane, times to emergences from anaesthesia and extubation, Aldrete score, cortisol and norepinephrine and the Mini Mental State Examination (MMSE) for the first 3 postoperative days were recorded. Perioperative changes in heart rate and mean arterial blood pressure were similar in both groups. The patients in the BIS targeted group showed significantly lower ET concentrations of desflurane, shorter times to eye opening, to follow commands and to tracheal extubation and higher Aldrete score and 24-hour MMSE values compared with those in the minimum alveolar concentration (MAC) targeted group(p<.05).Perioperative cortisol and norepinephrine plasma levels were similar in both groups. It was concluded that BIS-targeted desflurane anaesthesia provides faster recovery and improves the cognitive function in the elderly patients after spine surgery.

Keywords: Desflurane; anaesthesia; BIS; cognitive function; elderly patients.

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INTRODUCTION

As life expectancy of the population increases, a higher number of elderly presents for major surgery and anaesthesia (Oskvig, 1999). Degenerative conditions and advanced spondylosis in the lumbar or cervical vertebrae are common in the elderly who may present for different surgical spine interventions (Holly *et al.*, 2008). Elderly patients tend to have multiple comorbidities that enclose a high peri-operative risk (Owens, 1988). Biological ageing causing substantial physiological, pharmacokinetic and pharmacodynamic differences (Lauven *et al.*, 1993),which may result in inter-individual response variability to anaesthetic agents, and increased sensitivity to their adverse effects. The use of clinical signs may not be reliable for measuring the hypnotic component of anaesthesia (Drummond, 2000). Furthermore, in the geriatric patient, the effects of residual anaesthesia can delay postoperative mental and psychomotor recovery and consequently prolong the recovery stay (Nielson *et al.*, 1990) and (Fredman *et al.*, 1998).

The bispectral index score (BIS) is a continuous processed electroencephalography parameter that has been developed to measure the hypnotic effects of anaesthetic and sedative agents on the brain (Johansen *et al.*, 2000). The use BIS to guide the dose of anaesthetics may have certain advantages over clinical signs. It includes a significant reduction in the amount of general anaesthetic agents administered, a reduction in the frequency of hypnotic agent dosing error, better haemodynamic stability and improved patient satisfaction as well as faster recovery at the end of the procedure and shorter stay in the post-anaesthesia care unit (PACU) (Luginbuhl *et al.*, 2003) and (Lehamann *et al.*, 2003). The elderly population could therefore potentially benefit from depth of hypnosis monitoring to facilitate titration of anaesthetic agents.

We hypothesized that BIS guided titration of anaesthetics enhances early and late recovery as well as decrease the incidence and duration of cognitive impairment in the elderly patients undergoing spine surgery. We aimed to assess the changes in BIS and the end-tidal (ET) concentrations of desflurane, mean arterial blood pressure (MAP), and heart rate (HR), plasma cortisol and nor-adrenaline, time to recovery and the Mini Mental State Examination (MMSE) in the BIS-targeted compared with the minimum alveolar concentration (MAC) -targeted desflurane anaesthesia in the elderly patients undergoing spine surgery.

PATIENTS AND METHODS

After obtaining approval from the Ethical committee and written, informed consent, 40 ASA physical status I–III patients older than 60 yrs. undergoing elective spine surgery were enrolled in this study. Patients were randomly assigned into two standardized groups, namely group (A) (n=20) BIS targeted desflurane anaesthesia and group (B) (n=20) MAC targeted desflurane anaesthesia using a computer-generated randomization code. Patients with clinically significant cardiopulmonary, hepatic, renal disorders or other end-organ problems, history of any psychiatric or neurological problems, drugs or alcohol abuse, deafness or any hearing defects, non educated patients and known allergies of the used drugs were excluded from the study. Patients fasted for 8 h before surgery and received no premedication with reviewed all routine laboratories data. The patients were instructed about the postoperative use of patient-controlled analgesia (PCA), visual analog score (VAS) for assesment of pain and the preoperative Mini Mental State Examination (MMSE) was obtained during on the day before surgery.

The MMSE has standardized instructions, takes about 10 min to administer and consists of 11 questions that examine orientation to place (5 points), time (5 points), registration and recall of words (6 points), attention and calculation (5 points), language skills (8 points) and visual construction (1 point). The maximum MMSE score is 30 points, while a score ≤ 23 is a cut off for dementia (Folstein *et al.*, 1975).

The ambient operative room temperature was maintained at 23 C°. On arrival of the patient in the operating room, electrocardiogram (ECG), pulse oximetry, train-of four (TOF), and BIS monitor *(A-2000; Aspect Medical Systems, Natick, MA)* were placed. Non dominant radial artery was cannulated by (22G) cannula under local anaesthesia for continuous monitoring of blood pressure and blood sampling. Baseline means arterial pressure (MAP), heart rate (HR), and BIS were recorded before induction of anaesthesia.

The anaesthetic technique was standardized for both groups. After preoxygenation for 5 minutes, anaesthesia was induced by intravenous infusion of remifentanil 0.125 µg/kg over 5 minutes and propofol 1-2.5 mg/kg targeted to BIS <50. Tracheal intubation was facilitated using 0.15mg/kg cisatracurium. Nasopharyngeal temperature and end-tidal concentration of carbon dioxide and desflursne were continuously monitored. Ventilation was mechanically maintained at a fresh gas flow of 2L/min (50% oxygen in air) for five minutes, ,tidal volumes was 8ml /kg, inspiratory: expiratory ratio of 1: 2, and respiratory rate was adjusted to maintain end-tidal CO2 between 30-40 mmHg. Anaesthesia was maintained by desflurane, remifentanil 0.01 µg / kg/ min and cisatracurium. The patient was placed in the prone position and an enforced warming air blanket was placed over the lower part of the body.

General anaesthesia was maintained in the patients in group A (BIS-targeted anaesthesia) (n=20),using BIS-guided titration of anesthesia.BIS was maintained between 50-55.Inspired desflurane concentration was decreased in steps of 0.5% if BIS decreased less than 50 and it was increased in steps of 0.5% when BIS increased to or higher than 55.

In group B (n=20) (MAC targeted anesthesia); the BIS monitor was covered hidden away from the attendant anaesthesiologist. General anaesthesia was maintained using the standard clinical practice. The targeted inspired concentration of desflurane was adjusted to achieve an ET concentration of 1.1 minimum alveolar anaesthetic concentration (MAC). After ensuring of deep neuromuscular blockade with the absence of the second response on the TOF, inspired desflurane concentration was increased in steps of 0.5% if the MAC of desflurane was ≤ 1.1 and heart rate and/or blood pressure were 20% higher than their baseline values. If heart rate and/or blood pressure decreased 20% lower than their baseline values and the MAC of desflurane was ≥ 1.1, the inspired desflurane concentration was decreased in steps of 0.5%.

The recorded data in the BIS monitor was collected after surgery in both groups by an independent investigator who was unaware of the patient's randomization code.

After the achievement of the targeted BIS and MAC of desflurane in the group A and B, respectively, hypotension (defined as MAP value <20% of the baseline value on two consecutive readings within 2–3 min) was initially treated with a 200 mL of intravenous Voluven 6% and intravenous, boluses of phenylephrine, 100 µg, hypertension (defined as MAP value >20% of the baseline value on two consecutive readings within 2–3 min) with or without associated tachycardia (defined as HR value >20% of the baseline value > 2 min) was treated with labetalol, 5 mg IV, boluses. Bradycardia (HR <45) persisting for >2 min was treated with atropine, 0.5 mg IV, boluses.

At the end of surgery during last skin suturing, desflurane was discontinued. The fresh gas flow was increased to 10 L/min whereas the anaesthesia ventilator pattern remained unchanged. Paracetamol 1g IV was given and at the same time, reversal of the residual neuromuscular blockade was achieved after returning back to supine position by neostigmine (0.05mg/kg) and glycopyrolate (0.015 mg/kg), when a TOF ratio increased higher than 0.9. The patient was extubated when he/she became normotheric (core temperature > 36 C°), stable haemodynamics, fully conscious, obeying commands (e.g. squeeze the investigator's hand), able for a 5-second head lift. The times from discontinuing desflurane to eye opening, tracheal extubation, obeying commands (e.g. squeeze the investigator's hand) were recorded.

Subsequently, MAP, HR, BIS and ET concentrations of desflurane were recorded every 15 min after induction of anaesthesia. Blood samples for measuring cortisol and nor-adrenaline was extracted on the day before surgery, one hour after tracheal intubation and one hour after extubation as index of stress response.

After the arrival to PACU , a PCA using intravenous fentanyl therapy was started when the patient's Aldrete score ≥ 8 (Aldrete *et al.*, 1970). The PCA device was programmed to deliver bolus doses of 10 μg of fentanyl as needed, lockout interval 10 minute and four hour limit of 200 μg. Another independent investigator who was unaware of the patient's randomization code assessed the patient's VAS , the quality of psychomotor recovery using the MMSE and Aldrete score. The later was assessed at 15 minutes intervals from admission to PACU for 120 minutes. The criteria for discharge from PACU included, haemodynamic stability, normotheric, free of pain, fully conscious, well oriented to persons and place and Aldrete score 9-10.

MMSE and VAS were conducted at 60, 120, and 180 minutes after the transfer to the PACU and 24, 48, 72 hours postoperatively. Also, any symptom of cognitive disturbance noted by nurses or family members was recorded. An interview was done 72 hours after surgery, and the patient was asked about any intraoperative recall events.

Statistics analysis:

Data were analyzed using SPSS 16 software (SPSS Inc., Chicago, Illinois.). Data were tested for normality using the Kolmogorov-Smirnov test. An unpaired Student'st test was used to compare the parametric values of the two groups; Mann-Whitney U test was performed to compare the non-parametric values of the two groups.Serial changes in the patients' data at induction were analyzed with repeat measures analysis. Data were expressed as frequency, mean ± SD, number or median (range). A value of $P < 0.05$ was considered to represent statistical significance.

RESULTS

Age, gender distribution, ASA physical status, height, weight, types of surgery, the duration of surgery and anaesthesia were similar in both groups (Table1).

Perioperative changes in HR and MAP were similar in both groups (Table2)

Baseline ET concentrations of desflurane and BIS values were comparable among the two groups (Figure 1 and 2). Patients in group A (BIS-targeted desflurane anaesthesia) (n=20) showed significantly lower ET concentrations of desflurane and higher BIS values compared with those in group B (MAC-targeted desflurane) (n=20) (P<0.05) (Figures 1 and 2).

Perioperative cortisol and nor-adrenaline plasma levels were similar in both groups (Table 3).

Times to eye opening, to follow commands and to tracheal extubation were prolonged in the patients in group B (MAC-targeted desflurane) (n=20) (Table 1).

Aldrete score values were significantly lower in the patients in group B (MAC-targeted desflurane) (n=20) up to 120 minutes after their discharge to the PACU compared with those in group A (BIS-targeted desflurane anaesthesia) (n=20) (Table 4).

MMSE values were significantly lower in the group B (MAC-targeted desflurane) (n=20) during the first 24 hours after surgery (Table 5). VAS was similar in both groups.

There is neither cognitive change reported by the nurses or patients family nor recall.

Table1. Patients data in the two groups (mean ± SD):

	Group A (n = 20)	Group B (n= 20)
Age (years)	64 ± 4	65 ± 3
Gender (Male / Female)	11/9	12 / 8
ASA physical status(I/II/ III)	7 /10 /3	6 /11 / 4
Height(cm)	174 ± 6.67	174 ± 6.61
Weight(Kg)	76 ± 5.60	78 ± 6.90
Type of spine surgery		
Lumber discectomy	16	15
Lumber laminectomy	4	5
Duration of surgery(min.)	110 ± 5.34	112 ± 5.87
Duration of anaesthesia (min.)	130 ± 5.29	131 ± 5.31
Time to eye opening (min)	5.5 ± 0.65	9.2 ± 0.32 *
Time to follow commands (min)	6.6 ± 0.45	10.6 ± 0.35 *
Time to tracheal extubation (min)	7.5 ± 0.36	11.8 ± 0.52 *

*P<0.05 compared with group (A).

Group A: BIS-targeted desflurane anaesthesia, Group B: MAC-targeted desflurane

Table 2.Heart rate [HR] and mean arterial blood pressure [MAP] changes in the two groups (mean ± SD):

	HR (bpm)		MAP (mm Hg)	
	Group A (n = 20)	Group B (n = 20)	Group A (n = 20)	Group B (n= 20)
Baseline	86±5.78	83±5.22	95±10.32	93±7.74
15 minutes	79±4.71	76±4.83	75±5.95	75±4.09
30 minutes	75±4.53	77±3.82	70±3.79	72±2.12
45 minutes	70±3.83	70±4.72	68±2.81	71±1.77
60 minutes	73±5.09	73±4.00	68±3.65	69±2.69
75 minutes	69±4.11	69±2.62	70±5.96	69±2.41
90 minutes	68±2.26	69±3.20	69±3.22	70±2.10
105minutes	69±3.20	69±3.20	75±8.65	76±4.29
120 minutes	70±5.69	71±3.67	85±7.97	80±5.53
135 minutes	86±6.29	78±4.14	91±7.80	82±4.17

No significant difference between the two groups.

Group A: BIS-targeted desflurane anaesthesia, Group B: MAC-targeted desflurane

bpm; beat per minute, mm Hg; millimeter mercury.

Table3.Perioperative changes in cortisol and norepinephrine plasma levels in the two groups Data was presented as median (range):

	Cortisol (μ/dl)		Nor adrenaline (pg/mL)	
	Group A (n = 20)	Group B (n = 20)	Group A (n = 20)	Group B (n = 20)
Baseline	12.5 (9)	12.5(6)	320.5(219)	303 (155)
1h after intubation	26 (20)	25 (11)	598 (224)	588 (177)
1h after extubation	39 (19)	37.5(13)	852 (180)	843 (176)

No significant difference between the two groups.
Group A: BIS-targeted desflurane anaesthesia, Group B: MAC-targeted desflurane

Table 4. Aldrete score in the two groups. Data was presented as median (range):

	Group A (n = 20)	Group B (n = 20)
Baseline	9(0)	8(0) *
15 min	9(0)	8(0) *
30 min	9(1)	8(1) *
45 min	10(1)	9(1) *
60 min	10(1)	9(2) *
90 min	10(0)	9(1) *
120 min	10(0)	10(1) *

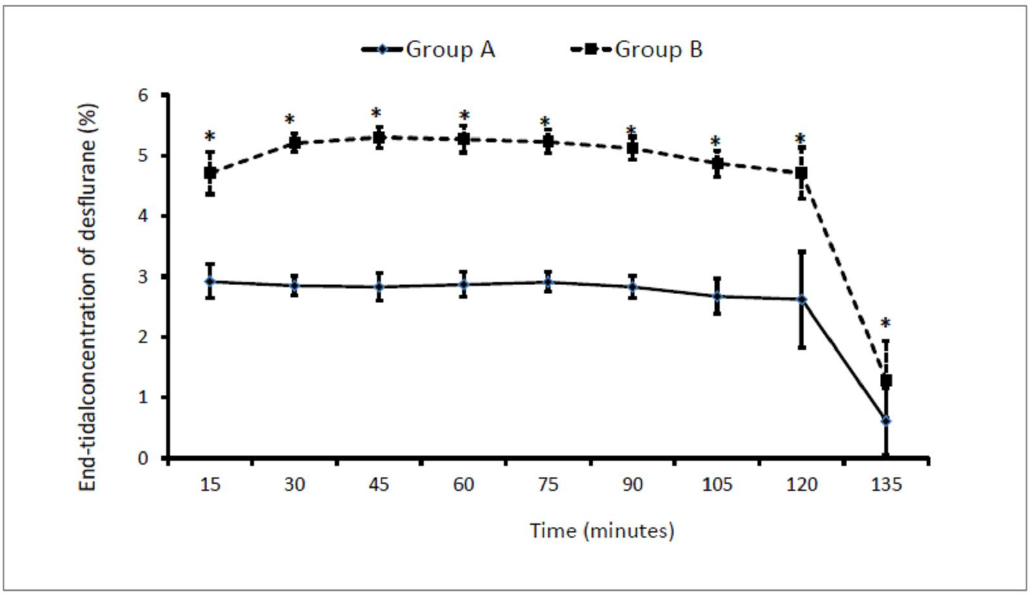
*P<0.05 compared with group (A).
Group A: BIS-targeted desflurane anaesthesia, Group B: MAC-targeted desflurane

Table 5. Minimental state examination (MMSE) in the two groups.
Data was presented as median (range):

	Group A (n = 20)	Group B (n = 20)
Baseline	28(3)	28(2)
1 hours	23(5)	20(4) *
2 hours	24(6)	20(4) *
3 hours	26(4)	22(4) *
24 hours	28(4)	26(6) *
48 hours	28(3)	28(2)
72 hours	28(3)	28(2)

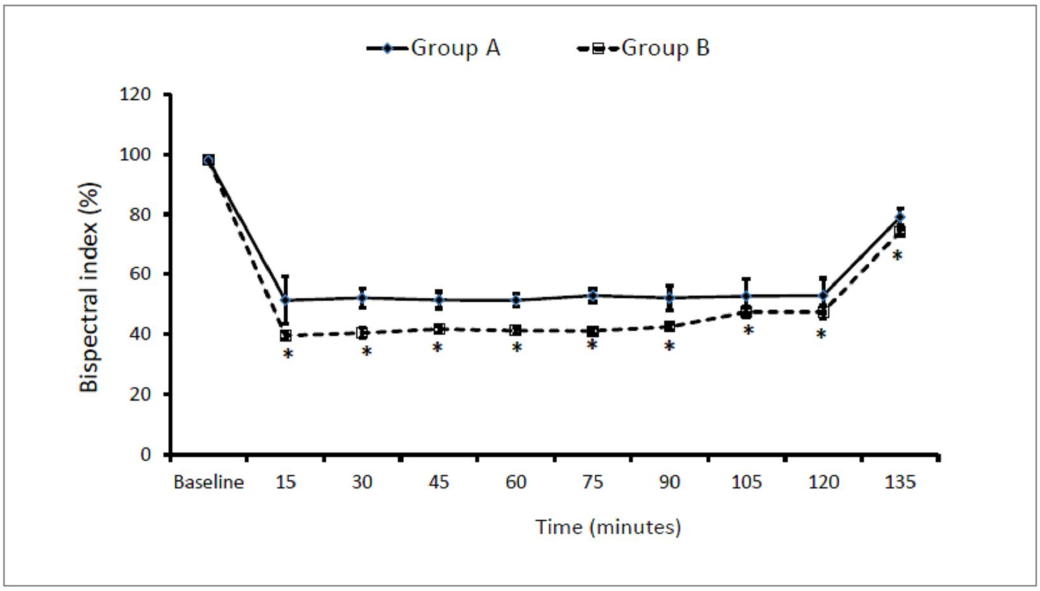
*P<0.05 compared with group (A).
Group A: BIS-targeted desflurane anaesthesia, Group B: MAC-targeted desflurane

Fig.1. Intraoperative changes of end tidal desflurane in the two groups:



*P<0.05 compared with group (A).
Group A: BIS-targeted desflurane anaesthesia, Group B: MAC-targeted desflurane

Fig.2. Intraoperative changes of BIS in the two



groups:
*P<0.05 compared with group (A).
Group A: BIS-targeted desflurane anaesthesia, Group B: MAC-targeted desflurane

DISCUSSION

Postoperative cognitive dysfunction is a condition characterized by impairment of memory and concentration, and the incidence has been reported to be extremely frequent in elderly patients undergoing major surgery. Postoperative cognitive dysfunction after desflurane anesthesia, especially in the elderly, is a well-recognized problem, although its known low blood-gas partition coefficient, contributing to its faster recovery from anaesthesia compared with the traditional volatile anaesthetics (Ghouri *et al.*, 1991) and (Tsai *et al.*, 1992). In the present study, the use of BIS monitoring to control the depth of desflurane anaesthesia reduces the used ET concentration of the drug and hasten the cognitive recovery in the elderly patients after spine surgery.

In our study, the intraoperative use of BIS-targeted desflurane anaesthesia was associated with significantly lower end-tidal desflurane concentrations than MAC-targeted anaesthesia. Similarly, Kreuer and colleagues,2005 recorded significantly less desflurane usage with the use of BIS-adjustment for the depth of anaesthesia than the use of standard practice for control of anaesthesia (416±99mg/min vs. 443±71 mg/min, respectively, [$P<0.05$]), however, recovery times were not significantly different between the groups (opening of eyes 4.7 ± 2.2 in standard practice versus 4.2 ±2.1 min in BIS).

In the present study, the elderly patients in the BIS-targeted group showed faster emergence from anaesthesia, namely, times to eye opening, follow commands and to tracheal extubation, than those in the MAC-targeted group. Similarly, other investigators demonstrated rapid emergence from desflurane anaesthesia in young adults, compared with sevoflurane anaesthesia (Nathanson *et al.*, 1995). Additionally, Chen and coworker's, 2001 reported faster emergence from desflurane anaesthesia and a shorter length of stay in the PACU in the elderly patients. Additionally, the postoperative pain score was similar in both groups.

We used the MMSE to assess the cognitive function after desflurane anaesthesia in elderly patients, because it combined high validity, good test–retest and inter-observer reliability, ease of application and not tiring for the elderly patients (Folstein *et al.*, 1975). This test concentrates on the cognitive aspect of mental function and excludes questions concerning mood and abnormal mental experiences and it can be repeated postoperatively to detect early changes of cognitive function (Parikh *et al.*, 1975) and (Wind *et al.*, 1997). Previous study have validated the MMSE found a sensitivity of 80% and an even higher specificity (98%) McKenzie *et al.*, 1996).

Cognitive dysfunction is well known adverse effects of general anaesthesia in the elderly patients which may extend up to 3 days after surgery (Papaioannou *et al.*, 2005).

Edwards and others,1981 found a progressive impairment in the mental function started from the second postoperative day and extended to the 7th postoperative day after anaesthesia. This impairment was maximal on the 4th and 5thdays after surgery. However Chen and coworker's,2001 reported lower mini-mental scores in the elderly patients at the first postoperative hour after sevoflurane and desflurane anaesthesia. Then, they returned to their preoperative baseline levels within 6 hours after surgery. The patients who underwent desflurane anaesthesia experienced significant cognitive impairment between the 1stand 3rd hour after surgery.

The differences between our results and Chen's results may be related to the smaller number of the studied population in our study (40 vs. 70 patients, respectively)

In the present study, the median durations of surgery and anaesthesia were about 110 and 130 minutes, respectively. This may be less likely to affect the cognitive function in the studied elderly patients. Therefore, Farag *et al.*, 2006 found that the depth of isoflurane anaesthesia during elective surgical procedures of intermediate duration [>220 min] may affect cognitive performance as late as 4–6 weeks postoperatively, specifically in the patients kept at somewhat lower BIS levels during the majority of the surgical procedures compared with those who somewhat more lightly anaesthetized.

Our study has an important limitation that it is a non-powered study, even though it clearly showed that the elderly displayed cognitive impairment during first postoperative day after desflurane anaesthesia. Further larger randomized clinical trials may be needed to validate the role of BIS monitoring to improve cognitive function in the elderly.

In conclusion, BIS-targeted desflurane anaesthesia provides faster recovery and improves the cognitive function in the elderly patients after spine surgery.

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