Bispectral index monitoring does not improve early recovery of geriatric outpatients undergoing brief surgical procedures

[Le monitorage avec l'index bispectral n'améliore pas la récupération précoce des patients ambulatoires âgés après une opération brève]

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Purpose: To assess if titration of sevoflurane using the bispectral index (BIS) monitor improves the early and intermediate recovery in geriatric outpatients undergoing brief urologic procedures under general anesthesia without muscle relaxants.

Methods: After a standardized induction with propofol and fentanyl, a laryngeal mask airway was inserted and sevoflurane was administered in combination with 60% nitrous oxide in oxygen for maintenance of anesthesia in spontaneously breathing outpatients. In the Control group (n = 25), sevoflurane and fentanyl were titrated according to standard clinical practice. In the BIS-directed group (n = 25), sevoflurane was titrated to maintain a BIS value between 50 and 60, and supplemental fentanyl, 25 μg *iv* boluses were administered to treat tachypnea. The intraoperative anesthetic and analgesic requirements, as well as the times to eye opening, removal of the laryngeal mask airway device, response to simple commands, orientation to person and place, and postanesthesia care unit discharge eligibility (fast-track score of 14) were assessed at specific time intervals.

Results: The minimum alveolar concentration-hour of sevoflurane (0.25 ± 0.15 and 0.31 ± 0.2) and end-tidal concentrations of sevoflurane at the end of surgery (0.3 ± 0.3 and 0.4 ± 0.20%) did not differ significantly between the Control and BIS-directed groups, respectively. Although the percentage of patients requiring supplemental boluses of fentanyl was reduced in the BIS-directed group (16 *vs* 48%, P <0.05), the intraoperative BIS values and recovery times were similar in the two groups.

Conclusion: In this non-paralyzed elderly outpatient surgery population, the use of BIS monitoring for titrating the maintenance anesthetic (sevoflurane) failed to improve the early recovery process.

***Objectif** : Évaluer si le titrage du sévoflurane à l'aide d'un moniteur d'index bispectral (BIS) améliore la récupération précoce et intermédiaire des patients ambulatoires âgés après une brève intervention urologique sous anesthésie générale sans myorelaxants.*

***Méthode** : Après une induction normalisée avec du propofol et du fentanyl, un masque laryngé a été inséré et le sévoflurane administré en combinaison avec un mélange de protoxyde d'azote et d'oxygène à 60 % pour maintenir l'anesthésie chez des patients en ventilation spontanée. Dans le groupe témoin (n = 25), le sévoflurane et le fentanyl ont été dosés selon la pratique courante. Dans le groupe sous monitorage BIS (n = 25), le dosage visait à maintenir une valeur de BIS entre 50 et 60, et du fentanyl complémentaire, en bolus de 25 μg iv, a été administré pour traiter la tachypnée. L'anesthésique peropératoire et les besoins d'analgésiques, de même que le temps précédant l'ouverture des yeux, le retrait du masque laryngé, la réponse à des commandes simples, la reconnaissance des gens et du lieu et la possibilité de quitter la salle de réveil (score séjour bref de 14) ont été notés à des intervalles spécifiques.*

***Résultats** : La concentration-heure de sévoflurane (0,25 ± 0,15 et 0,31 ± 0,2) et les concentrations télé-expiratoires de fin d'opération (0,3 ± 0,3 et 0,4 ± 0,20 %) n'affichaient pas de différence significative entre les groupes témoin et de monitorage BIS respectifs. Le pourcentage de patients qui ont eu besoin de bolus complémentaires de fentanyl était plus bas avec le BIS (16 vs 48 %, P < 0,05), mais les valeurs peropératoires de BIS et le temps de récupération étaient similaires dans les deux groupes.*

***Conclusion** : Dans cette population de patients ambulatoires âgés, opérés sans myorelaxants, l'usage du monitorage BIS pour le titrage de l'anesthésique de maintien (sévoflurane) n'a pu améliorer la récupération précoce.*

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SEVERAL studies have suggested that use of cerebral monitoring can facilitate the early recovery process by improving the titration of anesthetic and analgesic drugs during surgery.[1–4] However, in instances where intraoperative use of a bispectral index (BIS) monitoring device did not significantly alter the titration of the anesthetic drugs during the maintenance period, investigators have failed to find meaningful differences in the patients' recovery profiles following general anesthesia.[5,6] Most of the previous studies evaluating the impact of BIS monitoring on recovery from general anesthesia have involved young healthy patients who received muscle relaxants during surgery. However, Wong *et al.*[7] reported that titration of isoflurane using the BIS monitor decreased the emergence times for elderly inpatients undergoing major orthopedic joint replacement procedures. We were interested in determining if these findings would apply to elderly outpatients undergoing shorter ambulatory surgery procedures.

Therefore, we designed a prospective, double-blind controlled clinical study to test the hypothesis that BIS monitoring would improve titration of anesthetic drugs and decrease early recovery times in geriatric outpatients undergoing brief urologic procedures without muscle relaxants.

Methods

After obtaining Institutional Review Board approval (Meir Hospital, Kfar Saba, Israel) and written informed consent, 50 geriatric outpatients were enrolled in this prospective, randomized, assessor-blinded study involving two treatment groups: 1) a standard practice (control) group; and 2) an experimental (BIS-directed) group. All participants were 65 yr of age or older and were undergoing short elective transurethral surgical procedures. Patients with a history of unstable cardiovascular, pulmonary, hepatic, renal, neurologic, psychiatric or metabolic diseases were excluded from participating in this study.

No preanesthetic medication was administered. Upon arrival in the operating room, non-invasive blood pressure, electrocardiogram, and oxygen saturation monitors were applied. In addition, an A-2000 Bispectral Index™ monitoring system (Aspect Medical Systems, Natick, MA, USA) was used to record perioperative electroencephalographic BIS values. In the control group, the anesthesiologists were not permitted to observe the BIS values during the intraoperative period, and the inspired concentration of sevoflurane was varied based on standard clinical signs. In the BIS-directed group, the anesthesiologist was instructed to maintain the BIS value in the 50 to 60 range by varying the inspired concentration of sevoflurane. In both groups, the sevoflurane concentration was increased in response to signs of an inadequate "depth of anesthesia" (e.g., movement in response to surgical stimulation).

After obtaining baseline hemodynamic and bis values, all patients were allowed to breathe 100% oxygen for two to three minutes prior to induction of anesthesia with fentanyl 1.0 to 1.5 μg·kg *iv*, and propofol 1.5 to 2.0 $mg \cdot kg^{-1}$, *iv*. Following induction of anesthesia, a laryngeal mask airway (LMA) was inserted and sevoflurane was administered at an initial inspired concentration of 1.5% in combination with 60% nitrous oxide in oxygen. In all cases, the patients were permitted to breathe spontaneously. However, ventilation was transiently assisted in those patients who developed apnea immediately after induction of anesthesia. The inspired oxygen, and end-tidal concentrations of carbon dioxide, sevoflurane and nitrous oxide were continuously measured using an infrared gas analyzer (Datex, AS/3™ Helsinki, Finland). Supplemental "rescue" doses of fentanyl (25 μg *iv*) were administered in both groups when the patient manifested a sustained increase in respiratory rate (> 20 $beat \cdot min^{-1}$ lasting > two minutes).

Hemodynamic variables and anesthetic concentrations, as well as intraoperative BIS values, were recorded at one-minute intervals during the induction period, and at three- to five-minute intervals during the maintenance period. Upon discontinuation of the volatile anesthetic, the BIS value and end-tidal sevoflurane concentrations were recorded. The sevoflurane minimum alveolar concentration (MAC) during the maintenance period was calculated according to the following equation: MAC/hr = sum of end-tidal concentrations divided by the product of the MAC value multiplied by the time (hr) at that concentration. The inhaled anesthetics were discontinued at the end of surgery (i.e., upon withdrawal of the endoscope). Anesthesia time was measured from induction with propofol until discontinuation of sevoflurane and nitrous oxide.

Early recovery endpoints were recorded at one minute intervals following discontinuation of the maintenance anesthetics by a "blinded" observer, including spontaneous eye opening, removal of the LMA device, responding to simple verbal commands, and the ability to correctly state name, age, and personal identification number. In addition, the times to achieve fast-track eligibility (i.e., from removal of the LMA to a fast-track score ≥ 12),[8] and postanesthesia care unit (PACU) discharge eligibility (i.e., a fast-track score of

TABLE I Patient characteristics and intraoperative anesthetic and analgesic requirements in the two treatment groups*

	Control	*BIS-directed*
Number (*n*)	25	25
Age (yr)	76 ± 7	73 ± 8
Weight (kg)	76 ± 12	77 ± 14
Height (cm)	169 ± 7	170 ± 8
Sex (F/M) (*n*)	3 / 22	4 / 21
ASA physical status (I/II/III) (*n*)	2 / 20 / 3	2 / 19 / 4
Type of urologic surgery (*n*)		
transurethral prostatectomy	8	6
transurethral bladder resection	15	17
ureteroscopy	2	2
Propofol at induction ($mg \cdot kg^{-1}$)	1.9 ± 0.5	1.9 ± 0.5
Fentanyl at induction (μg)	93 ± 14	92 ± 28
Sevoflurane (MAC-hr)	0.31 ± 0.2	0.25 ± 0.15
Sevoflurane at end of surgery (ET %)	0.4 ± 0.2	0.3 ± 0.3
Fentanyl "rescue" required (*n*, μg)	12, 67 ± 24	4, 29 ± 17†
Surgery time (min)	28 ± 16	31 ± 22
Anesthesia time (min)	48 ± 16	51 ± 24

*Values are mean ± SD or numbers (*n*). †$P < 0.05$ *vs* control. ASA = American Society of Anesthesiologists; BIS = bispectral index; MAC = minimal alveolar concentration; ET = end-tidal concentration.

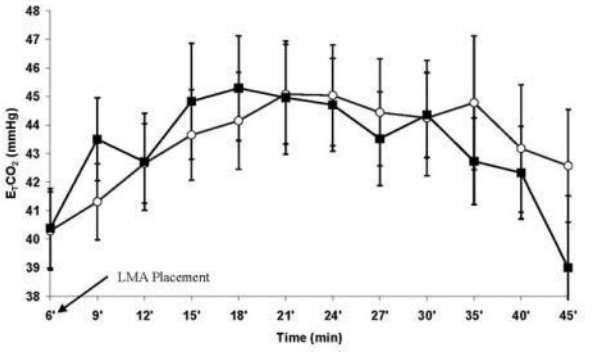

FIGURE Intraoperative end-tidal carbon dioxide (E_TCO_2) levels after insertion of the laryngeal mask airway (LMA) in the control group (open circles) and bispectral index (BIS)-directed group (filled squares). Values represent mean ± standard error of the mean. No significant differences were found between the two treatment groups.

14 on two consecutive evaluations) were assessed at five-minute intervals after awakening from anesthesia by the same blinded observer. The occurrence of any side effects and the need for therapeutic interventions by the nursing staff (e.g., supplemental oxygen, *iv* opioid analgesic, or antiemetic "rescue" medications) in the PACU were recorded in the patient's chart. At the time of discharge from the PACU, all patients were questioned about recall of any events during the operation, and an assessment of patient satisfaction with their anesthetic experience was performed using a four-point scale (with 0 = unacceptable, 1 = poor, 2 = good, and 3 = excellent).

Based on the results of previous studies involving geriatric patient populations,[7,9] the power analysis ($\alpha = 0.05$, ß = 0.8, SD = 12) suggested that 25 patients per group would be required to detect a mean difference of ten minutes in the time from discontinuation of the maintenance anesthetic drugs to achieving a fast-track score of 14.[10] In all cases, normality was assessed using the Kolmogorov-Smirnov test with Lilliefors' modification. Depending upon the results of the Kolmogorov-Smirnov analysis, either a parametric or non-parametric analysis was performed. Demographic, hemodynamic, and BIS values, as well as anesthetic drug dosage and recovery data were analyzed using student's t test and/or ANOVA (with Bonferroni's correction for multiple comparisons). Perioperative events requiring therapeutic interventions, as well as patient satisfaction, were analyzed using the Chi square test. Data are expressed as mean values ± standard deviation (or standard error of the mean), with *P*-values < 0.05 considered statistically significant.

Results

There were no significant differences between the two groups with regard to their demographic characteristics and the types of urologic surgery procedures performed (Table I). Similarly, the induction doses of propofol and fentanyl, as well as the average end-tidal sevoflurane concentrations and MAC-hr of sevoflurane during the maintenance period, were similar in the two groups. However, the number of patients receiving intraoperative "rescue" fentanyl was significantly higher in the control (*vs* BIS-directed) group (12 *vs* 4, $P < 0.05$). The mean intraoperative dose of fentanyl was also significantly higher in the control group (Table I). During the induction and maintenance periods, the hemodynamic variables were comparable in the two groups (data not reported). The respiratory rates and end-tidal carbon dioxide values were also similar in both groups (Figure). At the end of anesthesia, the mean end-tidal sevoflurane concentration was similar in both groups (0.4 ± 0.2% and 0.3 ± 0.3% for the control and BIS-directed groups, respectively).

Preoperative (baseline) BIS values, as well as the values observed at specific clinical endpoints dur-

TABLE II Comparative BIS values at specific endpoints during the perioperative period in the two monitoring groups*

	Control	*BIS-directed*
Awake "baseline" value	96 ± 3	96 ± 3
After induction of anesthesia	48 ± 11	46 ± 7
Prior to insertion of endoscope	58 ± 13	60 ± 11
After endoscope insertion	59 ± 15	65 ± 14
Average value during the operation†	59 ± 10	57 ± 10
Upon discontinuation of sevoflurane	58 ± 18	57 ± 17
Upon removal of airway device	81 ± 14	78 ± 13
After spontaneous eye opening	87 ± 15	89 ± 9
Responded to simple commands	93 ± 7	94 ± 5
Oriented to person and place	95 ± 4	95 ± 4

*Values are means ± SD. †From time of insertion to removal of the endoscope. No significant differences were observed between the two groups. BIS = bispectral index.

TABLE III Recovery times and postoperative therapeutic interventions in the two monitoring groups*

	Control	*BIS-directed*
Recovery times (min)		
Awakening	7.0 ± 2.2	7.8 ± 2.4
Response to simple commands	8.5 ± 2.3	9.3 ± 2.7
Orientation to person and place	9.8 ± 2.3	10.9 ± 2.9
Fast-track eligibility (score ≥ 12) (min)	7.0 ± 3.0	7.2 ± 4.0
Achieved fast-track score of 14 (min)	17 ± 20	16 ± 18
Postoperative nursing interventions (*n*, %)		
Need for *iv* morphine in PACU	3, 12	5, 20
Supplemental oxygen in PACU	2, 8	7, 28
Emetic symptoms in PACU	1, 4	3, 12
Eligible for PACU discharge (min)	35 ± 22	37 ± 18
Patient satisfaction (0, 1, 2, 3) (*n*)†	0, 2, 8, 15	0, 1, 10, 14

*Values are means ± SD, or numbers (*n*) and percentages (%). †Scores: 0 = unacceptable, 1 = poor, 2 = good, and 3 = excellent. No significant differences were found between groups. BIS = bispectral index; PACU = postanesthesia care unit.

ing the perioperative period, were similar in the two groups (Table II). The emergence times (e.g., awakening, orientation) and the times to fast-track eligibility (score > 12) were also similar in the two groups (Table III). The times to achieve PACU discharge eligibility were 35 ± 22 and 37 ± 18 min in the control and BIS-directed groups, respectively (Table III). Finally, the need for therapeutic interventions by the nurses in the PACU and the distribution of patient satisfaction scores were comparable in the two groups (Table III). None of the patients reported recall of intraoperative events when questioned at the time of PACU discharge.

Discussion

Electroencephalographic BIS monitoring has been reported to facilitate improved titration of anesthetic drugs, leading to reduced time intervals to achieve early and intermediate recovery endpoints after general anesthesia.[1,2,4,11–13] Interestingly, a recent meta-analysis by Liu[14] found a similar 19% decrease in the volatile anesthetic requirement with BIS-directed (*vs* non-BIS) monitoring. Analogous to the conclusion of this systematic review, we found that the anesthetic-sparing effect of BIS monitoring did not reduce the time spent in the PACU and/or the ambulatory surgery unit. As suggested by Pavlin *et al.* in a study involving younger outpatients,[5] the BIS has "a limited capacity to influence the duration of recovery when used to monitor unparalyzed patients undergoing short surgical procedures with a relatively insoluble anesthetic such as sevoflurane." This observation appears to be equally valid in our elderly outpatient surgery population.

The comparable intraoperative BIS values and volatile anesthetic requirements (MAC-hr sevoflurane) in the two monitoring groups also suggested that anesthesiologists did not alter their technique for administering sevoflurane with BIS monitoring. Importantly, the anesthesiologist's standard monitoring technique allowed patients in the control group to maintain BIS values in the "targeted" range without the additional information provided by the BIS monitor.[15] However, unlike the previous investigation by Ahmad *et al.*,[6] the end-tidal sevoflurane concentrations in this study were compatible with BIS values in the range of 50 to 60.[2,16]

The failure to demonstrate significant differences in recovery times between the two study groups was likely multifactorial. Firstly, the impact of a cerebral monitor in improving the titration of the maintenance anesthetic will be minimized when the device is used for relatively brief surgical procedures (28–31 min). These data suggest that the context-sensitive decrement time for a > 50% decrease in the brain concentration of sevoflurane may be too short to demonstrate clinically-significant differences in early recovery times.[14] Secondly, since the anesthesiologists participating in the study had previous experience using the BIS monitor for titrating volatile anesthetics, a "learning effect" may have carried over into the study. These data suggest that the anesthesiologist's previous knowledge regarding the relationship between the end-tidal concentrations of sevoflurane and the BIS value under similar surgical conditions minimized the differences in the titration of the volatile agent in the two study groups. Thirdly, it would appear that the anesthesiologists using the BIS monitor did

not significantly alter their "standard" anesthetic drug administration technique, and therefore, the use of this technology would not be expected to facilitate the recovery process.[15] Finally, if the policy of the recovery facility mandates a minimum length of stay and/or does not permit patients who quickly satisfy the PACU discharge criteria to more rapidly advance through the recovery process (i.e., fast-tracking), one would not expect to find differences in the recovery times.

Previous studies demonstrating that BIS-directed administration of volatile anesthetics can facilitate discharge after general anesthesia were performed in younger surgical populations receiving muscle relaxants. Analogous to earlier studies evaluating the effect of cerebral monitoring on recovery after ambulatory surgery,[5,17] none of the outpatients in the current study received muscle relaxants as they were allowed to breathe spontaneously throughout the surgical procedure. Since spontaneous ventilation provides significant feedback to the anesthesiologist on the adequacy of anesthesia, this technique would minimize the beneficial effect of BIS monitoring in improving recovery. It is also well-known that electromyogram (EMG) activity itself can falsely elevate the BIS measurements.[18] When non-paralyzed patients received sedation in an intensive care unit, use of the BIS to guide administration of midazolam exposed the patients to "unnecessary oversedation."[19] Thus, it would appear that in spontaneously breathing patients, the EMG-related "contamination" of the BIS value eliminates the beneficial effects of BIS monitoring in improving the titration of the maintenance volatile anesthetic.

In an attempt to expedite the early recovery process following general anesthesia, most anesthesiologists attempt to minimize the amount of anesthetic and opioid analgesic medication that they administer during surgery in the ambulatory setting. These data would suggest that anesthesiologists in both monitoring groups were equally successful in minimizing their use of the volatile anesthetic. Although concerns have been raised regarding the possibility of adverse outcomes related to BIS monitoring (e.g., intraoperative awareness, myocardial ischemia, increased postoperative pain),[20] this has not proven to be the case in routine clinical practice.[1–7,11–13] In our current study, the perioperative respiratory and hemodynamic variables were not significantly different in the two study groups. Furthermore, there were no perioperative complications in this geriatric patient population, and no patient reported recall of any intraoperative events. However, this study was not sufficiently powered to detect differences between the two groups with respect to these secondary outcome variables.

The methodologic limitations of this study which may have contributed to these negative findings included: 1) the short duration of the surgical procedures; 2) the sevoflurane-sparing effects of nitrous oxide; 3) the differing amounts of fentanyl administered in the two groups; and 4) the failure to utilize highly sensitive neurophysiological tests to assess early recovery from anesthesia. Nevertheless, despite these shortcomings, these data would suggest that BIS monitoring offers little advantage in this clinical setting.

In conclusion, BIS-directed administration of sevoflurane during brief urologic procedures in elderly spontaneously breathing outpatients failed to facilitate the fast-track recovery process.

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