

Propofol consumption and recovery times after bispectral index or cerebral state index guidance of anaesthesia

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Background. We compared the propofol requirements and recovery times when either the bispectral index (BIS) monitor or the cerebral state monitor (CSM) is used to guide propofol anaesthesia.

Methods. Forty patients undergoing laparoscopic cholecystectomy were studied. All patients were monitored with both monitors and were randomly allocated into two groups according to the monitor used to titrate propofol administration. Propofol was administered to maintain BIS or CSM within 40 and 60. Propofol consumption and clinical markers of recovery were assessed after surgery.

Results. In the CSM group, the values of cerebral state index (CSI) and BIS were 47 (5) and 38 (6), respectively ($P=0.00054$). In the BIS group, the values of CSI and BIS were 47 (5) and 45 (2), respectively ($P=0.15$). In the BIS group, the total amount of propofol used was lower [109 (20) $\mu\text{g kg}^{-1} \text{min}^{-1}$] than in the CSM group [130 (27) $\mu\text{g kg}^{-1} \text{min}^{-1}$] ($P=0.018$). The time to eye opening was lower in the BIS [7.2 (3.5) min] than in the CSM group [10.7 (6.6)] ($P=0.038$). There were no differences in fentanyl consumption, or in other clinical markers of recovery.

Conclusions. Compared with BIS, propofol anaesthesia guided with CSI resulted in 20% higher propofol doses. This, however, does not lead to clinically relevant differences in recovery times.

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The bispectral index monitor (BISTM, Aspect Medical Systems, Norwood, MA, USA) and the cerebral state monitor (CSM, Danmeter A/S, Odense, Denmark) are commercial devices to measure depth of hypnosis during anaesthesia. Both monitors use proprietary algorithms to process the EEG signal and estimate dimensionless indices that are expected to approach 100 for the awake patient and progressively decrease as hypnosis increases.^{1,2} Index values between 40 and 60 for BIS and the cerebral state index (CSI) have good correlation between them and indicate adequate depth of hypnosis levels for surgery.³ In a previous study designed to compare CSI and BIS during propofol induction, we showed that although both indices progressively decrease as hypnosis increased, the CSI

tended to stabilize in values of 60–40 at intermediate levels of hypnosis, whereas BIS stabilized in values of 40–20 at deeper anaesthetic levels. The clinical relevance of these discrepancies has not yet been assessed.⁴

Since the 40–60 recommended index range for surgery is within the less dynamic range of CSI, we hypothesize that higher doses of propofol might be required to maintain index values between 40 and 60 during surgery, if CSI is used instead of BIS to guide propofol administration. Moreover, this larger propofol requirement might result in a delayed recovery period.

The objective of this study is to compare propofol requirements and recovery times when BIS and CSM are used to guide propofol anaesthesia.

Methods

After approval by institutional ethics committee (Facultad de Medicina, Pontificia Universidad Católica de Chile), informed written consent was obtained from 40 ASA I or II patients, aged 18–60 yr, undergoing elective laparoscopic cholecystectomy under general anaesthesia. Exclusion criteria were a BMI $>30 \text{ kg m}^{-2}$, any known cerebrovascular disease, intake of any drug acting on the central nervous system, known pregnancy, and any known adverse effect to the study drugs.

After arrival at the operating theatre, standard monitoring was initiated (non-invasive arterial pressure, ECG, and pulse oximetry), and a peripheral i.v. line was inserted. At this time, the sensors of the Aspect A-2000 BIS[®] monitor (version 3.2 XP) and the standard electrodes of the CSM model 2 monitor were placed on each patient according to the manufacturer's recommendations.

The smoothing time period of the BIS monitor was set at 15 s. BIS values were automatically recorded every 5 s and transferred to computer hard disk using the Hyperterminal (Microsoft, Redmond, VA, USA) program. The CSM updates the CSI every second and has a fixed smoothing time of around 10 s.⁵

The data of CSI were recorded using the Danmeter A/S CSM capture V2.02 onto the computer hard disk. The BIS and the CSI were recorded simultaneously in each patient during the study period.

Before induction of anaesthesia, the patients were randomly allocated into two groups according to the monitor used to guide propofol administration (Groups BIS and CSM). Randomization was performed using a table of random numbers generated by a computer. A baseline period of 1 min was registered at this time. Anaesthesia was then induced with fentanyl $5 \mu\text{g kg}^{-1}$, and a target-controlled infusion (TCI) of propofol with the workstation Orchesta[®] Base Primea (Fresenius Vial Company, Brezins, France). Initially, an effect-site concentration of $4.5 \mu\text{g ml}^{-1}$ was targeted in both groups using Schnider pharmacokinetic parameters.⁶ Tracheal intubation was facilitated with atracurium 0.5 mg kg^{-1} and mechanical ventilation was adjusted to an \dot{V}_{CO_2} of 30–35 mm Hg. Neuromuscular blocking agents were given only during the induction of anaesthesia. Nitrous oxide was not used and all patients were ventilated with O_2 to 100% throughout the surgery. All patients received ketorolac 60 mg i.v. after induction of anaesthesia. The intra-abdominal pressure secondary to the pneumoperitoneum was 15 mm Hg in both groups. During maintenance of anaesthesia, additional 50 or 100 μg bolus doses of fentanyl were given as necessary to maintain mean arterial pressure (MAP) and heart rate (HR) between 20% of baseline values. Although MAP and HR were the primary endpoints to administer fentanyl, if the patient presented signs of inadequate anaesthesia, such as lacrimation or movements, the anaesthetist was allowed to administer

additional fentanyl boluses. Propofol TCI was adjusted to maintain the BIS or CSI within 40 and 60. Although all patients were simultaneously monitored with both EEG monitors, the anaesthetist was allowed to see only the monitor randomly assigned to guide propofol administration. The same clinician was in charge of the anaesthesia administration in all patients.

At the end of skin closure, \dot{V}_{CO_2} was increased to 40 mm Hg. Patients who had fade during tactile assessment to double burst stimulation received neostigmine and atropine, and propofol was stopped (T_0). After 5 min under the same ventilatory variables, patients were left in apnoea until spontaneous breathing. During this period, manual ventilations were given $2\text{--}3 \text{ min}^{-1}$, if required to avoid pulse oximetry values $<95\%$. No stimulation was applied to patients during the first 10 min after T_0 . From minute 11 after T_0 , patients were called by their names every minute until recovery of consciousness. The tracheal tube was removed, when subjects did not tolerate it any longer. The total amount of propofol and fentanyl administered throughout surgery were registered.

Beginning at T_0 , evaluation of recovery of anaesthesia was done by the time to spontaneous breathing (TSB) and time to eyes opening (TEO). Another collaborator who was blind to the group allocation carried out these measurements. Thirty minutes after arrival in the post-anaesthesia care unit (PACU), the modified Aldrete score was measured.⁷ Discharge of patients from PACU was left to the discretion of the PACU anaesthesiologists who were blinded to the monitor used during surgery.

Normality of data was tested with the Shapiro test. The data were judged adequate for calculations, if the signal quality index of BIS and CSI was $>20\%$. Comparisons of BIS and CSI values were performed during the maintenance period (5 min after intubation until the end of propofol infusion) with ANOVA for repeated measurements. All the other comparisons were done with non-paired Student's *t*-test, χ^2 test, or Mann–Whitney test. A value of $P < 0.05$ was considered significant.

Assuming mean infusion rates of propofol of 100 ($20 \mu\text{g kg}^{-1} \text{ min}^{-1}$), a sample size of 16 patients in each group was estimated necessary to detect a 20% difference in total propofol consumption (power=0.8, $\alpha=0.05$). Statistical analyses were performed using R (language and environment for statistical computing, freely available from <http://www.r-project.org/>).

Results

There were no significant differences in patient's characteristics or duration of anaesthesia (Table 1). Most of our patients were ASA I. Concomitant medications were levotiroxine, three patients in each group, enalapril, one patient in the CSM group, atenolol, one patient in the BIS group, and simvastatine, one patient in the CSM group.

All randomized patients were finally included in the analysis. No vasoactive drugs or fluid boluses were given before or during the period of study. Clinical signs of inadequate anaesthesia were not observed. Surgeries were done in down lithotomy position in all cases. Lactated Ringer's solution was administered between 8 and 10 ml $\text{kg}^{-1} \text{h}^{-1}$.

During the maintenance period of anaesthesia, the BIS values were within the target range, an 80.2% of time in the BIS group. On the other hand, the CSI values were

according to the desired range, an 85.5% of time in the CSM group ($P=0.91$).

The values of BIS and CSI measured during the maintenance of anaesthesia in both groups can be seen in Figures 1 and 2, respectively.

In patients of the BIS group, the values of CSI and BIS were 47.9 (5.8) and 45.9 (2.2), respectively ($P=0.15$). In patients of the CSM group, the values of CSI were higher than BIS, 46.8 (5.1) and 38.7 (6.2), respectively ($P=0.00054$).

There were no differences in fentanyl consumption between the BIS and the CSM groups, 5.05 (1.6) and 5.44 (1.2) $\mu\text{g kg}^{-1} \text{h}^{-1}$, respectively ($P=0.41$). In the BIS group, the total amount of propofol used was smaller [109 (20) $\mu\text{g kg}^{-1} \text{min}^{-1}$] than that used in the CSM group [130 (27) $\mu\text{g kg}^{-1} \text{min}^{-1}$] ($P=0.018$).

When anaesthesia was guided according to the BIS, poor quality of the signal was observed for on average 0.33 (0.12) min, with a minimum and maximum value of 0 and 2.58 min, respectively. In the CSM-guided group, poor quality of the signal was observed for 1.75 (0.68) min, with a minimum and maximum value of 0 and 9.41

Table 1 Patient characteristics and duration of anaesthesia. Data are mean (range) for age, or mean (sd). BIS, bispectral index monitor; BMI, body mass index; CSM, cerebral state monitor

	Group BIS	Group CSM
Age (yr)	40 (20–51)	43 (24–60)
Weight (kg)	71 (10)	72 (10)
Height (cm)	162 (7)	169 (10)
BMI (kg m^{-2})	27 (3)	25 (2)
Gender (female/male)	15/5	12/8
ASA I/II	16/4	15/5
Duration of anaesthesia (min)	80 (20)	85 (22)

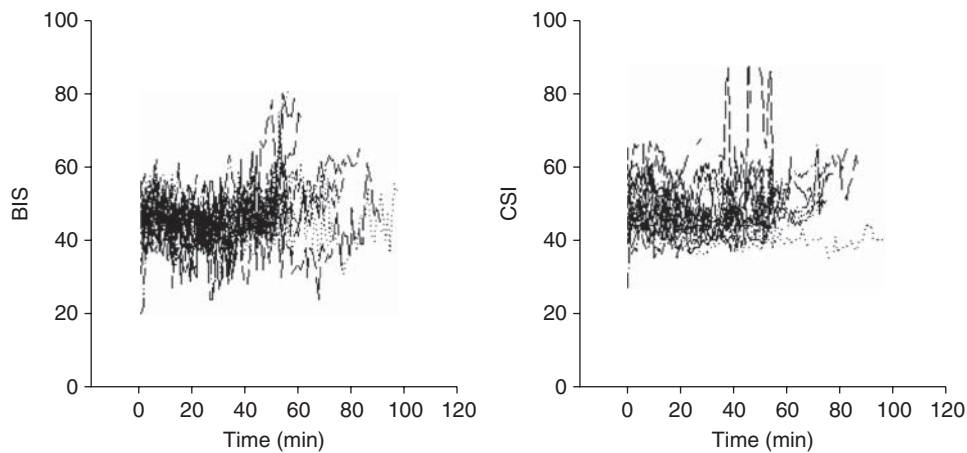


Fig 1 Variation of BIS and CSI during the maintenance when the anaesthesia was guided according to BIS.

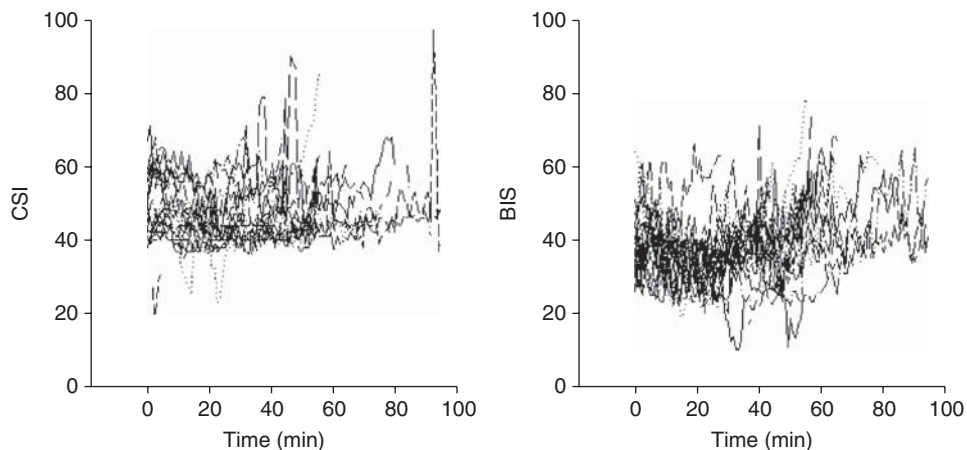


Fig 2 Variation of BIS and CSI during the maintenance when the anaesthesia was guided according to CSM.

Table 2 Evaluation of recovery from anaesthesia, discharge criteria, and discharge times from PACU. Data are mean (SD). * $P < 0.05$. BIS, bispectral index monitor; CSM, cerebral state monitor; TSB, time to spontaneous breathing; TEO, time to eyes opening; PACU, post-anaesthesia care unit

	Group BIS	Group CSM
TSB (min)	3.5 (3.8)	6.9 (6.6)
TEO (min)	7.2 (3.5)*	10.7 (6.6)
Modified Aldrete score	13 (0.8)	13 (0.6)
Discharge PACU (min)	114 (3.8)	114 (4.5)

min, respectively ($P=0.006$). The maximum continuous extension of time with bad quality signal was 85 and 90 s in the BIS and CSM groups, respectively ($P>0.05$).

Recovery times, modified Aldrete scores, and time to discharge to ward are shown in Table 2.

Discussion

The main finding of this study is that, compared with a BIS-guided anaesthesia, ~20% higher doses of propofol are required to keep CSI values within the same 40–60 range. In addition, although slightly shorter recovery times were observed after stopping propofol infusion in patients guided by BIS, no differences in modified Aldrete scores were observed 30 min after surgery.

To the best of our knowledge, there are no studies comparing propofol consumption and recovery profiles when BIS or CSM are used to guide anaesthesia. The findings of our study showing a 20% higher consumption of propofol when the anaesthesia was guided by CSM are consistent with our previous study findings showing that the CSM has a less dynamic profile compared with BIS within the 60–40 range.⁴ This less dynamic profile of CSM is probably explained because the CSM's algorithm does not incorporate frequencies below 6 Hz, which are characteristic of profound hypnotic levels.^{3–8} Therefore, this index is less sensitive than BIS to propofol concentration changes until much deeper hypnotic levels are reached, marked by the start of burst suppression activity.⁴ The less sensitivity to propofol effect observed with CSM at these intermediate levels of hypnosis is manifested by a stabilization tendency during increasing propofol concentrations,⁴ which explains the lower BIS values found in our study when CSI was used to guide propofol administration. In other words, it is difficult with this monitor to discriminate a too deep level of hypnosis until the appearance of burst suppression activity. According to the current results, showing higher propofol consumption and a wider range of BIS values during surgery when anaesthesia was guided by the CSM (Fig. 2), BIS seems more reliable than CSM to guide propofol administration at these lighter surgical hypnotic levels.

In our study, the significantly higher propofol infusion rates observed in patients guided by CSM lead to delayed TEO after stopping propofol infusions (Table 2). This

higher propofol consumption was observed in most patients in the CSM group, and it is not the result of a few outliers with a very high consumption.

The longer TSB and higher consumption of fentanyl observed in patients guided by CSM, however, did not reach statistical significance, most probably from lack of power of this study design. In the postoperative period, the differences observed in propofol infusion rates did not lead to prolonged recovery times. We did not find differences neither in the modified Aldrete scores at 30 min nor in the discharge times from the PACU between both groups.

Our findings are consistent with the favourable pharmacokinetic profile of propofol and agreed with clinical studies showing rapid recovery times after propofol anaesthetics at comparable infusion schemes.^{6–9–11} It might be possible that the 20% higher propofol consumption observed in the CSM group might lead to relevant prolonged recovery times after longer surgeries, since context-sensitive half-times of propofol increase as infusion times increase.¹²

The period of time without adequate signal secondary to artifacts was significantly higher in the CSM group than in the BIS group ($P=0.006$). However, the maximum continuous period of time with bad quality signal was not more than 1.5 min. Therefore, it is improbable that clinical decisions, such as change in propofol rate, have been made considering that information.

One limitation of this study was the lack of blind to the monitor used. This might have led to bias in propofol administration schemes according to the anaesthesiologist experience and confidence with each of the monitors used. However, considering that no differences exist in the time at which the values of BIS and CSI were maintained within the desired target range (80.2% of time in the BIS group and 85.5% of time in the CSM group) ($P=0.91$), we think this limitation is less relevant. Another potential limitation of our study is the awareness possibility, which was not investigated.

In conclusion, the guidance of propofol anaesthesia to keep CSI or BIS within the 40–60 range during surgery resulted in 20% higher propofol doses with the CSM guide. This higher propofol consumption, however, did not lead to clinically relevant prolonged recovery times.

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