

NEUROSCIENCES AND NEUROANAESTHESIA

Survey on the adequacy of depth of anaesthesia with bispectral index and isolated forearm technique in elective Caesarean section under general anaesthesia with sevoflurane[†]

F. Zand, S. M. R. Hadavi*, A. Chohedri and P. Sabetian

Shiraz Anaesthesiology and Critical Care Research Center, Department of Anaesthesia, Shiraz University of Medical Sciences, Faghihi Hospital, Zand Blvd, Shiraz, Iran

* Corresponding author. E-mail: hadavimr@sums.ac.ir

Editor's key points

- Bispectral index (BIS) monitoring is commonly used to monitor depth of anaesthesia.
- The authors studied parturients in whom standard techniques were used for general anaesthesia for Caesarean section.
- The isolated forearm test was used to study the ability of the BIS to detect consciousness.
- BIS values below 60 were commonly associated with IFT responses, particularly before delivery.

Background. Awareness during general anaesthesia for Caesarean section (C/S), although uncommon, remains a concern for anaesthesiologists. We examined the relationship between the bispectral index (BIS) and responses to the isolated forearm technique (IFT) to evaluate the adequacy of general anaesthesia in C/S and determine a suitable cut-off point for BIS values based on IFT results.

Methods. In 61 parturients, a standardized anaesthetic technique was applied. It included sodium thiopental and succinylcholine for induction, and O₂, N₂O, and sevoflurane for maintenance of anaesthesia. BIS values and IFT response were recorded at 16 predetermined events during anaesthesia.

Results. Positive IFT responses were seen in 41%, 46%, and 23% of the parturients at laryngoscopy, intubation, and skin incision, respectively. BIS could not reliably differentiate between IFT responders and non-responders during these three stages. The receiver operating characteristic curve cut-off points for BIS to predict IFT responders with 100% sensitivity were 34, 37, and 27, respectively, for these stages. In all stages of the operation *after* skin incision, more than 90% of parturients had no IFT test response, and BIS values between 40 and 63 were associated with negative IFT results. During a structured interview within 12–24 h after the operation, no patient had evidence of explicit recall of intraoperative events.

Conclusions. The BIS is not reliable for monitoring anaesthesia depth in C/S. Lower than previously recommended values are needed to avoid IFT test responses during laryngoscopy, intubation, and skin incision.

Keywords: anaesthetics, sevoflurane; awareness; bispectral index; Caesarean section; general anaesthesia

Accepted for publication: 26 September 2013

Awareness during general anaesthesia is a problem that has become increasingly recognized since the introduction of routine use of neuromuscular blocking agents.^{1 2} It has long been recognized that this is a particular problem during Caesarean section (C/S), because a lack of sedative premedication, a low inspired concentration of nitrous oxide and volatile agent, and the withholding of opioids until after delivery, all contribute to the risk of awareness.^{3 4}

The isolated forearm technique (IFT) is the gold standard test for detecting wakefulness during C/S.^{5 6} It relies on isolation of the forearm from the effects of the neuromuscular blocking drug by occlusion of the circulation with a pneumatic

tourniquet inflated before injection of neuromuscular blocking agent. Movement of the hand in response to a recorded command played to the patient is then monitored.

The bispectral index (BIS), a multivariate variable calculated from the processed electroencephalogram, is believed by some to be a useful aid to ensure adequate hypnosis during general anaesthesia,^{7–9} but others would dispute its accuracy, and believe that the BIS is of value only in that it gives some idea as to memory function and absence of subsequent explicit recall and is not a guarantee of lack of wakefulness.^{10 11}

We carried out an observational study to compare and correlate BIS values with IFT responses to find a cut-off point for

[†]This article is accompanied by Editorial V.

BIS values associated with the absence of wakefulness during general anaesthesia for C/S.

Methods

The study protocol was approved by the ethics committee of the Shiraz University of Medical Sciences, Shiraz, Iran. Sixty-one ASA I or II patients undergoing elective C/S under general anaesthesia gave informed consent to participation in the study. Exclusion criteria were uncooperative patients, language barrier problems, MgSO₄ administration before the study, psychological disorders, history of awareness, opium addiction, and neuromuscular disorders.

All patients were monitored with ECG, non-invasive arterial pressure, pulse oximetry (SpO₂), end-tidal gas analyser, and BIS monitoring. Anaesthesia was administered by senior residents, under the supervision of one of the authors.

The researcher, who supervised the anaesthesia, explained the concept of the study to the patients and placed a sphygmomanometer cuff around the right forearm of the patients after placing a cotton bandage and inflated it to 200 mm Hg immediately before induction. This isolated the right hand from the effects of the neuromuscular blocking agent. The headphones of an MP3 player were placed over the patient's ears and the following command was presented: 'open and close your right hand'. This was repeated every 30 s throughout the period of the trial until the time of tracheal extubation. The cuff was deflated after 20 min to prevent ischaemic paralysis, but was re-inflated before any further boluses of neuromuscular blocking drugs were administered. Arm activity was scored as no movement (0), non-specific movement (e.g. fine movements of fingers) (1), or firm clenching/flexing movement (2).¹² Before induction of anaesthesia, the Bispectral Index monitor (Aspect Medical Systems Inc., USA) was connected to the Aspect BIS sensor, which had been placed on the forehead of the patient as recommended by the manufacturers.

After 3 min of preoxygenation, rapid sequence induction was performed with sodium thiopental 4–5 mg kg⁻¹ and succinylcholine 1–2 mg kg⁻¹. Cricoid pressure was applied and tracheal intubation was performed. Anaesthesia was then maintained with 50% nitrous oxide in oxygen (7 litre min⁻¹) and sevoflurane. The inspired concentration of sevoflurane was set at 1.8–2.2% until delivery; thereafter, it was reduced to 1.2%. After delivery, i.v. morphine 0.15 mg kg⁻¹, midazolam 0.03 mg kg⁻¹, and fentanyl 100 µg were administered. After recovery of spontaneous respiration, 10 mg atracurium was administered. Sevoflurane administration was stopped at subcutaneous layer closure and nitrous oxide stopped at the start of skin closure.

The BIS value, IFT responses, and end-tidal sevoflurane concentrations were noted in association with the following events: baseline value, induction of anaesthesia (at the end of thiopental injection), laryngoscopy (at insertion of blade to hypopharynx), intubation (at the time of cuff inflation), at the end of skin incision, at the end of peritoneal incision, at the end of uterine incision, at the end of uterine retraction (widening the uterine incision by the surgeon), delivery (cord

clamping), start of uterine closure, start of muscle closure, start of subcutaneous layer closure, start of skin closure, 2 min after the end of skin closure, eye opening, and extubation.

BIS was read off the machine. BIS and IFT values were noted by two independent observers. All patients were interviewed 12–24 h after surgery regarding the experience of dreaming or recall using the following questions:¹³

- (1) What was the last thing you remembered before going to sleep?
- (2) What was the first thing you remembered on waking?
- (3) Do you remember anything between going to sleep and waking?
- (4) Did you dream while you were sleeping during the operation?

Receiver operating characteristic (ROC) analysis was used for determining the best cut-off point for BIS, that is, the BIS value with best (nearest to 100%) sensitivity and specificity to prevent wakefulness. Also, the Mann–Whitney test was used to determine the relationship between BIS and IFT values, after combining the data at laryngoscopy, intubation, and skin incision events.

Results

All 61 enrolled parturients completed the study. All collected data are presented. The median (range) Apgar scores of newborns were 9 (4–9) at minute 1 and 10 (9–10) at minute 5. Table 1 shows the percentage of patients who showed IFT responses of grades 2, 1, and 0 at various stages of surgery with the mean, SD, and range of BIS in each group. The BIS values and the end-tidal sevoflurane concentrations recorded at predetermined intraoperative events are shown in Figures 1 and 2, respectively. The mean BIS values were 37, 45, and 46 at induction, laryngoscopy, and intubation, respectively (i.e. before the start of sevoflurane). For the time points when BIS was recorded during sevoflurane administration, the median BIS values were between 45 and 59, except for delivery time, when the median BIS was 39.

Unlike routine sensitivity analysis of diagnostic tests that try to find a cut-off point with the best sensitivity and specificity, we believe that the best cut-off for BIS is the cut-off point associated with 100% sensitivity (i.e. below that value no patients showed evidence of wakefulness defined as IFT=2). Table 2 shows the cut-off points for BIS values with 100% sensitivity for preventing wakefulness and the cut-off point with best overall sensitivity and specificity. As the results show that to be 100% certain that a patient will not regain consciousness (IFT response=2), the BIS value must be below 27 in the pre-delivery stages.

The BIS and IFT values for laryngoscopy, intubation, and skin incision stages were combined to give 183 data points (3 for each patient). The BIS data were analysed according to whether there was a clear IFT response (IFT=2) vs no clear IFT response (IFT=0 or 1). At these times, amalgamated BIS values were not normally distributed. The BIS values were

Table 1 Percentage of different IFT states at each event (number of patients) with corresponding mean BIS values (BIS standard deviation) (range of BIS)

Events	IFT=2	IFT=1	IFT=0	All patients, BIS values
Baseline	100 (61); 98 (0.2) (97–98)	0	0	98 (0.21) (97–98)
Induction	0	0	100 (61), 37 (3.3) (30–52)	37 (3.3) (30–52)
Laryngoscopy	29 (18), 46 (5.4) (36–52)	11 (7), 31.1 (14.6) (38–80)	59 (36), 43 (16.4) (38–80)	45 (8) (31–80)
Intubation	36 (22), 49 (8.2) (36–70)	10 (6), 51 (16.3) (38–80)	54 (33), 43 (7) (31–66)	46 (9) (31–80)
Skin incision	13 (8), 55 (15.3) (28–70)	10 (6), 60 (13.2) (42–78)	77 (47), 45 (6.2) (34–66)	48 (9.8) (28–78)
Peritoneal incision	3 (2), 68 (4.2) (65–71)	2 (1), 42	95 (58), 46 (8.8) (22–78)	46 (9.5) (22–78)
Uterine incision	0	0	100 (61), 46 (8.7) (24–80)	46 (8.7) (24–80)
Uterine retraction	0	10 (6), 53 (6.7) (45–60)	90 (55), 48 (8.5) (31–78)	49 (8.4) (31–78)
Delivery	0	0	100 (61), 39 (7.1) (25–66)	39 (7.1) (25–66)
Uterine closure	0	3 (2), 43 (2.1) (41–44)	97 (59), 45 (7.3) (28–68)	45 (7.2) (28–68)
Muscles and fascia closure	0	5 (3), 51 (8) (43–59)	95 (58), 52 (6.9) (29–66)	52 (6.9) (29–66)
Subcutaneous closure	2 (1), 66	3 (2), 66 (66)	95 (58), 59 (6.5) (35–70)	59 (6.5) (35–70)
Start of the skin closure	2 (1), 64	3 (2), 70 (70)	95 (58), 63 (6) (40–78)	63 (6.0) (40–78)
2 min after the end of skin closure	0	12 (7), 74 (8.3) (64–84)	89 (54), 67 (5) (55–82)	68 (5.7) (55–84)
Eye opening	98 (60), 87 (3.5) (80–93)	0	2 (1), 83	87 (3.5) (80–93)
Extubation	100 (61), 88 (3.3) (81–92)	0	0	88 (3.3) (81–92)

Downloaded from https://academic.oup.com/bja/article/112/5/871/272581 by guest on 19 April 2024

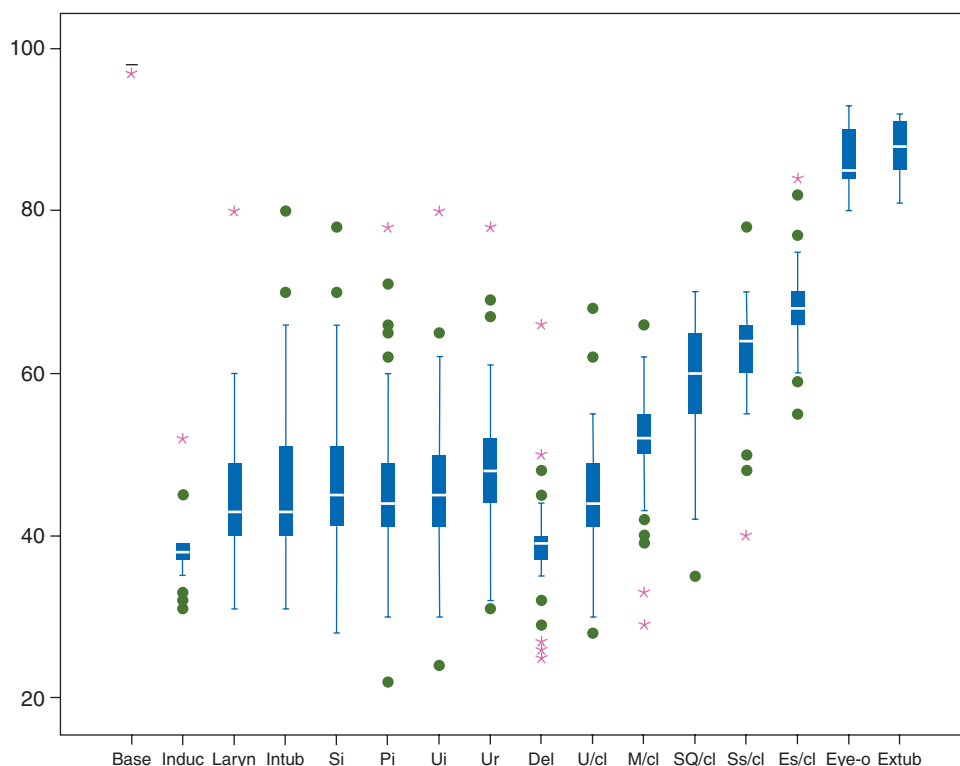


Fig 1 Box and whiskers plot of BIS vs 16 events (milestones). Boxes represent inter-quartile range. Whiskers represent maximal points that are not outliers. Circles represent points that are > 1.5 times the inter-quartile range. Asterisks represent points that are > 3 times the inter-quartile range. The 16 milestones are baseline (Base), induction (Induc), laryngoscopy (Laryn), intubation (Intub), skin incision (Si), peritoneal incision (Pi), uterine incision (Ui), uterine retraction (Ur), delivery (Del), uterine closure (U/cl), muscles and fascia closure (M/cl), subcutaneous closure (SQ/cl), start of the skin closure (Ss/cl), 2 min after the end of skin closure (Es/cl), eye opening (Eye-o), and extubation (Extub).

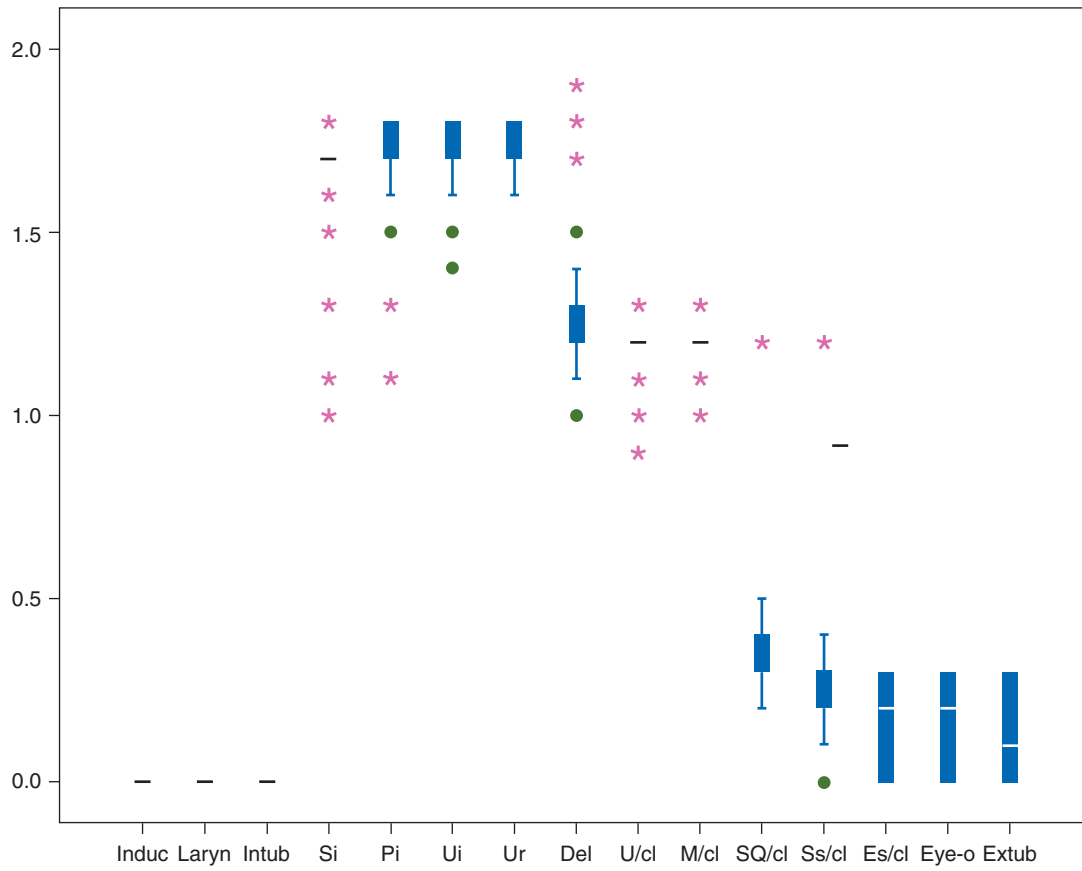


Fig 2 Box and whiskers plot of end-tidal sevoflurane vs 15 events (milestones). Boxes represent inter-quartile range. Whiskers represent maximal points that are not outliers. Circles represent points that are > 1.5 times the inter-quartile range. Asterisks represent points that are > 3 times the inter-quartile range. The 15 milestones are baseline induction (Induc), laryngoscopy (Laryn), intubation (Intub), skin incision (Si), peritoneal incision (Pi), uterine incision (Ui), uterine retraction (Ur), delivery (Del), uterine closure (U/cl), muscles and fascia closure (M/cl), subcutaneous closure (SQ/cl), start of the skin closure (Ss/cl), 2 min after the end of skin closure (Es/cl), eye opening (Eye-o), and extubation (Extub).

Table 2 The cut-off points of BIS with a sensitivity 100% at each event and the cut-off point with best overall sensitivity and specificity (sensitivity and specificity could not be calculated at the points that all the patients were either responding or non-responding to verbal command)

Events	Cut-off points of BIS for 100% sensitivity	Cut-off with best sensitivity and specificity	Sensitivity	Specificity
Laryngoscopy	34.5	41.5	72	51.2
Intubation	35.5	41.5	77	48.7
Skin incision	27	48.5	75	64.2
Peritoneal incision	63.5	63.5	100	99.9
Subcutaneous closure	65.5	65.5	100	80
Start of skin closure	63.5	63.5	100	46.7

significantly different between IFT responders and IFT non-responders (Mann–Whitney test; $P < 0.005$) (Table 3).

Using the ROC analysis, the best cut-off point for BIS, based on combined values of IFT in laryngoscopy, intubation, and skin incision, was 43 (sensitivity=68.8%, specificity=57.3%); but for this cut-off, the area under the curve (0.64) represents a poor level of accuracy (Fig. 3). Only at a BIS value of 27, 100% sensitivity could be reached.

Discussion

The current standard practice for induction and maintenance of anaesthesia for C/S is inadequate for preventing wakefulness. The main findings of our study are that the BIS is not a reliable method of monitoring anaesthetic depth in C/S, and that lower than previously recommended values are needed to avoid IFT test responses during laryngoscopy, intubation, and skin incision.

Table 3 Comparison of the combined BIS values at laryngoscopy, intubation, and skin incision according to the IFT response. *IFT response' is defined as IFT=2; †'No IFT response' is IFT=0 or 1

	<i>n</i>	Lower quartile (25%)	BIS median (50%)	Upper quartile (75%)	Range	<i>P</i> -value
IFT response*	67	41	49	52	28–80	<0.0005
No IFT response†	116	40	42	46.75	31–66	

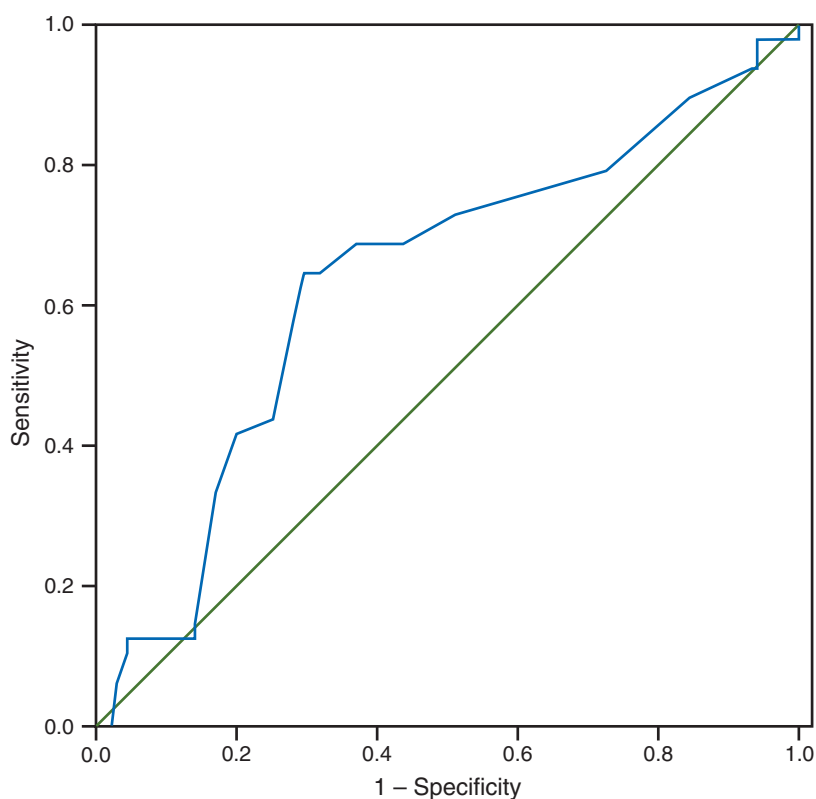


Fig 3 ROC curve of combined BIS and the IFT response of the patients at three points of laryngoscopy, intubation, and skin incision.

Even in countries where regional anaesthesia is common for C/S, general anaesthesia may be indicated because of the lack of time in emergencies, patients with coagulopathies, or because of patients' fear of dural puncture or concern about post-dural puncture headache.

Awareness with recall in association with general anaesthesia for C/S occurs more frequently than in other operations (0.1–0.2%).¹⁴ There are several reasons: (i) physiological changes during pregnancy such as higher cardiac output resulting in a wider distribution of drugs and thus lower blood levels of induction agents and volatile anaesthetics; and (ii) omission of, or decrease in the dose of some drugs to minimize their effects on uterine tone and to avoid fetal exposure.¹⁵ Such awareness with recall may cause severe postoperative psychological sequelae, including post-traumatic stress disorder, anxiety, neurosis, nightmares, fear of hospitals, and death. Standard clinical signs of inadequate anaesthesia such as increased arterial pressure or heart rate are controlled by the

autonomic nervous system, and therefore are affected by non-anaesthetic factors such as β -adrenergic receptor blocking drugs, hypovolaemia, hypoxaemia, hypercapnia, and pain. Thus, these signs are unreliable for evaluation of depth of anaesthesia.¹⁴

The IFT is recognized as the gold standard for consciousness monitoring in the presence of neuromuscular blocking agents.^{16,17} As shown in Table 1, in the current study, 18 (30%), 22 (36%), and eight patients (13%) had an IFT=2 during laryngoscopy, intubation, and skin incision, respectively. More surprising is the fact that 30 patients (49%) had positive IFT responses (IFT=2) at at least one of these events. From skin incision until subcutaneous layer closure, while sevoflurane was administered, more than 95% of patients had an IFT=0 or 1. From after skin incision to the end of the operation, only two patients (3.3%) showed positive responses at peritoneal incision and only one patient (1.6%) had positive responses at subcutaneous closure and

beginning of skin closure. The inability of the BIS to detect responsiveness in the early phases of C/S, where lower doses of sevoflurane were used, is concordant with other studies in gynaecological surgery, where lower doses of propofol or isoflurane were used with EEG-based depth of anaesthesia monitors (Narcotrend, MonitorTechnik, Germany; BIS, Covidien, USA).^{10 18}

The relationship between BIS, depth of anaesthesia, and memory functions is complex, and is influenced by multiple other factors, and by the type of memory function being studied. Kerssens and colleagues¹⁹ studied explicit and implicit memory for words presented during C/S under light isoflurane and N₂O anaesthesia (0.2% isoflurane; N₂O 50% until delivery, thereafter 70%). The mean BIS value during word presentation was 76.3. Interestingly, although no patient had explicit recall of intraoperative events, and no patients had conscious (cued) recall of previously heard words, the authors did find evidence of a subtle and weak form of explicit memory for previously presented words. In another study, in which deeper anaesthesia was administered (halothane 0.5% and 66% N₂O), no patients showed positive responses to the IFT, and none showed evidence of explicit and implicit memory, but these patients received temazepam premedication,²⁰ and the benzodiazepines are known to impair memory function.²¹ In the current study, although many patients showed signs of wakefulness and responding, none had any evidence of explicit recall, and this is concordant with the findings of other studies.^{19 20 22} In our study, the mean BIS of <48 before delivery, while not ensuring unconsciousness, was associated with lack of subsequent explicit recall. Among our patients, the lack of recall for events occurring after delivery may of course also be attributed to the use of midazolam after delivery.

BIS is commonly used to estimate the depth of anaesthesia during i.v. and volatile anaesthesia.¹⁹ The relationship between BIS and likelihood of movement appears to be influenced by the nature and intensity of noxious stimuli. In a previous study, the researchers used the BIS and the IFT for measuring depth of anaesthesia after a single dose of propofol or pentothal.²³ Although there were no hand movements when the BIS was <58, there were no painful stimuli such as laryngoscopy, intubation, or surgical incision.²³ But in the present study, which was done in patients with considerable stimulation, even a BIS <50 did not prevent patients from waking up and responding to command.

We divided the patients into three groups according to their IFT responses, but considered the patients with IFT=1 (non-specific movements) as non-responders for the following reasons: (i) we believe that depth of anaesthesia is either adequate or inadequate, and thus a third state does not exist; and (ii) non-specific movement cannot be considered as a meaningful indicator of wakefulness. Defining wakefulness as either IFT=1 or IFT=0, there appear to be three distinct phases during the course of the anaesthesia in our patients:

- (i) From laryngoscopy to skin incision: In this period, 24 patients (40%) were responsive at one or more of the events. This significant percentage could be related to

an inadequate dose of thiopental (4–5 mg kg⁻¹), and/or inadequate sevoflurane concentrations during the sevoflurane wash-in period, while thiopental concentrations were declining.

- (ii) Peritoneal incision to 2 min after skin closure: In this period, the number of patients showing wakefulness at different time points was between zero and two. This lower percentage (0–3%) can be attributed to either adequate uptake of sevoflurane, or administration of midazolam and opioids.
- (iii) Eye opening and extubation: In this period, more than 59 patients (98%) had IFT=2. This is to be expected as sevoflurane and nitrous oxide had been discontinued.

One significant point that can be concluded from the comparison of BIS values and IFT responses is that although there was a significant difference in the BIS values between those showing and not showing responses, this was not clinically useful. BIS is poor at predicting whether patients are conscious or not. At the time of laryngoscopy, 18 patients (30%) were responsive (IFT=2), despite the fact that their BIS values were between 36 and 52. Conversely, at laryngoscopy, some patients with high BIS values (up to 80) showed no specific responses to the IFT (IFT 0 or 1). The same problems were noted at other time points. For example, at skin closure, 58 patients (95%) had IFT=0, despite their BIS values being in the range 40–78. This apparent hysteresis phenomenon may be because the opioids alter the relationship between BIS and the likelihood of responsiveness to stimuli.²⁴ It should be noted too that neuromuscular blocking agents alone can decrease BIS while clearly not influencing the conscious state.²⁵

The poor sensitivity and specificity of the BIS for detecting wakefulness in our study is concordant with that of previous studies. In a study using BIS and patient state index for determining the depth of anaesthesia, with different combinations of propofol, sevoflurane, and remifentanyl, the median BIS at loss of consciousness was 66, whereas the median BIS at recovery of consciousness was 79; as a result, a threshold BIS of 60 was associated with 90% sensitivity and only 26% specificity for consciousness.²⁶ Likewise, in another study, BIS values between 50 and 60 were not reliably associated with the lack of responsiveness to the IFT during laryngoscopy and intubation.¹¹ We believe that patients, and anaesthetists, usually want to be completely certain of unconsciousness. Thus, we attempted to determine cut-off points for BIS associated with 100% sensitivity for unconsciousness, which we defined as IFT 0 or 1. As shown in Table 2, during laryngoscopy, intubation, and skin incision, these values were 35, 36, and 27, respectively. During subsequent surgery, a BIS <65 prevented consciousness.

The BIS means recorded in the current study at the different stages (Table 1) have a close correlation with the cut-off points for optimal sensitivity and specificity (Table 2) except for laryngoscopy, intubation, and skin incision. Because of the proximity in time, and similar high levels of stimulation, we amalgamated the data for these three data collection points, in an

ROC curve analysis. Based on these integrated data, an optimal threshold for this early part of surgery is a BIS of 40 (sensitivity=86.6%, specificity 14.7%). However, in clinical practice, the poor specificity associated with this threshold is probably not acceptable. To ensure that all patients are unconscious during these phases of surgery, our data for the cut-off point of BIS suggest that BIS should be lower than 27 (sensitivity 100%). This is very different from previous studies in which the range of BIS values considered to be associated with adequate anaesthesia was 40–60.^{23 24}

Our study has some limitations which may have limited our ability to identify all the patients who were conscious or who had recall. First, rather than assessing responses continuously, we checked for hand movements at specific discrete time points. Thus, we cannot exclude consciousness between these time points. Secondly, the tourniquet was not always placed on the dominant arm, so in the early stages of consciousness, there may have been confusion as to which hand to move. Another weakness is that the command did not include the patient's first name, and it may be that conscious patients may fail to respond to the IFT commands because they are uncertain that the instruction is intended for them. Also, we did not use a peripheral nerve stimulator to ensure that the hand on the side of the tourniquet had not become paralysed. Although we consider this highly unlikely, unexpected paralysis of the ipsilateral hand may account for some cases of failure to respond, despite higher BIS values later in surgery. Another possible weakness is that we only observed the patients—and thus did not attempt to verify indeterminate responses (IFT=1). Finally, we administered midazolam after delivery which may have prevented recall for subsequent events, and we did not perform three postoperative interviews as some have recommend.^{27 28} However, by their nature, all of these limitations would tend to reduce the number of patients identified as being conscious or with recall, and so do not detract from our basic observation that during C/S, the BIS monitor was poor at predicting whether patients were conscious or not.

A few other limitations should be mentioned. The addition of opioids and omission of N₂O could have had profound effects on our findings, and this limits the extent to which our findings can be extrapolated to other populations and situations when different drugs and drug combinations are used. Finally, the BIS values were read off the machine and not offline from downloaded data. As the BIS can vary rapidly during and after painful stimuli, it is better to download data and apply some averaging to evaluate recorded values more accurately.

In conclusion, the standard anaesthetic protocol we applied was not sufficient for providing adequate depth of anaesthesia, and the BIS performed poorly at detecting consciousness, during laryngoscopy, intubation, and skin incision.

Authors' contributions

F.Z.: helped design the study, analyse the data, and write the manuscript. F.Z. has seen the original study data, reviewed

the analysis of the data, and approved the final manuscript. S.M.R.H.: helped analyse the data and write the manuscript. S.M.R.H. has seen the original study data, reviewed the analysis of the data, and approved the final manuscript. P.S.: helped design the study, conduct the study, analyse the data, and write the manuscript. P.S. has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files. A.C.: helped conduct the study. A.C. has seen the original study data and approved the final manuscript.

Acknowledgements

The authors would like to thank all the anaesthesia staff at Zeinabieh Hospital, especially Mrs Taleii for her kind help during the conduct of this study and Miss R. Malek for typing and editing the manuscript.

Declaration of interest

None declared.

References

- 1 Bischoff P, Rundshagen I. Awareness under general anesthesia. *Dtsch Arztebl Int* 2011; **108**: 1–7
- 2 Leslie K, Davidson AJ. Awareness during anesthesia: a problem without solutions? *Minerva Anesthesiol* 2010; **76**: 624–8
- 3 Zand F, Allahyary E, Tabatabaee HR. Evaluation of the adequacy of general anesthesia in caesarean section by auditory evoked potential index : an observational study. *Acta Anaesthesiol Taiwan* 2008; **46**: 16–24
- 4 Lyons G, Macdonald R. Awareness during caesarean section. *Anesthesia* 1991; **46**: 62–4
- 5 Tunstall ME. Awareness, caesarean section and the isolated forearm technique. *Anaesthesia* 1990; **45**: 686
- 6 Andrade J, Deeprise C, Barker I. Awareness and memory function during paediatric anaesthesia. *Br J Anaesth* 2008; **100**: 389–96
- 7 Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. *Lancet* 2004; **363**: 1757–63
- 8 Klopman MA, Sebel PS. Cost-effectiveness of bispectral index monitoring. *Curr Opin Anaesthesiol* 2011; **19**: 234–9
- 9 Yeo SN, Lo WK. Bispectral index in assessment of adequacy of general anesthesia for lower segment caesarean section. *Anesth Intensive Care* 2002; **30**: 36–40
- 10 Russell IF. The Narcotrend 'depth of anaesthesia' monitor cannot reliably detect consciousness during general anaesthesia: an investigation using the isolated forearm technique. *Br J Anaesth* 2006; **96**: 346–52
- 11 Schneider G, Wagner K, Reeker W, Hanel F, Werner C, Kochs E. Bispectral index (BIS) may not predict awareness reaction to intubation in surgical patients. *J Neuro Anesth* 2002; **14**: 7–11
- 12 Bogod DG, Orton JK, Yau HM, Oh TE. Detecting awareness during general anesthetic caesarean section. *Anesthesia* 1990; **45**: 279–84
- 13 Abouleish E, Taylor FH. Effect of morphine–diazepam on signs of anesthesia, awareness and dreams of patients under N₂O for cesarean section. *Anesth Analg* 1976; **55**: 702–6
- 14 Robins K, Lyons G. Intraoperative awareness during general anaesthesia for cesarean section. *Anesth Analg* 2009; **109**: 886–90

- 15 Paech MJ, Scott KL, Clavisi O, Chua S, MacDonell N. A prospective study of awareness and recall associated with general anaesthesia for cesarean section. *Int J Obstet Anesth* 2008; **17**: 298–303
- 16 Jessop J, Jones JG. Conscious awareness during general anaesthesia—what are we attempting to monitor? *Br J Anaesth* 1991; **66**: 635–63
- 17 Barker I, Deeprose C, Andrade J. Response to editorial by Davidson. *Paediatr Anaesth* 2003; **13**: 644
- 18 Russell IF. The ability of bispectral index to detect intra-operative wakefulness during isoflurane/air anaesthesia, compared with the isolated forearm technique. *Anaesthesia* 2013; **68**: 1010–20
- 19 Kerssens C, Lubke GH, Sebel PS, Gershon RY. Memory formation during general anaesthesia for emergency cesarean section. *Anesthesiology* 2000; **92**: 1029–34
- 20 Russell IF, Wang M. Absence of memory for intraoperative information during surgery under adequate general anaesthesia. *Br J Anaesth* 1997; **78**: 3–9
- 21 Savic MM, Obradovic D, Bokonjic D, Ugresic N. Memory effects of benzodiazepines: memory stages and types versus binding-site subtypes. *Neural Plas* 2005; **12**: 289–98
- 22 Chin KJ, Yeo SW. Bispectral index values at sevoflurane concentrations of 1% and 1.5% in lower segment cesarean delivery. *Anesth Analg* 2004; **98**: 1140–4
- 23 Flaishon R, Windsor A, Sigl J, Sebel PS. Recovery of consciousness after thiopental or propofol. Bispectral index and isolated forearm technique. *Anesthesiology* 1997; **86**: 613–9
- 24 Sebel PS, Lang E, Rampil IJ, White PF, Cork R, et al. A multicenter study of bispectral electroencephalogram analysis for monitoring anesthetic effect. *Anesth Analg* 1997; **84**: 891–9
- 25 Messer M, Beese U, Romstok J, Dinkel M, Tschakowsky K. The bispectral index declines during neuromuscular block in fully awake persons. *Anesth Analg* 2003; **97**: 488–91
- 26 Schneider G, Gelb AW, Kochs E, Schmeller B, Tschakert R. Detection of awareness in surgical patients with EEG-based indices: bispectral index and patient state index. *Br J Anaesth* 2003; **91**: 329–35
- 27 Samuelsson P, Brudin L, Sandin R. Late psychological symptoms after awareness among consecutively included surgical patients. *Anesthesiology* 2007; **106**: 26–32
- 28 Shalev A, Peri T, Canetti L, Schreiber S. Predictors of PTSD in injured trauma survivors: a prospective study. *Am J Psychiatry* 1996; **153**: 219–25

Handling editor: A. R. Absalom