Worcestershire Acute Hospitals NHS Trust

Use of Bispectral Index (BIS) depth of anaesthesia monitors

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Contents

Aims

Guidance for anaesthetists on the patients who may benefit from use of depth of anaesthesia monitoring.

Summary

Consider using BIS as an option in the following settings:
Concern about increased risk of intraoperative awareness
TIVA, in particular with use of neuromuscular blocking agents, or when cannula cannot be visualised.
Concern regarding postoperative delirium in patients undergoing anaesthesia
High risk of adverse events – ASA 3 or 4 patients >60 years, and likely to be anaesthetised for > 2 hours.
Record use of BIS consumables in BIS log book

Introduction

The simplest method employed by anaesthetists to assess depth of anaesthesia is the interpretation of clinical signs. These include blood pressure, heart rate, sweating, tearing, pupillary response, and muscle reflexes. Whilst routinely used to aid depth of anaesthesia assessment, many of these signs when taken individually, are subject to change based on events unrelated to depth of anaesthesia. Consequently, inaccurate assessments can be made, leading to potential under or overdosing of anaesthetic agents.

Bispectral Index Monitor (BIS)

The Bispectral Index (BIS) monitor, (BIS™ Medtronic-Covidien, Dublin, Ireland), converts a single channel of frontal electroencephalograph into an index between 0 and 100, with specific ranges (45-60) reflecting low probability of consciousness. A suppression ratio (SR) or burst count can also be measured on the BIS monitors, representing the proportion of the total time on the EEG spent in 'burst suppression' – associated with very deep anaesthesia.

Important considerations when using BIS

As is well understood by all anaesthetists, the depth of anaesthesia is influenced by the degree of stimulation of the patient, and as when monitoring the anaesthetic without such a monitor, vigilance is required during periods with changes in level of stimulation. A BIS score ~50 immediately before a stimulating event (e.g. laryngoscopy, intubation, skin incision) is potentially inadequate to avoid accidental awareness. More opiate-based anaesthetics (e.g. remifentanil infusion) have fewer variations in BIS and result in a smaller increase in BIS following painful stimuli such as intubation.

The BIS index and EMG are measured/monitored in two separate frequency ranges (0-45 HZ for BIS and 70-110Hz for EMG). Therefore, technically neither should affect the other. In reality however, particularly in situations where there is a high degree of EMG artefact, some EEG signals may overlap into the lower ranges where BIS is measured, leading to elevation in BIS score. Clinicians need to be able to spot the difference between clinical and artefactual EMG signal and not 'over rely' on the BIS score in this situation. Of course, genuine increased muscle activity (where NMB's are not active) can be a useful and early sign of emergence.

Nitrous oxide has no direct effect on BIS when used as a sole agent or when administered with propofol, but has a small additive effect with sevoflurane. It may lead to a 'smoother' BIS trend during general anaesthesia due to the added analgesic effect. Its use with BIS might result in an unintentionally deep level of anaesthesia. Ketamine is not only a general anaesthetic agent but also has unique dissociative properties which distinguishes it from many other anaesthetic agents, and as such can have the effect of increasing the BIS index. Etomidate can also affect the BIS index.

Potential Benefits of BIS monitoring

Areas in which BIS can potentially be useful during anaesthesia can be divided into reduction in perioperative adverse outcomes (mortality and morbidity), reduction of risk of anaesthetic awareness, and the more accurate titration of anaesthetic dosing to reduce anaesthetic overdosing and time to emergence.

Prevention of Adverse Outcomes

There is building evidence that considerable morbidity, and potentially increased mortality can be caused by the deliberate or inadvertent excessive dosing of anaesthetic agents to vulnerable individuals.

Post-op Morbidity/Mortality and BIS

Recent studies have found an association between deep anaesthesia and increased post-operative mortality in elderly and infirm patients undergoing major surgery. Six of the seven published studies have shown a correlation between relatively deep anaesthesia and increased mortality (see table 1 in appendix).[1-5] Increasing morbidity included an increased risk of myocardial infarction and stroke when deep anaesthetics were administered. The largest database, of 24,000 patients found three independent risk factors for mortality (low blood pressure, low requirement of volatile anaesthetic, and BIS score <40. A large multicentre randomised controlled trial has recently completed recruitment, to address the question of anaesthetic depth and mortality/morbidity (BALANCED trial).

Delirium:

A Cochrane analysis, published in May 2018 looked at using depth of anaesthesia monitors for the amelioration of postoperative delirium and cognitive dysfunction. They identified evidence that optimised anaesthesia using depth of anaesthesia (DOA) monitoring could reduce the risk of postoperative delirium and postoperative cognitive dysfunction in patients over the age of 60 years.[6-12] Results from three studies (2529 participants) indicate that using the processed EEG to help deliver the optimal depth of anaesthesia could reduce the incidence of delirium from 21.3% to 15.2%. Results from three studies (2051 participants) indicate that this could also reduce the incidence of postoperative cognitive dysfunction at three months from 9.1% to 6.4%.

Guidelines Favouring the Use of DOA monitoring to prevent adverse outcomes:

Current advice from **NICE (2012)**, recommends the Bispectral Index monitor (BIS monitor) be available as an option for monitoring depth of anaesthesia during any type of general anaesthesia in patients considered at higher risk of adverse outcomes.[13]
The 2015 European Society of Anaesthesiology **(ESA) guideline for the prevention and treatment of postoperative delirium**, recommends monitoring of a patient's depth of

anaesthesia during surgery specifically to help prevent postoperative delirium, citing evidence from ASA 3 or 4 patients over the age of 60 undergoing prolonged surgery (> 2hrs).[17]

Prevention of awareness and titration of anaesthetic depth

Total Intravenous Anaesthesia (TIVA/TCI)

TIVA is commonly used during intra-hospital transfers and for remote anaesthesia, as well as in main theatres where indicated. Indications for TIVA include history of malignant hyperpyrexia, a history of severe postoperative nausea and vomiting, a need for clear and crisp post-anaesthetic wakeup, and remote anaesthesia. There is mounting evidence that the choice of anaesthetic may have mortality benefits in certain groups, with Wigmore *et al* showing in a retrospective analysis a difference in long term mortality of 16% and 23% when comparing TIVA vs volatile anaesthetic for solid organ cancer resections. [14]

Guidelines Favouring the Use of DOA monitoring when using TIVA

2012 NICE guidelines:
recommend that BIS is available for monitoring depth of anaesthesia in all patients receiving total intravenous anaesthesia, because it is not possible to measure end-tidal anaesthetic concentration, and as it is recognised as a cost effective solution.[13]

The NAP5 awareness audit:
UK National anaesthetic audit specifically noted an increased risk of awareness when using TIVA, with those receiving a muscle relaxant as part of general anaesthesia most at risk.[16]

AAGBI Minimum Monitoring Standards 2015:
'Use of depth of anaesthesia monitors, for example processed EEG monitoring, is recommended when patients are anaesthetised with total intravenous techniques and neuromuscular blocking drugs, to reduce the risk of accidental awareness during general anaesthesia'[15]

Joint Guidelines for Safe Practice of TIVA 2019: AAGBI and Society of Intravenous Anaesthesia:
'Use of a processed EEG (pEEG) monitor is recommended when a neuromuscular blocking drug is used with TIVA.'

Volatile Anaesthetic Agents

Early evidence for reduced anaesthetic awareness when using BIS was fairly convincing, including a randomised controlled trial comparing BIS guided anaesthesia versus standard practice in 2500 patients at high risk of awareness.[18] Explicit recall reduced from 0.91% to 0.17% ($p<0.02$) in the BIS group. One Chinese randomised controlled trial of over 5000 patients demonstrated a reduction in awareness when using titration of propofol intravenous anaesthesia to predefined BIS levels ($p=0.002$), however, the rates of awareness in the control arm (no BIS titration) were much higher than found in other publications at 0.65% of anaesthetics.[19] Other trials have demonstrated benefits including reduced time to wakening, and reduced anaesthetic drug usage with BIS monitoring, although further evidence of reduced awareness has been lacking. A recent publication of anaesthesia in patients at high risk of awareness was unable to find an improvement when titrating volatile anaesthesia to BIS compared to titrating anaesthesia to within predefined volatile MAC (albeit with an audible alarm when MAC strayed from a predefined level).[20]

Guidelines Favouring the Use of DOA monitoring when using Volatile Anaesthetic Agents

Given the mixed evidence, and the very low levels of anaesthetic awareness found in the UK NAP5 national audit, it is not possible to categorically state that BIS leads to reduced levels of awareness in all groups, although is likely to reduce volatile consumption. The **NAP 5 audit** did demonstrate higher levels of awareness when a neuromuscular blocking agent was used, and suggested that DOA monitoring such as BIS should be considered to reduce this risk when these agents are used.[16] A balanced approach for considering BIS use is suggested until a higher level of evidence is published, such as:

(a) the patient falls into a 'high-risk' of awareness category
(b) the patient has had an experience of accidental awareness under anaesthesia or expresses specific fears of such
(c) other measures such as heart rate or blood pressure indicate very high levels of agent are required
(d) other measures such as blood pressure are unusually low despite low levels of agent.

Worcestershire Acute Trust Guidance for Use of BIS

Currently BIS consumables (on the basis of the supply of hardware by the manufacturers without cost) are around £15 per patient. As the benefits of such monitors are most defined in certain circumstances, this guidelines has outlined the patient categories most likely to benefit based on current evidence, and in whom it is agreed that anaesthetists can use the technology should they wish.

Consider using BIS in the following settings:

- Concern about increased risk of intraoperative awareness
- TIVA, in particular with the use of neuromuscular blocking agents, or when cannula cannot be easily visualised.
- Concern regarding postoperative delirium in patients undergoing anaesthesia (risk increases with age, ASA grade, and duration of anaesthesia).
- High risk of adverse events – ASA 3 or 4 patients over the age of 60, likely to be anaesthetised for at least 2 hours.

Logistics

Currently, Medtronic have loaned us one stand alone BIS monitor for Worcester Royal Hospital, and one at the Alexandra Hospital, both located in the anaesthetic recovery room. Number of monitors loaned by the company would be dependent on clinical need of the trust, although a reasonable use is required in order to make supply of the monitors feasible using this model.

Clinical Support

Medtronic have provided both lecture-based teaching, and one on one sessions in theatres, but are happy to attend for follow up session for further training. Dr Cowley has the contact details and can organise additional training sessions if required.

References

1. Monk TG, Saini V, Weldon C, Sigl JC. Anesthetic management and one-year mortality after non-cardiac surgery. *Anesth Analg.* 2005; 100:4-11.
2. Lindholm M, Traff S, Granath F, Greenwald SD, Ekbom A, Lennmarken C, Sandin RH. Mortality within 2 years after surgery in relation to low intraoperative bispectral index values and preexisting malignant disease. *Anesth Analg.* 2009; 108:508-12.
3. Saager L, Greenwald SC, Kelley SD, Schubert A, Sessler Dl. Hospital stay and mortality are increased by a triple low of blood pressure, BIS and anesthetic depth. *International Society of Anesthetic Pharmacology Abstracts,* New Orleans 2009; 3-9.
4. Searleman AC, Leitner A, Ridley C, Zhang L, Avidan MS. Deep hypnotic time and one-year mortality in non-cardiac and cardiac surgical patients. Anesthesiology 2008; 109 Al.
5. Leslie K, Myles PS, Andrew Forbes, Chan MTV. The effect of BIS Monitoring on long-term survival in the B-Aware trial. *Anesth Analg.* 2010; 110:816-22.
6. Kertai MD, Pal N, Palanca BJA, Lin N, Searleman SA, Zhang L, Burnside BA, Finkel KJ, Avidan MS; B-Unaware Study Group. Association of perioperative risk factors and cumulative duration of low bispectral index with intermediate-term mortality after cardiac surgery in the B-unaware trial. *Anesthesiology.* 2010; 112:1116-27.
7. Kertai MD, Palanca BJA, Pal N, Burnside BA, Zhang L, Sadiq F, Finkel KJ, Avidan MS; B- Unaware Study Group. Bispectral index monitoring, duration of bispectral index below 45, patient risk factors, and intermediate-term mortality after noncardiac surgery in the B-aware trial. Anesthesiology. 2011: 114:545-56
8. Aldecoa C, Bettelli G, Bilotta F, et al. European Society of Anaesthesiology evidence-based and consensus-based guidelines on postoperative delirium. Eur J Anaesthesiol. 34(4):192–214, APR 2017
9. Radtke FM, Franck M, Lendner J, Krüger S, Wernecke KD, Spies CD. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. Br J Anaesth. 2013;110(suppl 1):i98-105.
10. Chan MT, Cheng BC, Lee TM, Gin T; CODA Trial Group. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol. 2013;25(1):33-42.
11. Sieber FE, Zakriya KJ, Gottschalk A, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. Mayo Clin Proc. 2010;85(1):18-26.
12. **http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD011283.pub2/abstract**
13. National Institute for Health and Care Excellence. Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M, 2012. https://www.nice.org.uk/guidance/dg6(accessed 03/03/2016).

14. Wigmore TJ, Mohammed K, Jhanji S. Long-term Survival for Patients Undergoing Volatile versus IV Anesthesia for Cancer Surgery A Retrospective Analysis. Anaesthesiology 2016: 124:1
15. Checketts MR, Alladi R, Ferguson K, et al. Recommendations for standards of monitoring during anaesthesia and recovery 2015: AAGBI. *Anaesthesia* 2016; **71**: 85–93.
16. Pandit JJ, Andrade J, Bogod DG, et al. 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors. *Anaesthesia*2014; **69**: 1089–101.
17. Aldecoa C, Bettelli G, Bilotta F et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol. 2017 Apr;34(4):192-214
18. 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 May 29;363(9423):1757-63.
19. Zhang C, Xu L, Ma YQ, Sun YX. Bispectral index monitoring prevent awareness during total intravenous anesthesia: a prospective, randomized, double-blinded, multi-center controlled trial. Chin Med J (Engl). 2011 Nov;124(22):3664-9.
20. Avidan MS, Jacobsohn E, Glick D. Prevention of intraoperative awareness in a high-risk surgical population. N Engl J Med. 2011 Aug 18;365(7):591-600.

Appendix

Table 1: Observational studies of the relationship between depth of anaesthesia and subsequent mortality

Author	N	ASA 3&4 *	1 y mortality	Increased risk of death if 'deep' #
Monk 2005 [12]	1064	35%	5.5	RR = 1.24
Lindholm 2009 [13]	4087	6%	4.3	HR = 1.18
Saager 2009 [14]	23,999	~30%	4.8	RR = 1.63
Searleman 2010 [15]	1791	71%	10.7	OR = 1.25/h
Leslie 2010 [16]	2463	74%	10.8	PS = 1.42 (at 4y)
Kertai 2010 (cardiac) [17]	460	100%	17.8	HR = 1.29 (at 3y)
Kertai 2011 (non-cardiac) [18]	1473	60%	24.3	HR = 1.03 (at 3y)

*ASA=American Society of Anaesthesiologists physical status scale, 1=normal health, 2=mild to moderate systemic disturbance, 3=severe systemic disturbance which limits activity, 4=incapacitating life threatening disease, 5=moribund.

#RR=relative risk, HR=hazard ratio, OR=odds ratio, PS=propensity score