

## Critical Review Form

### Therapy

Gan TJ, et al, BIS allows faster emergence AND Improved Recovery from Propofol, Alfentanil and Nitrous Oxide Anesthesia, *Anesthesiology*.1997.**87**:4;808-815

**Objectives:** To show the efficacy of bispectral index (BIS) monitoring as a pharmacodynamic measure of patient response to propofol during general anesthesia. A secondary objective was to show whether guiding drug administration by BIS changes the number of unwanted somatic and hemodynamic responses operatively.

**Methods:** Multicenter, prospective, randomized clinical study comparing standard practice (SP) with standard practice plus BIS monitoring. Randomization occurred by sequential coded envelopes with treatment sequence in blocks of 10 after patients' informed consent had been obtained. Adults ages 18-80 years were eligible with exclusion for "known neurologic disorders, uncontrolled hypertension, baseline systolic blood pressure < 106, or any serious medical conditions that would interfere with cardiovascular response assessment." In the BIS group, the anesthesiologist dosed propofol to achieve a target BIS score of 45-60. In the SP group, the BIS monitor was covered with an opaque card, so dosage adjustments were made at the discretion of the primary anesthesiologist based only on standard clinical signs. All patients received midazolam (1-2 mg IV), fluid load (500 mL), and propofol (1-2 mg/kg and alfentanil 30mcg/kg) with infusions of propofol and alfentanil with 50% N2O plus (if necessary) a neuromuscular blocking agent. Outcomes included drug use, intraoperative responses, and patient recovery parameters.

<b>Guide</b>		<b>Comments</b>
<b>I.</b>	<b>Are the results valid?</b>	
<b>A.</b>	<b>Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)?</b>	
1.	Were patients randomized?	Yes. Blocks of 10 (5 BIS/5 SP) Generated by random #.
2.	Was randomization concealed (blinded)?	Anesthesiologist not blinded (the purpose of the study.)
3.	Were patients analyzed in the groups to which they were randomized?	No. 28 patients excluded from analysis entirely. NO INTENTION TO TREAT ANALYSIS. This is important. All subjects must be analyzed in the group to which they were originally assigned to avoid missing important implications of the data. The data can be analyzed with and without the intention to treat, but there was no effort made here.

4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	No. this was facilitated by inclusion criteria limits of ASA class, procedure time, etc. But no assessment of risk for increase procedure noted.
<b>B.</b>	<b>Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?</b>	
1.	Were patients aware of group allocation?	Not stated
2.	Were clinicians aware of group allocation?	Yes. BIS recorded on all pt, but only available to clinicians in BIS group
3.	Were outcome assessors aware of group allocation?	Anesthesiologist not blinded, which affects all time management portions of the study. Recovery room RN blinded, but unsure what they measured. They never do mention if there are independent assessors or if they were blinded.
4.	Was follow-up complete?	240/268 included for analysis. Of these, no drop outs.
<b>II.</b>	<b>What are the results (answer the questions posed below)?</b>	
1.	How large was the treatment effect?	Saves around 4 minutes to extubation & 6 min to PACU discharge. Is this large? I doubt it. The decision to discharge is complex and not solely affected by the variables they report. Also, there was a change from their pilot numbers to their study numbers, implying a change in technique or learning curve was present.
2.	How precise was the estimate of the treatment effect?	As SP is better than historical control, they have likely underestimated treatment effect (see discussion, 2 <sup>nd</sup> p)
<b>III.</b>	<b>How can I apply the results to patient care (answer the questions posed below)?</b>	
1.	Were the study patients similar to my patient?	<ol style="list-style-type: none"> <li>1. We rarely use this combo of drugs although propofol is used in the ED.</li> <li>2. OR patients, not ED pt's , but conscious sedation included pt's whose proc were &gt; 1 hour. Those &lt;30 min were dropped.</li> <li>3. No ASA class E patients or class 4-5 pt's, but all of our patients are class E by definition.</li> <li>4. Paralytics allowed – which we rarely use in the ED for procedural sedation. Dr. DeWitt had some excellent comments regarding the use of BIS in unparalyzed patients.</li> </ol>

2.	Were all clinically important outcomes considered?	Intention to treat analysis is necessary for conclusions. Did not thoroughly assess effectiveness of anesthesia. No report of time of procedure
3.	Are the likely treatment benefits worth the potential harm and costs?	<p>Study is too weak for conclusions to be drawn. Also, difficult to place a cost on time-savings of such small magnitude.</p> <p>Most importantly, there is potential harm from the BIS. A low BIS in an awake patient could cause inappropriately light sedation, while a high BIS in a sedated patient could yield oversedation.</p>

### **Limitations**

- 1) Poorly blinded
- 2) Poorly defined 1° and 2° outcomes (see last page methods section)
- 3) No subjective measures of anesthesia adequacy (physiologic changes only)
- 4) Many post-hoc analyses without providing numbers (cost-savings, changes in somatic movements, etc.)

### **Bottom Line**

**The technology is conceptually intriguing, but probably not ready for prime time. From the discussion and from Dr. DeWitt's experience, we might be able to use it in paralyzed patients (since clinical exam is unreliable), but using for brief procedures, associated with little clinically significant respiratory depression, isn't indicated, and could potentially cause harm. Also note that in comparison with the B-AWARE RCT (4<sup>th</sup> Year Paper), the current cohort is healthier, but has no class E's or procedures under 30 minutes (our typical ED population).**

