# Quando o Índice Bispectral (BIS) Pode Fornecer Valores Espúrios\*

When the Bispectral Index (Bis) can Give False Results\*

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#### RESUMO

Duarte LTD, Saraiva RA — Quando o Índice Bispectral (BIS) Pode Fornecer Valores Espúrios.

JUSTIFICATIVA E OBJETIVOS: O índice bispectral (BIS) é um parâmetro multifatorial derivado do eletroencefalograma (EEG) que permite a monitorização do componente hipnótico da anestesia. Foi obtido a partir de algoritmo derivado da análise de grande número de EEGs de voluntários e pacientes submetidos a sedações e anestesia geral com diferentes agentes anestésicos. Além de outros benefícios, o uso do BIS para monitorização da profundidade da anestesia reduz a ocorrência de despertar e memória intra-operatória. Esta revisão teve o objetivo de apresentar situações clínicas em que o BIS aponta valores espúrios, falsamente elevados ou reduzidos, em decorrência de condições do paciente ou ações de anestésicos não-previstos quando da elaboração do seu algoritmo.

**CONTEÚDO:** Os valores do BIS podem sofrer alteração e influência em variadas situações clínicas em que há padrões anormais do EEG; efeito de diferentes anestésicos e outros fármacos nãoincluídos na elaboração de seu algoritmo; interferência de equipamentos elétricos; bem como decorrentes de peculiaridades do monitor.

**CONCLUSÃO:** Apesar de o algoritmo do BIS ter sofrido diversas alterações desde a sua primeira versão, essas situações que determinam variações espúrias dos valores do BIS devem ser reconhecidas pelo anestesiologista a fim de evitar complicações, sejam conseqüentes à sobredose anestésica, sejam por subdoses que poderão causar despertar e memória intra-operatória.

Unitermos: ANESTESIA: Geral; MONITORIZAÇÃO: índice bispectral, consciência.

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#### SUMMARY

Duarte LTD, Saraiva RA — When the Bispectral Index (BIS) Can Give False Results.

**BACKGROUND AND OBJECTIVES:** The bispectral index (BIS) is a multifactorial parameter derived from the electroencephalogram (EEG), which allows monitoring of the hypnotic component of anesthesia. It was obtained from the algorithm based on the analysis of a large number of EEGs from volunteers and patients undergoing sedation and general anesthesia with different anesthetic agents. The use of BIS to monitor the depth of anesthesia reduces the incidence of intraoperative awakening and recall, among other benefits. The objective of this review was to present clinical situations in which the BIS gives false results, either elevated or decreased, due to conditions related to the patient or anesthetic actions unforeseen when the algorithm was elaborated.

**CONTENTS:** The bispectral index can be altered and influenced in different clinical situations in which abnormal EEG patterns are present; the effects of different anesthetics and other drugs not included when the algorithm was elaborated; interference from electrical equipment; as well as peculiarities of the monitor.

**CONCLUSIONS:** Although the BIS algorithm underwent several changes since its first version, the anesthesiologist should be aware of situations that cause false BIS readings to avoid complications, may it be secondary to anesthetic overdose or underdosing, which might cause intraoperative awakening and recall.

Key Words: ANESTHESIA: General; MONITORING: bispectral index, awareness.

# INTRODUÇÃO

O índice bispectral (BIS) é um parâmetro multifatorial derivado do eletroencefalograma (EEG) que permite a monitorização do componente hipnótico da anestesia <sup>1</sup>. É um número nãodimensionável que varia entre 0 e 100. Em pacientes nãoanestesiados, o BIS está entre 90 e 100. Por outro lado, a supressão total da atividade elétrica cortical resultará em um valor de BIS de 0. Valores de BIS entre 40 e 60 se associam a baixa probabilidade de despertar e consciência intra-operatória <sup>2</sup>.

A monitorização do BIS permite reduzir o consumo dos agentes anestésicos, manter nível adequado de hipnose e evitar tanto níveis demasiadamente profundos de anestesia quanto o despertar e a formação de memória, implícita e explícita, durante a anestesia geral <sup>1,2</sup>. De fato, em 1996, o FDA (*Food and Drug Administration*) recomendou o uso do BIS para monitorização da profundidade da anestesia com Um estudo demonstrou que a lentificação do EEG associada à demência alterou os valores do BIS acordado <sup>44</sup>. Pacientes com demência decorrente de doença de Alzheimer, múltiplos infartos encefálicos, apresentaram quando acordados valores menores do BIS que indivíduos idosos, na mesma faixa etária, usados como controle (89 × 95) <sup>44</sup>. Esses valores diminuídos do BIS nos pacientes com demência se correlacionaram com testes do estado mental (*Mini-Mental State Examination*). Apesar dos resultados desse estudo, a utilidade do BIS na detecção de demência necessita ainda de novos estudos.

Crianças com paralisia cerebral apresentaram valores de BIS muito menores que crianças normais, seja durante a manutenção da anestesia com sevoflurano, seja durante o despertar da anestesia <sup>45</sup>. Um relato descreveu o comportamento do BIS em um paciente em estado vegetativo permanente e submetido a procedimento cirúrgico dentário <sup>46</sup>. O valor basal reduzido do BIS (74 a 85) devido à lesão neurológica sofreu redução com a administração de sevoflurano. Todavia, como ocorreria em indivíduos normais, surpreendentemente, ao final da operação, o BIS se elevou até 98 a 100. Esse relato vem demonstrar que o BIS não é capaz de distinguir a atividade cortical integrada e a não-integrada. No indivíduo normal, o valor elevado do BIS refere-se a grande atividade cortical que se manifesta na forma de consciência. Todavia, no indivíduo com lesão neurológica, o valor elevado do BIS nem sempre significa atividade cortical integrada. Além dessas situações, o algoritmo do BIS é também muito vulnerável a artefatos quando há ausência (morte encefálica) ou grande supressão (hipotermia profunda) dos sinais do EEG. Em dois indivíduos com morte encefálica confirmada, o valor do BIS se elevou de 0 a 5 até 38 em virtude da sincronização do sinal do eletrocardiograma com o BIS, que interpretou o sinal do ECG como atividade do EEG 47.

# Condições Clínicas Que Alteram o Valor do BIS

Diferentes situações clínicas que determinem a diminuição do débito cardíaco e, em conseqüência, a perfusão encefálica determinarão a redução dos valores do BIS. Exemplo dessa situação ocorreu com um paciente que apresentou assistolia e foi reanimado com sucesso <sup>48</sup>. Padrão isoelétrico do EEG surgiu dez segundos após o início da assistolia. Com o início das compressões torácicas e aumento da perfusão encefálica, surgiu padrão de baixa voltagem e alta freqüência no EEG. Com o retorno do ritmo cardíaco e restauração do fluxo sanguíneo encefálico, o sinal do EEG voltou ao normal.

Em casos de parada cardíaca por hipovolemia, houve uma diminuição paralela dos valores do BIS até zero, com EEG isoelétrico <sup>49</sup>. À medida que a pressão arterial foi restaurada e a perfusão encefálica restabelecida, o BIS se elevou até os níveis anteriores à complicação <sup>48</sup>. As alterações do BIS podem ocorrer antes mesmo do surgimento das alterações hemodinâmicas <sup>50</sup>. É provável que tal fato ocorra em decorrência de alterações provocadas na farmacocinética dos

anestésicos. Por outro lado, durante a desordem hemodinâmica, as variações do BIS devem-se às mudanças sobre a perfusão encefálica.

Apesar de o BIS não ter sido desenhado, tampouco validado para detectar lesão isquêmica encefálica, a monitorização do BIS poderá auxiliar na sua detecção. O BIS pode refletir não apenas a forma global de isquemia encefálica, mas também formas focais de isquemia. Em intervenções cirúrgicas sobre a carótida, os valores do BIS se reduzem durante o pinçamento arterial e retornam ao normal com o restabelecimento da circulação <sup>51</sup>.

A hipotermia é outro fator que deve ser considerado durante a monitorização do BIS. Estimou-se em pacientes anestesiados com isoflurano e submetidos a *bypass* cardiopulmonar com hipotermia que o valor do BIS diminui 1,12 unidades para cada grau centígrado reduzido na temperatura corporal <sup>52</sup>. O fenômeno decorre da redução linear nas necessidades anestésicas, bem como da diminuição da atividade cerebral.

A hipoglicemia (até 72 mg.kg<sup>-1</sup>) causa pequeno aumento na freqüência de ondas  $\delta \in \theta$  de baixa freqüência <sup>53</sup>. A redução da glicemia até 54 mg.kg<sup>-1</sup> provoca um aumento difuso das ondas ä e è. Em 32 mg.kg<sup>-1</sup>, o aumento das ondas ä e è se associa à redução das ondas  $\alpha$ , um padrão muito semelhante ao da anestesia geral <sup>53</sup>. De fato, relatos descrevem a ocorrência de valores de BIS tão baixos quanto 45 em pacientes em coma hipoglicêmico e que se elevaram após a normalização da glicemia <sup>54</sup>.

# CONCLUSÃO

Apesar de o algoritmo do BIS ter sofrido diversas alterações desde sua primeira versão, há ainda situações que determinam variações espúrias dos valores do BIS e que devem ser reconhecidas pelo anestesiologista a fim de serem evitadas complicações durante a anestesia geral, sejam conseqüentes à sobredose anestésica, sejam por subdoses que poderão causar o despertar intra-operatório, o aparecimento de memória e suas conseqüências.

Os valores do BIS devem ser entendidos como dado adicional na monitorização da anestesia geral e interpretados à luz de outros dados clínicos e de outros monitores.

# When the Bispectral Index (Bis) can Give False Results\*

Leonardo Teixeira Domingues Duarte, TSA<sup>1</sup>, Renato Ângelo Saraiva, TSA<sup>2</sup>

## INTRODUCTION

The bispectral index (BIS) is a multifactorial parameter derived from the electroencephalogram (EEG) that allows mo-

nitoring of the hypnotic component of anesthesia<sup>1</sup>. It is a dimensionless number that varies from 0 to 100. In nonanesthetized patients the bispectral index varies from 90 to 100. On the other hand, total suppression of cortical electrical activity results in a BIS of zero. A BIS between 40 and 60 is associated with a low probability of intraoperative awakening and awareness<sup>2</sup>.

Monitoring of the bispectral index allows the reduction of anesthetics, maintenance of adequate levels of hypnosis, and prevents both extremely deep anesthesia levels and awakening and formation of implicit and explicit memory during general anesthesia<sup>1,2</sup>. In fact, in 1996 the FDA recommended the use of BIS to monitor the depth of anesthesia to reduce the incidence of intraoperative awakening and recall. It also allows faster awakening and reduces the length of stay in the post-anesthetic recovery room, which reduces costs<sup>2</sup>.

The bispectral index was obtained from an algorithm derived from the analysis of a large number of EEGs of volunteers and patients under sedation and general anesthesia with different anesthetics<sup>3</sup>. Although the BIS algorithm was modified several times to improve its performance and decrease the interference of artifacts, its results can still be changed and influenced by different clinical situations and anesthetics that were not included during its elaboration<sup>4</sup>.

During surgery, the anesthesiologist needs to know whether the depth of anesthesia, composed of hypnosis, amnesia, and analgesia, is adequate in all moments of the nociceptive stimulation. However, those gualities cannot be discriminated just through parameters derived from the EEG. Despite the efficacy of BIS in reducing intraoperative recall<sup>2</sup>, its occurrence even when the monitor is used is still reported in the literature. Thus, the BIS is not 100% specific in predicting intraoperative awakening and recall, which is one of the limitations of this monitoring. Even though it is not realistic to expect that any monitor will not show false-negative results, there are reports in the literature of cases in which the patient had intraoperative recall despite BIS values characteristics of hypnosis and adequate anesthetic depth. A precise correlation between sedation scales and BIS values recorded during anesthesia is not consistently present. Electrical equipment, specific clinical conditions, abnormal EEG patterns, and neuromuscular blockers (NMB) can interfere with BIS monitoring.

The objective of this review was to present clinical situations in which BIS results are erroneously elevated or decreased by conditions related to the patient or anesthetic effects not foreseen when the algorithm was elaborated. The anesthesiologist should recognize those situations to avoid errors in anesthetic management.

#### **Monitor-Related Situations**

To use the BIS to monitor the depth of hypnosis based on the levels recorded, the monitor should be predictably influenced by different anesthetics and show good inter- and intra-pa-

tient reproducibility. In fact, a study suggested different placements of BIS electrodes (frontal and occipital) in the same patient showed strong correlation between readings<sup>5</sup>. However, in two recent studies the concomitant use of older BIS versions and the BIS-XP, the most recent version of the monitor, gave different results<sup>6</sup>. The results of the XP monitor (version 4.0) were significantly lower than that of the A-2000 monitor (version 3.4) (33 x 40)<sup>7</sup>. Besides, the concomitant use of two BIS-XP monitors in the same patient showed that different readings in 10% of the cases, suggesting different anesthesia depths8. The monitors showed a concordance coefficient of 0.65. The results of this study suggest that the BIS-XP does not have consistent intra-patient reproducibility8. One should emphasize that the performance of a BIS model will not be necessarily the same as other models. The most recent algorithm of the BIS monitor (BIS XP version 4.0) may have resulted in lower BIS scores than those of older models for the same level of hypnosis. This difference is secondary to the inclusion in more recent models of mechanisms that reduce the level of noise, interferences, and electromyographic activity, resulting therefore in lower BIS values. Anyway, one should not forget that the model of BIS monitor can influence the interpretation of the results.

All monitors currently available need different times to calculate and update the index in response to changes in the depth of anesthesia. The time to update BIS records can range from 14 to 155 seconds<sup>9</sup>. The latency of the bispectral index may indicate a limitation of the efficacy of this monitor on the prevention of intraoperative recall and in the transition from alertness to unconsciousness.

Falsely elevated BIS can occur when electrode impedance is elevated due to erroneous placement or reduced adherence<sup>10</sup>. The bispectral index requires specific electrodes that, although they are comfortable, easy to use, and guarantee low impedance when capturing the EEG signal, they are very expensive. Thus, the use of ECG electrodes has been suggested as a lower cost alternative<sup>11</sup>. However, although their use is feasible, after adaptation of specific models of monitor<sup>11</sup>, it is problematic. First, impedance to the EEG signal can remain elevated and very variable, even with adequate skin preparation<sup>10</sup>. Second, depending on monitor model, it might be impossible to connect them to the monitor.

Electromyographic (EMG) activity and neuromuscular blockers (NMB) can influence significantly BIS monitoring. Elevated EMG activity increases BIS, while the subsequent administration of NMBs reduces it<sup>12</sup>. Electromyographic activity represents artifacts superimposed on the frequency band of EEG signals used by the algorithm of the monitor to determine BIS values. Since the frequency limits range of EMG (30 to 300 Hz) and ECG (0.5 to 30 Hz) signals are very close, low frequency EMG signals can be erroneously interpreted as high frequency EEG signals, leading to a false elevation of BIS<sup>13</sup>. Therefore, EMG frequencies can simulate the component of EEG frequency associated with being awake and superficial anesthesia (30 – 47 Hz). From this moment on,

the BIS interprets erroneously EMG signals, making patients in deep anesthesia seem more awake than they really are. In this situation, the administration of NMBs decreases BIS values by reducing artifacts, revealing their real value.

The evolution of BIS algorithm includes a reduction in the impact of EMG contamination, both in sedation ranges and anesthesia. A correlation between the EMG and the false elevation of BIS does not exist. The anesthesiologist should be attentive and verify signal quality (SQI), EMG activity, and the tendency of BIS values regarding the clinical status of the patient before making any decisions.

# Anesthetic Effects and Other Drugs

Different situations in which BIS values did not coincide with the clinical status of sedation or did not correlate with the expected anesthetic effects have been described in the literature.

Nitrous oxide (N<sub>2</sub>O) has weak cortical action. This effect is not detected by the BIS algorithm<sup>14</sup>. Inhalation of 50% N<sub>2</sub>O does not change BIS and does not reduce the level of consciousness<sup>15</sup>. At the 70% concentration, the response to vocal commands is lost, but BIS remains unchanged<sup>15</sup>. The addition of N<sub>2</sub>O to volunteers receiving target-controlled infusion of propofol decreased the probability of response to a range of stimuli at any level of BIS16. When 55 to 63% of N<sub>2</sub>O was added to anesthesia with propofol and remifentanil it did not change BIS, but it prevented movements during laryngoscopy and tracheal intubation<sup>17</sup>. Based on those results, N<sub>2</sub>O seems to have a small role on the hypnotic state, but it seems to work predominantly as analgesic. One should be attentive because BIS monitoring might not be sensitive enough to give an adequate measurement of the depth of sedation and hypnosis when N<sub>2</sub>O is used as a single agent. In those cases, clinical monitoring of sedation is the best option<sup>14</sup>.

One study reported paradoxal reduction of BIS 6 minutes after interruption of  $N_2O$ , from 95 - 81 to 30 - 50<sup>15</sup>. The EEG recorded simultaneously showed an increase in the activity of low frequency ä and è waves, similar to the pattern seen in deep anesthesia. This result can be attributed to a with-drawal and suppression phenomenon unique to the sudden interruption of  $N_2O$ .

Ketamine, on the doses of 0.25 to 0.5 mg.kg<sup>-1</sup>, can block the response capacity of patients, but it does not reduce the BIS<sup>18</sup>. This drug increases â activity associated with reduction in ä power<sup>19</sup>. This EEG pattern was reflected on the paradoxal increase in BIS values<sup>20</sup>. When used during sedation in combination with propofol, ketamine increased hypnosis without affecting BIS levels<sup>20</sup>.

Different inhalational anesthetics can cause peculiar changes in the EEG. As a consequence, BIS values are not the same with equipotent concentrations of different anesthetics. The bispectral index was significantly greater with halothane than with equipotent doses of sevoflurane<sup>21</sup> or isoflurane<sup>22</sup>. This indicates that the BIS algorithm, which was not described for halothane, does not reflect the hypnotic effects of this anesthetic. Therefore, when BIS is used to monitor anesthesia with halothane, one should be careful to avoid inadvertent anesthetic overdose.

On the other hand, while BIS was more elevated during anesthesia with halothane than with sevoflurane<sup>21,23</sup> in adults and children, it had similar behavior during anesthesia with sevoflurane or halothane in newborns<sup>23</sup>.

A case in which the inspired fraction of isoflurane was increased from 0.9% to 1.26%, causing a paradoxal increase in BIS, has been reported<sup>24</sup>. This paradoxal awakening reaction was, in reality, due to an increase in á and â waves in the EEG. The bispectral index returned to baseline levels after reducing the concentration of isoflurane.

A report using the A1000 monitor resented two volunteers whose BIS remained unchanged, between 35 and 40, despite the progressive increase in propofol plasma concentration<sup>25</sup>. On the other hand, the EEG recorded simultaneously indicated burst suppression. The authors speculated that BIS levels of 35 to 40 would represent the uncertainty range between the beta ratio and burst suppression in which the BIS algorithm would be less sensitive to the effects of propofol<sup>25</sup>. The effects of opioids on BIS also require attention. In comparison to intravenous and inhalational anesthetics, opioids cause minimal electrophysiological changes in the cerebral cortex. Subcortical structures are involved with the mechanism of action of opioids that are not detected by the EEG. Combined with a constant target concentration of propofol, a progressive increase or reduction in the dose of remifentanil does not change BIS<sup>26</sup>. On the other hand, the addition of fentanyl, sufentanil, remifentanil, or alfentanil to the targetcontrolled infusion of propofol results in loss of consciousness with lower concentrations of propofol, but the associated values of BIS are higher<sup>27,28</sup>. Studies have demonstrated that even high doses of remifentanil do not change BIS during continuous infusion with propofol<sup>26</sup>. The bispectral index is not accurate when fentanyl associated or not with propofol<sup>29</sup> or midazolam<sup>30</sup> is used during coronary bypass surgeries.

Those results demonstrated clearly that the hypnotic effects of propofol are increased by opioids, but monitoring with BIS does not show this effect, which can lead to inadvertent anesthetic overdose. However, despite requiring attention, BIS monitoring during anesthesia with propofol and opioids is in fact very useful. When this combination is balanced during surgery, it produces BIS values that can be used as a baseline from which an elevation in the response to surgical stimuli will indicate awakening due to a deficiency of the analgesic component of anesthesia; in this case, one should increase the dose of the opioid.

Unexpected variations in BIS during general anesthesia in response to the administration of different drugs were described. A case report referred to the elevation of BIS above 70 in response to beta-adrenergic stimulation resulting from the administration of isoproterenol<sup>31</sup>. The increase in BIS did not seem to be related with surgical stimulation and the patient

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did not have intraoperative recall. The administration of successive doses of methylene blue to increase methemoglobinemia caused simultaneous sudden and severe reduction in BIS followed by recovery to the levels before the administration of the drug<sup>32</sup>. Other causes for the reduction in BIS were not identified and, consequently, the temporal relationship between the administration of the drug and the reduction in BIS favors the theory that there might be an interaction between methylene blue and the electroencephalographic monitoring.

#### Interference from Electrical Equipment

The bispectral index also demonstrated to be somewhat weak when artifacts are present. Different electrical devices, besides the electric scalpel, can affect BIS monitoring. During cardiac surgeries a rise in BIS up to 90 during the use of the atrial pacemaker, which decreased when the pacemaker was turned off, was seen<sup>31</sup>. The quality of the electroencephalographic signal was low when the pacemaker was turned on, and electrical interference was responsible for the artifact observed in BIS.

However, the signal quality bar does not show the artifact every time. False elevations in BIS, when the thermal blanket was turned on and placed directly on the face of the patient, have been reported<sup>34</sup>. The bispectral index returned to 35 to 60 when the device was turned off. Similarly, BIS increased suddenly during shoulder arthroscopy when the oscillations produced by the shaver started<sup>35</sup>. Besides, an ENT system created an electromagnetic field around the head of the patient leading to an increase in BIS<sup>36</sup>. Those electrical devices can cause vibrations or minimal frequency on BIS electrodes, simulating EEG waves found in superficial anesthesia or during alertness. Those signal interferences were not identified by the monitor as interferences. Therefore, once more, conditions for inadvertent anesthetic overdose are created.

#### **Changes in BIS Secondary to Abnormal EEG Patterns**

There are different reports and situations in which the BIS shown by the monitor does not coincide with the clinical state of sedation, due to the pathophysiology of brain function or limitations in the performance of the monitor. One report described an awake patient with a BIS of 4737. On the other hand, sometimes painful stimulation during surgery in the presence of inadequate anesthesia results in EEG suppression. One study demonstrated a significant reduction in BIS immediately after peritoneal irrigation in abdominal surgeries<sup>38</sup>. Administration of fentanyl before abdominal irrigation abolished this abnormal BIS response, which did not change during irrigation. These data show that stimulation during peritoneal irrigation can cause a paradoxal response characterized by a reduction in EEG-derived parameters<sup>38</sup>. One should be attentive for the development of this paradoxal response to avoid inappropriate superficiality of the anesthetic plane.

Some individuals have a specific genetically-determined EEG variant, which manifests with low voltage<sup>39</sup>.This is a normal variant that affects 5 to 10% of the population and it is not associated with any cerebral dysfunction. Since the BIS algorithm was developed in volunteers with normal EEG, this abnormal EEG pattern is not recognized by the monitor. For this reason, it is important to confirm the BIS in all patients before anesthetic induction.

However, a low voltage EEG can also be induced by drugs. A fast and paradoxal reduction in BIS was seen during the elimination phase of remifentanil in six patients<sup>40</sup>. The same effect was reported with inhalational anesthetics during the elimination of sevoflurane and isoflurane<sup>41</sup>. In those two reports, the EEG showed very low voltage (< 15  $\mu$ V), which was interpreted by the monitor as burst suppression.

In electroconvulsive therapy, after recovering consciousness, patients have a peculiar EEG pattern characterized by very slow ä waves, resembling deep planes of anesthesia. Therefore, the BIS reflects this postictal state (which is independent of the anesthetic used) with very slow levels, from 45 to 57<sup>42</sup>. The case of a patient with spontaneous eyes opening who had a BIS of 7 has also been reported.

The BIS algorithm was developed using data from individuals with normal EEG and, consequently, neurologic disorders that manifest with abnormal EEG patterns will, most likely, affect BIS monitoring. Although recent studies using the bispectral index in patients with brain lesions reported good correlation with sedation scales<sup>43</sup>, unusual situations during BIS monitoring in patients with neurologic disorder have been reported.

One study showed that slowing of the EEG associated with dementia changed awaken BIS<sup>44</sup>. In patients with dementia secondary to Alzheimer's and multiple brain infarcts the BIS, while awaken, was lower than that of elderly individuals in the same age range used as control (89 x 95)<sup>44</sup>. Reduced BIS levels in individuals with dementia correlate with the Mini Mental State Examination. Despite the results of this study, further studies are needed to confirm the usefulness of BIS to detect dementia.

Children with cerebral palsy had significantly lower BIS than normal children, both during anesthesia maintenance with sevoflurane and during awakening from anesthesia<sup>45</sup>. One report described BIS behavior in a patient in permanent vegetative state who underwent dental surgery<sup>46</sup>. Baseline BIS was reduced (74 to 85) due to neurologic damage, but it was reduced even further after the administration of sevoflurane. However, similar to normal individuals, at the end of the surgery BIS rose to 98 - 100. This report demonstrates that BIS cannot differentiate integrated and non-integrated cortical activity. In normal individuals, elevate BIS reflects the great cortical activity manifested by being conscious. However, in individuals with neurological lesions, elevated BIS does not indicate, necessarily, integrated cortical activity.

Besides those situations, the BIS algorithm is also very vulnerable to artifacts when EEG signals are absent (brain death) or profoundly depressed (severe hypothermia). In two individuals with confirmed brain death, BIS rose from 0-5 to 38 due to synchronization of the electrocardiogram signal with the BIS, which interpreted ECG signals as EEG activity<sup>47</sup>.

#### **Clinical Conditions That Cause Changes in BIS**

Different clinical situations that lead to a reduction in cardiac output and, consequently, brain perfusion, cause a reduction in BIS. This was seen in a patient with asystole who was successfully resuscitated<sup>48</sup>. An isoelectric EEG pattern occurred 10 minutes after the beginning of asystole. When thoracic compressions were instituted, leading to an increase in brain perfusion, a low-voltage, high-frequency EEG pattern developed. With the return of the cardiac rhythm, which restored blood flow to the brain, the EEG signal returned to normal. A parallel reduction in BIS down to zero with isoelectric EEG is associated with cardiac arrest secondary to hypovolemia<sup>49</sup>. As blood pressure is restored to normal levels and brain perfusion is resumed, BIS increased to the levels seen before the complication<sup>48</sup>. Changes in bispectral index can occur even before the development of hemodynamic changes<sup>50</sup>. This can probably be explained by the changes induced in anesthetic pharmacokinetics. On the other hand, during hemodynamic changes variations in BIS are secondary to changes in brain perfusion.

Although the BIS was not designed or validated to detect brain lesion, BIS monitoring can help detect it. The bispectral index can reflect, besides global encephalic ischemia, focal ischemia. In surgeries of the carotid artery, BIS is reduced during arterial clamping and it returns to normal when blood flow is reestablished<sup>51</sup>.

Hypothermia is another factor that should be considered during BIS monitoring. In patients anesthetized with isoflurane on cardiopulmonary bypass with hypothermia, it was estimated that BIS decreased 1.12 units for each Celsius degree reduction in body temperature<sup>52</sup>. This is secondary to the linear reduction in the need of anesthetics as well as a reduction in brain activity.

Hypoglycemia (down to 72 mg.kg<sup>-1</sup>) causes a small increase in the frequency of low frequency ä and è waves<sup>53</sup>. Reduction in glucose levels to 54 mg.kg<sup>-1</sup> causes a diffuse increase in ä and è waves. At 32 mg.kg<sup>-1</sup>, the increase in ä and è waves is associated with a reduction in á waves, a pattern very similar to that of general anesthesia<sup>53</sup>. In fact, BIS as low as 45 in patients with hypoglycemic coma, which rose after blood glucose levels were restored to normal, has been reported<sup>54</sup>.

# CONCLUSION

Although the BIS algorithm has changed since its first version, false variations in BIS still occur, and they should be recognized by the anesthesiologist to avoid complications during general anesthesia due to anesthetic overdose or low doses, which can lead to intraoperative wakening and recall, and their consequences. The bispectral index should be seen as additional datum of general anesthesia monitoring and interpreted in the context of other clinical data and monitors.

# **REFERÊNCIAS** — *REFERENCES*

- Liu J, Harbhej S, White PF Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. Anesth Analg, 1997;84:185-197.
- Punjasawadwong Y, Boonjeungmonkol N, Phongchiewboon A Bispectral index for improving anaesthetic delivery and postoperative recovery. Cochrane Database Syst Rev, 2007;(4): CD003843.
- Rampil IJ A primer for EEG signal processing in anesthesia. Anesthesiology, 1998;89:980-1002.
- Dahaba AA Different conditions that could result in the bispectral index indicating an incorrect hypnotic state. Anesth Analg, 2005;101:765-773.
- 05. Shiraishi T, Uchino H, Sagara T et al. A comparison of frontal and occipital bispectral index values obtained during neurosurgical procedures. Anesth Analg, 2004;98:1773-1775
- Tonner PH, Wei C, Bein B et al. Comparison of two bispectral index algorithms in monitoring sedation in postoperative intensive care patients. Crit Care Med, 2005;33:580-584.
- Dahaba AA, Mattweber M, Fuchs A et al. Effect of different stages of neuromuscular block on the bispectral index and the bispectral index-XP under remifentanil propofol anesthesia. Anesth Analg, 2004;99:781-787.
- Niedhart DJ, Kaiser HA, Jacobsohn E et al. Intrapatient reproducibility of the BISxp monitor. Anesthesiology, 2006;104:242-248.
- Pilge S, Zanner R, Schneider G et al. Time delay of index calculation: analysis of cerebral state, bispectral, and narcotrend indices. Anesthesiology, 2006;104:488-494.
- Johansen JW, Sebel PS Development and clinical application of electroencephalographic bispectrum monitoring. Anesthesiology, 2000;93:1336-1344.
- Hemmerling TM, Harvey P Electrocardiographic electrodes provide the same results as expensive special sensors in the routine monitoring of anesthetic depth. Anesth Analg, 2002;94: 369-371.
- Vivien B, Di Maria S, Ouattara A et al. Overestimation of bispectral Index in sedated intensive care unit patients revealed by administration of muscle relaxant. Anesthesiology, 2003;99:9-17.
- Baldesi O, Bruder N, Velly L et al. Spurious bispectral index values due to electromyographic activity. Eur J Anaesthesiol, 2004;21:324-325.
- Park KS, Hur EJ, Han KW et al. Bispectral index does not correlate with observer assessment of alertness and sedation scores during 0.5% bupivacaine epidural anesthesia with nitrous oxide sedation. Anesth Analg, 2006;103:385-389.
- Rampil IJ, Kim JS, Lenhardt R et al. Bispectral EEG index during nitrous oxide administration. Anesthesiology 1998;89:671-677.
- Kearse Jr LA, Rosow C, Zaslavsky A et al. Bispectral analysis of the electroencephalogram predicts conscious processing of information during propofol sedation and hypnosis. Anesthesiology 1998;88:25-34.
- Coste C, Guignard B, Menigaux C et al. Nitrous oxide prevents movement during orotracheal intubation without affecting BIS value. Anesth Analg, 2000;91:130-135.
- Hans P, Dewandre PY, Brichant JF et al. Comparative effects of ketamine on Bispectral Index and spectral entropy of the electroencephalogram under sevoflurane anaesthesia. Br J Anaesth, 2005;94:336-340.

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- Hering W, Geisslinger G, Kamp HD et al. Changes in the EEG power spectrum after midazolam anaesthesia combined with racemic or S-(+) ketamine. Acta Anaesthesiol Scand, 1994;38: 719-723.
- Vereecke HE, Struys MM, Mortier EP A comparison of bispectral index and ARX-derived auditory evoked potential index in measuring the clinical interaction between ketamine and propofol anaesthesia. Anaesthesia, 2003;58:957-961.
- 21. Edwards JJ, Soto RG, Thrush DM et al. Bispectral index scale is higher for halothane than sevoflurane during intraoperative anesthesia. Anesthesiology, 2003;99:1453-1455.
- Davidson AJ, Czarnecki C The bispectral index in children: comparing isoflurane and halothane. Br J Anaesth, 2004;92: 14-17.
- Edwards JJ, Soto RG, Bedford RF Bispectral index values are higher during halothane vs. sevoflurane anesthesia in children, but not in infants. Acta Anaesthesiol Scand, 2005;49: 1084-1087.
- Detsch O, Schneider G, Kochs E et al. Increasing isoflurane concentration may cause paradoxical increases in the EEG bispectral index in surgical patients. Br J Anaesth, 2000;84:33-37.
- Bruhn J, Bouillon TW, Shafer SL Onset of propofol-induced burst suppression may be correctly detected as deepening of anaesthesia by approximate entropy but not by bispectral index. Br J Anaesth, 2001;87:505-507.
- Koitabashi T, Johansen JW, Sebel PS Remifentanil dose/electroencephalogram bispectral response during combined propofol/regional anesthesia. Anesth Analg, 2002;94:1530-1533.
- Struys MM, Vereecke H, Moerman A et al. Ability of the bispectral index, autoregressive modelling with exogenous inputderived auditory evoked potentials, and predicted propofol concentrations to measure patient responsiveness during anesthesia with propofol and remifertanil. Anesthesiology, 2003; 99: 802-812.
- Lysakowski C, Dumont L, Pellegrini M et al. Effects of fentanyl, alfentanil, remifentanil and sufentanil on loss of consciousness and bispectral index during propofol induction of anaesthesia. Br J Anaesth, 2001;86:523-527.
- Barr G, Anderson RE, Owall A et al. Effects on the bispectral index during medium-high dose fentanyl induction with or without propofol supplement. Acta Anaesthesiol Scand, 2000;44:807-811.
- Barr G, Anderson RE, Samuelsson S et al. Fentanyl and midazolam anaesthesia for coronary bypass surgery: a clinical study of bispectral electroencephalogram analysis, drug concentrations and recall. Br J Anaesth, 2000;84:749-752.
- Matthews R Isoproterenol-induced elevated bispectral indexes while undergoing radiofrequency ablation: a case report. AANA J, 2006;74:193-195.
- Matisoff AJ, Panni MK Methylene blue treatment for methemoglobinemia and subsequent dramatic bispectral index reduction. Anesthesiology, 2006;105:228.
- Gallagher JD Pacer-induced artifact in the bispectral index during cardiac surgery. Anesthesiology, 1999;90:636.
- Hemmerling TM, Fortier JD Falsely increased bispectral index values in a series of patients undergoing cardiac surgery using forced-air-warming therapy of the head. Anesth Analg, 2002;95: 322-323.
- Hemmerling TM, Migneault B Falsely increased bispectral index during endoscopic shoulder surgery attributed to interferences with the endoscopic shaver device. Anesth Analg, 2002; 95:1678-1679.
- Hemmerling TM, Desrosiers M Interference of electromagnetic operating systems in otorhinolaryngology surgery with bispectral index monitoring. Anesth Analg, 2003;96:1698-1699.
- Mychaskiw G, Horowitz M, Sachdev V et al. Explicit intraoperative recall at a Bispectral Index of 47. Anesth Analg, 2001; 92:808-809.

- Morimoto Y, Matsumoto A, Koizumi Y et al. Changes in the bispectral index during intraabdominal irrigation in patients anesthetized with nitrous oxide and sevoflurane. Anesth Analg, 2005; 100:1370-1374.
- Schnider TW, Luginbuehl M, Petersen-Felix S et al. Unreasonably low bispectral index values in a volunteer with genetically determined low-voltage electroencephalographic signal. Anesthesiology, 1998;89:1607-1608.
- Muncaster ARG, Sleigh JW, Williams M Changes in consciousness, conceptual memory, and quantitative electroencephalographical measures during recovery from sevoflurane- and remifentanil-based anesthesia. Anesth Analg, 2003;96:720-725.
- Hagihira S, Okitsu K, Kawaguchi M Unusually low bispectral index values during emergence from anesthesia. Anesth Analg 2004; 98:1036-1038.
- Gunawardane PO, Murphy PA, Sleigh JW Bispectral index monitoring during electroconvulsive therapy. Anesth Analg, 2002; 88:184-187.
- Deogaonkar A, Gupta R, DeGeorgia M et al. Bispectral index monitoring correlates with sedation scales in brain-injured patients. Crit Care Med, 2004;32:2403-2406.
- Renna M, Handy J, Shah A Low baseline bispectral index of the electroencephalogram in patients with dementia. Anesth Analg, 2003;96:1380-1385.
- Choudhry DK, Brenn BR Bispectral index monitoring: a comparison between normal children and children with quadriplegic cerebral palsy. Anesth Analg, 2002;95:1582-11585.
- Pandit JJ, Schmelzle-Lubiecki B, Goodwin M et al. Bispectral index-guided management of anaesthesia in permanent vegetative state. Anaesthesia, 2002;57:1190-1194.
- 47. Myles PS, Cairo S Artifact in bispectral index in a patient with severe ischemic brain injury. Anesth Analg, 2004;98:706-707.
- Azim N, Wang CY The use of bispectral index during a cardiopulmonary arrest: a potential predictor of cerebral perfusion. Anaesthesia, 2004;59:610-612.
- 49. Engl MR The changes in bispectral index during a hypovolemic cardiac arrest. Anesthesiology, 1999;91:1947-1948.
- Honan DM, Breen PJ, Boylan JF et al. Decreasing in bispectral index preceding intraoperative hemodynamic crisis: evidence of acute alteration of propofol pharmacokinetics. Anesthesiology, 2002;97:1303-1305.
- Merat S, Levecque JP, Le Gulluche Y et al. BIS monitoring may allow the detection of severe cerebral ischemia. Can J Anaesth, 2001;48:1066-1069.
- 52. Mathew JP, Weatherwax KJ, East CJ et al. Bispectral analysis during cardiopulmonary bypass: the effect of hypothermia on the hypnotic state. J Clin Anesth, 2001;13:301-305.
- Tribl G, Howorka K, Heger G et al. EEG topography during insulin-induced hypoglycemia in patients with insulin-dependent diabetes mellitus. Eur Neurol, 1996;36:303-309.
- Vivien B, Langeron O, Riou B Increase in bispectral index (BIS) while correcting a severe hypoglycemia. Anesth Analg, 2002;95:1824-1825.

#### RESUMEN

Duarte LTD, Saraiva RA — Cuando El Índice Bispectral (BIS) Puede Suministrar Valores Falsos.

JUSTIFICATIVA Y OBJETIVOS: El índice bispectral (BIS) es un parámetro multifactorial derivado del electroencefalograma (EEG), que permite la monitorización del componente hipnótico de la anestesia. Fue obtenido a partir de algoritmo derivado del análisis de un gran número de EEG de voluntarios y pacientes sometidos a sedaciones y anestesia general con diferentes agentes anestésicos. Además de otros beneficios, el uso del BIS para la monitorización de la profundidad de la anestesia, reduce el aparecimiento del despertar y memoria intraoperatoria. Esa revisión tuvo el objetivo de presentar situaciones clínicas en que el BIS denota valores no verdaderos, que están falsamente elevados o reducidos, debido a condiciones del paciente o a acciones de anestésicos no previstos cuando se elaboró su algoritmo.

**CONTENIDO:** Los valores del BIS pueden sufrir la alteración y el influjo en múltiples situaciones clínicas en que existen estándares

anormales del EEG; efecto de diferentes anestésicos y otros fármacos no incluidos en la elaboración de su algoritmo; interferencia por equipos eléctricos; o debido a peculiaridades del monitor.

**CONCLUSIÓN:** A pesar de que el algoritmo del BIS haya sufrido diversas alteraciones desde su primera versión, esas situaciones que determinan variaciones falsas de los valores del BIS, deben ser reconocidas por el anestesiólogo para evitar complicaciones, sean a causa de la sobredosis anestésica, o por subdosis que podrán causar el despertar y la memoria intraoperatoria.