Falsely increased bispectral index values caused by the use of a forced-air-warming device

EDITOR:
The bispectral index (BIS) is an electroencephalogram (EEG)-derived index which has been proposed to monitor the hypnotic component of anaesthesia. It is a dimensionless number between 0 and 100. In non-anaesthetized patients, BIS ranges between 90 and 100. Total suppression of cortical activity results in a BIS of 0. BIS values below 60 are associated with a low probability of consciousness and reflect sufficient anaesthesia. However, BIS might be inaccurate in some instances, e.g. during hypothermia, nitrous oxide administration or the use of electrocautery (for review see [1]). Forced-air-warming therapy has also been shown to produce falsely high BIS values when the monitors Aspect A-1000 (v. 3.12) [2] or the newer A-2000 (both monitors Aspect Medical Systems, Natick, MA, USA) [3] are used. Here we report a similar case using the latest available version of the Aspect BIS XP monitor (Aspect Medical Systems, Natick, MA, USA).

CASE REPORT: A 65-yr-old male patient with squamous cell carcinoma was scheduled for abdomino-thoracic resection of the oesophagus. After placement of an epidural catheter at the T5 level, anaesthesia was induced using 2 mg kg\(^{-1}\) propofol and 10 µg sufentanil; intubation was facilitated with 0.6 mg kg\(^{-1}\) rocuronium. Anaesthesia was maintained with 0.7 minimum alveolar concentration (MAC) sevoflurane in 40% oxygen and air. For analgesia, 10 mL of ropivacaine (7.5 mg mL\(^{-1}\)) were administered approximately every 2 h via the epidural catheter. Neuromuscular blockade was provided by repeated injections of 0.2 mg kg\(^{-1}\) rocuronium. After induction of anaesthesia, catheters were placed in the left radial artery and the right internal jugular vein. A new original BIS XP sensor was placed on the patient’s forehead according to the manufacturer’s instructions to monitor the hypnotic component of anaesthesia. For warming, the patient’s upper body, arms and head were surrounded by a tent of blankets and a WarmTouch air warming system (Mallinckrodt, Hazelwood, MO, USA) was inserted above the left arm. From the first reading – after induction of general anaesthesia – BIS ranged around 40, no change was noticed after surgical incision. When the WarmTouch was turned on, the BIS value climbed to ~80 within 10 s. The signal quality index ranged between 80% and 100% during electrocautery and the electromyogram (EMG) bar increased slightly. No clinical sign of insufficient hypnosis was observed. The high BIS value dropped back to ~40 when the WarmTouch was turned off again. This phenomenon could be repeated several times (Fig. 1). During usage of the WarmTouch system, no interference with other electrical devices, i.e. electrocardiogram, were noted. This is consistent with the results of the testing of the WarmTouch devices by our medical physics group, which is routinely performed every 2 yr. After extubation and on postoperative day 1, the patient did not recall any intraoperative events.

Figure 1. Recording of BIS of an anaesthetized patient warmed using a forced-air-warming device. When the device was turned on, BIS values quickly increased to ~80. When the device was turned off, BIS values rapidly decreased to ~40. The recording was started during the operation when the device was on. Values of signal quality index (SQI) and EMG are also shown. An EMG level of 30 corresponds to an empty EMG bar on the BIS display.

Correspondence to: Robert Zanner, Klinik für Anaesthesiologie, Klinikum rechts der Isar, Technische Universität München, Ismaninger Strasse 22, D-81675 München, Germany. E-mail: Robert.Zanner@lrz.tum.de; Tel: +49 89 4140 4291; Fax: +49 89 4140 4886

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Since its introduction in 1996, the BIS system has been improved to generate stable signals that are more robust against artefacts to make the interpretation of BIS values more reliable. In the XP system, a new electrode position was added to further enhance artefact detection and reduce the influence of high frequencies on BIS values. According to the manufacturer, this results in better stability against artefacts and more reliable BIS values. Here we report a case where the latest version of the BIS XP system produced falsely high values due to the use of a forced-air-warming system. This problem has been described for older versions of the BIS [2,3]. However, in contrast to these reports, the XP system displayed an increase on the EMG bar.

R. Zanner, G. Schneider, E. Kochs
Department of Anaesthesiology
Klinikum rechts der Isar der
Technischen Universität München
Munich, Germany

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Atrioventricular sequential pacing causing haemodynamically significant mitral regurgitation immediately following cardiopulmonary bypass

EDITOR:
Mitral regurgitation can be induced or exacerbated by artificial pacemakers. What is not always so clear is the mechanism by which it occurs. Loss of atrioventricular synchrony when the ventricle is paced independently of the atrium has been blamed in some cases [1,2]. At least one attempt to study this phenomenon found that ventricular pacing was no more likely to produce new mitral regurgitation than dual chamber pacing [3] leading the authors to conclude that abnormal ventricular activation was more of a factor than atrioventricular synchrony. It has also been shown that rapid atrial pacing may produce mitral regurgitation through ischaemic dysfunction [4]. Here we present a case of haemodynamically significant severe mitral regurgitation produced transiently by atrioventricular pacing immediately after cessation of cardiopulmonary bypass.

Case report
A 68-yr-old female was admitted to our institution with unstable angina. Her past medical history included hypertension, insulin-dependent diabetes mellitus and myocardial infarction. Her medications included aspirin, metoprolol, insulin, furosemide, prinivil and heparin. Physical examination revealed a blood pressure (BP) of 148/84 mmHg and a heart rate of 68 beats min⁻¹. Her laboratory results were normal. Chest roentgenogram revealed a mildly enlarged cardiac silhouette. Electrocardiogram revealed non-specific ST changes. Surface echocardiography demonstrated a mildly enlarged left ventricle, a moderately reduced global left ventricular systolic function and multiple regional wall motion abnormalities. The ejection fraction was 38% and mild mitral regurgitation was demonstrated. Cardiac catheterization revealed severe stenoses of the right coronary artery, left anterior descending artery and circumflex artery. She was taken to surgery for coronary artery bypass grafting (CABG).

After placement of a large bore intravenous access and invasive monitors (pulmonary artery catheter and right radial arterial line) an uneventful induction of
general anaesthesia was performed. Intraoperative transoesophageal echocardiography (TOE) confirmed a moderately reduced global left ventricular systolic function and mild mitral regurgitation. The patient underwent left internal mammary artery grafting to the left anterior descending artery, and saphenous vein grafting to the right coronary and circumflex arteries. Temporary epicardial right atrial and ventricular pacing wires were placed as per routine.

In preparation for separation from cardiopulmonary bypass, epinephrine infusion at 0.05 µg kg\(^{-1}\) min\(^{-1}\) and milrinone at 0.5 µg kg\(^{-1}\) min\(^{-1}\) were instituted and atrioventricular sequential pacing at a rate of 90 beats min\(^{-1}\) with an atrioventricular delay of 150 ms was begun. On the initial attempt at separation, systolic BP decreased to 60 mmHg and pulmonary artery pressure increased to 44/23 mmHg. Cardiopulmonary bypass was reinstituted to address bleeding at the left anterior descending artery graft. A second attempt at separation failed due to low BP. The milrinone infusion was increased to 0.75 µg kg\(^{-1}\) min\(^{-1}\) and the heart was reperfused for 10 min. On the third attempt at separation, BP increased quickly above 100 mmHg systolic, but then decreased to 85/55 mmHg with a pulmonary artery pressure of 70/49 mmHg (Fig. 1).

TOE demonstrated severe mitral regurgitation (Fig. 2) without new segmental wall motion abnormalities. Electrocardiogram demonstrated pacemaker spikes with good capture of both the atrium and ventricle. The ventricular tracing was consistent with a left bundle-branch block pattern. Pausing the pacemaker revealed that the native rhythm had returned to sinus at 82 beats min\(^{-1}\) and pacing was discontinued. BP rapidly rose to 130/60 mmHg as the pulmonary artery pressure fell to 35/20 mmHg. The mitral regurgitation, as visualized by TOE, was once again mild (Fig. 3).

Protamine infusion and decanulation were then well tolerated by the patient. Trial reinstiution of atrioventricular sequential pacing within minutes of successful termination of cardiopulmonary bypass again resulted in severe mitral regurgitation. Thirty minutes after cessation of cardiopulmonary bypass, the pacemaker could be restarted without worsening the baseline mild mitral regurgitation or creating adverse haemodynamic effects. The patient was transferred to the intensive care unit in stable condition on infusions of epinephrine and milrinone. Her post-operative hospital course was uneventful and she was subsequently discharged to home.

Discussion

This case demonstrates severe mitral regurgitation, as confirmed by TOE and pulmonary artery pressures, induced by atrioventricular sequential pacing.
Glutamine and chronic obstructive pulmonary disease

EDITOR:
The association between weight loss and chronic obstructive pulmonary disease (COPD) has been recognized since the late Nineteenth Century. Critically ill patients have severe impairment of protein metabolism including muscle protein breakdown, increased transfer of amino acids from the periphery to the splanchnic area, increased use of amino acids for gluconeogenesis and synthesis of acute phase proteins [1]. Certain alterations involve specific amino acids, such as glutamine, which plays...
a key role in the maintenance of organ and tissue functions. No other single amino acid has received so much attention in recent clinical nutrition research [2]. Glutamine is a conditionally essential amino acid, i.e., a nonessential amino acid under physiologic conditions that may become an essential amino acid in catabolic illness. During severe stress, cellular requirements of glutamine-using tissues increases and use of this amino acid outpaces its production leading to depletion of its plasma pool [1]. The purpose of the present study was to evaluate the effects of intravenous (i.v.) glutamine in enterally feed patients on haemodynamic and biochemical parameters, serum cytokine levels and patient outcome.

The Ethics Committee of Trakya Hospital approved the study protocol and each patient or relative gave written informed consent before the study. The study was prospective, placebo-controlled, randomized and double-blinded. Forty patients with COPD, requiring mechanical ventilation to manage acute respiratory failure due to an acute exacerbation of chronic airflow obstruction, were studied. The diagnosis of COPD was based on clinical history, physical examination and prior pulmonary function tests. Following a protocol already in use in the ICU for COPD patients receiving invasive ventilation, the preset inspiratory pressure was adjusted to obtain an exhaled tidal volume of 6–8 mL kg⁻¹ (ideal body weight). Positive end-expiratory pressure (PEEP) was initially set at 5 cmH₂O. FIO₂ was adjusted to maintain oxygen saturation between 92% and 94% as measured by pulse oximetry. Further adjustments of the ventilator settings were made on the basis of continuous monitoring, clinical data and arterial blood-gas assessments. Mechanical ventilation in controlled mode was used for less than 24 h. When spontaneous breathing reappeared, pressure support ventilation was initiated. The preset inspiratory pressure was set to achieve a tidal volume of 6–8 mL kg⁻¹, while PEEP was initially set at 5 cmH₂O for all patients.

Randomization was achieved according to computer determined permuted block design. The study was a planned prospective, randomized, double-blind, placebo-controlled study. To perform the study in a double-blind fashion, drug solution and infusion set were covered with foil and administered to all patients by a nurse without any knowledge about the study protocol. A nasogastric tube was placed and its correct location in the gastric lumen confirmed radiologically. All patients were placed on continuous infusion of enteral tube feeding. The enteral feed was delivered by a pump device and 25–30 kcal kg⁻¹ day (Pulmocare; Abbott Laboratories BV Ross Product Manufacturer, Zwolle, Holland, carbohydrate 28%, lipid 55.5%, protein 16.5%, 383 mOsm L⁻¹) as the caloric requirement. After achieving caloric target in 24 h, the study was started. Glutamine solutions 100 mL (Dipeptiven® 100 mL (N₂-l-alanine l-glutamine 20 g L⁻¹), Fresenius Kabi, Austria GmbH, Graz, Austria) (n = 20, Group I) i.v. was administered as a continuous infusion for 12 h everyday for 5 days. In the placebo group (n = 20, Group II), patients were given saline in the same volume and dosing regimen.

Arterial blood samples were simultaneously withdrawn for measurements of pH, PO₂, PCO₂ and SaO₂ (Medica Easy BloodGas, Massachussets, USA). Haemodynamic parameters were continuously monitored (SpaceLabs Inc., Redmond, USA). All measurements were obtained at baseline (before start of the study) and were repeated at 24, 48, 72, 96 and 120 h after glutamine administration. Platelets, albumin, leukocytes, bilirubin, alanine aminotransferase and creatinine were determined at the same times (Vitalab Flexor; Dieren, Netherlands).

Tumour necrosis factor alpha (TNF-α), interleukin (IL)-1β, IL-2 receptor, IL-6 and IL-8 levels were measured at the same times. Venous blood was collected into a 10 mL sterile plain tube (without anticoagulant) before administration of any medications and stored at −20°C. TNF-α, IL-1, IL-2 receptor, IL-6, IL-8 levels were measured with a solid-phase, two-site chemiluminescent enzyme immunometric assay method (Immulite TNF-α, Immulite IL-1β, Immulite IL-2 receptor, IL-6 Immulite and IL-8 Immulite, EURO/DPC, Llanberis, UK). The antibodies used in this procedure have no known crosreactivities with other cytokines.

According to power analysis we calculated that 20 patients would be needed in each group (α = 0.05, β = 0.2). Repeated measures ANOVA was used to evaluate the differences between and within groups. In the case of significance the groups were tested further by independent sample t-test to determine which difference was significant. Data were expressed as mean ± SD. A P-value of <0.05 was considered significant.

Twenty patients received glutamine solution i.v. (Group I) and 20 received placebo (Group II). APACHE II scores (16.10 ± 4.4 and 15 ± 4.2, Groups I and II, respectively) were similar (P > 0.05, Table 1). There was no significant difference between the groups with respect to pH, PO₂, PCO₂, PaO₂/FiO₂ ratio and SaO₂. No significant change was found in haemodynamic and biochemical parameters between the groups.

Five patients had septic shock on admission (2 in Group I and 3 placebo-treated patients). All non-survivors died while being mechanically ventilated. In Groups I and II, ventilation duration was 7 ± 3 and 6 ± 3 days, respectively (n.s.). The ICU stay of Group I treated survivors was not significantly different to...
that of the placebo-treated survivors (13 ± 8 vs. 15 ± 3 days). TNF-α, IL-1β, IL-2 receptor, IL-6 and IL-8 levels remained unchanged during the study.

COPD is characterized by airway inflammation which is considered to play a pathogenic role in this disorder [3]. The proinflammatory cytokines TNF-α and IL-1 are thought to play a central role in inflammatory processes, and increased levels of TNF-α have been reported in sputum and in the circulation of patients with COPD [4]. Furthermore, both TNF-α and IL-1 have been detected in bronchial submucosal cells in patients with chronic bronchitis, and during exacerbations the number of TNF-α positive cells is significantly increased [5]. Although the chronic inflammatory state in COPD suggests an imbalance between pro- and anti-inflammatory mediators, to date there are no data on the levels of anti-inflammatory mediators in this disease [6]. It also triggers the release of other cytokines, which themselves mediate an increase in energy expenditure as well as mobilization of amino acids and muscle protein catabolism. In this study, proinflammatory cytokines were elevated.

Although glutamine also is a prime substrate for monocyte metabolism the effect of glutamine on monocyte TNF-α and IL-6 production is unknown. Souba and colleagues [7] have suggested that in times of stress glutamine also support macrophage production of the cytokine mediators of the catabolic response. Glutamine is required for the production of IL-1 by cultured macrophages and it seems likely that it is required for the production of other proinflammatory cytokines such as IL-6 or TNF-α [8]. However, glutamine improves gut barrier function and by the attenuation of portal endotoxemia it might indirectly reduce the production of proinflammatory cytokines such as TNF-α or IL-6 by the peripheral blood mononocytes or related cells of the reticuloendothelial system. Our results failed to observe a significant change in systemic cytokine levels during glutamine administration in patients with COPD. Cytokine levels in the plasma do not necessarily reflect the local synthesis of cytokines by cells. Many cells have surface receptors for these cytokines with high binding properties, and target cells and soluble receptors trap cytokines. Thus, cytokines released at the local level may remain undetected in the plasma. In our study we found that plasma cytokine levels remained unchanged during a period of 120 h.

We found that the effect of i.v. glutamine did not alter haemodynamic and biochemical parameters or cytokine levels or outcome in patients with COPD. Due to the limited number of patients in our study and the short period of observation our findings need to be confirmed by larger clinical trials of i.v. glutamine patients with COPD.

Table 1. Patient and clinical characteristics.

<table>
<thead>
<tr>
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<th>Group I (n = 20)</th>
<th>Group II (n = 20)</th>
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<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td>68 ± 6</td>
<td>70 ± 5</td>
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<tr>
<td><strong>APACHE II score</strong></td>
<td>16.1 ± 4.4</td>
<td>15 ± 4.2</td>
</tr>
<tr>
<td><strong>Male/female</strong></td>
<td>10/10</td>
<td>13/7</td>
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<tr>
<td><strong>Cause of acute respiratory failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exacerbation of chronic disease</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Arterial pH before ventilation</strong></td>
<td>7.17 ± 0.05</td>
<td>7.18 ± 0.06</td>
</tr>
<tr>
<td><strong>PaO₂ before ventilation (mmHg)</strong></td>
<td>43 ± 9</td>
<td>44 ± 8</td>
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<tr>
<td><strong>PaCO₂ before ventilation (mmHg)</strong></td>
<td>99 ± 14</td>
<td>100 ± 13</td>
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<tr>
<td><strong>HCO₃ before ventilation (mmol L⁻¹)</strong></td>
<td>39 ± 4</td>
<td>38 ± 4</td>
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| **Outcomes**             |                  |                  |
| ICU mortality            | 2                | 3                |
| Post-ICU hospital mortality | 1             | 1                |
| **Duration of ventilation (days)** | 7 ± 3          | 6 ± 3            |
| **ICU stay (days)**      | 13 ± 8          | 15 ± 3           |

ICU: intensive care unit; APACHE II: acute physiologic and chronic health evaluation. There were no significant statistical differences between groups. Data are mean ± SD or numbers of patients.

References