Cardiovascular and arousal responses to laryngoscopy and tracheal intubation in patients with complete spinal cord injury

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Background. We aimed to determine whether the autonomic and arousal responses to laryngoscopy and tracheal intubation were altered in patients with spinal cord injury (SCI).

Methods. One hundred and sixteen patients with traumatic complete SCI were grouped according to the time elapsed after the injury (<3 days and >9 months) and the level of injury (above T5 and below T5): acute high (AH, n=25), chronic high (CH, n=26), acute low (AL, n=20), and chronic low (CL, n=45). Twenty-five patients without SCI served as a control group. Bispectral index (BIS) response, systolic arterial pressure (SAP), heart rate (HR), and plasma concentrations of catecholamines and arginine vasopressin were measured.

Results. Both CH and CL groups showed a greater reduction in BIS values after induction of anaesthesia with thiopental compared with controls (P<0.05). However, BIS values after intubation increased similarly in all groups from the value measured just before laryngoscopy. SAP increased in the AL and CL and control groups but not in the AH and CH groups. HR increased significantly in all groups; though to a lesser degree in the AH compared with the other groups. Plasma norepinephrine concentrations increased in all except the AH group, but vasopressin concentrations were unchanged.

Conclusions. The arousal response to laryngoscopy and tracheal intubation as measured by BIS is not altered in SCI, but cardiovascular and catecholamine responses may be changed depending on time elapsed and the level of the injury. However, an identical dose of thiopental may reduce BIS value after intubation more profoundly in patients with chronic SCI.


Keywords: complications, intubation tracheal; complications, spinal injury; monitoring, bispectral index; sympathetic nervous system, sympathoadrenal responses

Accepted for publication: October 7, 2008

In addition to cardiovascular responses, laryngoscopy and tracheal intubation induce an arousal response on the EEG.1–3 Animal studies have shown that EEG responses to noxious stimulation may occur when the depth of anaesthesia is changed.4 Moreover, the depth of anaesthesia depends on the intensity of the noxious stimulation.5

Neuraxial block, such as with spinal or epidural anaesthesia, has sedative effects depending on the level of sensory block6–7 and markedly reduces the amount of sevoflurane required to maintain adequate depth of anaesthesia.8 Epidural anaesthesia also reduces the minimum alveolar concentration of sevoflurane required to suppress movement in response to noxious electric stimuli applied even above the level of sensory block.9 A complete spinal cord injury (SCI) or transection not only results in the loss of sensory and motor functions, but also an interruption of sympathetic outflow below the level of injury.10 SCI may simulate spinal or epidural anaesthesia in terms of spinal deafferentation. In this context, SCI may reduce the arousal and cardiovascular responses to tracheal intubation by a general anaesthetic effect, by interrupting the sympathetic efferent fibres innervating the heart and vascular beds, or by both.

The bispectral index (BIS), obtained by bispectral analysis of the EEG, has been related to the hypnotic component of anaesthesia.11 It has been used successfully
to identify the arousal associated with noxious stimulation such as tracheal intubation during anaesthesia. We hypothesized that SCI per se would attenuate both the arousal response assessed by BIS and autonomic responses to laryngoscopy and tracheal intubation during induction of anaesthesia. Thus, anaesthetic requirements to provide adequate depth of anaesthesia for tracheal intubation would be reduced in patients with SCI.

**Methods**

The study was performed in 116 patients with traumatic clinically complete SCI undergoing a spinal or non-spinal surgery under general anaesthesia at our University Hospital from January 2003 to December 2007. The study protocol was approved by the University Hospital Ethics Committee. One hundred and thirty-one patients were initially approached to take part in the study. When patients were unable to give written consent because of their injury, consent was taken from the next of kin. Fifteen patients denied their consent and were excluded. Patients were classified into acute (<3 days) and chronic (>9 months) groups according to the interval after injury. As life-threatening cardiovascular disturbances frequently occur in acute stage of SCI and a life-threatening hyperkalaemic response to suxamethonium may occur during the period between 4 days and 9 months after SCI, patients were not recruited at these times. Patients were further divided into high and low groups according to the most cephalic level of complete motor and sensory lesions. Thus, the groups comprised: acute high level-injured, AH (interval <3 days, level of injury above T5; n=25), chronic high level-injured, CH (interval >9 months, level of injury above T5; n=26), acute low level-injured, AL (interval <3 days, level of injury below T5; n=20), and chronic low level-injured CL (interval >9 months, level of injury below T5; n=45) groups.

Twenty-five age-matched patients without neurological impairment undergoing spinal surgery for trauma served as a control group. Exclusion criteria included: (i) history of any cardiovascular, pulmonary, or metabolic disease; (ii) medications that would influence arousal or cardiovascular response to intubation; (iii) spinal neurogenic shock state with or without vasopressors; (iv) acute trauma to other organ systems including brain than the spine or changes in level of consciousness; (v) chronic pain associated with the SCI; and (vi) SCI that involved long periods of ICU stay. Spinal neurogenic shock was defined as a systolic arterial pressure (SAP) ≤85 mm Hg at the beginning of anaesthesia and surgery in acutely cord-injured patients.

Neurological examinations were performed by the University Hospital Spine Center according to the 1996 American Spinal Injury Association standards. Motor function was examined using key muscles for levels C5 through T1 and L2 through S1, and total paralysis of motor strength was regarded as a complete lesion. Sensory level was examined by light touch and pinprick at each dermatome, and anaesthesia and analgesia were regarded as a complete lesion.

Patients received no premedication. Before arrival in the operating theatre, an i.v. catheter was placed to allow the administration of fluids and medications and a 20 gauge catheter inserted into a radial artery to measure arterial pressure and for blood sampling. Heart rate (HR), pulse oximetry, and capnography were recorded continuously using an S/5 Anaesthesia Monitor (GE Healthcare, Helsinki, Finland). A standard BIS electrode montage (BIS Sensor—Aspect Medical Systems, Inc., Natick, MA, USA) was applied to the forehead before induction of anaesthesia, and BIS was measured continuously using an Aspect A-2000 BIS monitor (BIS® XP, software version 3.31; Aspect Medical Systems, Inc.). The anaesthetist who participated in the anaesthetic care was blinded to the BIS value. All external stabilizing devices—including soft and hard collars, halo vest, and weighted traction—were removed before anaesthesia induction. For each patient, a rest period of at least 30 min was provided between the time of i.v. and arterial cannulation and the start of the study.

After baseline values were recorded and breathing oxygen 100%, anaesthesia was induced at time ~90 s with thiopental 5 mg kg⁻¹ administered i.v. over 20 s, followed by suxamethonium 1 mg kg⁻¹ over 5 s. Direct laryngoscopy and tracheal intubation were performed when neuromuscular block was achieved (time 0), and anaesthesia was maintained with nitrous oxide 50% and sevoflurane (2% inspired) in oxygen with a fresh gas flow of 4 litre min⁻¹ maintained throughout the study. Manual ventilation, laryngoscopy, and tracheal intubation were performed in all patients by an experienced faculty anaesthetist. No effort was made to fully expose the glottis during laryngoscopy; exposure was limited to that necessary to allow passage of the tracheal tube through the vocal cords under direct vision. In patients with unstable cervical spine fracture, cervical immobilization was maintained manually by a member of a skilled anaesthesia team to reduce the likelihood of secondary neurological injury during the process of intubation. Lungs were mechanically ventilated with a ventilator to maintain an end-tidal CO₂ tension between 4 and 4.5 kPa. Data from patients in whom intubation required longer than 15 s were excluded.

BIS values, SAP, and HR were recorded by an independent investigator before induction of anaesthesia (baseline), just before laryngoscopy and intubation, and at 1 min intervals up to 5 min thereafter. BIS values were recorded as the maximum value displayed within each minute. These values were confirmed by downloading data from the electronic memory of the monitor at the end of surgery. Arousal response (defined by an increase in BIS to intubation) was determined by calculating the difference of highest BIS value observed after intubation (for 5 min after intubation) and BIS value measured just before starting laryngoscopy. Hypertension was defined as an SAP
characteristic data were compared using a one-way analysis of variance. Serial changes in cardiovascular, hormonal, and BIS data were analysed using two-way analysis of variance with repeated measures, with time as within-group factor, group (SCI/control) as between-group factor, and the interaction between time and group also compared. A difference among the groups in BIS increase at intubation from the value measured just before starting laryngoscopy to peak value (arousal) was analysed using analysis of variance. The Scheffé test was used for multiple pairwise comparisons when a significant difference was indicated with analysis of variance. Complication rates among the groups were analysed by using the $\chi^2$ test where appropriate. A $P$-value of $<0.05$ was considered statistically significant.

**Results**

There were no significant differences among the groups with respect to sex ratio, age, weight, or height. Haemoglobin concentrations were significantly lower in the SCI group compared with the control, whereas blood loss was greater in the AL group (Table 1). All acutely injured patients (AH and AL) received anterior, posterior, or both spinal fusions. Fifteen (58%) in the CH group and 41 (91%) in the CL group had local flap surgery because of decubitus ulcer. Baseline BIS value and HR were similar among the groups including the control. Baseline SAP was lower in the AH and CH groups than in the control.

There was a significant decrease in BIS values after induction of anaesthesia in all groups; the degree of which was greater in the CH and CL groups than in the control ($P<0.05$). BIS values increased similarly (14–19 BIS units) in response to tracheal intubation, from the value measured just before starting laryngoscopy (arousal) in the cord-injured and control groups. Mean (95% confidence intervals) of the difference between AH and control was 0.4 (−10.2 to 10.9), between AL and control −0.3 (−11.5 to 10.9), between CH and control 5.3 (−5.2 to 15.8), and between CL and control 3.5 (−5.8 to 12.8) ($P=0.34$). Mean (SD) peak BIS values after intubation were significantly smaller in the CH [56 (12)] and CL [58 (10)] groups compared with the control [67 (9)] but not in the AH and AL groups where peak BIS values were [63 (11)] and [66 (11)], respectively. The maximal increase in BIS was noted within the first 4 min in every patient (Fig. 1). The day after the surgery, no patients recalled awareness during anaesthesia and tracheal intubation.

SAP decreased after induction of anaesthesia in all groups. In response to tracheal intubation, however, SAP increased in the control and the low level-injured (AL and CL), whereas it remained unaltered in the high level-injured (AH and CH). The maximum increase in SAP was noted within 60 s, which persisted until 2 min after the intubation. SAP then decreased to the control value or even less than

>130% of the baseline value or >160 mm Hg, whereas hypotension was defined as SAP <70% of the baseline value or <90 mm Hg. Tachycardia and bradycardia were defined as HR more rapid than 120 and <60 beats min$^{-1}$, respectively. The incidences of hypertension, hypotension, tachycardia, and bradycardia were recorded throughout the study. A dysrhythmia was defined as any ventricular or supraventricular premature beat or any sustained rhythm other than sinus.

Blood loss, assessed by measuring suctioned blood and by weighing gauzes and drapes, was replaced with Ringer’s lactate solution in a ratio of 1:4 or with packed cells if haemoglobin concentration was <10 g dl$^{-1}$. Intraoperative hypotension was treated with ephedrine 8 mg i.v. boluses if SAP decreased to <85 mm Hg. At the completion of surgery, volatile anaesthetic agents were discontinued and residual neuromuscular block was reversed with atropine 1.0 mg and neostigmine 2.5 mg. Estimated blood loss and amount of ephedrine administered during the surgery were recorded. All patients were interviewed for recall on the first postoperative day using a standardized set of postoperative questions, which included enquiring for the recall of any unpleasant dreams during intubation or surgery and explicit memory recall for operative events.

Arterial samples were drawn before (baseline) and 1 min after the onset of intubation for measurement of plasma catecholamine and arginine vasopressin (AVP) concentrations. Samples were collected into pre-chilled tubes containing EDTA/Na$^+$ and immediately centrifuged at 3000 rpm for 10 min at 4°C. The plasma was stored at −70°C until assayed. Plasma concentrations of epinephrine and norepinephrine were measured in duplicates using high-pressure liquid chromatography. The assay sensitivity was 10 pg ml$^{-1}$, and the within-run precision coefficients of variation were 14.2% and 13.5% for epinephrine and norepinephrine, respectively. Plasma concentrations of AVP were measured by radioimmunoassay (Bühlmann Laboratories, Allschvil, Switzerland). Assay sensitivity for AVP was 2.5 pg ml$^{-1}$.

**Statistical analysis**

The sample size calculation was based on the primary endpoint of BIS value at tracheal intubation. In our pilot study, the mean and standard deviation of maximum BIS in the control group were 68 and 10. A power analysis suggested a sample size of 17 patients in each group should be adequate to detect a 15% difference in peak BIS at intubation with a two-sided significance level $\alpha$ of 0.05 and a power of 0.8. Taking into account possible dropouts, we aimed to recruit about 20 patients in each group. However, there were 45 patients in the CL group during the period of the study, without prejudice.

Data are expressed as number or mean (SD). They were analysed using StatView software version 4.0 (Abacus Concepts, Berkeley, CA, USA) on a Macintosh computer. Sex was analysed using Fisher’s exact test. The other patient
baseline values, which occurred earlier in the high level-injured (AH and CH) groups than in the control and low level-injured groups (Fig. 2). An increase of SAP >130% of baseline values or 160 mm Hg was noted in 49 (42%) of 116 SCI patients. The incidence of hypertension was significantly lower and that of hypotension was significantly higher in the high level-injured than in the control (Table 2). Thirteen (52%) patients in the AH group received ephedrine to treat the hypotension during the surgery.

HR increased after induction of anaesthesia in all groups \((P<0.05)\) and increased after tracheal intubation, though peak values were smaller in the AH group than in the others (Fig. 3). Although basal bradycardia was common and the incidence of bradycardia was more frequent in the AH group, no patient showed further slowing of HR during the study period. Premature ventricular contractions appeared immediately after tracheal intubation in two of 25 control patients and in four of 45 CL patients and in all cases disappeared spontaneously without treatment (Table 2).

Baseline norepinephrine concentrations were lower in both AH and CH groups compared with controls. Tracheal intubation increased plasma norepinephrine concentrations in all but the AH group. However, the magnitude of increase was attenuated in the CH group, whereas not affected in the AL and CL groups compared with the controls. No groups showed significant changes in plasma epinephrine concentrations after intubation, although the baseline values of the AH and CH groups were smaller compared with those in the control. Plasma AVP concentrations did not differ among the groups both at baseline and after intubation. Neither group showed changes in AVP concentrations in response to intubation (Table 3).

**Discussion**

The main finding in the present study was that the arousal response to laryngoscopy and tracheal intubation (as assessed by BIS) was not altered in SCI, either by the time elapsed or by the affected level, although chronic (CL and CH) groups showed a smaller peak BIS value. It has been shown that a neuraxial block produces inhibition

**Table 1** Patient characteristics, presented as mean (range), mean (SD) or number. Control, uninjured patients; AH, acute high-level cord-injured patients; CH, chronic high-level cord-injured patients; AL, acute low-level cord-injured patients; CL, chronic low-level cord-injured patients; \(n\), number of patients. *\(P<0.05\) vs the control group.

<table>
<thead>
<tr>
<th></th>
<th>Control ((n=25))</th>
<th>AH ((n=25))</th>
<th>CH ((n=26))</th>
<th>AL ((n=20))</th>
<th>CL ((n=45))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>20/5</td>
<td>21/4</td>
<td>23/3</td>
<td>17/3</td>
<td>40/5</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>39 (22–63)</td>
<td>41 (17–60)</td>
<td>39 (17–58)</td>
<td>37 (20–58)</td>
<td>44 (24–59)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>64 (12)</td>
<td>62 (9)</td>
<td>62 (11)</td>
<td>67 (19)</td>
<td>58 (12)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168 (7)</td>
<td>167 (8)</td>
<td>172 (6)</td>
<td>172 (7)</td>
<td>169 (9)</td>
</tr>
<tr>
<td>Haemoglobin concentration (g dl(^{-1}))</td>
<td>13.4 (1.8)</td>
<td>12.1 (1.3)*</td>
<td>12.0 (1.7)*</td>
<td>12.3 (1.9)*</td>
<td>12.4 (1.5)*</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>450 (208)</td>
<td>312 (168)*</td>
<td>502 (225)</td>
<td>838 (203)*</td>
<td>565 (350)</td>
</tr>
<tr>
<td>Time after injury (months)</td>
<td>—</td>
<td>—</td>
<td>79 (74)</td>
<td>—</td>
<td>147 (109)</td>
</tr>
</tbody>
</table>

**Fig 1** BIS before and after tracheal intubation in patients with SCI and in control patients. Values are mean (SD) or number. AH, acute high-level injury; CH, chronic high-level injury; AL, acute low-level injury; CL, chronic low-level injury; Control, normal patients; Ind, just before intubation; Int-1, 2, 3, 4, and 5, responses at 1, 2, 3, 4, and 5 min after intubation. *\(P<0.05\) vs the control group.

**Fig 2** SAP before and after tracheal intubation in patients with SCI and in control patients. Values are mean (SD) or number. AH, acute high-level injury; CH, chronic high-level injury; AL, acute low-level injury; CL, chronic low-level injury; Control, normal patients; Ind, just before intubation; Int-max, maximum response within 1 min after intubation; Int-1, 2, 3, and 5, responses at 1, 2, 3, and 5 min after intubation. *\(P<0.05\) vs baseline; †\(P<0.05\) vs the control group; ‡\(P<0.05\) vs the AH group.
Spinal cord injury and BIS responses to intubation

Fig 3 HR before and after tracheal intubation in patients with SCI and in control patients. Values are mean (SD) or number. AH, acute high-level injury; CH, chronic high-level injury; AL, acute low-level injury; CL, chronic low-level injury; Control, normal patients; Int, just before intubation; Int-max, maximum response within 1 min after intubation; Int-1, 2, 3, and 5, responses at 1, 2, 3, and 5 min after intubation. *P<0.05 vs baseline; †P<0.05 vs the control group; ‡P<0.05 vs the AH group.

Table 2 Incidence of adverse effects presented as number (%). Control, uninjured patients; AH, acute high-level cord-injured patients; CH, chronic high-level cord-injured patients; AL, acute low-level cord-injured patients; CL, chronic low-level cord-injured patients; HR, heart rate. *P<0.05 vs baseline; †P<0.05 vs the control group;

<table>
<thead>
<tr>
<th></th>
<th>Control (n=25)</th>
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<th>CH (n=26)</th>
<th>AL (n=20)</th>
<th>CL (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>17 (68%)</td>
<td>3 (12%)</td>
<td>3 (12%)</td>
<td>12 (60%)</td>
<td>33 (73%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>3 (12%)</td>
<td>13 (50%)</td>
<td>1 (5%)</td>
<td>4 (9%)</td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>6 (24%)</td>
<td>3 (12%)</td>
<td>5 (25%)</td>
<td>11 (24%)</td>
<td></td>
</tr>
<tr>
<td>(HR &gt;120 beats min⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Bradycardia</td>
<td>2 (8%)</td>
<td>9 (36%)</td>
<td>1 (4%)</td>
<td>6 (13%)</td>
<td></td>
</tr>
<tr>
<td>(HR &lt;60 beats min⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyssrhythmia</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
<td>2 (8%)</td>
<td>4 (9%)</td>
<td></td>
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</tbody>
</table>

Table 3 Mean (SD) plasma catecholamine and AVP concentrations. Control, uninjured patients; AH, acute high-level cord-injured patients; CH, chronic high-level cord-injured patients; AL, acute low-level cord-injured patients; CL, chronic low-level cord-injured patients; PI-1, 1 min post-intubation. *P<0.05 vs baseline; †P<0.05 vs the control group; ‡P<0.05 vs the AH group.

<table>
<thead>
<tr>
<th></th>
<th>Control (n=25)</th>
<th>AH (n=25)</th>
<th>CH (n=26)</th>
<th>AL (n=20)</th>
<th>CL (n=45)</th>
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<tbody>
<tr>
<td>Norepinephrine (pg ml⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>192 (103)</td>
<td>69 (56)</td>
<td>105 (71)</td>
<td>279 (111)</td>
<td>232 (112)</td>
</tr>
<tr>
<td>PI-1</td>
<td>345 (171)</td>
<td>74 (61)</td>
<td>134 (108)</td>
<td>346 (135)</td>
<td>345 (136)</td>
</tr>
<tr>
<td>Epopinephrine (pg ml⁻¹)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>81 (49)</td>
<td>14 (14)</td>
<td>16 (11)</td>
<td>111 (85)</td>
<td>83 (85)</td>
</tr>
<tr>
<td>PI-1</td>
<td>63 (47)</td>
<td>12 (13)</td>
<td>20 (17)</td>
<td>87 (55)</td>
<td>65 (60)</td>
</tr>
<tr>
<td>AVP (pg ml⁻¹)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.4 (0.6)</td>
<td>2.1 (3.1)</td>
<td>1.2 (1.3)</td>
<td>2.5 (2.8)</td>
<td>1.2 (1.2)</td>
</tr>
<tr>
<td>PI-1</td>
<td>2.3 (1.6)</td>
<td>2.7 (2.9)</td>
<td>2.2 (2.2)</td>
<td>3.0 (3.5)</td>
<td>1.4 (0.9)</td>
</tr>
</tbody>
</table>

of tonic afferent spinal signalling to the brain that produces sedative, general anaesthetic, or both effects.6–9 In the present study, just before starting laryngoscopy and intubation, the degree of cortical depression as assessed by the BIS was significantly greater in chronically injured patients (CH and CL groups). These results imply that chronic patients are more sensitive to thiopental. The sedative, general anaesthetic effects, or both of SCI itself may have potentiated the effects of thiopental on brain cortical function. However, this is unlikely because patients with an acute SCI showed similar BIS responses compared with the normal controls. Furthermore, the BIS values between SCI and control patients before induction of anaesthesia (baseline) did not differ, suggesting that SCI per se does not affect the BIS.

The subsequent laryngoscopy and intubation caused a similar increase (14–19 BIS units) of BIS values in every group (P=0.34), although chronic SCI patients showed lower BIS values after intubation than the control. These findings suggest that subcortical antinoception may not be affected in SCI, either by the level or by the time of injury. Thus, possible general anaesthetic effects resulting from spinal deafferentation are unlikely to affect the arousal response to tracheal intubation in SCI. Clinical evidence suggests that acute (i.e. ischaemic nerve block) and chronic (i.e. SCI) sensory deafferentation is associated with widespread changes in the somatosensory pathways and cortical information processing, which do not necessarily go in the same (acute vs chronic) direction.16 17 A different BIS response from that observed in patients with neuraxial anaesthesia8 could have resulted from neuromodulatory changes or reorganization within the cortex in SCI.

Patients with chronic SCI have been reported to have low blood volume and reduced lean tissue mass,18 19 implying a smaller volume of distribution for i.v. anaesthetic agents and a smaller vessel-rich compartment. Therefore, a higher brain concentration of the anaesthetic would be expected for a given dose. Indeed, it has been found that the dose requirement of propofol for induction of anaesthesia is related to lean tissue mass rather than total body mass.20 The greater sensitivity to thiopental and smaller increase of BIS values, although statistically insignificant, in response to tracheal intubation in chronic groups may be attributed to altered pharmacokinetics. An identical dose of thiopental 5 mg kg⁻¹ used in the present study is more likely to be associated with deeper planes of anaesthesia in chronic SCI than in acute SCI or control patients.
The cardiovascular responses to laryngoscopy and intubation are attributed to a reflex sympathetic discharge. In patients with spinal cord lesions, the sympathetic nervous system may be differentially affected according to the level of injury.\(^1\) In addition, cardiovascular responses to noxious stimuli may differ according to the time elapsed since the injury.\(^1\) We have previously shown that the cardiovascular and catecholamine responses to tracheal intubation differed according to the timing and the level of injury in SCI.\(^2\) The present study confirmed that the pressor response was abolished in the high level-injured (AH and CH groups). The chronotropic response was not affected in the CH group but was attenuated in the AH group, whereas the catecholamine response was increased significantly, though small, in the former and abolished in the latter. In contrast, cardiovascular and catecholine responses were not altered in either AL or CL groups.

AVP and renin–angiotensin systems are specifically activated to maintain the arterial pressure after epidural anaesthesia in humans,\(^3\) where sympathetic nervous activities are blocked. In addition, AVP is released by a number of stimuli including severe hypotension and decreased intrathoracic blood volume.\(^4\) Moreover, its concentrations may be changed more dramatically in response to surgical stimuli than catecholamines.\(^5\) High SCI causing quadriplegia is accompanied by significant hypotension due to impairment of sympathetic nervous activity. In the present study, whether AVP system activity would be changed in response to tracheal intubation and whether it would compensate for the decrease in arterial pressure were examined in the high SCI. However, AVP concentrations were not different between the cord-injured and the control either at baseline or after intubation. These findings suggest that AVP may not play an important role in maintaining arterial pressure in patients with complete SCI.

The BIS monitor has been used to detect arousal responses,\(^6\) and to measure depth of sedation and anaesthesia.\(^7\) In the present study, BIS responses to laryngoscopy and tracheal intubation were not altered in SCI. Therefore, in SCI patients who were unable to mount a haemodynamic response to painful stimulation because of impaired sympathetic activity or who were unable to move because of impaired motor activity, BIS variability with painful stimuli may be useful to titrate the analgesic component of general anaesthesia. However, given the severance of EEG generator sites from surgical location, BIS, which is derived from cortical EEG, is unlikely to predict cardiovascular reflex responses when noxious stimuli are applied at dermatome below the level of injury in the cord-injured.

BIS ≤60 is widely used as an endpoint of hypnosis during general anaesthesia.\(^8\) BIS values after intubation increased above 60, which represents a risk for awareness,\(^9\) in the acutely cord-injured and normal controls. This is consistent with a previous finding,\(^10\) in which tracheal intubation was also performed after induction of anaesthesia with thiopental 5 mg kg\(^{-1}\) i.v. In contrast, BIS reached values of just more than 40 after induction with thiopental, and it remained below 60 after tracheal intubation in the chronic cord-injured. Thus, the dosage and pharmacokinetics may have to be considered during induction of anaesthesia with i.v. anaesthetics to minimize the risk of unwanted side-effects, i.e. a small dosage may lead to an arousal reaction to tracheal intubation or an excessive dosage to hypotension in the SCI.

This study has several limitations. First, since a rapid sequence technique with suxamethonium is preferable in acute SCI patients who are at increased risk of pulmonary aspiration. To standardize the study technique, this was used in all patients and so patients who were at increased risk of hyperkalemia after suxamethonium were excluded.\(^11\) Secondly, peak BIS values after intubation in the control and acutely injured patients reached the critical BIS value for awareness of >60.\(^12\) One may thus argue that the use of thiopental 5 mg kg\(^{-1}\) alone is inadequate to prevent an awareness reaction to tracheal intubation during sevoflurane–N\(_2\)O anaesthesia. However, no patients recalled awareness during anaesthesia in the present study, such as in the previous study where BIS reached above 60 after tracheal intubation.\(^13\) Thirdly, the data collection was not performed in a blinded fashion, though since many of the observations are objective (e.g. BIS value, SAP, and HR), we feel that a lack of blinding is unlikely to have influenced our results. Finally, the arousal response was examined only by using BIS. However, awareness may occur at BIS levels that indicate adequate depth of hypnosis (≤60),\(^14\) although studies using BIS monitoring showed a low incidence of awareness during the surgery.\(^15\) Therefore, it may have been better if other additional parameters (e.g. isolated forearm test) have been studied to determine the effects on ‘arousal’.

In summary, the arousal response to laryngoscopy and intubation as measured by BIS was not altered, although cardiovascular and catecholamine responses differed according to the time elapsed and the level of injury in patients with SCI. However, an identical dose of thiopental given to induce anaesthesia before tracheal intubation caused a greater reduction in BIS value in the chronic, but not in acute cord-injured patients, suggesting that doses of i.v. induction agents should be adjusted according to the time elapsed after the injury in cord-injured patients.

**Funding**

This study was supported by a grant (#CRI07011-1) from Chonnam National University Hospital Research Institute of Clinical Medicine, 8 Hak-dong, Gwangju 501-757, South Korea.

**References**

1. Wilder-Smith OH, Hagon O, Tassonyi E. EEG arousal during laryngoscopy and intubation: comparison of thiopentone or

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2 Coppins MJ, Versichelen LE, Mortier EP, Struys MM. Do we need inhaled anaesthetics to blunt arousal, haemodynamic responses to intubation after i.v. induction with propofol, remifentanil, rocuronium? Br J Anaesth 2006; 97: 835–41


8 Hodgson PS, Liu SS. Epidural lidocaine decreases sevoflurane requirements for adequate depth of anesthesia as measured by the bispectral index monitor. Anesthesiology 2001; 94: 799–803


12 Lehmann KG, Lane JG, Piepmeier JM, Batsford WP. Cardiovascular abnormalities accompanying acute spinal cord injuries in humans: incidence, time course and severity. J Am Coll Cardiol 1987; 10: 46–52

13 Martyn JA, Richards M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. Anesthesiology 2006; 104: 158–69


17 Raineau O. Plastic responses to spinal cord injury. Behav Brain Res 2008; 192: 114–23


20 Leslie K, Crankshaw DP. Lean tissue mass is a useful predictor of induction dose requirements for propofol. Anaesth Intensive Care 1991; 19: 57–60


