European Journal of Anaesthesiology 2005; **22:** 392–402

ISSN 0265-0215

Correspondence

Changes in bispectral index values during lumbar arthrodesis*

EDITOR:

Several authors have reported sudden increases of the bispectral index values during different procedures such as endoscopic shoulder surgery [1], deep hypothermic circulatory arrest [2] or after using an upper-body blanket for warming [3]. In addition, spurious bispectral index values can be observed when the electromyogram activity of the bispectral index monitor reaches a value of 50 [4]. In all these reports there is a general agreement that the bispectral index monitor shows an erroneous value, which must be interpreted carefully.

In the present report we present four cases of patients who underwent general anaesthesia for lumbar arthrodesis, in which the depth of anaesthesia was assessed with the BIS A-2000™ bispectral index monitoring system (Aspect Medical Systems, Natick, MA, USA). In all patients, we observed a sudden increase in the bispectral index values coinciding with an intense surgical stimulation of the spinal roots.

Cases 1–3

These three patients were two males (66 and 41 yr) who underwent lumbar arthrodesis in the prone position and a female (60 yr) who had a resection of a thoracic vertebral body in the supine position. During surgery, when the surgeon adjusted a screw in the vertebral pedicles or in the course of the vertebral body resection there was a sudden increase of bispectral index values from 55–60 up to more than 90 while the heart rate (HR) and the blood pressure (BP) remained unaltered. The bar indicating signal quality in the monitor was of good quality, and the electromyogram did not show muscle activity. In none of the cases there were clinical signs of inadequate depth of anaesthesia (e.g. tachycardia, hypertension) and thus we did not increase the rates of infusion of remifentanil or propofol. At the time of the increase in bispectral index value, the surgeons were informed and they immediately interrupted the procedure and/or changed the direction of the screws. Afterwards the bispectral index values returned to below 60 within 30–180 s.

In all three patients general anaesthesia was achieved with an infusion of propofol ($2\,mg\,kg^{-1}\,h^{-1}$), a mixture of $O_2:N_2O$ (40 : 60) and an infusion of remifentanil ($0.2–0.5\,\mu g\,kg^{-1}\,min^{-1}$) which was increased or decreased in order to maintain the HR and the mean arterial pressure within a 20% range of baseline values. Neuromuscular blockade was monitored by the train-of-four (TOF) technique using a neurostimulator (Innervator 252; Fisher & Paykel Healthcare, New Zealand) with the electrodes placed on the anterior aspect of the wrist and hand. Boluses of 2 mg of cisatracurium were given to maintain an adequate level of neuromuscular blockade (two twitches of the TOF).

No changes in oxygen saturation (pulse oximetry) or body temperature (oesophageal probe) were observed at the time of the increased values of bispectral index. None of the patients had any recall evaluated 48 h after surgery.

Case 4

A 69-yr-old, 80-kg male undergoing lumbar arthrodesis (L5–S1), was anaesthetized with sevoflurane (0.8% end tidal) in a mixture of $O_2:N_2O$ (40 : 60) and an infusion of alfentanil ($0.72–1.0\,\mu g\,kg^{-1}min^{-1}$) administered at a rate to maintain the mean arterial pressure and HR within a 20% range of the baseline values. Neuromuscular blockade was obtained with boluses of 2 mg of cisatracurium titrated to preserve two twitches in the TOF.

At the time of rhizolysis, we observed a sudden increase in bispectral index which reached values between 90 and 100, together with an increase in mean arterial pressure from 91 to 122 mmHg and an increase in HR from 48 to 62 beats min^{-1}. The event was not associated with cough or movement. The rate of alfentanil infusion was increased from 0.72 to $1.0\,\mu g\,kg^{-1}min^{-1}$ for a period of 10 min. BP and HR returned to the previous values (89 mmHg and 48 beats min^{-1}) and the bispectral index value decreased to 60. Therefore, the alfentanil infusion was

*The results were presented at the ESA Meeting held in Lisbon, Portugal, 5–8 June 2004.

Correspondence to: Margarita M. Puig, Department of Anaesthesiology, Hospital Universitario del Mar, UAB, Paseo Maritimo 25–29, 08003 Barcelona, Spain. E-mail: MpuigR@imas.imim.es; Tel: +34 93 248 3527; Fax: +34 93 248 3254

Accepted for publication January 2005 EJA 2101

returned to the initial rate ($0.72\,\mu g\,kg^{-1}\,min^{-1}$). Afterwards, while the cardiovascular parameters remained unchanged, the bispectral index number increased again to values above 90, where it remained throughout the rest of the surgery, approximately 30 min after the event. Postoperatively, the patient stated that he dreamed about his granddaughter but there was no recall of the surgery.

These abrupt changes of the bispectral index observed during spinal surgery could have been due to a number of factors. Interferences with electrical devices in the operating room, such as the electrocautery, were considered. In all patients, we had good signal quality at the time of the event. It is possible, that the surgical tools used in this type of procedure could produce some kind of interference. However, if this were the case, changes in bispectral index would have appeared more frequently when performing this type of surgery. Moreover, when electrical interference occurs, the signal usually fades from the screen in a characteristic manner. Thus, we do not think that this type of interference could explain the change observed in our patients.

All of our patients were paralysed with cisatracurium and the electromyogram column in the bispectral index monitor showed no change in activity.

In Case 4, we observed high bispectral index values together with an increase in BP and HR. We were able to abolish the haemodynamic response and return the bispectral index value to 60 using alfentanil. This suggests the presence of pain. Afterwards, as the alfentanil infusion was returned to the initial rate, the bispectral index value increased again, a fact that could be related to the transmission of the nociceptive stimuli induced by the excision of a spinal root, to supraspinal sites. The presence of dreaming in this case could be a sign of a light level of anaesthesia [5].

In Cases 1–3 we observed a short increase in bispectral index values without haemodynamic changes. This could be due to a more transient stimulation and/or to the administration of remifentanil, a more effective opioid than alfentanil.

The adrenergic response induced by the intense nociceptive stimulation during spinal surgery can be blocked by the administration of opioids, combined with intravenous (i.v.) or inhalation anaesthetics. But, in order to avoid the activation of the cerebral cortex observed in these cases, it would be necessary to administer higher doses of hypnotics to maintain bispectral index values close to 40. However, the manifestation of sudden increases in bispectral index (associated or not with changes in cardiovascular parameters) could be a reliable indication of manipulation of the spinal roots or fibres. It is possible that bispectral index could be an early clinical indicator to warn the surgical team about possible nerve injury.

E. Barrera, S. Fernández-Galinski, E. Arbonés
F. Escolano, M. M. Puig
Anaesthesiology Service
Hospital Universitario del Mar
UAB, Barcelona, Spain

References

1. 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.
2. Mychaskiw G, Heath BJ, Eichhorn JH. Falsely elevated bispectral index during deep hypothermic circulatory arrest. *Br J Anaesth* 2000; **85**: 798–800.
3. Guignard B, Chauvin M. Bispectral index increases and decreases are not always signs of inadequate anesthesia. *Anesthesiology* 2000; **92**: 903.
4. Baldesi O, Bruder N, Velly L, Gouin F. Spurious bispectral index values due to electromiographic activity. *Eur J Anaesthesiol* 2004; **21**: 330–331.
5. Myles PS, Leslie K, McNeil J, Forbes A, Chan MTV, for the B-Aware trial group. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. *The Lancet* 2004; **363**: 1757–1763.

Total intravenous anaesthesia with propofol for myasthenic patients

EDITOR:

Myasthenia gravis is a neuromuscular disorder characterized by weakness and fatigue of voluntary muscles due to a decreased number of acetylcholine receptors at the neuromuscular junction [1]. The use of muscle relaxants has remained controversial because patients with myasthenia gravis are known to be sensitive to their effects [2]. Experience with the use of propofol induction and maintenance of anaesthesia in patients with myasthenic gravis is limited [3,4].

The aim of this study was to investigate the use of propofol in myasthenic patients by evaluating endotracheal intubation, surgical conditions, undesirable

Correspondence to: A. Bouaggad, Department of Anaesthesiology and Intensive Care, CHU Ibn Rochd, Casablanca 20000, Morocco. E-mail: Bouaggad@hotmail.com; Tel: +212 61 791 791; Fax: +212 22 29 94 83

Accepted for publication February 2004 EJA 1291

side-effects and duration of postoperative ventilatory support. After institutional Ethics Committee approval and patients' consent, 22 patients with myasthenia gravis were studied. They were all scheduled to undergo transsternal thymectomy. They were classified according to Osserman (8 class IIA; 14 class IIB). All were receiving anticholinesterase drugs and 10 were receiving oral prednisone. This treatment was withdrawn on the morning of surgery. No premedication was used. Anaesthesia was induced using fentanyl $3\,\mu g\,kg^{-1}$ and propofol $2\,mg\,kg^{-1}$. Direct laryngoscopy was performed 60 s after propofol injection. Intubating conditions were evaluated by Viby-Mogenson's criteria [5]. Anaesthesia was maintained using a continuous infusion of propofol $10\,mg\,kg^{-1}\,h^{-1}$ for the first 10 min, $8\,mg\,kg^{-1}\,h^{-1}$ for the next 10 min and $6\,mg\,kg^{-1}\,h^{-1}$ thereafter with further titration of the infusion rate as necessary according to haemodynamic response. Mechanical ventilation with oxygen and nitrous oxide (F_iO_2 of 0.5) was continued throughout anaesthesia. No inhalational anaesthetic agent was used. In cases of poor intubating conditions, vecuronium $0.05\,mg\,kg^{-1}$ was used. Unwanted effects (e.g. cough, airway obstruction), patient movement in response to surgery and time to extubation were recorded. Of the 22 patients, two could not be intubated without the addition of vecuronium. Of the remainder, intubating conditions were excellent in 12 cases, and good in 8 cases. No unwanted effects or patient movement were recorded. In 18 patients the trachea was extubated at the end of the anaesthesia. Four required ventilatory support for 1 to 4 h.

Our results suggest that total intravenous anaesthesia with propofol infusion is a suitable technique for transsternal thymectomy in myasthenic patients. It offers a smooth induction and good conditions for tracheal intubation in the majority of patients. Satisfactory surgical conditions, and early extubation and recovery are also benefits.

A. Bouaggad, M. A. Bouderka, O. Abassi
Department of Anaesthesiology and Intensive Care
CHU Ibn Rochd
Casablanca, Morocco

References

1. Drachman DB. Myasthenia gravis. *New Engl J Med* 1994; **330**: 1797–1810.
2. Azar I. The response of patients with neuromuscular disorders to muscle relaxants. A review. *Anesthesiology* 1984; **61**: 173–187.
3. El Dawlatly AA, Ashour MH. Anaesthesia for thymectomy in myasthenia gravis: a non-muscle relaxant technique. *Anaesth Intens Care* 1994; **22**: 458–460.
4. O'Flaherty D, Pennant JH, Rao K, Giesecke AH. Total intravenous anaesthesia with propofol for transsternal thymectomy in myasthenia gravis. *J Clin Anesth* 1992; **4**: 241–244.
5. Viby-Mogenson J, Engback J, Eriksson LI, *et al*. Good clinical research practice (GCPP) in pharmacodynamic studies of neuromuscular blocking agents. *Acta Anaesthesiol Scand* 1996; **40**: 59–74.

Rapid injection reduces pain on injection with propofol

EDITOR:

A major disadvantage of propofol administration is pain on injection. Pre-treatment with lidocaine, opioids, metoclopramide, ephedrine, magnesium sulphate, neostigmine, ketorolac and injection into a large vein have all been reported to reduce the incidence and severity of pain. In principle, the speed of injection might influence pain since a slow rate will prolong the contact time with the endothelium, but rapid injection allows the propofol to be cleared from the vein and replaced with blood. There are conflicting data about the influence of speed of injection on pain with one study [1] showing no difference and another showing slow injection increased pain [2]. In the following randomized, double-blind placebo-controlled trial, we compared pain during fast administration of propofol to that during slow administration with and without lidocaine pre-treatment.

We studied 120 unpremedicated females (ASA I–II, aged 18–70 yr) undergoing elective surgery. Ethics committee approval from the University of Tsukuba and written informed consent were obtained. Patients were excluded if they were allergic to propofol, had

Correspondence to: Joseph R. Brimacombe, Department of Anaesthesia and Intensive Care, Cairns Base Hospital, The Esplanade, Cairns 4870, Australia. E-mail: jbrimaco@ bigpond.net.au; Tel: +61 7 40514999; Fax: +61 7 40506854

Accepted for publication March 2005 EJA 1879

communication difficulties, a history of cardiovascular or neurological disease, a body mass index $>30\,kg\,m^{-2}$ or were unsuitable for intravenous (i.v.) induction.

Patients were randomized into four equal-sized groups and the treatment group determined by opening an opaque envelope. In Group A, patients were pre-treated with normal saline 5 mL and then given propofol $2\,mg\,kg^{-1}$ at a rate of $3.3\,mg\,s^{-1}$. In Group B, patients were pre-treated with preservative-free lidocaine $0.5\,mg\,kg^{-1}$ adjusted to a volume of 5 mL and then given propofol $2\,mg\,kg^{-1}$ at a rate of $3.3\,mg\,s^{-1}$. In Group C, patients were pre-treated with preservative-free lidocaine $1.0\,mg\,kg^{-1}$ adjusted to a volume of 5 mL and then given propofol $2\,mg\,kg^{-1}$ at a rate of $3.3\,mg\,s^{-1}$. In Group D, patients were pre-treated with normal saline 5 ml then given propofol $2\,mg\,kg^{-1}$ at a rate of $50\,mg\,s^{-1}$.

An 18-G cannula (BD Insyte Autoguard, BD Medical Systems Inc., Utah, USA) was inserted into the largest visible vein on the radial side of the non-dominant forearm, attached to a three-way tap and flushed with Ringer's lactate solution. A 5 mL syringe containing the randomized pre-treatment drug at room temperature was attached to one limb of the tap and a propofol infusion at 5°C attached to the other limb of the tap. A venous tourniquet was applied just above the elbow and the pre-treatment drug was given. The tourniquet was released after 3 min and the propofol infusion commenced. The infusion was prepared immediately before use by drawing unmodified propofol (Diprivan 1%; AstraZeneca, Milano, Italy) without the use of a filter into a 60 mL syringe from three 20 mL glass vials. An i.v. infusion was not commenced during induction and co-induction agents were not administered.

Patients were asked by the anaesthetist, 'does it hurt' at 10 s intervals until unresponsive. Any spontaneous movements of the wrist, elbow or shoulder were noted. A second anaesthesiologist, blinded to the type of pre-treatment and rate of propofol infusion, evaluated the response as follows: 0: no verbal pain or movement; 1: verbal pain, but no movement; 2: verbal pain and movement of wrist; and 3: verbal pain and movement of elbow or shoulder. The pain score for the patient was taken as the most severe pain documented.

Following induction of anaesthesia, the laryngeal mask airway was inserted and anaesthesia maintained with 67% nitrous oxide and 1–2% sevoflurane in oxygen. Systolic blood pressure was measured every minute after the completion of propofol infusion and ephedrine 5 mg administered, if it was 30% lower than pre-induction baseline values.

Sample size was selected to detect a projected difference of 50% in the mean pain score between the groups for a Type I error of 0.05 and a power of 0.8. Patient characteristics data was tested by analysis of variance (ANOVA) (Scheffé as a *post hoc* test), pain intensity by Kruskal–Wallis test and the intensity of pain by χ^2-test with $P < 0.05$ taken as significant.

None of the patients were excluded from the analysis. Patient characteristics data were similar among groups (Table 1). Pain scores are given in Table 2. Rapid injection was less painful than slow injection ($P < 0.00001$). Rapid injection was similarly painful to slow injection after pre-treatment with lidocaine 1.0%, but less painful than after pre-treatment with lidocaine 0.5% ($P < 0.00001$). Pre-treatment with lidocaine 0.5% and 1.0% reduced pain during slow injection (both, $P < 0.00002$). During slow injection, pre-treatment with lidocaine 1.0% was more effective at reducing pain than lidocaine 0.5% ($P < 0.00001$). No patient required ephedrine.

We found that pain was reduced by rapid injection of propofol. Scott and colleagues [2], in a study of 30 patients using an induction dose of propofol at room temperature, reported that pain was more severe with slow injection. However, Grauers and colleagues [1], in a study of 30 patients using a sub-induction dose of propofol at room temperature, reported that infusion rate did not affect local pain on injection when comparing $2\,mg\,s^{-1}$ with $10\,mg\,s^{-1}$. The differences in study findings may be related to differences in the infusion rates or the total dose of propofol, but are

Table 1. Patient characteristics.

Group	Age (yr)	Height (cm)	Weight (kg)
A. Saline/slow propofol	48 ± 5	156 ± 6	52 ± 5
B. Lidocaine 0.5%/ slow propofol	46 ± 5	156 ± 4	52 ± 4
C. Lidocaine 1.0%/ slow propofol	48 ± 4	157 ± 3	52 ± 4
D. Saline/fast propofol	47 ± 4	157 ± 3	52 ± 4

Data are mean ± SD.

Table 2. Pain scores.

	Pain score			
Group	0	1	2	3
A. Saline/slow propofol	0	0	7	23
B. Lidocaine 0.5%/slow propofol	2	9	13	6
C. Lidocaine 1.0%/slow propofol	19	8	3	0
D. Saline/fast propofol	21	6	3	0

0: no verbal pain or movement.
1: verbal pain, but no movement.
2: verbal pain and movement of wrist.
3: verbal pain and movement of elbow or shoulder.

probably not related to injection temperature, since this has no impact on pain [3].

We found that during slow injection, lidocaine pre-treatment reduced pain and that the effect was dose related, with 1.0% being more effective than 0.5%. The efficacy of lidocaine pre-treatment is well established. A recent meta-analysis found that the best prevention of pain with propofol is lidocaine 0.5 mg kg^{-1} given with a rubber tourniquet before propofol injection and this will prevent pain in approximately 60% of patients [3]. Our study suggests that 0.5 mg kg^{-1} will prevent pain in 7%, but 1 mg kg^{-1} will prevent pain in 63%. The lower dose of lidocaine may have been less effective due to the slowness of the propofol injection.

Our study has four limitations. First, we did not compare haemodynamic responses between fast and slow injection. A potential hazard of rapid injection is a more marked fall in blood pressure than after slow injection [4]; however, no patient given rapid propofol had a fall in systolic blood pressure >30%, suggesting that rapid injection is probably safe in healthy patients. Second, we did not collect data about apnoea; however, we encountered no problems with ventilation using the laryngeal mask airway in the event of apnoea. Third, we did not collect data about whether patients remembered the pain they experienced; however, we recall that some patients did remember mild pain while others failed to remember severe pain. Fourth, our findings may not be applicable where pre-anaesthesia drugs, such as fentanyl and/or midazolam, are given.

We conclude that fast administration of propofol reduces pain and is comparable to slow administration with lidocaine 1.0% pre-treatment.

T. Shimizu, S. Inomata, S. Kihara, H. Toyooka
Department of Anesthesiology
University of Tsukuba
Tsukuba, Ibaraki, Japan

J. R. Brimacombe
Cairns Base Hospital
James Cook University
The Esplanade, Cairns, Australia

References

1. Grauers A, Liljeroth E, Akeson J. Propofol infusion rate does not affect local pain on injection. *Acta Anaesthesiol Scand* 2002; **46**: 361–363.
2. Scott RP, Saunders DA, Norman J. Propofol: clinical strategies for preventing the pain of injection. *Anaesthesia* 1988; **43**: 492–494.
3. Picard P, Tramèr MR. Prevention of pain on injection with propofol: a quantitative systematic review. *Anesth Analg* 2000; **90**: 963–969.
4. Ludbrook GL, Upton RN, Grant C, Martinez A. The effect of rate of administration on brain concentrations of propofol in sheep. *Anesth Analg* 1998; **86**: 1301–1306.

Mechanism of action of metoprolol in reducing propofol-induced pain

EDITOR:

Asik and colleagues recently reported on the efficacy of metoprolol in relieving the pain on injection of propofol [1] besides others who have proposed mechanisms for this effect. Although the mechanism for this action of metoprolol is still open to conjecture, that proposed by the authors, i.e vasodilatation, in view of its concomitant β_2-antagonist action, seems inappropriate. Metoprolol is a β_1-selective (cardioselective) adrenergic antagonist. However, this selectively is not absolute and β_2-antagonism is seen at higher doses [2,3]. In neurologically intact limbs in animal models, the intravenous infusion of metoprolol in larger doses has rather been found to increase peripheral vascular resistance and produce vasoconstriction [4,5]. Cardioselective β_1-antagonists have minimal effect on vascular tone and they do not possess vasodilator action in their own mode. Furthermore, metoprolol does not possess intrinsic sympathomimetic action which could explain the vasodilating effect as proposed by the authors [1–3].

Albeit weak, metoprolol is known to possess a membrane stabilization action [3]. This action may have assumed significant proportions in view of the high concentration of the drug achieved locally – distal

Correspondence to: Rajesh Mahajan, House No. F-35, Patel Chowk, Jammu, Jammu and Kashmir, India-180001. E-mail: drmahajanr@rediffmail.com; Tel: +91 2549948

Accepted for publication January 2004 EJA 1665

to the site of venous occlusion – and may in fact explain the beneficial effect of metoprolol in reducing propofol-induced pain rather than its direct effect on vascular tone.

R. Mahajan
ASCOMS, Jammu
Jammu and Kashmir, India

References

1. Asik I, Yorukoglu D, Gulay I, Tulunay M. Pain on injection of propofol: comparison of metoprolol with lidocaine. *Eur J Anaesthesiol* 2003; **20**: 487–489.
2. Moss J, Renz CL. The autonomic nervous system. In: Miller RD, ed. *Anesthesia*, 5th edn. Philadelphia, USA: Churchill Livingstone, 2000: 523–577.
3. Hoffman BB. Catecholamines, sympathomimetic drugs and adrenergic receptor antagonists. In: Hardman JG, Limbbird LE, eds. *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 10th edn. New York, USA: McGraw Hill, 2000: 215–268.
4. Benfield P, Clissold SP, Brogden RN. Metoprolol. An updated review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficiency in hypertension, ischemic heart disease and related cardiovascular disorders. *Drugs* 1986; **31**: 376–429.
5. Gorezynski RJ. Basic pharmacology of esmolol. *Am J Cardiol* 1985; **56**: 3F–13F.

Remifentanil and high thoracic epidural anaesthesia: a successful combination for patients with myasthenia gravis undergoing transsternal thymectomy

EDITOR:

Myasthenia gravis is an autoimmune disorder of the motor endplate. Medical treatment of myasthenia gravis includes improving neuromuscular transmission by anticholinesterases, suppressing the immune system by corticosteroids and immunosuppressants, and decreasing circulating antibodies by plasmapheresis [1]. Myasthenia gravis is frequently associated with morphological abnormality of the thymus gland. Patients with generalized myasthenia and patients with ocular symptoms poorly controlled by anticholinesterases often benefit from thymectomy [2]. After transsternal thymectomy, postoperative pain, analgesics and residual effects of anaesthetics can adversely affect pulmonary function which is already limited by the myasthenia gravis itself. This report describes the anaesthetic management of two patients with myasthenia gravis undergoing transsternal thymectomy using a high thoracic epidural and total intravenous (i.v.) anaesthesia with propofol and remifentanil.

In the last year two patients with myasthenia gravis were admitted to the Department of Thoracic Surgery for elective transsternal thymectomy. The first patient was a 32-yr-old female. Thoracic computed tomography revealed a thymoma in the thymus gland. The patient had an Ossermann and Genkins classification score of IIa [3] and was taking 90 mg pyridostigmine daily. The second patient was a 25-yr-old female with hyperplasia of the thymus gland. This patient had an Ossermann and Genkins classification score of IIb and was taking 120 mg pyridostigmine daily. Preoperative blood chemistry, respiratory and thyroid function test were normal in both patients.

On the day of surgery each patient received their usual dose of pyridostigmine and a premedication of diazepam 5 mg orally. Prior to surgery, an i.v. cannula was inserted and an infusion of 10 mL kg^{-1} of Ringer's lactate started. A radial artery catheter was placed under local anaesthesia. Electrocardiogram (lead II), invasive arterial pressure, pulse oximetry and capnography were continuously monitored, recorded and stored in an IBM-compatible computer. An epidural catheter was placed at the T5–6 level and a test dose of lidocaine 2% 3 mL was given. After 5 min, the patient received bupivacaine 0.5% 5 mL with 50 µg fentanyl via the epidural catheter. Anaesthesia was induced after preoxygenation with an infusion of propofol 6 mg kg^{-1} h^{-1}, remifentanil 0.5 µg kg^{-1} min^{-1} and atracurium 0.2 mg kg^{-1}. Five minutes after induction, the patients were intubated. After intubation the infusion of propofol was decreased to 4.5 mg kg^{-1} h^{-1} and the infusion of remifentanil to 0.2 µg kg^{-1} min^{-1}. The patients were ventilated with a 50% mixture of oxygen and air to maintain end-tidal CO_2 between 4 and 4.5 kPa. Patients were haemodynamically stable during the whole surgical procedure. Ten minutes before

Correspondence to: Dušan Mekiš, Department of Anesthesiology, Intensive Care and Pain Management, Maribor Teaching Hospital, Ljubljanska 5, 2000 Maribor, Slovenia. E-mail: dmekis@siol.net; Tel: +386 2 3211568; Fax: +386 2 3312393

Accepted for publication January 2005 EJA 1973

termination of the surgical procedure, the patients received bupivacaine 0.25% 5 mL via epidural catheter. At the end of surgery, the patients received neostigmine 1.5 mg and atropine 0.5 mg and the infusions of propofol and remifentanil were stopped. Five minutes later the patients were fully orientated, had no pain and were breathing spontaneously. They were extubated and transferred to the intensive care unit (ICU).

In the ICU the patients were haemodynamically stable without any subjective or objective impairment of respiratory function (Table 1). Analgesia was excellent with bupivacaine 0.125% 5 mL and 1 mg morphine epidurally every 6 h. The patients were discharged from the ICU 24 h after surgery.

In patients with myasthenia gravis, the combination of high thoracic epidural analgesia (TEA) and general anaesthesia for transsternal thymectomy is recommended by many authors [3]. Many authors combined TEA with light general anaesthesia using inhalation anaesthetics [3] or with i.v. general anaesthesia. Lorimer and Hall [4] used total i.v. anaesthesia with propofol and remifentanil for transsternal thymectomy in myasthenia gravis. The combination allowed excellent control of heart rate and pressor response during surgery, an early return to spontaneous ventilation and extubation within 9 min after termination of anaesthesia. Remifentanil is hydrolysed by non-specific tissue and plasma esterases, and its duration of action is not prolonged in patients with cholinesterase deficiency [5]. As remifentanil is not a substrate for pseudocholinesterase the metabolism of remifentanil is not affected by a cholinesterase inhibitor [6]. Baraka and colleagues [7] did, however, report a delayed postoperative arousal for 12 h following sevoflurane and remifentanil anaesthesia in a patient with myasthenia gravis undergoing thymectomy. Those authors believed that delayed postoperative arousal was due to prolonged remifentanil metabolism caused by pyridostigmine.

Table 1. Respiratory function before and after surgical procedure and blood-gas analyses after surgical procedure in patient no. 2.

	Before surgical procedure	After surgical procedure		
		0 h	2 h	4 h
VC (mL)	4130	2140	2420	2980
FEV_1 (mL)	3610	1430	2160	2100
Respiratory rate (min^{-1})	12	20	17	14
PaO_2 (kPa)	–	28.6	26.5	16.22
$PaCO_2$ (kPa)	–	5.08	5.87	6.11

VC: vital capacity; FEV_1: forced expiratory volume in 1 s; PaO_2: partial pressure of arterial oxygen; $PaCO_2$: partial pressure of arterial carbon dioxide.

In our two patients we used a combination of high TEA and total i.v. anaesthesia with remifentanil and propofol. To our knowledge this combination has not yet been reported in the literature. High TEA suppresses hormonal and metabolic stress response to pain allowing stable haemodynamics during surgery and excellent postoperative analgesia without compromising pulmonary function. We combined this technique with light i.v. anaesthesia using remifentanil and propofol. In our opinion, although TEA alone offers very stable haemodynamics during sternotomy, spontaneous breathing during this procedure would be most uncomfortable for the patient. Due to the fast elimination of remifentanil it is possible to rapidly alter its concentration in plasma by altering the speed of infusion. This enabled us to adjust the depth of analgesia to the phase of the operation. Since adequate analgesia for surgery was achieved in our patients by the use of TEA, only light general anaesthesia was needed for the patient to tolerate the tracheal tube allowing adequate mechanical ventilation. Therefore we could lower the dose of remifentanil for general anaesthesia in our patients. This may be one of the reasons why we observed no clinically important differences in the duration of remifentanil action in our patients also receiving pyridostigmine in contrast to the experiences described by Baraka and colleagues [7]. Excellent analgesia enabled us also to minimize the dose of atracurium to facilitate tracheal intubation during the induction of anaesthesia. After that, no additional muscle relaxant was given during surgery.

Our experiences show that the combination of high TEA and total i.v. anaesthesia with remifentanil and propofol is an effective technique for transsternal thymectomy providing haemodynamic stability during surgery followed by rapid awakening, a quick transition to spontaneous breathing, excellent postoperative analgesia and an uneventful recovery.

D. Mekiš, M. Kamenik
Department of Anesthesiology, Intensive Care and Pain Management
Maribor Teaching Hospital
Maribor, Slovenia

References

1. Richman DP, Agius MA. Treatment of autoimmune myasthenia gravis. *Neurology* 2003; **61**: 1652–1661.
2. Wilkins KB, Bulkley GB. Thymectomy in the integrated management of myasthenia gravis. *Adv Surg* 1999; **32**: 105–133.
3. Akpolat N, Tilgen H, Gursoy F, Saydam S, Gurel A. Thoracic epidural anaesthesia with bupivacaine for transsternal thymectomy for myasthenia gravis. *Eur J Anaesthesiol* 1997; **14**: 220–223.

4. Lorimer M, Hall R. Remifentanil and propofol total intravenous anaesthesia for thymectomy in myasthenia gravis. *Anaesth Intens Care* 1998; **26**: 210–212.
5. Manullang J, Egan T. Remifentanil's effect is not prolonged in a patient with pseudocholinesterase deficiency. *Anesth Analg* 1999; **89**: 529–530.
6. Rosow C. Remifentanil: a unique opioid analgesic. *Anesthesiology* 1993; **79**: 875–876.
7. Baraka AS, Haroun-Bizri ST, Gerges FJ. Delayed postoperative arousal following remifentanil-based anesthesia in a myasthenic patient undergoing thymectomy. *Anesthesiology* 2004; **100**: 460–461.

Malposition of internal jugular catheter into internal mammarian vein in coronary artery bypass grafting

EDITOR:

We report a case of misplacement of an internal jugular catheter into the internal mammary vein before coronary artery bypass grafting (CABG). Internal jugular vein catheterization is commonly used in anaesthesiology and critical care, but its appropriate application is unknown. Proper placement is essential for the use of central venous catheters (CVC). It has been reported that the incidence of catheter malposition depends on a number of factors including the site of insertion and the type of material used but not on the experience of the physician who inserted the catheter [1]. Proper positioning of the catheter with the tip just above the superior vena cava (SVC) and right atrial junction is important to minimize associated complications such as dysrhythmias, thrombus formation and perforation with associated hydrothorax, pneumothorax, hydromediastinum, bleeding and tamponade. Malpositioning of the catheter occurs approximately 2% of the time when subclavian or internal jugular vein approaches are used [2]. Malpositioning in the left mediastinum is a rare event. A case of left internal thoracic vein cannulation is described.

This 76-yr-old and obese female had a long history of effort dyspneoa and angina. At cardiac catheterization it was shown that the left anterior descending and right coronary arteries (RCx) were occluded. She was therefore scheduled for CABG.

Anaesthesia was induced with etomidate 20 mg, fentanyl 2 $\mu g\,kg^{-1}$ and endotracheal intubation was facilitated with vecuronium bromide 0.01 $mg\,kg^{-1}$. Anaesthesia was maintained with isoflurane 2%, nitrous oxide 50% in oxygen and fentanyl. Venous access in obese patients may be difficult. Initial difficulty with cannulation of the right internal jugular vein was encountered and so the left internal jugular vein was used instead. Correct cannulation using a Secalon T 16 G® (Becton Dickinson Critical Care Systems – Franklin Lakes, New Jersey, USA) cannula initially appeared to be obtained without any difficulty. Return of venous blood was observed and intravenous (i.v.) fluid flowed easily into the catheter. Central venous pressure (CVP) was measured as 4 mmHg.

Following a median sternotomy, the exact anatomical location of the catheter was seen. The surgeons informed us that the catheter had entered the left internal mammary vein (Fig. 1) and they used the catheter as a guide during dissection of the internal mammary artery. After the dissection we withdrew the catheter and inserted another catheter into the right femoral vein. Surgery was completed without any complication and the patient was transferred to the intensive care unit (ICU). One week later the patient was discharged from the hospital.

Proper positioning of CVC is important to ensure optimal catheter function and to decrease complications. Malposition can lead to inaccurate CVP evaluation, inability to aspirate blood samples, dysrhythmias, thrombus formation and perforation with associated hydrothorax, pneumothorax, hydromediastinum, bleeding and tamponade. Catheter malpositioning utilizing subclavian and internal jugular vein approaches is uncommon occurring 2% of the time. Many of the

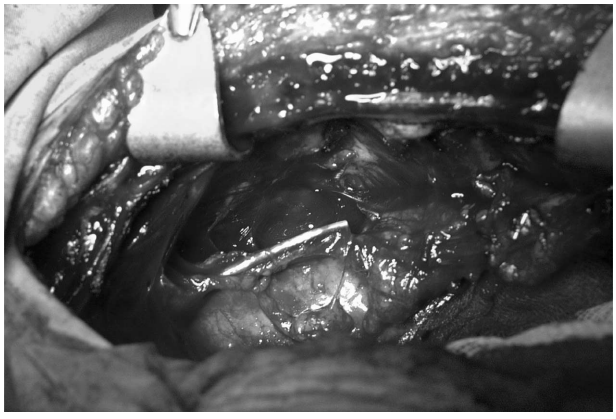

Figure 1.
Internal jugular catheter in left internal mammary vein.

Correspondence to: Heves Karagöz, Bestekar Sok. 28/9, Kavaklıdere-Ankara, Turkey 06680. E-mail: heves@ada.net.tr; Tel: +90 312 4171817; Fax: +90 312 3109600

Accepted for publication September 2004 EJA 1910

cases of left superior intercostal vein cannulation in the literature document the findings with no report of patient symptoms, catheter function, or management.

Smith described an asymptomatic patient with a normal functioning catheter [3]. Although in our patient there was no unexpected anatomical aberration, we discovered a malpositioned catheter. A case has been reported of a pulmonary artery catheter being inserted via the left internal jugular approach without complication although it was later found to have passed through an unknown residual ventricular septal defect into the left ventricle, aorta and right carotid artery [4].

Although left-sided catheter malpositioning is a rare event [5], Şekerci and colleagues [6] reported inadvertent malpositioning of a drum catheter in the left internal mammary vein following an attempt at central venous cannulation via the right antecubital fossa. Similar to this, we report misplacement of an internal jugular catheter into the internal mammary vein. Although different type of catheters had been used, we should not forget that internal mammarian vein cannulation is possible. In CABG, this can be complicated by injury to the internal mammary vein and artery thus compromising an important graft source. To use X-ray imaging to assist correct replacement would be an alternative. Intraoperative transoesophageal echocardiography is gaining acceptance as a diagnostic tool for controlling the proper placement of catheters. Fortunately, our patient was undergoing open heart surgery and we had a chance to see the placement of it directly during the operation.

M. Kanbak, A. H. Karagöz
Department of Anaesthesiology and Reanimation
Hacettepe University Faculty of Medicine
Ankara, Turkey

M. Öç, İ. Uçar
Department of Cardiovascular and Thoracic Surgery
Hacettepe University Faculty of Medicine
Ankara, Turkey

B. Çelebioglu
Department of Anaesthesiology and Reanimation
Hacettepe University Faculty of Medicine
Ankara, Turkey

R. Dogan
Department of Cardiovascular and Thoracic Surgery
Hacettepe University Faculty of Medicine
Ankara, Turkey

References

1. Muhm M, Sunder-Plassmann G, Apsner R, *et al*. Malposition of central venous catheters. Incidence, management and preventive practices. *Wien Klin Wochenschr* 1997; **109**: 400–405.
2. Kaufman JL, Rodriquez JL, McFadden JA, *et al*. Clinical experience with the multiple lumen central venous catheter. *J Parenteral Enteral Nutr* 1986; **10**: 487–489.
3. Smith DC, Pop PM. Malposition of a total parenteral nutrition catheter in the accessory hemiazygous vein. *J Parenteral Enteral Nutr* 1983; **7**: 289–292.
4. Kanbak M, Öcal T. Inadvertent placement of pulmonary artery catheter into right carotid artery. Inadvertent placement of pulmonary artery catheter into right carotid artery. *Can J Anaesth* 2000; **47**: 460–462.
5. Moskal TL, Ray Jr CE. Left mediastinal central line malposition: a case report. *Angiology* 1999; **50**: 349–353.
6. Şekerci S, Mercan Ş, Dönmez A, *et al*. Malpositioning of the central venous catheter necessitating sternotomy. *Eur J Anaesthesiol* 1999; **16**: 69–70.

Anaesthetic management of a patient with tricho-rhino-phalangeal syndrome

EDITOR:

Tricho-rhino-phalangeal syndrome (TRPS) presents a number of anaesthetic challenges, including airway and skeletal abnormalities, frequent respiratory infections, as well as cardiac defects and anaemia. The particular constellation of issues depends on the specific form of TRPS. Anaesthesiologists should be aware of these potential problems when caring for patients with TRPS.

TRPS occurs rarely, but is associated with a number of potential anaesthetic challenges. The most important are airway considerations, positioning issues, and cardiac abnormalities.

Correspondence to: Marcel E. Durieux, Department of Anaesthesiology, University of Virginia Health System, Charlottesville, VA 22908-0710, USA. E-mail: durieux@virginia.edu; Tel: +1 434 924 2283; Fax: +1 434 982 0019

Accepted for publication March 2005 EJA 2023

Case report

A 14-yr-old female, diagnosed with vaginal agenesis, was scheduled for exploratory laparotomy and cystoscopy. At a previous laparotomy for possible appendicitis, 2 months prior to this procedure, a pelvis filled with chocolate-coloured blood and an arcuate uterus with bilateral haemosalpinx had been found. The patient was known to have TRPS types 1 and 3 with a family history extending back five generations. She had also been recently diagnosed with a seizure disorder of unknown aetiology that was not believed to be related to her syndrome and was controlled with carbamazepine and gabapentin. According to her parents a ventricular septal defect had been diagnosed at birth, but the patient was not being followed by a cardiologist and she was not limited by it symptomatically. No murmur was auscultated. She was very anxious, of an apparently normal level of intelligence, with extremely short stature (weight 29 kg), fine hair, a pear-shaped nose, very irregular dentition and mild micrognathia (Fig. 1). Despite her micrognathia, her airway appeared to be Mallampatti Class I.

After premedication with midazolam 1 mg intravenously (i.v.), the patient was taken to the operating room. Routine monitors were placed and she was preoxygenated. Induction was accomplished with propofol 100 mg and lidocaine 50 mg i.v. Mask ventilation was found to be very easy even without the use of an oral airway. Muscle relaxation was induced with rocuronium 40 mg. Intubation was accomplished atraumatically with a Macintosh 3 blade and a 6.0-mm cuffed tracheal tube was placed. Relaxation was maintained with vecuronium; fentanyl and morphine were titrated for pain control. The patient was stable throughout the procedure from an anaesthetic standpoint. The surgery, however, was complicated and prolonged due to the patient's unusual pelvic anatomy and multiple adhesions and lasted a total of 4 h. The surgeons were unable to satisfactorily locate viable cervical tissue and decided to perform a hysterectomy instead of attempting a reconstruction.

At the conclusion of surgery, the patient was taken to the postanaesthesia care unit with the tracheal tube in place. When she was fully awake, she was extubated without difficulty. Her postanaesthesia course was uncomplicated and she was discharged on postoperative day 4.

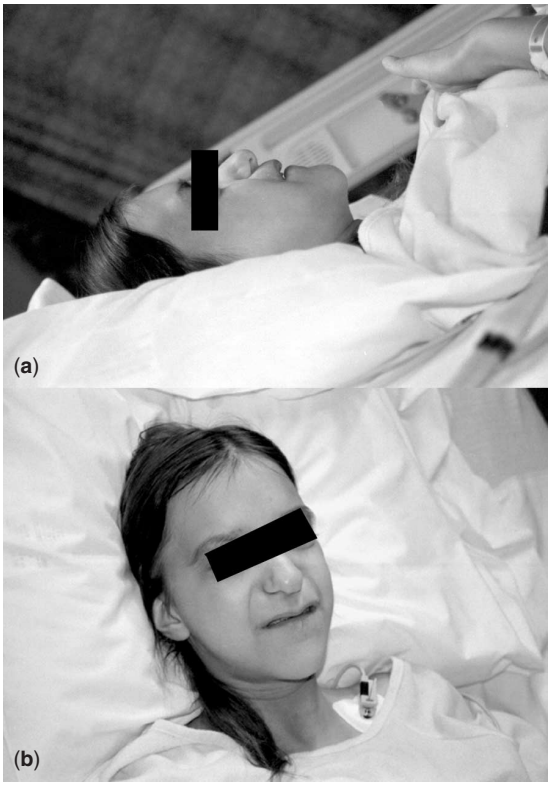

Figure 1.
*Side (**a**) and (**b**) front views of patient with TRPS.*

Discussion

Three forms of the TRPS have been described [1,2]. Type 1 is characterized by normal intelligence, a characteristic facies with sparse hair, laterally thinning eyebrows, pear-shaped nose, abnormal dentition and mild micrognathia, and has been associated with recurrent respiratory infections although not associated with any specific immunologic defect [3]. These patients typically have short stature, cone-shaped epiphyses, and may have premature degenerative hip disease [4]. It is typically inherited in an autosomal dominant fashion and is due to a mutation in the TRPS 1 gene on chromosome 8 [3]. An autosomal recessive form may exist [4]. TRPS 3 appears to result from a specific missense mutation in the TRPS 1 gene. It is phenotypically very similar to TRPS 1, but is differentiated by severe brachydactyly and short stature. Langer–Giedon syndrome, also referred to as TRPS type 2, has similar phenotypic findings, but also includes mental retardation, multiple exostoses, redundant skin in infancy, and a higher incidence of congenital cardiac defects, seizure disorders, hypochromic anaemia and hyperextensible joints. These patients may have other facial deformities (including thick alae nasi and a thin upper lip) and various bone abnormalities [2]. It occurs in a sporadic fashion and is due to a large deletion on chromosome 8 [2].

TRPS offers a number of potential challenges to the anaesthesiologist. Individuals with types 1 and 3 may present difficulties during laryngoscopy and intubation caused by the combination of irregular

dentition with varying degrees of micrognathia. Frequent respiratory infections may cause cancellation of non-emergent cases, and may be associated with a greater incidence of respiratory adverse events during and after surgery. Patients and parents should be aware of this potential increase in perioperative risk. Bone abnormalities and premature degenerative hip joint disease warrant particular care in positioning, with extremities placed as much as possible in natural positions. Type 2 presents similar anaesthetic concerns, but in addition these patients may require antibiotic prophylaxis for congenital heart defects. Also, there may be a greater likelihood of transfusion requirement if anaemia is present. Hyperextensible joints and bone abnormalities warrant great care in positioning these patients. If nasal intubation is required (e.g. for procedures on the affected dentition), a smaller tube size may be needed because of the hypertrophied alae nasi.

In conclusion, although the case reported was uncomplicated from an anaesthetic standpoint, a number of concerns should be considered by the anaesthesiologists in individuals with TRPS, and potential increased risk should be communicated clearly to patients and parents.

L. S. Graybeal, V. C. Baum, M. E. Durieux
Department of Anaesthesiology
University of Virgina Health System
Charlottesville, USA

References

1. Buhler EM, Buhler UK, Beutler C, Fessler R. A final word on the tricho-rhino-phalangeal syndromes. *Clin Genet* 1987; **31**: 273–275.
2. Hall BD, Langer LO, Giedion A, *et al.* Langer–Giedion syndrome. *Birth Defect* 1974; **10**: 147–164.
3. Ludecke HJ, Schaper J, Meinecke P, *et al.* Genotypic and phenotypic spectrum in tricho-rhino-phalangeal syndrome types I and III. *Am J Hum Genet* 2001; **68**: 81–91.
4. Noltorp S, Kristoffersson UL, Mandahl N, Stigsson L, Svensson B, Werner CO. Trichorhinophalangeal syndrome type 1: symptoms and signs, radiology and genetics. *Ann Rheum Dis* 1986; **45**: 31–36.