

## Correspondence

---

# Sedation in dentistry: current sedation practice in Italy

doi: 10.1017/S0265021506001785

### EDITOR:

The power of patient sedation to blunt the stress response to surgery is important in dentistry [1,2]. The advantages of the available sedation techniques should be evident to teachers of Dental Schools, to dental students, to dentists, to all involved dental practitioners and, obviously, to dental patients [3–5]. Unfortunately, this knowledge is not so widely shared in Italy, so that the use of patient sedation is still a limited practice among Italian dentists [4,6]. We report information about the current sedation practice in Italy within both academic and private practice. An E-mail or telephone survey was performed in January 2005 to collect data about current sedation practice in Italy. The survey covered all the 33 Dental Schools of Italy and 110 private dental offices of the Veneto region in the north-east of Italy. Data from a previous study [6] of private dental practice in the Friuli Venezia Giulia region were added. The two Italian regions, Friuli Venezia Giulia and Veneto, have 5 730 000 inhabitants, about 10% of the whole Italian population. In Italy there are 18 921 dentists and 34 625 physicians working as dentists. Results from the survey on the education of undergraduate dental students and of private dental practice in Italy are reported in Table 1.

Sedation in Italian Dental Schools is provided mainly by anaesthesiologists (94%) with the remainder by dentists (6%). In private dental practice the situation is different with the anaesthesiologists performing the sedation in about 20% of cases, the remainder being performed by dentists and physicians. Since the foundation of Dental Schools in Italy, in 1981, the teaching of Anaesthesia in Dentistry presented many problems defining a didactic model according to the goal of this specialty. This situation had not improved 20 yr later, after the introduction of the new European Standards (2001) in the

academic didactic organization that included teaching of patient evaluation and information, anxiety and pain control, emergency prevention and treatment. This is due to a lack of clinical facilities in Dental Schools and theoretical but not practical adjustment to European Standards together with lack of information among dentists. In Italian Dental Schools all the sedation masters are anaesthesiologists with a clear preference toward topics for anaesthetists and not for dentists: many anaesthesiologists had little knowledge of the training presently available to dentists wishing to practise conscious sedation. It is of great concern that a considerable number of these anaesthesiologists do not feel that is appropriate for dentists to be administering even the simplest method of sedation including the use of nitrous oxide/oxygen inhalation.

The sedation techniques taught and performed in the Dental Schools depend on the knowledge and wisdom of the teachers, skill of clinical staff and available resources of the Institution. Oral sedation is widely employed because it is simple to teach, to learn and to perform. Intravenous (i.v.) sedation needs special skill but is suitable for titration. Inhalation of nitrous oxide and oxygen is a relatively frequent technique, but intranasal and sublingual routes of drug administration are less used. The drugs studied in most of the Italian Dental Schools are benzodiazepines and nitrous oxide but general i.v. anaesthetics (ketamine, propofol, barbiturates, opioids, etc.) and halogenated anaesthetics (sevoflurane, desflurane) are, erroneously, also taught. We believe erroneously because these are topics for anaesthesiologists and not for dentists. Special sedation techniques, for children and/or disabled patients are carried out only in a minority of cases because these are considered, mostly, as patients for anaesthesiologists requiring general anaesthesia in the majority of the Institutions. Education is carried out on a theoretical basis, while practice on the patient is lacking in the majority of the Dental Schools. The nearly total absence of academic continuing education about this topic is evident as only two Universities perform such education: Bologna University, where

---

Correspondence to: Gastone Zanette, Department of Medico-Surgical Specialties, Chair of General and Special Anaesthesiology in Dentistry, University of Padua, Via Giustiniani 2, 35100 Padova, Italy. E-mail: gastone.zanette@unipd.it; Tel: +39 49 8212041; Fax: +39 49 8218229

**Table 1.** Survey on undergraduate dental students education and on private dental practice in Italy: patient evaluation, sedation techniques, drugs and practice in Dental Schools and private dental offices.

Sedation techniques and drugs	Dental Schools performing the teaching, <i>n</i> (%)	Dental Schools with practice on the patient, <i>n</i> (%)	FVG + VE: practice in 218 private dental offices, <i>n</i> (%)
Patient evaluation	32 (97)	0	175 (80.3)
Conscious sedation	26 (79)	12 (36)	153 (70.2)
General anaesthesia	20 (60)	0	0
Oral benzodiazepine	26 (79)	8 (24)	109 (50)
i.v. benzodiazepine	24 (72)	12 (36)	14 (6.5)
N <sub>2</sub> O/O <sub>2</sub> inhalation	22 (66)	7 (21)	49 (22.5)
Intranasal benzodiazepine	12 (36)	0	7 (3.2)
Sublingual benzodiazepine	9 (27)	0	33 (15.1)
General i.v. anaesthetics	9 (27)	–	–
Halogenated anaesthetics	3 (9)	–	–

FVG: Friuli Venezia Giulia region; VE: Veneto region; i.v.: intravenous.

there is an active education programme about Basic Life Support and Defibrillation and Padua University with an education programme regarding patient evaluation and information, anxiety and pain control in dentistry. At Padua University Dental School, sedation is provided by the 'sedationist' [7,8], a dentist with a high level of competence based on a solid foundation of theoretical and practical supervised training. In this scenario, the anaesthesiologist is supervisor for the sedationist, and performs also general anaesthesia for particular and limited indications. In other Universities, with few exceptions, the anaesthesiologist performs most of the sedations because the lack of a sedationist. Consequently, in these Institutions there is a prevalence of general anaesthesia compared with sedation. What sort of sedation is practised in private dental practice? The answer is more difficult, because the situation is heterogeneous and depends on many factors such as knowledge, skill, clinical experience of the staff and prevalent activity performed in the dental office. In the private dental practice younger, well-educated and skilled dentists perform conscious sedation techniques, but older well-known dentists depend on anaesthesiologists, who are more likely to perform so-called 'light general anaesthesia'.

The Italian reality is embarrassing: there are no guidelines produced by the Italian Health Ministry, the Italian University Dental Schools or the Italian National Dental Associations. Italian guidelines for sedation in dentistry were published in 2001, by the Italian Association of Dental Anaesthesia (AINOS), in its official publication the 'Journal of Dental Anaesthesia' and cover all the aspects of perioperative medicine in dentistry. AINOS is a member of the International Federation of Dental Anaesthesiology Societies (IFDAS) and of the European Federation for the Advancement of Anaesthesia in Dentistry (EFAAD). Effective management of anxiety and pain

is very important for patients requiring dental care and conscious sedation techniques are a fundamental component of this [3,4,7,8]. Competently provided conscious sedation is safe, valuable and effective to blunt the stress response to surgery. A high level of competence based on a solid foundation of theoretical and practical supervised training, progressive updating of skills and continuing experience is the key to safe practice.

*G. Zanette*  
 Department of Medico-Surgical Specialties  
 Chair of General and Special  
 Anaesthesiology in Dentistry  
 University of Padua  
 Padova, Italy

*N. Robb*  
 Dental School  
 University of Glasgow  
 Glasgow, UK

*E. Facco*  
 Department of Pharmacology and Anaesthesiology  
 University of Padua  
 Padova, Italy

*L. Zanette*  
 Disability Psychology Service  
 Azienda Sanitaria  
 Tolmezzo, Italy

*G. Manani*  
 Department of Medico-Surgical Specialties  
 Chair of General and Special  
 Anaesthesiology in Dentistry  
 University of Padua  
 Padova, Italy

## References

1. Kaufer D, Friedman A, Seidman S, Soreq H. Acute stress facilitates long-lasting changes in cholinergic gene expression. *Nature* 1998; **393**: 373–377.
2. Brand HS, Gortzak RA, Palmer-Bouva CC, Abraham RE, Abraham-Inpijn L. Cardiovascular and neuroendocrine responses during acute stress induced by different types of dental treatment. *Int Dent J* 1995; **45**: 45–48.
3. Manani G, Baldinelli L, Cordioli G, Consolati E, Luisetto F, Galzigna L. Premedication with chlordemethyldiazepam and anxiolytic effect of diazepam in implantology. *Anesth Prog* 1995; **42**: 107–112.
4. Manani G, Alberton L, Bazzato MF *et al.* Analysis of an anxiolytic technique applied to 1179 patients undergoing oral surgery. *Minerva Stomatol* 2005; **54**: 551–568.
5. Alberton M, Cocilovo F, Scarpa D *et al.* Analysis of dental anxiety in three different subjects populations. *J Dent Anaesth* 2002; **29**: 46–53.
6. Floreani S, Battisti A, Boscolo G *et al.* Polycentric study on some dental anesthesia practices in an out-patients population of the Friuli-Venezia-Giulia region. *J Dent Anaesth* 2003; **1**: 33–41.
7. European Federation for the Advancement of Anaesthesia in Dentistry (EFAAD). Recommendations by the Council of EFAAD concerning European Standards for anaesthesia, analgesia and sedation in dentistry. Proceeding of Consensus Conference on 'Conscious sedation in dentistry' Trier/Germany, 26 October 2002.
8. Standing Dental Advisory Committee (SDAC). Conscious sedation in the provision of dental care: new guidelines. *SAAD Digest* 2004; **21**: 20–23.

## Ketamine-induced emergence reactions after desflurane anaesthesia

doi: 10.1017/S0265021506001773

### EDITOR:

We would like to report a case who suffered from ketamine-induced postoperative psychological sequelae after low-dose ketamine and desflurane anaesthesia. A 45-yr-old male, weighing 81 kg and standing 181 cm, was scheduled for shoulder arthroscopic surgery. His past history was unremarkable and laboratory tests were all within normal limits. Intravenous (i.v.) induction of anaesthesia was performed with fentanyl 100 µg, lidocaine 80 mg and thiamylal 400 mg. Tracheal intubation was facilitated with succinylcholine 100 mg. Desflurane 10–12% in 100% O<sub>2</sub> at flow rate of 0.5 mL min<sup>-1</sup> was used to maintain anaesthesia and cisatracurium for neuromuscular blockade. Eight minutes after tracheal intubation, ketamine 30 mg i.v. was administered for pre-emptive analgesia. At this moment, the exhaled concentration of desflurane was 7.9%. The surgery lasted for 2 h. After recovery from anaesthesia, the patient complained of dizziness and extracorporeal experiences, described as sense of floating out of his body. This

unpleasant memory persisted until discharge 5 days after operation.

It is well known that ketamine may produce undesirable psychological sequelae during emergence from ketamine anaesthesia. They are termed emergence reactions and manifest themselves as vivid dreams, extracorporeal out-of-body experience, floating sensations, 'weird trips' and body image alterations [1]. The possible mechanisms have been proposed that ketamine may depress auditory and visual relay nuclei leading to misperception and/or misinterpretation of auditory and visual stimuli [2]. In addition, Olney and colleagues [3] demonstrated that, in the rat, ketamine causes damage to neurons in the posterior cingulate and retrosplenial cortex, areas postulated to mediate affective and emotional responses. The incidence is wide ranging from 3% to 100% [2]. Various factors have been proposed to modify the occurrence of the ketamine-induced emergence reactions include age, dose, gender, people who commonly dream or a history of personality problems [1]. Benzodiazepines [1] or dexmedetomidine [4] have been reported to reduce the incidence of this unwanted side-effects. Previously, the occurrence of these adverse effects of ketamine has been reported in patients who received ketamine as the main anaesthetic. In this case, just a small dose of ketamine (30 mg) was

Correspondence to: Chen-Hwan Cherng, Department of Anesthesiology, Tri-Service General Hospital, National Defense Medical Center, No. 325, 2 Sec. Cheng-Gung Road, Nei-Hu, 114, Taipei, Taiwan. E-mail: cherng1018@yahoo.com.tw; Tel: +886 2 87927128; Fax: +886 2 87927127

Accepted for publication 27 May 2006 EJA 3935  
First published online 11 October 2006

administered and the patient was under 1.5 MAC of desflurane anaesthesia when the ketamine was given. Postoperatively, we evaluated the patient's personality by Eysenck Personality Questionnaire [5] and it showed no particular finding. It is difficult to explain why the ketamine-induced emergence reactions occurred in this patient. We did not give benzodiazepine prior to ketamine administration. It would seem that desflurane has no preventive effect on this reaction. We suggest that a benzodiazepine should be given prior to ketamine administration even in a patient receiving desflurane anaesthesia.

C.-H. Cherng, C.-S. Wong  
 Department of Anesthesiology  
 Tri-Service General Hospital  
 National Defense Medical Center  
 Taipei, Taiwan

## References

1. White PF, Way WL, Trevor AJ. Ketamine – its pharmacology and therapeutic uses. *Anesthesiology* 1982; 56: 119–136.
2. Reves JG, Glass PSA, Lubarsky DA, McEvoyHull MD. Intravenous nonopioid anesthetics. In: Miller RD, ed. *Miller's Anesthesia*, 6th edn. Philadelphia, PA: Elsevier Churchill Livingstone, 2005: 317–378.
3. Olney JW, Labruyere J, Price MT. Pathological changes induced in cerebrocortical neurons by phencyclidine and related drugs. *Science* 1989; 244: 1360–1362.
4. Levanen J, Makela ML, Scheinin H. Dexmedetomidine premedication attenuates ketamine-induced cardiostimulatory effects and postanesthetic delirium. *Anesthesiology* 1995; 82: 1117–1125.
5. Eysenck SBG, Eysenck HJ, Barrett P. A revised version of the psychoticism scale. *Pers Individ Diff* 1985; 6: 21–29.

## Downbeat nystagmus as a manifestation of intrathecal morphine toxicity

doi: 10.1017/S0265021506001724

### EDITOR:

Downbeat nystagmus (DBN) is most commonly associated with lesions affecting the lower brain stem or the cerebellum. Aetiologies include congenital anomalies, multiple sclerosis, vascular, metabolic and toxic causes [1,2]. Opiate-related toxicity nystagmus seems rare, but possibly underrecognized. Its pathophysiological mechanism is unknown. We report a patient who presented postoperative isolated transient DBN linked to intrathecal administration of a single high dose of morphine.

A previously healthy 59-yr-old woman underwent a rectal resection for adenocarcinoma. The patient received 7.5 mg oral midazolam as preoperative sedation. Fifteen minutes before surgery, 7.5 mg of intrathecal bupivacaine and 0.6 mg of intrathecal morphine were administered according to local practice. The intervention was performed under general anaesthesia. No intraoperative complications occurred,

and the awakening phase was unremarkable. No additional medications were administered. Ten hours after morphine administration, the patient acutely developed nausea and vomiting, and complained of blurred vision. Examination revealed DBN, persistent with equal amplitude and direction in downward and horizontal gaze and decreasing in upward gaze. This finding contrasted with an otherwise unremarkable neurological examination. The brain CT-scan was normal. The patient's complaints rapidly improved and completely disappeared within 24 h. She did not receive naloxone.

The strictly isolated symptomatology and the normal brain imaging allowed the hypothesis of a large posterior fossa lesion to be reasonably ruled out. The spontaneous complete resolution of symptoms within hours favours a drug toxicity-related mechanism.

The drugs most commonly incriminated in the appearance of DBN are anticonvulsants (phenytoin [2,3], carbamazepine [2,4], phenobarbital [4], felbamate [5]), alcohol [6] and lithium [7]. Until now, neither general anaesthetic agents nor bupivacaine have been reported to cause this effect. Several cases of vertical nystagmus related to opiates have been reported [8–10].

Correspondence to: Christian Korff, Neuropédiatrie, Hôpital des Enfants, 6 rue Willi-Donzé, CH-1211 Genève 14, Switzerland. E-mail: christian.korff@hcuge.ch; Tel: +41 22 382 45 72; Fax: +41 22 382 54 89

Accepted for publication 5 July 2006 EJA 3825  
 First published online 11 October 2006

Henderson and colleagues observed DBN in a patient several hours after a surgical procedure for which he had received a total of 56 mg continuous intravenous morphine. The symptoms completely disappeared 12 h after discontinuation of treatment [9]. Rottach and colleagues observed similar transient symptoms in three patients who had received intravenous meperidine and fentanyl [11].

Epidural morphine has also been implicated in the appearance of vertical nystagmus. Fish and colleagues observed transient upbeat nystagmus in a patient who had received 11 mg of epidural morphine in two separate doses and subcutaneous morphine several hours earlier. Their causal hypothesis was reinforced by the fact that the symptoms completely disappeared after several doses of naloxone [8]. Stevens and colleagues described a similar case. Their patient presented DBN after having received a total dose of 5.2 mg epidural morphine in continuous administration [10]. Uyeama and colleagues reported the appearance of naloxone-reversible horizontal nystagmus observed after the administration of a single 0.1 mg intrathecal morphine dose [12].

Physiopathological mechanisms for opioid effects on eye movements have been proposed by Rottach and colleagues. Their hypothesis is based on opiate-mediated inhibition of binding sites in the cerebellum and the vestibular nuclei [13].

Considering what precedes, we strongly believe that morphine is responsible for the appearance of DBN in our patient. Although we do not explain the long period that separates drug administration and symptoms observation, such an interval has been described by other authors [9].

We suggest that the assessment of a patient presenting with DBN after having received morphine should include the possibility of self-limiting opiate-related toxicity. Naloxone administration should be considered in suspected cases in order to confirm the hypothesis. This could prevent expensive and unnecessary diagnostic procedures being performed.

C. Korff  
Department of Neurology  
University Hospital of Geneva  
Geneva, Switzerland

M. Peter  
Department of Anesthesiology  
University Hospital of Geneva  
Geneva, Switzerland

P. R. Burkhard  
Department of Neurology  
University Hospital of Geneva  
Geneva, Switzerland

## References

1. Leigh RJ, Averbuch-Heller L. Nystagmus and related ocular motility disorders. In: Miller NR, Newman NJ, eds. *Walsh and Hoyt's Clinical Neuro-Ophthalmology*, 5th edn, Vol. 1. Baltimore, MD: Williams and Wilkins, 1998: 1461–1505.
2. Yee R. Downbeat nystagmus: characteristics and localization of lesions. *Trend Am Ophthalmol Soc* 1989; **LXXXVII**: 985–1032.
3. Alpert JN. Downbeat nystagmus due to anticonvulsant toxicity. *Ann Neurol* 1978; 4: 471–473.
4. Wheeler SD, Ramsay RE, Weiss J. Drug-induced downbeat nystagmus. *Ann Neurol* 1982; 12: 227–228.
5. Hwang TL, Still CN, Jones JE. Reversible downbeat nystagmus and ataxia in felbamate intoxication. *Neurology* 1995; 45: 846.
6. Rosenberg ML. Reversible downbeat nystagmus secondary to excessive alcohol intake. *J Clin Neuro-Ophthalmol* 1987; 71: 23–25.
7. Halmagyi GM, Lessell I, Curthoys IS, Lessell S, Hoyt W. Lithium-induced downbeat nystagmus. *Am J Ophthalmol* 1989; 107: 664–670.
8. Fish DJ, Rosen SM. Epidural opioids as a cause of vertical nystagmus. *Anesthesiology* 1990; 73: 785–786.
9. Henderson RD, Wijdicks EFM. Downbeat nystagmus associated with intravenous patient-controlled administration of morphine. *Anesth Analg* 2000; 91: 691–692.
10. Stevens RA, Sharrock NE. Nystagmus following epidural morphine. *Anaesthesiology* 1991; 74: 390–391.
11. Rottach KG, Dzaja AE, Wohlgemuth WA, Eggert T, Straube A. Effects of intravenous opioids on eye movements in humans. *Ann NY Acad Sci* 2002; 956: 595–597.
12. Uyeama H, Nishimura M, Tashiro C. Naloxone reversal of nystagmus associated with intrathecal morphine administration. *Anaesthesiology* 1992; 76: 153.
13. Rottach KG, Wohlgemuth WA, Dzaja AE, Eggert T, Straube A. Effects of intravenous opioids on eye movements in humans: possible mechanisms. *J Neurol* 2002; 249: 1200–1205.

# Tension pneumocephalus following deep brain stimulation surgery with bispectral index monitoring

doi: 10.1017/S0265021506001736

## EDITOR:

Deep brain stimulation (DBS) is increasingly being used for treatment of movement disorders associated with Parkinson's disease (PD). The procedure involves functional lesioning of subthalamic nucleus (STN) and globus pallidus internus (GPI) after placement of stimulator leads via burr hole craniotomies. The procedure is usually performed under monitored anaesthesia care with minimal or no sedation. During these procedures we use bispectral index (BIS) monitoring regularly along with the routine monitors because it may reflect the hypnotic effect of anaesthetics and sedative drugs. Various complications have been reported associated with DBS surgery [1] although tension pneumocephalus has never been reported. We report a case where a patient undergoing DBS surgery developed tension pneumocephalus associated with lowering of BIS value intraoperatively.

A 63-yr-old male weighing 58 kg was scheduled for magnetic resonance imaging guided, stereotactic frame based bilateral placement of electrodes for DBS. His past medical history was significant for coronary artery disease 6 yr previously. A 2-D echocardiogram showed concentric left ventricular hypertrophy with mild aortic regurgitation along with a left ventricular ejection fraction of 45%. The patient was kept fasting overnight. The first part of the procedure, that is electrode placement, was done under monitored anaesthesia care. In the operating theatre intravenous access was secured using an 18-G cannula on the dorsum of the left hand. Monitoring included 5-lead ECG, non-invasive blood pressure, pulse oximetry, and A-2000 BIS monitor (Aspect Medical Systems, Newton). The BIS sensor was placed on the right side of the forehead. Supplemental O<sub>2</sub> was administered via nasal prongs at a flow rate of 2 L min<sup>-1</sup>. The patient was positioned supine on the operating table in a stereotactic frame with 10° head up tilt. At the initiation of surgery, the heart rate and blood pressure were 64 beats min<sup>-1</sup> and 130/56 mmHg, respectively and BIS was 98. After local anaesthetic infiltration, burr holes were made bilaterally. Electrodes were placed on both the

subthalamic nuclei. The patient's responses to the test stimulation as assessed by the neurologist were satisfactory. This part of procedure lasted approximately 5 h. It was then noticed that the patient had become drowsy but was still obeying to verbal commands. The BIS monitor showed a value of 75–85.

The second part of the DBS surgery was placement of a battery in the anterior chest wall for further regulation of the stimulations. This was performed under general anaesthesia. General anaesthesia was induced with fentanyl 2 µg kg<sup>-1</sup> and thiopentone 200 mg intravenously. Tracheal intubation was facilitated with rocuronium 60 mg intravenously. Anaesthesia was maintained with isoflurane in a mixture of O<sub>2</sub> and N<sub>2</sub>O (1:2). BIS was maintained at 40–60. The procedure was completed uneventfully in 30 min. At the end of the procedure the patient was reversed from residual neuromuscular blockade with neostigmine and glycopyrrolate. As the patient was maintaining adequate tidal volume and responding to verbal commands, though drowsy, the trachea was extubated. After 15 min, he was still drowsy with a BIS of 65–75. Oxygen was given by facemask and the patient was transferred to the intensive care unit (ICU). The drowsiness persisted even after 1 h in the ICU so a computed tomographic (CT) scan was performed which revealed a tension pneumocephalus (Fig. 1). As the patient was haemodynamically stable with no lateralizing signs, no active intervention was considered except close monitoring. BIS was continuously monitored in the postoperative period. For the initial 10 h after surgery, BIS remained in the range 65–80. Later, it started to rise gradually coinciding with improving conscious level. The patient was moved to the postoperative ward after 18 h fully orientated and with a BIS value of 98. A CT scan 18 h after surgery showed a complete resolution of the pneumocephalus.

Pneumocephalus has been known to occur after any craniotomy procedure with an incidence reported to be 100% following supratentorial craniotomies [2]. Generally it is asymptomatic but occasionally high pressure may build up in the air cavity with development of tension pneumocephalus. Although tension pneumocephalus is more common after posterior fossa or cervical spine surgery in the sitting position, it is rare following the supine position. It may manifest as deterioration of consciousness with or without lateralizing signs, severe restlessness, generalized

Correspondence to: Girija P. Rath, Department of Neuroanaesthesiology, All India Institute of Medical Sciences, New Delhi, India. E-mail: girijarath@yahoo.co.in; Tel: +91 9868398204; Fax: +91 11 26588663

Accepted for publication 9 July 2006 EJA 4035  
First published online 11 October 2006



**Figure 1.**  
CT scan showing collection of air in the frontal region.

convulsions or focal neurological deficits. Several contributing factors have been implicated in the development of tension pneumocephalus. Prominent among them are surgical position of the patient, duration of surgery, gross hydrocephalus, excessive cerebrospinal fluid (CSF) loss, a functional VP shunt, nitrous oxide anaesthesia, and intraoperative administration of dehydrating agents like mannitol and furosemide [3].

Perioperative complications associated with DBS surgery include haemorrhage, seizure, confusion [1] and venous air embolism [4] but tension pneumocephalus has never been reported. During DBS surgery, there occurs a slow but continuous egress of CSF from the cranial burr holes. However, due to the prolonged duration of surgery, the loss of CSF may become significant over a period of time. The space created by the CSF loss may become filled with air causing pneumocephalus. This seems to be the likely cause of development of pneumocephalus in our case. It is also likely that during closure of the dura mater, subdural injection of saline to fill such space was insufficient.

We believe that the drowsiness along with resultant fall in BIS value could have been due to pneumocephalus. It is also suggested that the use of nitrous oxide during general anaesthesia for the placement of the battery could have further expanded the collected air resulting in development of tension pneumocephalus. This manifested as persistent drowsiness with a low BIS value in the postoperative period. It is probable that over a period of time, the accumulated

air became reabsorbed, resulting in improved BIS values with simultaneous improvement in neurological status.

Diagnosis of pneumocephalus requires a high index of suspicion in DBS surgery. We believe the persistent low BIS after extubation indicated a neurological deterioration. The treatment of tension pneumocephalus requires burr-hole aspiration [3]. No active intervention was required in our patient, as he remained haemodynamically stable with no further neurological deterioration. However the patient was monitored closely.

BIS monitoring in neurosurgical procedures has not gained popularity due to difficulty in placement of sensors in the recommended location. Nevertheless we believe that this monitoring can provide valuable information in diagnosing neurological events as literature has shown its utility in diagnosing global cerebral ischaemia during asystole [5] and other forms of localized cerebral ischaemia and brain injuries [6]. Sen and colleagues highlighted the usefulness of BIS for detection of cerebral ischaemia secondary to vasospasm in neurointerventional procedures [7]. In our case, the patient had frontal pneumocephalus, and the BIS monitor displayed readings that correlated with the neurological status of the patient.

V. Jain, H. Prabbakar  
G. P. Rath, D. Sharma

Department of Neuroanaesthesiology  
All India Institute of Medical Sciences  
New Delhi, India

## References

- Beric A, Patrick J, Ali R, Sterio D, Mogilner A, Zonenshayn M, Kopell B. Complications of deep brain stimulation surgery. *Stereotact Funct Neurosurg* 2001; 77: 73–78.
- Reasoner DK, Todd MM, Scamman FL, Warner DS. The incidence of pneumocephalus after supratentorial craniotomy. Observations on the disappearance of intracranial air. *Anesthesiology* 1994; 80: 1008–1012.
- Satapathy GC, Dash HH. Tension pneumocephalus after neurosurgery in the supine position. *Br J Anaesth* 2000; 84: 115–117.
- Deogaonkar A, Avitsian R, Henderson JM, Schubert A. Venous air embolism during deep brain stimulation surgery in an awake supine patient. *Stereotact Funct Neurosurg* 2005; 83: 32–35.
- Azim N, Wang CY. The use of bispectral index during a cardiopulmonary arrest: a potential predictor of cerebral perfusion. *Anaesthesia* 2004; 59: 610–612.
- Mérat S, Lévecque JP, Gulluche YL, Diraison Y, Brinquin L, Hoffmann JJ. BIS monitoring may allow the detection of severe cerebral ischemia. *Can J Anaesth* 2001; 48: 1066–1069.
- Sen I, Puri GD, Bapuraj JR. Early detection of cerebral vasospasm during a neurointerventional procedure using the BIS. *Anaesth Intens Care* 2005; 33: 691–692.

## With bleomycin, that's too much oxygen

doi: 10.1017/S0265021506001797

### EDITOR:

Patients who have been treated with bleomycin should not receive high concentrations of oxygen during subsequent general anaesthesia as this can lead to respiratory failure [1,2]. Marzetti and colleagues described the conduct of general anaesthesia in two cases of testicular germ cell tumour following recent chemotherapy and highlighted the risk of neural injury related to cisplatin exposure [3]. Their patients also had received bleomycin as part of the chemotherapy but their general anaesthetic technique involved the use of 50% inspired oxygen. The risk of respiratory failure with general anaesthesia and high inspired oxygen in patients who have received bleomycin is not well known amongst anaesthetists; hence this communication which we hope will increase awareness of this hazard.

Two major risk factors for the development of bleomycin-induced pulmonary damage related to hyperoxia exposure are evidence of pre-existing pulmonary damage from bleomycin and prior exposure to bleomycin within a 1–2-month period. Other risk factors for bleomycin-induced pulmonary damage are total dose of bleomycin >450 mg and a creatinine

clearance <35 mL min<sup>-1</sup>. Cisplatin, when used with bleomycin can increase the lung toxicity of bleomycin because it is nephrotoxic and can delay renal clearance of bleomycin [4]. The current recommendations are that patients with one or both major risk factors present should be maintained on the lowest F<sub>i</sub>O<sub>2</sub> to maintain S<sub>p</sub>O<sub>2</sub> > 90% [4,5].

C. M. Frerk, N. George  
Department of Anaesthesia  
Northampton General Hospital  
Northampton, UK

Correspondence to: C. M. Frerk, Department of Anaesthesia, Northampton General Hospital, Northampton, NN1 5BD, UK. E-mail: Chris.Frerck@ngh.nhs.uk; Tel: +44 1604 545671; Fax: +44 1604 545670

Accepted for publication 29 May 2006 EJA 3932  
First published online 11 October 2006

### References

1. Bleomycin. In: British National Formulary (51). London, England: BMJ Publishing Group Ltd and RPS Publishing, March 2006: 433.
2. Luis M, Ayuso A, Martinez G *et al*. Intraoperative respiratory failure in a patient after treatment with bleomycin: previous and current intraoperative exposure to 50% oxygen. *Eur J Anaesth* 1999; 16: 66–68.
3. Mazaretti G, Marret E, Lotz JP *et al*. Brachial plexus injury during anaesthesia in patients receiving cisplatin-based chemotherapy. *Eur J Anaesth* 2006; 23: 262–265.
4. Mathes DD. Bleomycin and hyperoxia exposure in the operating room. *Anaesth Analg* 1995; 81: 624–629.
5. Huettemann E, Sakka SG. Anaesthesia and anti-cancer chemotherapeutic drugs. *Curr opin Anaesthesiol* 2005; 18: 307–314.

## Opioid-induced hyperalgesia

doi: 10.1017/S0265021506001700

### EDITOR:

There is evidence to suggest that acute administration of opioids results in analgesia and delayed induced hyperalgesia [1]. N-methyl-D-aspartate (NMDA) receptors play a critical role in the development of hyperalgesia and opioids are known to activate or

potentiate these receptors through different mechanisms [2,3]. The analgesic effects of fentanyl are known to be followed by a dose dependent decrease in pain threshold and morphine following fentanyl enhances this induced hyperalgesia [4].

A 62-yr-old man, ASA Grade III, 72 kg, 165 cm, was scheduled for revascularization of the right femoral artery. He had undergone an aorto-bifemoral bypass 9 yr before and suffered again from lower limb claudication. Relevant medical history included essential hypertension, ischaemic heart disease (stenting of the anterior interventricular artery 1 yr before),

Correspondence to: Emmanuel Guntz, Department of Anesthesiology, Centre Hospitalier Universitaire Saint-Pierre, Université Libre de Bruxelles, Rue Haute, 322, 1000 Brussels, Belgium. E-mail: eguntz@ulb.ac.be; Tel: +32 2 535 35 94; Fax: +32 2 535 40 70

Accepted for publication 9 July 2006 EJA 4009  
First published online 11 October 2006



non-insulin dependant diabetes mellitus, chronic lymphoid leukaemia, oesophagitis, alcohol addiction, depression and chronic pain related to the arteritis of the lower limbs. Smoking was stopped 6 months ago. Daily treatment included: amlodipine 10 mg, carvedilol 25 mg, lorazepam 2.5 mg, amitriptyline 50 mg, metformin 1700 mg and artovastatin 20 mg. The analgesic treatment included: tramadol 150 mg, paracetamol 3 g per day and a 75 µg patch of fentanyl every 3 days. The fentanyl patch had not been changed for 2 days prior to the operation.

The placement of a new aorto-femoral bypass from the previous prosthesis to the deep femoral artery was performed without complications. Anaesthesia was induced with 150 mg propofol, 100 µg remifentanyl and 14 mg cisatracurium and maintained with continuous administration of propofol, remifentanyl and cisatracurium. The patient received a total dose of 6.3 mg remifentanyl during the 5 h operative time period. He was intubated with an 8.5 mm tracheal tube (Portex, Keene, NH, USA) and extubated at the end of the surgery. Two grams of proparacetamol and 10 mg of piritramide were given respectively 30 and 10 min before the end of surgery. Continuous monitoring included electrocardiography, pulse, oxygen saturation, end-tidal carbon dioxide, invasive arterial pressure and central venous pressure.

Once admitted to the intensive care unit, the patient complained of intense epigastric pain and therefore received 2 mg of morphine. This injection dramatically increased the pain. A second injection induced a similar result. He then received a bolus of 5 mg ketamine that markedly reduced his pain. Consequently, ketamine, 60 mg per day was continuously infused over 3 days with additional bolus of 5 mg ketamine if required.

This case report of opioid-induced hyperalgesia illustrates the putative role of opioids as activators of both a pronociceptive and an antinociceptive pathway [4].

In rats fentanyl dose-dependently decreases the nociceptive threshold and reduces morphine-induced analgesia. Moreover, morphine enhances for several days fentanyl-induced hyperalgesia. This effect is described as related to the activation of pronociceptive pathways by morphine administration and is prevented by repeated boluses of ketamine [4,5]. Ketamine inhibition of opioid-induced hyperalgesia underlines the involvement of NMDA receptors in the activation of pronociceptive pathways.

Remifentanyl has also been involved in promoting hyperalgesia. Guignard and colleagues described this effect as an acute opioid tolerance prevented by the administration of ketamine [1,6]. Two recent electrophysiological studies showed that remifentanyl is able either to activate NMDA receptors or to potentiate their activity [2,3]. The potentiation of NMDA

receptors by opioids is related to the activation of an intra-cellular pathway triggered by the activation of  $\mu$ -opioid receptors [3].

This report suggests that the fentanyl patch induced hyperalgesia subsequently enhanced by the post-operative boluses of morphine. We assume that intra-operatively remifentanyl activated the pro- and antinociceptive pathways. The potency of remifentanyl allowed surgery but as soon as it was stopped, the antinociceptive  $\mu$  pathway was ineffective whereas the pronociceptive NMDA pathway remained active and sensitive to the administration of morphine. As described in rats by Laulin and colleagues, morphine is able to enhance opioids induced hyperalgesia and not potent enough to blunt it [4]. The analgesic-hyperalgesic equilibrium is unbalanced in favour of the pronociceptive pathways and is restored by ketamine.

The administration of ketamine decreased after 12 h. This length of time corresponds to the time required for the fentanyl release from the patch to be active. It implies that during 12 h the blockade of the pronociceptive pathway by ketamine was efficient enough to relieve the patient from his pain. Secondly, morphine did not relieve pain as expected but worsened the pain which is unusual. Since the patient had been using a fentanyl patch for a long period of time, we postulate that the down-regulation left less receptors available. Remifentanyl and fentanyl have a high potency than morphine [7]. Thus the morphine that remained active on the pronociceptive pathway became inactive on the antinociceptive pathway whereas fentanyl would have, probably, been active on both pathways, as shown by the progressive antinociceptive effect of fentanyl.

This report describes an unusual situation that can be encountered when a patient is treated with opioids for a long period of time undergoes surgery. Although opioids remain the gold standard for post-operative analgesia, in this type of case morphine must be used with caution. We suggest to favour the use of a high efficacy agent (remifentanyl) in association with ketamine.

*H. Dumont, E. Guntz, M. Sosnowski, G. Talla*  
 Department of Anesthesiology  
 Centre Hôpitalier Universitaire Saint-Pierre  
 Université Libre de Bruxelles  
 Brussels, Belgium

*A. Roman*  
 Department of Intensive Care Unit  
 Centre Hôpitalier Universitaire Saint-Pierre  
 Université Libre de Bruxelles  
 Brussels, Belgium

B. Segers  
 Department of Vascular Surgery  
 Centre Hospitalier Universitaire Saint-Pierre  
 Université Libre de Bruxelles  
 Brussels, Belgium

## Acknowledgement

Work attributed to Department of Anesthesiology, Centre Hospitalier Saint-Pierre, Université libre de Bruxelles (ULB), Rue Haute, 322, 1000 Brussels, Belgium.

## References

1. Guignard B, Bossard AE, Coste C *et al.* Acute opioid tolerance: intraoperative remifentanyl increases postoperative pain and morphine requirement. *Anesthesiology* 2000; **93**: 409–417.
2. Hahnenkamp K, Nollet J, Van Aken HK *et al.* Remifentanyl directly activates human N-methyl-D-aspartate receptors

expressed in *Xenopus laevis* oocytes. *Anesthesiology* 2004; **100**: 1531–1537.

3. Guntz E, Dumont H, Roussel C *et al.* Effects of remifentanyl on N-methyl-D-aspartate receptor: an electrophysiologic study in rat spinal cord. *Anesthesiology* 2005; **102**: 1235–1241.
4. Laulin JP, Maurette P, Corcuff JB *et al.* The role of ketamine in preventing fentanyl-induced hyperalgesia and subsequent acute morphine tolerance. *Anesth Analg* 2002; **94**: 1263–1269.
5. Rivat C, Laulin JP, Corcuff JB *et al.* Fentanyl enhancement of carrageenan-induced long-lasting hyperalgesia in rats: prevention by the N-methyl-D-aspartate receptor antagonist ketamine. *Anesthesiology* 2002; **96**: 381–391.
6. Guignard B, Coste C, Costes H *et al.* Supplementing desflurane-remifentanyl anesthesia with small-dose ketamine reduces perioperative opioid analgesic requirements. *Anesth Analg* 2002; **95**: 103–108.
7. Sosnowski M, Yaksh TL. Differential cross-tolerance between intrathecal morphine and sufentanyl in the rat. *Anesthesiology* 1990; **73**: 1141–1147.

# Concentration of levobupivacaine solutions is labelled differently than that of other local anaesthetic solutions

doi: 10.1017/S0265021506001712

## EDITOR:

It seems to be difficult for both clinicians and investigators to realize that there is a difference between the *base* and the *salt* of the drug molecule when local anaesthetic concentrations are reported. Di Donato and colleagues [1] have made an error when reporting the concentration of levobupivacaine in their paper published recently in EJA.

In contrast to the labelling principle of all other clinically used local anaesthetics the concentration of levobupivacaine (Chirocaine®) on the marketed ampoule is given as the concentration of the base-form of the molecule. Therefore, a 0.5% levobupivacaine concentration is, in fact, 0.56% when the concentration of the solution would be given according to the hydrochloride-form (salt) of the molecule, i.e., the form in which it exists in the injectable solution.

This error has been pointed out repeatedly in the anaesthesiology literature, the most recent note was published in 2005 [2].

Perhaps such a small error in actual levobupivacaine concentration does not make any difference in clinical practice, but this 12.6% difference may influence scientific evaluation and the interpretation of equipotency in comparison with other local anaesthetics. It can be assumed that the small difference in favour of levobupivacaine in the study by Di Donato and colleagues [1] would have been eliminated had the correct concentration (0.5% instead of 0.56%) and dose (45 mg instead of 50.4 mg) of levobupivacaine-HCl been chosen.

P. H. Rosenberg  
 Department of Anaesthesiology and  
 Intensive Care Medicine  
 Helsinki University Hospital  
 Helsinki, Finland

## References

1. Di Donato A, Fontana C, Lancia F, Celleno D. Efficacy and comparison of 0.5% levobupivacaine with 0.75% ropivacaine for peribulbar anaesthesia in cataract surgery. *Eur J Anaesthesiol* 2006; **23**: 487–490.
2. Rosenberg PH, Schug SA. Levobupivacaine base and levobupivacaine hydrochloride. *Br J Anaesth* 2005; **94**: 544.

Correspondence to: Per H. Rosenberg, Department of Anaesthesiology and Intensive Care Medicine, Helsinki University Hospital, PB 340, Helsinki, 00029 HUS, Finland. E-mail: per.rosenberg@hus.fi; Tel: +358 9 47172510; Fax: +358 9 47174017

Accepted for publication 9 July 2006 EJA 4020  
 First published online 11 October 2006

