



Anesthetic management for neurosurgery in awake patients

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ABSTRACT

Neurosurgery without general anesthesia is based on the necessity to avoid any interference between brain electrophysiological recordings and anesthetic agents, and the opportunity to have a patient able to follow commands and to cooperate during surgery. It includes not only several minimally invasive procedures, but also craniotomies for epilepsy surgery or the removal of tumors located close to brain eloquent areas. Before surgery, the patient must be carefully evaluated, correctly informed and appropriately prepared. In the operating room, monitoring is important for conducting the anesthetic management, ensuring patient's comfort and safety, and meeting surgical requests. Propofol and remifentanyl are frequently used for anesthesia, but sufentanil, local anesthetics and α_2 -agonists are also of primary interest. Patient's ventilation may be spontaneous, assisted or controlled. Airway management is a key point strongly related to the anesthesia technique and the type of surgery. Airway may be secured with different airway devices and the laryngeal mask appears to progressively replace the endotracheal tube. Respiratory, hemodynamic, and neurologic complications as well as nausea and vomiting and loss of patient's cooperation may have disastrous consequences and should be prevented rather than cared.

Key words: Anaesthesia, methods - Neurosurgery - Surgery.

Nowadays, a quite important part of neurosurgery does not necessarily require completely anesthetized patients, but does certainly require skilled and experienced anesthesiologists. This type of surgery is not limited to awake craniotomies only and can be discussed in the field of a more general context.

Basically, neurosurgery without general anesthesia is not a new story. In the second half of the 19th century, awake craniotomies for epilepsy surgery were already performed in patients under local anaesthesia.¹ Today, the concept of neurosurgery in awake or waking up patients has considerably evolved and extended, in strong relationship with the outstanding progresses made in neurosurgical technology, monitoring of anesthesia,

and also anesthetic agents and the way they are delivered to the patients. Consequently, anesthesiologists are more and more frequently involved in this setting. This review paper aims at discussing the role of the anesthetic management of patients undergoing neurosurgical procedures without general anesthesia.

Indications and objectives

Indications

We may consider three main reasons for performing neurosurgery without general anesthesia. The first reason is that no real benefit is expected from general anesthesia. This situation may con-

cern simple ventriculostomies, cerebral biopsies under stereotactic conditions and even some endoscopic procedures performed in cooperative patients. Indeed, a simplified endoscopic third ventriculostomy under local anesthesia has been reported in the literature.² The second reason for performing neurosurgery in awake patients is the necessity to avoid any type of interference between anesthetic agents and either the spontaneous or the evoked electrical activity of the brain, as it may be required during electrodes placement for deep brain stimulations or the realization of electrocortical mapping in epilepsy surgery. The last reason of those awake neurosurgical procedures, which is certainly the most important one, is the opportunity to take advantage of the awake state of the patient and specifically of his capacity to co-operate during surgery. That will be the case when the surgeon wants to test the therapeutic efficacy of deep brain stimulations, such as in Parkinson surgery, and also for the removal of tumors or even vascular lesions located close to functional eloquent areas of the brain such as motor, vision or language areas. In this particular situation, the neurosurgeon has to cope with a difficult dilemma.³ Indeed, a large resection will decrease the risk of recurrence of the lesion and increase the chance of patient's survival but, in the meantime, it may favor the occurrence of a neurological deficit that could badly affect brain function and quality of life. Therefore, the challenge of tumor surgery performed in awake patients is to remove the maximum amount of lesion without impairing neurological function.

Objectives

Minimally invasive surgery is usually performed either under local anesthesia or under sedation and analgesia. In contrast, craniotomies will more frequently, although not systematically require one or two phases of general anesthesia that are part of the so-called "asleep awake asleep technique", as described by Huncke et al. for intraoperative language mapping in 1998.⁴

Whatever the strategy of anesthesia, the objectives of patients' management are twofold: allow the neurosurgeon to take advantage of the patient's cooperation, and preserve general homeostasis. Achievement of the first objective will require opti-

mal analgesia during nociceptive stimulations, sedation and anxiolysis with regard to specific surgical events, immobility and comfort throughout the procedure, and finally prevention of occurrence of side effects or unpleasant events, such as nausea, vomiting or seizures. The second objective aims at maintaining airway permeability, adequate ventilation, hemodynamic stability and brain relaxation. It will also imply to avoid any interference between anesthetic agents and the electrophysiological activity of the brain. Hence, the anesthetic management of patients undergoing awake neurosurgical procedures can be rationally discussed in two stages: what has to be done before surgery and how to proceed in the operating room?

What has to be done before surgery?

The preoperative phase includes the assessment of the patient, the preparation of the patient and the premedication.

Patient's assessment

In addition to the classical issues commonly addressed before any type of general anesthesia, the anesthesiologist should pay a particular attention to specific points. He must anticipate a difficult intubation and detect any risk factor that could favor upper airway obstruction or respiratory depression, such as obesity or a sleep obstructive apnea syndrome. In epileptic patients, he should be aware of the type and frequency of seizures as well as the routine anticonvulsant therapy of the patient. He should know the propensity of the patient to present nausea and vomiting. In brain tumor patients, he should evaluate the degree of intracranial hypertension according to clinical signs and imaging. He should also evaluate the hemorrhagic risk of the procedure, depending on the type of lesion, history of the patient and routine medications. Finally, he should evaluate the degree of anxiolysis, the tolerance to pain and any neurological deficit that could impede the patient's cooperation during surgery.

Preparation of the patient

Obtaining the patient's confidence and agreement for cooperating during surgery is a key fac-

tor of success. The psychological preparation must be considered as a team work that should involve all the actors of the scene, namely surgeon, anesthesiologist and nurse. The patient must be informed regarding the sequence of events during surgery, the specific times where his cooperation will be required, and also the potential side effects or complications and the way they will be managed.⁵ It can also be useful to repeat a functional test the day before surgery.

Premedication

Regarding premedication, there is no general rule but a case by case discussion that should refer to different points. A conversation may be better than any medication, although drugs such as benzodiazepines, clonidine and atropine, are commonly administered. Routine anticonvulsive medication should be continued in patients undergoing tumor surgery and maintained in the therapeutic range. Steroids must be considered to reduce brain edema in tumor surgery and also to prevent nausea and vomiting in combination with specific anti-emetic drugs, such as metoclopramide or ondansetron.⁵ Finally in patients undergoing surgery for Parkinson disease or epilepsy, no specific therapy will be given the day of surgery in an attempt to avoid any interference with electrophysiological recordings and evaluation of the patient's response to deep brain stimulations.

How to proceed in the operating room?

In the operating room, the general philosophy is to make the patient as comfortable as possible, in a safe environment and throughout the entire period of surgery. This intraoperative management includes a preparation phase, the choice of a strategy of anesthesia, the airway care, and finally the diagnosis and treatment of potential complications.

Preparation

In the operating room, drugs and equipment should be ready in advance. One or two intravenous lines are placed. Patients are regularly equipped with an ECG monitor, a blood pressure measurement device, a pulse oxymeter and, ideal-

ly, a depth of anesthesia monitor. According to the type of surgery, blood pressure can also be measured invasively, at the discretion of the anesthesiologist. A urinary catheter and a temperature probe are usual. Pillows, mattress and warming blanket may improve the patient's comfort and are useful to prevent pressure lesions.⁵

Anesthesia

Anesthesia for awake neurosurgery sounds first as a paradoxical issue, but is nevertheless completely justified. It most frequently relies on the concept of monitored anesthesia care (MAC).⁶ In any case, the anesthetic management of patients should fulfill the following criteria: a sufficient depth of anesthesia during opening and closure, a full consciousness during electrical mapping and functional testing, a smooth transition between anesthesia and consciousness and, finally, adequate ventilation, immobility and comfort of the patient throughout the entire procedure.⁷ The two main available options that are susceptible to meet those criteria are either sedation or analgesia, or the so-called asleep awake asleep technique.

Looking at the literature since 1988 to 2006, drugs and anesthetic agents that have been used to provide sedation, analgesia or anesthesia to those patients include local anesthetics, different drugs such as droperidol, midazolam, propofol and thiopental, morphine and synthetic opioids, volatile anesthetics and nitrous oxide, α_2 agonists and ketamine. Today, the main agents actually employed are bupivacaine and ropivacaine, sufentanil, remifentanil, and propofol. Regarding α_2 agonists, clonidine is used occasionally and dexmedetomidine appears of increasing interest although it is not yet available in most European countries. Drugs such as esmolol, labetalol and hydralazine may also be part of the pharmacological armamentarium.

Local anesthesia of the surgical field using ropivacaine or levobupivacaine with epinephrine 5 $\mu\text{g}/\text{mL}$ has been reported to be safe and efficacious.^{8, 9} Regional blocks of upper and lower extremity nerves have also been proposed to prevent involuntary movements in patients undergoing awake craniotomy.¹⁰ Today, this technique appears to be abandoned or remains exceptional in this particular setting. The three classical synthet-

ic opioids alfentanil, sufentanil and fentanyl have been used and combined with other drugs such as droperidol, midazolam, propofol, etc.^{4, 11-17} More than 10 years ago, they have been reported to have similar properties in patients undergoing epilepsy surgery.¹⁸ Nowadays, sufentanil is still commonly used, but remifentanil is gaining more and more popularity.¹⁹⁻²¹ Remifentanil has well known advantages over the other synthetic opioids. Its interesting pharmacokinetic properties make it a good choice to provide excellent analgesia on request, and obtain a patient alert and able to cooperate rapidly after stopping infusion. However, it may favor respiratory depression.²² Propofol is the first choice hypnotic. It can be administered using a target control infusion technique, and its administration can be guided by a depth of anesthesia monitor and combined to remifentanil infusion.¹⁹⁻²² Dexmedetomidine is not available in all countries but appears to be promising when used in patients undergoing awake craniotomies.²³⁻²⁵ It provides sedation close to natural sleep, has anxiolytic and analgesic properties, decreases the use of opioids and antihypertensive drugs without causing clinically relevant respiratory depression²⁶ and can be administered when sophisticated neurologic testing is required.²³ Finally, it is worth to note that awake craniotomy is perfectly feasible in pediatric patients. In particular, drugs such as propofol and dexmedetomidine have been successfully used for managing anesthesia in the pediatric population.^{24, 27-29}

Airway care

Airway management is a major challenge during surgery in awake patients, and often strongly related both to the type of surgery and the strategy of anesthesia.¹⁷ Usually, spontaneous ventilation is maintained during sedation and analgesia as well as during the awake phase of the asleep awake asleep technique. In contrast, ventilation will be more frequently controlled or assisted during the phases of general anesthesia. Spontaneous ventilation is quite common in minimally invasive procedures although it carries on some risk of upper airway obstruction and respiratory depression. In spontaneously breathing patients, airway can be managed with a face mask, a nasal or a laryngeal mask airway (LMA), an oropharyngeal

or a nasopharyngeal device. All of them neither necessarily secure the airway nor prevent pulmonary aspiration, but some may allow to apply ventilatory support such as biphasic positive airway pressure and proportional assist ventilation.^{30, 31} In a recent report, a positive inspiratory and expiratory pressure has been successfully applied through bilateral cannulation of the nares during the asleep phases of craniotomy and was shown to successfully improve ventilation parameters in a patient with an obstructive sleep apnea.³² Ventilation is more often controlled during the asleep phases of the asleep awake asleep technique. A couple of years ago, the old fashion to proceed was to keep the trachea intubated during opening and closure of the skull, and extubated for functional testing or electrical mapping. It has also been reported that lidocaine could be delivered to the upper airway in order to avoid cough and gag reflexes.⁴ Endotracheal intubation is known to prevent aspiration and ensure adequate ventilation, but is not always easy to perform. It may require a fiberoptic guide and is quite uncomfortable for the patient. The less aggressive and more comfortable alternative solution is to "secure" the airway either with a laryngeal mask inserted under general or even local anesthesia, or with a nasal mask which allows non invasive positive pressure ventilation.^{7, 12, 17, 22, 33} The LMA has been proven effective for airway management in pediatric patients.^{34, 35} Finally, it is also possible to control the patient's ventilation only during the opening phase of the surgical procedure, and to complete surgery after electrical mapping or functional testing under sedation and analgesia in a patient breathing spontaneously without any tracheal or laryngeal device.

Complications

Potential complications of awake craniotomies include upper airway obstruction and respiratory depression, tight brain, nausea and vomiting, seizures, decrease in the level of consciousness, neurological deficit and loss of patient's cooperation.^{5, 21, 36, 37} In this setting, prevention is better than care and the anesthesiologist may play a key role.

The incidence of complications is quite variable and may be related to the strategy of anesthe-

sia. Recently, a general evaluation of monitored anesthesia care for functional neurosurgery in 178 patients emphasized a 16% overall complications rate.³⁷ In a retrospective study on patients undergoing awake craniotomy for tumor surgery, Sarang *et al.* analysed the incidence of complications according to the anesthesia regimen.¹⁷ In the 99 reviewed procedures, the incidence of respiratory and hemodynamic complications was the lowest in patients who received total intravenous anesthesia with propofol and remifentanyl with a controlled ventilation using the LMA, compared to total i.v. anesthesia and spontaneous breathing through a LMA, and to sedation and spontaneous breathing through a nasal airway. In another retrospective study performed on 96 patients undergoing functional neurosurgery and receiving propofol and remifentanyl under spontaneous ventilation, at least one 30 s episode of apnea was detected in 69 patients.²¹ Finally, in more than 450 patients undergoing epilepsy surgery under propofol and remifentanyl, the asleep awake asleep technique without a secured airway was associated to a higher rate of hypoxemia and hemodynamic complications than general anesthesia with an endotracheal tube.³⁶

Therefore, respiratory complications are not rare and may be life threatening. In a recent paper on injury and liability associated with monitored anesthesia care, respiratory depression after absolute or relative overdose of sedative or opioid drugs appears to be the most common damaging specific mechanism in MAC claims, with a reported incidence higher than 20%.³⁸ As mentioned in the editorial accompanying this paper, MAC should stand for maximum anesthesia caution, not for minimal anesthesiology care.³⁹ Respiration complications are prevented first by preoperative detection of risk factors and selection of patients, but also by appropriate choice and titration of the anesthetic agent, monitoring respiratory rate and expired CO₂, attention paid to the patient's position and continuous free access to the head. Experienced anesthesiologists are required to manage those cases.²² The incidence of nausea and vomiting is variable, depending on patient's history, type of lesion, medications, and anesthesia.^{11, 17} It can be minimized by a judicious selection of anesthetic drugs combined to the administration of steroids

and specific anti-emetic medications. Seizures can occur at any time in brain tumor patients during the perioperative period. They are best prevented by an appropriate therapy before surgery. Their management involves administration of anticonvulsants to stop the crisis while maintaining adequate ventilation, and may require a conversion to general anesthesia. Finally, the patient's refusal to cooperate may be due to different reasons including bad preoperative preparation, inappropriate and excessive sedation, insufficient analgesia, uncomfortable position and a too long surgical procedure. Some of them can be prevented, but the loss of patient's cooperation may also require a conversion to general anesthesia for completing surgery.

Conclusions

Neurosurgery in awake or waking up patients is an exciting challenge and has become common practice in several neurosurgical centers for many years.^{13, 15, 21} Management of those patients is a team work that requires skilled and experienced anesthesiologists. The patient's cooperation is a determinant factor of success. Strategy of anesthesia should be defined before surgery. Complications must be anticipated and managed according to pre-established guidelines. Last, there is a crucial need for high quality clinical trials to improve the safety and efficacy of this technique, and also to validate it in comparison to more conventional procedures.

References

1. Horsley V. Brain surgery. *BMJ* 1886;2:670-5.
2. Longatti P, Perin A, Rizzo V, Comai S, Bertazzo A, Allegri G. Endoscopic selective sampling of human ventricular CSF: a new perspective. *Minim Invasive Neurosurg* 2004;47:350-4.
3. Lanier WL. Brain tumor resection in the awake patient. *Mayo Clin Proc* 2001;76:670-2.
4. Huncke K, Van de WB, Fried I, Rubinstein EH. The asleep-awake-asleep anesthetic technique for intraoperative language mapping. *Neurosurgery* 1998;42:1312-6.
5. Manninen P, Contreras J. Anesthetic considerations for craniotomy in awake patients. *Int Anesthesiol Clin* 1986;24:157-74.
6. Berkenstadt H, Ram Z. Monitored anesthesia care in awake craniotomy for brain tumor surgery. *Isr Med Assoc J* 2001;3:297-300.
7. Yamamoto F, Kato R, Sato J, Nishino T. Anaesthesia for awake craniotomy with non-invasive positive pressure ventilation. *Br J Anaesth* 2003;90:382-5.

8. Costello TG, Cormack JR, Hoy C, Wyss A, Braniff V, Martin K et al. Plasma ropivacaine levels following scalp block for awake craniotomy. *J Neurosurg Anesthesiol* 2004;16:147-50.
9. Costello TG, Cormack JR, Mather LE, LaFerlita B, Murphy MA, Harris K. Plasma levobupivacaine concentrations following scalp block in patients undergoing awake craniotomy. *Br J Anaesth* 2005;94:848-51.
10. Gebhard RE, Berry J, Maggio WW, Gollas A, Chelly JE. The successful use of regional anesthesia to prevent involuntary movements in a patient undergoing awake craniotomy. *Anesth Analg* 2000;91:1230-1.
11. Archer DP, McKenna JM, Morin L, Ravussin P. Conscious-sedation analgesia during craniotomy for intractable epilepsy: a review of 354 consecutive cases. *Can J Anaesth* 1988;35:338-44.
12. Tongier WK, Joshi GP, Landers DF, Mickey B. Use of the laryngeal mask airway during awake craniotomy for tumor resection. *J Clin Anesth* 2000;12:592-4.
13. Taylor MD, Bernstein M. Awake craniotomy with brain mapping as the routine surgical approach to treating patients with supratentorial intraaxial tumors: a prospective trial of 200 cases. *J Neurosurg* 1999;90:35-41.
14. Herrick IA, Craen RA, Gelb AW, Miller LA, Kubu CS, Girvin JP et al. Propofol sedation during awake craniotomy for seizures: patient-controlled administration versus neurolept analgesia. *Anesth Analg* 1997;84: 1285-91.
15. Bernstein M. Outpatient craniotomy for brain tumor: a pilot feasibility study in 46 patients. *Can J Neurol Sci* 2001;28:120-4.
16. Blanshard HJ, Chung F, Manninen PH, Taylor MD, Bernstein M. Awake craniotomy for removal of intracranial tumor: considerations for early discharge. *Anesth Analg* 2001;92:89-94.
17. Sarang A, Dinsmore J. Anaesthesia for awake craniotomy: evolution of a technique that facilitates awake neurological testing. *Br J Anaesth* 2003;90:161-5.
18. Gignac E, Manninen PH, Gelb AW. Comparison of fentanyl, sufentanil and alfentanil during awake craniotomy for epilepsy. *Can J Anaesth* 1993;40:421-4.
19. Johnson KB, Egan TD. Remifentanil and propofol combination for awake craniotomy: case report with pharmacokinetic simulations. *J Neurosurg Anesthesiol* 1998;10:25-9.
20. Hans P, Bonhomme V, Born JD, Maertens dN, Brichant JF, Dewandre PY. Target-controlled infusion of propofol and remifentanil combined with bispectral index monitoring for awake craniotomy. *Anaesthesia* 2000;55:255-9.
21. Keifer JC, Dentshev D, Little K, Warner DS, Friedman AH, Borel CO. A retrospective analysis of a remifentanil/propofol general anesthetic for craniotomy before awake functional brain mapping. *Anesth Analg* 2005;101:502-8.
22. Berkenstadt H, Perel A, Hadani M, Unofrievich I, Ram Z. Monitored anesthesia care using remifentanil and propofol for awake craniotomy. *J Neurosurg Anesthesiol* 2001;13:246-9.
23. Mack PF, Perrine K, Kobylarz E, Schwartz TH, Lien CA. Dexmedetomidine and neurocognitive testing in awake craniotomy. *J Neurosurg Anesthesiol* 2004;16:20-5.
24. Ard J, Doyle W, Bekker A. Awake craniotomy with dexmedetomidine in pediatric patients. *J Neurosurg Anesthesiol* 2003;15:263-6.
25. Bekker AY, Kaufman B, Samir H, Doyle W. The use of dexmedetomidine infusion for awake craniotomy. *Anesth Analg* 2001;92:1251-3.
26. Hsu YW, Cortinez LI, Robertson KM, Keifer JC, Sum-Ping ST, Moretti EW et al. Dexmedetomidine pharmacodynamics. Part I: crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. *Anesthesiology* 2004;101:1066-76.
27. Tobias JD, Jimenez DF. Anesthetic management during awake craniotomy in a 12-year-old boy. *Paediatr Anaesth* 1997;7:341-4.
28. Soriano SG, Eldredge EA, Wang FK, Kull L, Madsen JR, Black PM et al. The effect of propofol on intraoperative electrocorticography and cortical stimulation during awake craniotomies in children. *Paediatr Anaesth* 2000;10:29-34.
29. Klimek M, Verbrugge SJ, Roubos S, van der Most E, Vincent AJ, Klein J. Awake craniotomy for glioblastoma in a 9-year-old child. *Anaesthesia* 2004;59:607-9.
30. Hormann C, Baum M, Putensen C, Mutz NJ, Benzer H. Biphase positive airway pressure (BIPAP): a new mode of ventilatory support. *Eur J Anaesthesiol* 1994;11:37-42.
31. Younes M. Proportional assist ventilation (PAV). In: Toby MJ, editor. Principles and practice of mechanical ventilation. New York, USA: McGraw-Hill Inc; 1994 .p. 349-70.
32. Gonzales J, Lombard FW, Borel CO. Pressure support mode improves ventilation in "asleep-awake-asleep" craniotomy. *J Neurosurg Anesthesiol* 2006;18:88.
33. Fukaya C, Katayama Y, Yoshino A, Kobayashi K, Kasai M, Yamamoto T. Intraoperative wake-up procedure with propofol and laryngeal mask for optimal excision of brain tumour in eloquent areas. *J Clin Neurosci* 2001;8:253-5.
34. Hagberg CA, Gollas A, Berry JM. The laryngeal mask airway for awake craniotomy in the pediatric patient: report of three cases. *J Clin Anesth* 2004;16:43-7.
35. Brunson CD, Mayhew JF. Laryngeal mask airway for awake craniotomy in pediatric patients. *J Clin Anesth* 2005;17:149-50.
36. Skucas AP, Artru AA. Anesthetic complications of awake craniotomies for epilepsy surgery. *Anesth Analg* 2006;102:882-7.
37. Venkatraghavan L, Manninen P, Mak P, Lukitto K, Hodaie M, Lozano A. Anesthesia for functional neurosurgery: review of complications. *J Neurosurg Anesthesiol* 2006;18:64-7.
38. Bhananker SM, Posner KL, Cheney FW, Caplan RA, Lee LA, Domino KB. Injury and liability associated with monitored anesthesia care: a closed claims analysis. *Anesthesiology* 2006;104:228-34.
39. Hug CC, Jr. MAC should stand for maximum anesthesia caution, not minimal anesthesiology care. *Anesthesiology* 2006;104:221-3.

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