ANESTHETIC MANAGEMENT OF AWAKE CRANIOTOMY : OUR STANDARDISED PROTOCOL AND REVIEW OF THE LITERATURE

Review Article

UYANIK KRANİYOTOMİ DE ANESTEZİ YÖNETİMİ: STANDART PROTOLÜMÜZ VE LİTERATÜRÜN GÖZDEN GEÇİRİLMESİ

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ABSTRACT

Paralel to the development of new anesthetics, and advanced technological changes, anesthesia is being more safer for the patients. At the same time, surgical procedures are becoming longer and much more complex. Awake craniotomy is the technique of choice for certain neurosurgical procedures, including excision of lesions from eloquent cortical areas and procedures for epilepsy and movement disorders. The anesthesiologist should be maintain patient comfort, analgesia, immobility and cooperation adequately during the awake craniotomy. Due to extensive and effective use of modern aneasthetic methods, its indications are getting less.

In this study we aimed to give our standardized anesthetic protocol for awake craniotomy and review of the literature.

ÖZET

Yeni anestezik ajanların bulunması ve teknolojik değişikliklerdeki ilerlemelerle anestezi hastalar için daha güvenli bir hale gelmiştir. Aynı zamanda, cerrahi uygulamalarda daha uzun ve daha kompleks olmaya başlamıştır. Uyanık kraniyotomi, hassas kortikal lezyonlar and epilepsi ve hareket bozukluklarının cerrahisinde tercih edilebilen bir tekniktir.

Uyanık kraniyotomi sırasında, anestezist hastanın konforunun, analjezisinin,hareket sizliğinin ve kooperasyonunun yeterli olmasını sağlamalıdır. Modern anestezi yöntemlerinin artmış ve etkin kullanımıyla, uyanık kraniyotomi endikasyonları azalmaktadır.

Bu çalışmada, uyanık kraniyotomide standart anestezi protokolümüz ve litera-türün gözden geçirilmesi amaçlan-mıştır.

INTRODUCTION

Awake craniotomy is the technique of choice for certain neurosurgical procedures, including excision of lesions from eloquent cortical areas and procedures for epilepsy and movement disorders (1). Use of awake craniotomy can result in a considerable reduction in resource utilization without compromising patient care by minimizing intensive care time and total hospital stay. The anesthesiologist should be maintain patient comfort, analgesia, immobility and cooperation adequately during the awake craniotomy (1,2). Due to extensive and effective use of modern aneasthetic methods, its indications are getting less. Today, there are no differences between awake and general anesthesia for postoperative mortality and morbidity except speech center pathologies. However, these results are directly related with the anesthetic and surgical skills and options of the clinics.

In this study we aimed to give our standardized anesthetic protocol and review of the history, indications, contraindications, and complications of awake craniotomy in light of the literature.

HISTORY

History of aneasthesia is parallel with the history of surgical interventions. In every civilization, aneasthesia approaches proper to the conditions of the period have been used during surgical intervention for the relief of pain. In ancient civilizations, it can be observed that besides the plants, which contain the parent material of many drugs used today, such as, belladonna alkaloids and coca leaves, vasoconstrictive effect of the cold and pressuring the aorta were used to relieve the pain during bewitchment, thaumaturgy, exorcism, evil spirit and the therapeutic surgical intervention (1,2).

Until 18th century, no reliable aneasthesia method to relieve pain completely during surgical interventions was develoved.Discovery of carbondioxide by Von Helmont and its being isolated by Black in 1754, discovery of oxygen and nitrous oxide formed a basis for modern and real aneasthesia. Aneasthesia entered a new period with Horace Wells' putting forward the aneasthetic effects of ether which had been used for fun at the parties. As of this date, modern aneasthesia could progress as a science. Application of endotracheal intubation safely is a milestone in anesthesia. However, even in these periods, due to the insufficiency of both monitorization methods and pharmacological agents, surgical mortality and morbidity rates related to aneasthesia are still very high. This leads to the continuance of craniotomy application under local aneasthesia which has already been used. In complicated operations such as brain and nerve surgery, use of general aneasthesia reliably could become a standart through the technological and pharmacological developments that gained acceleration in the last century. Application of aneasthesia in neurosurgery is paralel with this historical process.The period we call modern neurosurgery starts with Dr. Harvey Cushing (1,2).

INDICATIONS

In order to perform a better neurological monitorization during craniotomy opera-tions, to protect motor functions at sensitive neurosurgery and as a result to prevent neurologic deficit, awake craniotomy is prefered (2,3).

Awake craniotomy is used in debulking posterior frontal operculum tumours (broca's area) in dominant hemisphere and wernicke (angular girus) tumours in dominant hemisphere, in epilepsy surgery, and movement disorders.

Even if broca's area tumours are reported as the only real indication, if there is a lesion in motor area and if this causes an attack, awake cranitomy can be used. However, epilepsy surgery, amygdalohipolamectomy, is not an awake craniotomy indication by itself.

Wernicke's Area: It is one third of superior temporal gyrus as a center. Clinically, the patient does not understand what is told.

Broca's Area: It covers left lateral frontal, preeolandic, supra-sylvian region and it is just in front of anterior of precentral gyrus. Clinically, the patient understands what is told and written but suffers from not being able to express what he/she thinks.

CONTRAINDICATIONS

Patient selection is the key point for the success of awake craniotomy. Despite to the conflicted cantraindications, confusion and communication difficulties are absolute contraindications for awake surgeries (3). Awake craniotomy is relatively contraindicated for long surgical durations, extremely aged patients, patients with the moderate to severe cardiovascular system pathologies, in the conditions where surgical position may cause respiratory problems and in surgical operations where there is massive bleeding and dura related tumours. Another point should be keep in mind, the awake craniotomy is not safe for procedure being performed by an inexperienced neurosurgeon.

Recently, Garavaglia et al. reported that they had applied a successful awake craniotomy with the patients suffering from anxiety, difficult airway, obesity, big tumour and intracranial hypertension. They reported that the sedation with dexmedetomidine infusion and cranial block using by bupivacaine are effective for high risk patients without any airway problems (3). However, they did not discuss prevention for the patient safety for high risk patient. Also they did not explain their surgical indications for high risk patients for sedation instead of general anesthesia (3).

PREOPERATIVE EVALUATION

Selection of the patient for awake craniotomy is the important. Appropriate patient evaluation, selection and education; planning and communication among surgeon, neurologist, and anesthesiologist are essential. Having the same anesthesiologist evaluating the patient preoperativelycan be help for the Preoperative evaluation should be include the patient history of obstructive sleep apnea symptoms, and snoring. Table 1 shows the details to consider at preoperative anesthetic preparation of the patient for awake craniotomy. In addition to preoperative anesthetic examination; laboratory tests, neuropsychological tests, neuromonitoring (EEG, SSEP, MEP etc.), imaging techniques such as magnetic resonance and functional magnetic resonance (fMRI), positron emission tomography (PET) are also important for preoperative preparation. When temporal lobectomy was extensively used, dominant hemisphere of the patient was determined by injecting intra-arterial substance (Wada Test). But today more reliable information can be obtained by fMRI, PET (hypermetabolism in epileptic foci).

Preoperative preparation	Anesthetic evaluation Neuro-physiological evaluation Neuro-psychological evaluation
Premedication	Continue to the dexamethasone dosages Continue to the routine anticpilcptic medication Proton pump inhibitor (lansoprazole 30 mg) Serotonin receptor antagonist (ondansetron 8 mg/iv) Midazolam (max. 0.02-0.035 mg/kg/iv)
Medications	Furosemide 20 mg/kg Antibiotic prophylaxis Perioperative control of hypertension: Esmolol
Monitoring	Heart rate (ECG) Invasive blood pressure (Radial artery cannulation*) Oxygen saturation (SpO_2) Respiratory rate Transcutaneous /End tidal carbon-dioxide Urinary output Temperature (from urinary catheter) Depth of anesthesia (BIS) Neuromonitoring
Cranial Block	Bupivacaine + Adrenaline (20 minutes before pin head holder)
Sedation**	Propofol 25-50 mcg/kg/minute infusion +/- Remifentanil 0.05-0.1 mcg/kg/minute infusion

Table 1. *Preoperative anesthetic evaluation*

Neuropsychological tests are performed by specialist clinical psychologists in order to test cognitive function differences related to patients' disorder. Mental processing speed, attention, memory, visuo-spatial ability, operational functions, emotional state, language-speech, social sufficiency, fine motor ability, academic ability, reasoning and decision making abilities can be evaluated using by these test during the perioperative period. Neuropsychological tests are performed by the specialists and experienced clinical psychologist who will apply them during the surgery in perioperative period.

Communication between anesthesiologist and patient has e key role for peroperative surgical success. During the preoperative visit the following details should be explained to the patient;

•Why this method is chosen,
•What is the benefit,
•How it will be applied,
•What is the stages of surgery,
•Who will be in the environment,
•Who have been applied this before,
•What are the possible complications,
•Music the patient wants to listen during the surgery,
•Determining the support points for the patient to lie in a comfortable operation position,
•Demonstration of sounder kit,
•Showing operation room environment if required.
•If possible, have the patient watch videos of the patient who experienced awake craniotomy before.

Operation Room Preparation

On the door of the operating room, attention note should be written about the awake patient is in the operating room. All of the equipment should be ready before the patient came to the operating room. Room temperature should not be annoying for the patient. Patients should be covered immediately. Operating Room should be quiet and silent (monitor alarms, drill, CUSA...). Under the head and knees should be supported with pillows. Lumbar lordosis of patients having waist problem should be supported. Sounder toy, and music that the patient wants to listen should be prepared.Emergency airway equipments, and iced water with serum physiologic or ringer lactate should be ready for to use in case of emergency.

Premedication

The aim of the anesthetic management is to reduce patient's anxiety, prevention of pulmonary aspiration risk and maintaining the hemodynamic stability during the awake craniotomy (4). Premedication may changed according to the patient's clinical condition, preference of the anesthesiologist and the standards of the clinic. Table2 shows that the agents can be used for this purpose. Anxiety can be reduce with midazolam at the maximum dose of 0.02 mg/kg. However, benzodiazepine and opioids can be decrease the pharyngeal muscle tone and cause of respiratory depression. Deterioration in cognitive functions related to benzodiazepines may lead to confusion in electrocorticography since it pressures the agitation/ delirium and epileptic focus (5). Hipertansiyon in this period can be treated with titration of atenolol (25 mg) or esmolol (1 mg/kg). Glycopyrolate and Scopolamine should be prefered due to their antisialogogue effect without central side effects. Extrapyramidal side effects of metoclopramide should not be underestimated, if antiemetic treatment is required.

Aspiration Prophylaxis	H_2 receptor antagonists Proton pump inhibitors Sodium citrate
Anti-emetic prophylaxis	Ondansetron (4-8 mg) Metoclopramide (10 mg) Droperidol (0.625-2.5 mg)
Treatment of Hypertension	Clonidine (4 µg/kg) Atenolol (25 mg) Esmolol (0.5-1 µ/kg)
Anti-sialagogue agents	Glycopyrolate Atropine
Anxiolytic agents	Midazolam (maks. 0.02 mg/kg/iv) ± fentanil 50-100 mcg/iv Alprazolam Clonidine (Po) (2-3 mcg/kg 1 hour before)

Table 2. *Premedication for awake craniotomy*

MONITORIZATION

Besides the factors that belong to the patient, experience of the surgical team and possible complications should be evaluated and monitorization techniques should be applied. It should be considered that the one of the most frequent problem is hemodynamic changes. Heart rate, oxygen saturation, non-invasive or invasive blood pressure, end-tidal carbondioxide or transcutaneous carbondioxide pressure and temperature should be monitorized in all patients. Urinary output, depth of aneastesia, neuromonitoring and monitoring of the brain tissue oxygen pressure should be decided on patient basis (4,5). Brain tissue oxygen pressure may help to determine the limit of surgical resection. Arterial cannulation is required for blood pressure measurement, blood sampling for to check the metabolic condition and partial carbondioxide pressure. The pulse oxymeter should be placed to the oposite side extremity at which the motor responses will be controlled during the operation with spontenous movements. Central venous catheter is not routinely required for awake craniotomy. Urinary catheter should be placed, if diuretics are used, surgical duration is longer, or surgery has high risk for surgical bleeding. Arterial and urinary catheterizations should be applied after providing adequate depth of sedation. Local anesthetic infiltration for arterial catheterization and topical local aneasthetic lubricants during urinary catheterization should be used. Depth of the sedation should be adequate while the needle electrodes is inserted for neuromonitoring.

Border of the surgical resection can be determine using by intropeative mapping with patient is expected to recognize, name and pronounce the cards or objects shown. During awake craniotomy, limit where neurological deficit starts to develop was identified as resection limit, today since neurological deficit recovers in early stages of postoperative period and leads to residue of tumour, it has become debatable. Besides, still there is no scientific data related to which deficit will be temporary or permanent.

ANESTHETIC MANAGEMENT

Awake craniotomy can be performed under local anesthetic infiltration or cranial block, or sedation, or general anesthesia (4-12). General anesthesia is induced and the patient is intubated or ventilated through a laryngeal mask and kept asleep until the brain is exposed; then anesthesia is discontinued and the tracheal tube or LMA removed and the patient is allowed to fully awake for brain mapping and monitoring of neurological functions to be spared. Following the awake period, anesthesia is induced again, the patient re-intubated or the LMA reinserted, or just lightly sedated until the end of surgery. Monitored anesthesia care consists of sedation and analgesia. This technique does not require the airway instruments, however requires good local anesthetic infiltration or cranial block.

Pain should be relieved while pin head holder is fixing, opening the bone flap and dura. Patient's cooperation should be provided during neuromonitoring, with sufficient ventilation and stable hemodynamics. Immobility and comfort of the patient should be provided during the all surgery. The following 3 topics are important in anesthesia management in awake craniotomy; protection of the patient's cooperation with decreasing psychological-physical stres, optimal analgesia, enough sedation and anxiolisis, comfortable position, and preventing nausea and vomitting; effective hemostasis with airway safety and sufficient ventilation, hemodynamic stabilization, and normal intracranial pressure maintanence; minimal effect on electrophysiological records during the surgery (1-6). Providing these conditions, monitorized aneasthesia care, sedation or asleep-awake-asleep techniques can be used.

i- Cranial block / Local anesthetic infiltration

For maximum efficiency, block should be done about 20 minutes before head holder fixation. Also, local aneasthetic infiltration to incision line and head holder points may be helpful (12).

Block can be done with 23gauge needle. In choosing local aneasthetic agent, prilocain by itself will be effective for a shortterm and at maximum dosage methemoglobinemia risk is to be considered. Bupivacaine has longterm effect with the high cardiovascular side effects. Using levobupivacain instead of bupivacain due to less side effects. During the operation, lidocain can be attached to the painful points at the dura.

Ropivacain 3-4 mg/kg, levobupivacain 2-3 mg/kg and Bupivacain 2-3 mg/kg are the dosages most commonly to be used. Table 3 shows local aneasthetic dosages for cranial block. Non-pharmacological and pharmacological methods are identified for monitored anesthesia care (Table 4).

ii- Monitored anesthesia care / Sedation

Non-pharmacological and pharmacological methods are identified for monitored anesthesia care (Table 4).

Drugs	Concentration (%)	Volume (mL)	Adrenalin
Ropivacaine	0.75	20-40	1/200 000
	0.25	60	-
Bupivacaine	0.5	30-40	1/200 000
Bupivacaine	0.5	15	1/100 000
+Lidocaine	0.1	15	1/100 000
Levobupivacaine	0.5	20-30	1/200 000

Table 3. *Local anesthetics and dosages for cranial block*

	Bolus Dosages (mcg/kg)	Infusion (mcg/kg/min)
Propofol	1000-2000	1000-5000
		4000-7000
Dexmedetomidine	1-3	0.1-0.2
Dexmedetomidine	2	0.1-0.5
+Fentanyl	1	-
Fentayl	0.5-1	0.5-2
Alfentanil	7	0.5
Sufentanil	0.075	0.0015
Remifentanil	0.05-2	0.05-0.1

Table 4. *Most commonly used anesthetic agents and dosages for awake craniotomy*

Giving a comfortable position to the patient, supporting the pressure points, establishing sense of trust, appropriate room temperature, silent and quiet environment are non-pharmacological methods which are helpful in this aspect. In addition to this, all aneasthetic agents can be used at appropriate dosage and application forms (6-10).

It is stated that manual or target controlled infusion of propofol by itself or with opioids provides a good pain control. However, in the recent publications, fentanyl or opioid at a low dose is also added. In our clinic, propofol and remifentanyl infusions are used together (propofol 25-50 mcg/kg/min with remifentanyl 0.05-0.1 mcg/kg/min). Dexmedotimidine is being used increasingly in the recent years. The most important advantage of this agent is it does not cause respiratory depression. But it is conflicted for neuro cases cause of the hemodynamic changes (1,4).

Depth of the sedation can be titrated with propofol. It reduces cerebral oxygen consumption, increases cerebral perfusion and reduces intracranial pressure. It has antiepileptic and antiemetic effect. It can be given with manually or target

controlled infusion. It should be discountinued at least 15 minutes before electrocorticograpic recording. It has side effects such as respiratory depression and pseudo tonic-clonic seizures. Although its pro- and anti-convulsant properties are still under debate, propofol sedation is popular and does not appear to interfere with electrocorticography, provided it is suspended at least 15 minutes before recording.

Propofol and remifentanyl can be use together for sedation. Propofol TCI is then set to reach an effect site concentration around 0.5 mcg/ml (range 0.2 to 1.5) and remifentanil between 0.075 and 0.1 mcg/kg/min. This should provide an adequate sedation without respiratory depression during bone and dura mater opening.

Dexmedotimidine is a selective alfa-2 agonist, has an analgesic and anxiolytic effect without respiratory depression. However, if dexmedotimidine combine with benzodiazepine and opioids, respiratory depression can be ocur. It is valuable in awake neurocognitive tests. However, results related to its reliability in neuroaneasthesia are inconsistent (9,10,12). Recently, there are import publications about sedation with dexemedotimidine for awake craniotomy, or sedational procedures in neurosurgery. A Ramsay sedation score of 3 to 4 is the goal and accurate titration of sedation.

iii-Asleep-awake-asleep techique

In this technique, following the general aneasthesia induction, patient is inventilated using by endotracheal intubation or supraglottic devices, then patient kept asleep until the brain is exposed (13). Then anesthesia is discontinued and the tracheal tube or supraglottic devices removed to enable verbal communication and patient collaboration. Following the surgical resection, anesthesia is induced again, the patient is reintubated or supraglottic device reinserted and surgery is completed. Some of the anesthesiologist prefer to use sedation instead of general anesthesia with spontaneous ventilation during the closure period (11). Brain relaxation is better with this method, but it is more complex anesthetic procedures. Extubation may induce airway irritation and coughing, leading to patient movement which are related with the brain bulging. Short acting agents should be prefer fort his technique. Most frequently used agent is propofol for induction of anesthesia, sevoflurane, desflurane, propofol, dexmedotimidine for maintenance of anesthesia. Local inflitration/cranial block should be applied to all patients.

AWAKE CRANIOTOMY AT PREGNANCY

Publications on awake craniotomy at pregnancy are limited. It was reported that propofol and alfentanyl or propofol and dexmedotimine had been used safely (14).

AWAKE CRANIOTOMY AT PEDIATRIC PATIENTS

Although craniotomy at pediatric patients is conflicted, it was reported that aneasthesia was applied successfully during awake craniatomy by Psaquet in 1954 to a10-year-old patient, by Archer in 1989 to 354 patients older than 12, by Klimek in 2004 to a 9 year-old patient (15-19). In these series, patient were sedated with propofol, dexmedotimidine or remfentanyl infusions.

Preoperative preparation	Anesthetic evaluation Neuro-physiological evaluation Neuro-psychological evaluation
Premedication	Continue to the dexamethasone dosages Continue to the routine antiepileptic medication Proton pump inhibitor (lansoprazole 30 mg) Serotonin receptor antagonist (ondansetron 8 mg/iv) Midazolam (max. 0.02-0.035 mg/kg/iv)
Medications	Furosemide 20 mg/kg Antibiotic prophylaxis Perioperative control of hypertension: Esmolol
Monitoring	Heart rate (ECG) Invasive blood pressure (Radial artery cannulation*) Oxygen saturation (SpO_2) Respiratory rate Transcutaneous /End tidal carbon-dioxide Urinary output Temperature (from urinary catheter) Depth of anesthesia (BIS) Neuromonitoring
Cranial Block	Bupivacaine+ Adrenaline (20 minutes before pin head holder)
Sedation**	Propofol 25-50 mcg/kg/minute infusion +/- Remifentanil 0.05-0.1 mcg/kg/minute infusion

Table 5. *Anesthetic protocol for awake craniotomy*

*Radial artery catheter, urinary catheter, and neuromonitoring needle electrodes should be placed at BIS around 60-70

**Infusions should be started following the patient is transferred to the operation table and bolus propofol should be given if necessary (0.25-1 mg/kg)

COMPLICATIONS

Awake craniotomy complications and treatments are shown in the table (Table6).Recently, neurological deficits related with the awake craniotomy and posttraumatic stress syndrome are started to discuss following these procedures (13,20,21). They have led awake craniotomy to be questioned again.

i- postoperative neurological deficit

Since neurological deficit which is formed while determining surgical limit could be permenant or temporary related to oedema and inflammation, the method has started be debated again. While in some patients it leads to tumour residue but neurological deficit can be temporary, or in others there is no deficit during the resection, however it can be occur following the resection. This problem is completely a contradictory result with awake craniotomy philosophy.

In a research conducted by Nossek et al.488 patients who had awake craniotomy between 2003-2010 were observed retrospectively and no postoperative neurological deficit difference was found between the patients who could not continue due to seizure and intolerance and the patients who experienced awake craniotomy. However, tumour resection was found to be insufficient (13).

ii-post-traumatic stress syndrome

In the article published by Millian et al. in 2013, took the lid off a problem of awake craniotomy which had not been considered before (21); Posttraumatic stress syndrome which is more frequent among young and female patients. Fear of the same experience to be repeated and a bad dream (44%), refusing to talk about awake surgery (18.8%), stress when remembered (62.5%) and permanent posttraumatic stress are new data related to clinical table. Even this reveals how important is the choice of patients.

Description	Details	Management
Respiratory Depression	Decreased respiratory rate Desaturation Hypercarbia	Increase the oxygen flow Decrease the depth of sedation Give tactile/verbal stimulus Airway management (jaw thrust, oral airway, supraglottic devices)
Hemodynamic Changes	Hypertension is high in sedated patient Hypotension occurs with venous air embolism	Reduce the anxiety of patient Give additional analgesic Inject additional local anesthetic Check the partial carbon-dioxide pressure Give anti-hypertensive medication (Labetalol, esmolol, clonidine, uradipil..)
Seizure	Triggered with; Cortical and subcortical stimulation 50-70 Hz stimulation Continuously use of CUSA and bipolar	Check antiepileptic blood level preoperatively Prepare iced serum physiologic/ringer lactate Less use opioids **Treatment** Stop stimulation Irrigate the surgical area with iced fluid Give additional dosage of antiepileptic Give midazolam, diazepam, or propofol if necessary Switch to the general anesthesia, if required
Nausea and Vomiting	Manipulation of dural/cerebral vessels High dosage opioids	Can be reduce with antiemetic prophylaxis, dexamethasone, and propofol Treatment Stop the surgical manipulation Precaution of pulmonary aspiration Give the medication: Metoclopramide (10 mg) Ondansetron (4-8 mg) Granisetron (3-9 mg)

Table 6. *Management of the complications during awake craniotomy*

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CONCLUSION

Postoperative less side effects in early and late stages, early recovery and early mobilization, shorter intensive care stay, early discharge and low cost are the main advantages of the awake craniotomy. However, due to extensive and effective use of modern anesthetic methods and advanced monitoring techniques, its indications should be discuss and reevaluate again. Further researches are require for advantages of awake craniotomy for prevention of the neurological defisit and awake craniotomy related posttraumatic stress syndrome.

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