Options to manage post-craniotomy acute pain: no protocol available

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Abstract

The physical process of incision, traction and tissue cut utilized to proceed craniotomy stimulate nervous terminations and specific nociceptors, resulting in postoperative pain. Post operative cephalalgia is present in the majority of patients submitted to craniotomy procedures. The management of this clinical entity is yet to be standardized. Moreover, addressing outcome related to pain therapy is always a challenge due to the subjectiveness of pain. The goal of this study is to perform a review of the therapeutic options available in clinical practice in order to help clinicians and neurosurgeons when dealing with this common pain disorder. This is a narrative review of the literature from 1970 to December 2011 including reports, systematic reviews, all types of study and other literatures concerning acute pain management after craniotomy. The data was collected by doing a search of PubMed, EMBASE, Cochrane Reviews, and a manual search of all pertinent references in the literature. Sixty five researches were included and discussed on present review. Literature includes pharmacological treatment for post-craniotomy pain management as use of opioids like codeine, tramadol and morphine, non-steroidal anti-inflammatory drugs like cyclo-oxygenase 2 Inhibitors, gabapentin and scalp nerve block. Non-pharmacological strategies were identified in form of electromyography and criotherapy. The lack of an ideal protocol to treat patients suffering from post-craniotomy pain may represent an incomplete understanding of the physiopathology and neural mechanisms related to this syndrome. Future investigations focused on ideal protocols to control of pain after craniotomies are needed.

Key words: Analgesia, Clinical protocol, Cranial pain, Craniotomy, Patient care management, Treatment outcome.

Introduction

The physical process of incision, traction and tissue cut utilized in craniotomy stimulate nervous terminations and specific nociceptors resulting in postoperative pain. Literature refers that 60% to 84% of patients submitted to craniotomy presents a variation level of pain from light to severe. Particular sites of craniotomy, characteristics of surgical approaches or technique may result in post-craniotomy pain of different intensities. However, Irefin et al., (2003) reported that infratentorial craniotomy is not related with an increased necessity for immediate postoperative pain control compared to supratentorial craniotomy or spinal surgeries when local anesthetic infiltration is not used. A recent research demonstrates that, during the first 24 hours after surgery, 87% of patients present pain after craniotomy, and that the possibility of suffering post-craniotomy pain decreases 3% for each year of life. This pain syndrome, despite the introduction of novel drugs and analgesic techniques, is frequently untreated because of the risks related to medical therapy. Mordhorst et al., (2010) pointed that the continued use of sevoflurane and the absence of corticosteroids therapy, during anesthesia, decreased post-craniotomy pain syndrome occurrence by 147% and 119%, respectively. Some authors consider clinical guidelines indispensable tools to deal with pain secondary to craniotomy. According to Bardiau et
Opioids may lead to respiratory depression, increased blood flow and intracranial pressure. Codeine, oxycodone, hydrocodone, propoxyphene, and morphine are customarily used for post-craniotomy pain management. These drugs stimulate specific opioid receptors in the central and peripheral nervous system. The use of narcotics can generate several side effects, possibly resulting in delay recovery and ambulation, and extended hospital stays.

According to Goldsack et al. (1996), neurosurgeons resist to prescribe opioids in cases of post-craniotomy pain because of their latent risk to cause respiratory depression, decrease level of consciousness, nausea and vomiting. Acetaminophen or morphine are typically used on an as-needed basis because of their side effects, in particular their association with respiratory depression.

**Methods**

This is a narrative review of the literature from 1970 to December 2011 including reports, systematic reviews, all types of study and other literatures concerning acute pain management after craniotomy. The data was collected by doing a search of PubMed, EMBASE, Cochrane Reviews, and a manual search of all pertinent references in the literature. The keywords used were craniotomy, post-craniotomy, pain management, analgesia and outcome.

**Opioids**

Opioids may lead to respiratory depression, CO₂ retention, increased blood flow and intracranial pressure. Codeine, oxycodone, hydrocodone, propoxyphene, and morphine are customarily used for post-craniotomy pain management. These drugs stimulate specific opioid receptors in the central and peripheral nervous system. The use of narcotics can generate several side effects, possibly resulting in delayed recovery and ambulation, and extended hospital stays.

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**Tramadol**

This lower cost analgesic propitiates efficient pain relief without the side effects of narcotic drugs. It’s use do not results in the side effects classically associated with opioids or the inhibition on platelets induced by NSAIDs. However, this medication is underused for the management of postoperative pain in neurosurgical patients.

Tramadol presents a small risk of seizure in addition to the high incidence of vomiting. Adverse events have been noted after tramadol administration, such as higher nausea and vomiting scores than morphine, codeine, or placebo.

The analgesic effects of tramadol are related to inhibition of serotonin and norepinephrine re-uptake, although the exact mechanism is not known. Tramadol do not produce alterations on coagulation function, but has a weak interaction with opioid receptors which can lead to nausea, vomiting, dry mouth, and dizziness. Use of tramadol after craniotomy appears to achieve better pain control, while allowing for the administration of smaller doses of narcotics with acetaminophen for pain control.

After 100 mg bolus administration, this monoaminergic drug achieves peak effect in about 60 minutes. However, after intravenous injection of nalbuphine this analgesic effect begins two to three minutes after injection, and the action peak is observed after 30 minutes. A recent research studied patients who underwent elective craniotomy for vascular, tumor and epilepsy procedures through blindly randomization into 1 of 2 groups. A control group of 25 patients received acetaminophen and a placebo (narcotics group) while 25 patients of experimental group received tramadol twice daily associated to narcotic pain.
medications (tramadol group). The authors concluded that tramadol group reduced the length of stay in hospital, reduced visual analogue scale (VAS) scores, and morphine need, when compared to control group. According Verchère (2002)\textsuperscript{12}, after supratentorial craniotomy, remifentanil cannot be managed with paracetamol alone. Addition of tramadol or nalbuphine is necessary to maintain a good analgesic level (VAS less than 30 mm). However, to reach this objective more rapidly and for a longer period of time is better to use nalbuphine.

Morphine

PCA propitiate to the patient a mechanism that permits control over their own pain. This method was reported as a subjectively better analgesic provider and results in overall lower opioid requirement\textsuperscript{43}. Its recommended that the total dose in 4 h should not exceed 40 mg. Ondansetron is routinely combined with PCA morphine to achieve higher satisfaction in analgesia and control of nausea and vomiting\textsuperscript{44}.

In a prospective randomized trial\textsuperscript{20} it was compared intramuscular codeine with PCA morphine (1 mg-bolus) with a 10-minute lockout and no background infusion. Results leaded to a non-significant reduction in pain scores in PCA group, however without any side effect related to use of morphine. In 1996, Goldsack et al.\textsuperscript{22}, compared use of 10mg intramuscular morphine and 60mg of intramuscular codeine in a double-blind trial. They demonstrated that morphine was more effective than codeine in terms of pain relief, fewer doses of morphine than codeine were required, and none of patients exhibited any form of respiratory depression, sedation, papillary constriction or unwanted cardiovascular effects.

Non-steroidal anti-inflammatory drugs (NSAIDS)

Non-steroidal anti-inflammatory drugs (NSAIDs) apparently are a good option in post-craniotomy pain management because reduce pain and morphine use necessity by 25% to 50\textsuperscript{45,46} and decrease opioid-induced side effects\textsuperscript{47}. The inhibition of prostaglandins caused by these agents reduces pain and inflammation\textsuperscript{48}.

The NSAIDs reduce thrombocyte aggregation, and their use generates risks for postoperative intracranial hematoma\textsuperscript{49}. However, despite paracetamol does not interfere with haemostatic system, this is not a popular choice to promote postoperative analgesia after craniotomy\textsuperscript{50}. They also inhibit the cyclooxygenase enzyme which has 2 distinct isomers: cox-1 and cox-2\textsuperscript{49}. Cox-2 isomers are useful in promote analgesia, but cox-1 isomers may lead to platelet dysfunction and increased bleeding times.

Diclofenac 100 mg rectally may be used every 18 h if there is a bleeding problem or renal insufficiency\textsuperscript{30}. However, administration of NSAIDs after craniotomy represents the major risk factor to perioperative bleeding\textsuperscript{40,41}.

In 1996, Quiney et al.\textsuperscript{4} defended use of NSAIDs for control the post-craniotomy pain. Paracetamol alone has failed to provide satisfactory analgesia after supratentorial surgery, but when associated with nalbuphen/tramadol\textsuperscript{42}, and ketoprofen and paracetamol with patient-controlled analgesia using oxycodone have proven to be effective\textsuperscript{48}.

Cyclo-oxygenase 2 inhibitors (COXIBS)

Risk of intracranial bleeding limits use of NSAIDs in neurosurgery, but cyclooxygenase 2 inhibitors (COXIBS) don’t present the same risk\textsuperscript{43-47}. These medications are capable of decrease post-operative craniotomy pain without an increased risk of postoperative hemorrhage\textsuperscript{16}. COXIBs are effective in perioperative analgesics for a variety of surgical procedures and presents morphine-sparing effects from 30% to 50\textsuperscript{16}. The limitation for use this drugs is related to increased risk of cardiovascular disease due to thromboembolic events\textsuperscript{55}.

A recent paper\textsuperscript{56} indicated only limited evidence to support parecoxibe as a post-craniotomy analgesic. The use of these alternative analgesics after craniotomy can lead to decreased use of narcotic medications, can decrease length of hospital stay, and improve patient satisfaction after a surgical procedure\textsuperscript{57}.

Gabapentin

Literature\textsuperscript{57} indicates that this new generation antiepileptic presents antinociceptive and antihyperalgesic properties. Ture et al. (2009)\textsuperscript{58}, verified that gabapentin (3 x 400 mg), seven day preoperatively and after surgery, was successful in relieve acute postoperative pain.

In this research\textsuperscript{59}, patients that received gabapentin had a lower anesthetic and analgesic requirement during and after craniotomy for supratentorial tumor resection. However, some collateral effects occurred such as larger sedation and delayed tracheal extubation. Authors suggest that new investigations, using varying doses of gabapentin, are needed. The same study relates that patients who received gabapentin presented a lower necessity of antiemetic therapy than those who received phenytoin (3 x 100 mg) apart from reduced necessity of opioid consumption and lower VAS.

Scalp nerve block

Infiltration of scalp with local anesthetic, scalp nerve block (SNB), is an accepted method for preventing and/or attenuating the post-craniotomy stress responses\textsuperscript{52,54}, however, this method remain under-utilized\textsuperscript{90}. Nguyen et al. (2001)\textsuperscript{16}, demonstrate in their study that a ropivacaine scalp block (20 ml of ropivacaine 0.75%) is efficient in decreasing postoperative pain after craniotomy. Authors purpose that pain management with the ropivacaine scalp block may be justified because of dense C fibers scalp innervation and main cause of pain after craniotomy seems to come from skin incision and muscle disinsertion, instead brain manipulation or resection.

Nevertheless, a prospective, randomized, single-blinded, controlled study\textsuperscript{41} suggests that scalp infiltration in the wound margins with ropivacaine (20 ml of ropivacaine 0.75%) have a limited efficacy to decrease acute postoperative pain after intracranial tumor resection. This research suggests that effects are much more pronounced in limiting the development of the chronic pain state, regardless of its inflammatory or neuropathic component.

In a prospective, randomized double-blind study Biswas and Bithal (2003)\textsuperscript{62} submitted patients to scalp infiltration with 25 ml of bupivacaine (0.25%) without adrenaline. Infiltration was effected over proposed line of incision after preparation of skin and before draping the patient with the intention of allowing a minimum of 10 minutes to pass prior to incision. Authors concluded that
compared with administration of intravenous fentanyl at 2 µg/kg diluted with normal saline to a volume of 5 ml/kg, five minu-tes prior to craniotomy, bupiva-caine scalp infiltration delayed the onset of demand for rescue analgesic. Another investigation involving bupi-vacaine scalp infiltration at 0.25% in 1:200,000 adrenaline before incision and after skin closure, demonstrated a decreased pain on admission to post-anesthesia care unit up to one hour. However is important to remember that use of adrenaline may lead to unprecid-t-able vasomotor activity. Ayoub et al. (2006), suppose that morphine at 0.1 mg/Kg administered after dural closure and a scalp nerve block (SNB) performed with 20 ml of 0.9% saline immediately after surgery seems to be equivalent to a SNB with 10 ml of 0.9% saline solution after dural closure and SNB performed with a 1:1 mixture of bupivacaine 0.5% and lidocaine 2% immediately after surgery, for temporary analgesia after remifentanil-based anesthesia.

**New trends**

Electromyography is a non invasive method that may lead to a more specific diagnosis of muscular unbalance pre-sented after craniotomy. The execution of this exam could contribute to a more effective therapeutic planning. In 2009, a research indicated that cryotherapy may be useful to control post-craniotomy pain through application of ice bags on surgical wound and cold gel packs on periorbital areas, initiating three hours after surgery, during three days, for 20 minutes per hour. This study contemplates 97 patients subjected to elective supratentorial craniotomy, separated in cryotherapy and control groups. The level of pain (visual analogue scale) three hours after craniotomy was the same to both groups, but cryotherapy significantly reduced pain three days after surgery.

**Conclusion**

Even with conventional pain management, the major part of patients experience post-craniotomy pain. The use of unusual approaches, such as scheduled nonopiods, associated to narcotics may reduce collateral effects related to nartocotic medications, stimulates precocious physical functional recovery, diminish the period of hospital internment and decline cost during hospitalization period. Is important that researchers establish future investigations focused on ideal protocols to control of pain after craniotomy, because only by this way will be possible to promote an improved and individualized pain management to this special group of patients.

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