Headache Medicine

Cephalalgia in Palliative Neuro-oncology: Understanding and Managing Discomfort

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Introduction
Headaches are experienced by 30-70% of patients with brain tumors and are the prevailing source of pain within this cohort, with the predominant etiologies often including elevated intracranial pressure, edema formation and direct cranial nerve compression. This manifestation becomes notably pronounced in palliative care scenarios, where the meticulous management of pain assumes notable significance to ensure the optimal comfort of the patient. Therefore, there arises a need for a comprehensive exploration of the treatment modalities specific to this category of cephalalgia, with a dedicated focus on therapeutic potential and specificity.

Objectives
Produce a comprehensive analysis of the therapeutic modalities accessible for palliative care in patients experiencing cephalalgia subsequent to the presence of brain tumors or following neuro-oncological interventions.

Methods
This systematic review adheres to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We conducted database searches using the keywords "Neuro-oncology," "Palliative," and "Headache", combined with the Boolean operator "AND," on PubMed and on ScienceDirect.

Results
Search across databases yielded a total of 17 relevant articles, with 9 being included in this study. The literature indicates that tumor- directed therapies generally lead to an improvement in headache symptoms. However, to refine the management of cephalgia associated with intracranial tumors, it becomes essential to delve into the underlying mechanisms of its pathogenesis. Regarding tumor-related edema, the conventional palliative therapeutic approach involving dexamethasone with gastric protection has demonstrated substantial efficacy in ameliorating symptoms, mainly due to its low short-term side-effect profile. Nevertheless, dexamethasone, being a corticosteroid, may pose diagnostic challenges when primary central nervous system lymphoma is under consideration, as it has the potential to compromise diagnostic accuracy and should be used judiciously. Furthermore, in end-of-life stages, advantages of corticosteroids should be weighed against side- effects, as it is paramount to administer steroids at the minimal effective dose, minimizing potential side effects. Additionally, a phased reduction in the steroid regimen should be contemplated upon achieving satisfactory control of symptoms. It is noteworthy that, within this clinical context, the concurrent use of non- steroidal anti-inflammatory drugs is generally discouraged due to their propensity to engender hemorrhagic complications at the tumor site and an elevated risk of gastric ulceration when coadministered with steroids. Neuropathic pain may originate from cranial nerve involvement, such as occipital nerve compression in cranio-medullary junction tumors. Near death, use of opioids increases and predominates, with opioid combinations such as hydrocodone or oxycodone with nonopioid analgesics being often needed to treat moderate headaches, while more severe cases may need higher potency opiates, such as morphine or hydromorphone. A potentially more effective alternative to corticosteroids in reducing cerebral edema is the VEGF inhibitor bevacizumab, although large prospective trials are lacking. Treatment-related headache is also very recurrent, as it often occurs in radiotherapy, with radiation-induced neurotoxicity occurring in 50– 90% of brain tumor patients, and also being the more frequent side effect after craniotomy, being treated, in this last case, with occipital nerve blocks, duloxetine, gabapentin, and tizanidine.

Conclusion
Managing headaches associated with intracranial tumors presents multifaceted challenges. Careful consideration of diagnostic implications, medication choices, and potential side effects is crucial, and tailoring treatment to the individual patient's needs is essential.

Keywords: Headache; Palliative Care; Neoplasms; Brain Neoplasms; Terminal Care.