

Review Article

Perioperative Seizure Prophylaxis in Supratentorial Meningioma Surgery

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Abstract

Background: Supratentorial meningioma is the most common primary intracranial tumor in adults. Perioperative seizures are a recognised concern, and prophylactic antiepileptic drugs (AEDs) are used inconsistently.

Objective: To synthesise evidence on perioperative seizure risk and prophylactic AED efficacy and safety in supratentorial meningioma surgery.

Methods: Narrative review of randomised trials, meta-analyses, cohort studies, and society guidelines on seizure prophylaxis in meningioma and brain tumor craniotomy.

Findings: Postoperative seizures affect roughly one in ten to one in five patients. Risk is concentrated among those with peritumoral oedema, convexity or parasagittal tumors, brain invasion, or subtotal resection. Trials of phenytoin and valproate show no reduction in seizures with routine prophylaxis, only added toxicity. Levetiracetam is comparably effective and better tolerated when prophylaxis is used.

Conclusions: Guidelines now recommend against routine prophylaxis in seizure-naïve patients, favouring individualised, risk-based decisions and prompt treatment once a seizure occurs.

Keywords: Meningioma; Seizure prophylaxis; Antiepileptic drugs; Levetiracetam; Craniotomy

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Keywords: meningioma; seizure prophylaxis; antiepileptic drugs; levetiracetam; craniotomy

Introduction

Meningiomas account for approximately 37-40% of primary intracranial tumors in adults, making them the most frequently encountered extra-axial neoplasm in neurosurgical practice [1]. Under the current World Health Organization classification, meningiomas are graded from I to III, with brain invasion alone now sufficient to upgrade a tumor's grade regardless of other atypical features [2]. Supratentorial meningiomas, particularly those over the cerebral convexity, parasagittal region, or falx, sit adjacent to cortex that is intrinsically epileptogenic, and both tumor-associated seizures before

surgery and new or recurrent seizures after resection are well-documented complications [3,4].

Because a perioperative seizure can precipitate raised intracranial pressure, aspiration, falls, or prolonged hospitalisation, many neurosurgeons have historically prescribed prophylactic antiepileptic drugs (AEDs) around the time of craniotomy for meningioma, extrapolating from broader brain tumor and traumatic brain injury literature. Phenytoin was for decades the default agent, followed more recently by levetiracetam, which requires no serum level monitoring and interacts less with other perioperative medications. Yet the evidence base for this practice, when scrutinised specifically, has consistently failed to demonstrate a clear benefit, while documenting real drug-related harm.

Practice in this area has also been shaped by parallel literatures on traumatic brain injury and other supratentorial craniotomies, where prophylactic phenytoin became routine in the 1980s and 1990s before its efficacy was ever confirmed specifically for tumor surgery. Meningioma surgery raises distinct considerations from trauma or glioma resection: many patients are seizure-naïve at presentation, tumors are frequently extra-axial and slow-growing, and the decision to operate is often elective, allowing more deliberate perioperative planning than emergency craniotomy permits. These features make meningioma surgery a particularly useful setting in which to ask whether blanket AED prophylaxis is justified, or whether a more selective, evidence-based approach targeting genuinely high-risk patients would better balance seizure prevention against drug toxicity, cost, and the burden of unnecessary medication in an already vulnerable postoperative population.

This review synthesises the epidemiology and risk factors for perioperative seizures in supratentorial meningioma

surgery, the randomised and observational evidence for and against prophylactic AED use, comparative data on phenytoin versus levetiracetam, and the resulting guideline recommendations from the American Academy of Neurology (AAN), the Society for Neuro-Oncology and European Association of Neuro-Oncology (SNO/EANO), and the Congress of Neurological Surgeons (CNS), with the goal of clarifying when, if ever, prophylaxis is justified.

Epidemiology and Risk Factors for Perioperative Seizures

Preoperative, tumor-associated seizures are common in supratentorial meningioma, particularly with convexity and parasagittal-falcine tumors, which lie closer to eloquent, seizure-prone cortex than skull-base lesions [4,5]. Early and late postoperative seizure rates reported across contemporary single- and multi-centre cohorts cluster broadly in the 10-20% range, varying with the definition of "early" (commonly the first postoperative week) versus longer follow-up, and with how rigorously seizures are ascertained [6,3,7,5].

A meta-analysis pooling risk-factor data across multiple series identified four independent predictors of postoperative seizures after meningioma surgery: a history of preoperative seizures, peritumoral oedema, non-skull-base (convexity or parasagittal) location, and subtotal rather than gross-total resection [8]. Peritumoral oedema has since been examined in a dedicated systematic review and meta-analysis, which confirmed its association with both preoperative and postoperative seizure risk, likely reflecting oedema-related cortical irritability and disruption of the blood-brain barrier around the tumor [9]. Brain invasion, the histological feature that alone upgrades a meningioma's WHO grade, has similarly been proposed as a factor worth exploring for its seizure-related and other prognostic implications, given its association with more aggressive local growth and peritumoral change [10]. A further single-centre

retrospective analysis corroborated the importance of tumor location and perioperative variables in distinguishing patients who develop early from those who develop late postoperative seizures, reinforcing that risk is not uniform across the meningioma population [11].

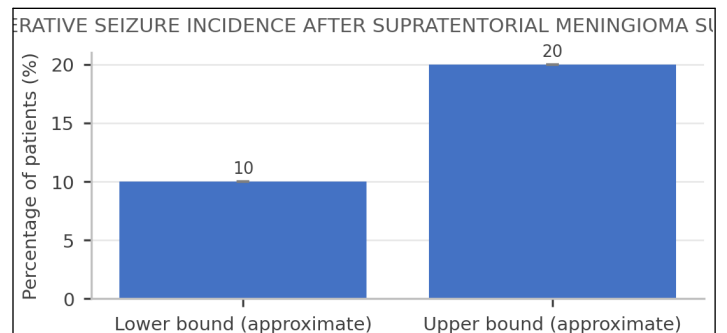


Figure 1: Approximate range of reported postoperative seizure incidence after supratentorial meningioma surgery across contemporary cohort studies, roughly 10-20% [6,3,7,5].

Together, these data support a risk-stratified rather than uniform view of perioperative seizure risk: patients with large convexity or parasagittal tumors, substantial peritumoral oedema, radiological or histological evidence of brain invasion, incomplete resection, or a preoperative seizure history are measurably more likely to seize than patients with small, skull-base, oedema-free tumors resected completely.

The clinical implication is that a single perioperative seizure incidence figure poorly describes the population undergoing supratentorial meningioma surgery, since it averages across groups with meaningfully different underlying risk. A patient with a small, incidentally discovered skull-base meningioma and no oedema faces a materially lower seizure risk than one with a large convexity tumor, marked oedema, and a preoperative seizure history, yet both have historically received similar perioperative AED regimens under blanket-prophylaxis policies. Recognising this heterogeneity is the first step toward the individualised approach discussed later in this review, and it also explains why trials enrolling unselected

supratentorial tumor or craniotomy populations may dilute any true effect of prophylaxis in the small subgroup that stands to benefit most.

Randomized and Observational Evidence on Prophylactic Antiepileptic Drugs

The randomised evidence for prophylactic AEDs in supratentorial tumor and craniotomy populations, including meningioma, is remarkably consistent in showing no benefit. An early double-blind trial of phenytoin versus placebo after craniotomy found no significant reduction in postoperative seizures, with more adverse effects in the phenytoin arm [12]. A subsequent trial addressing immediate and early postcraniotomy seizures reached a similar conclusion, finding no clear protective effect of prophylactic anticonvulsants [13]. A randomised, blinded, placebo-controlled trial of divalproex sodium in newly diagnosed brain tumor patients likewise failed to demonstrate a seizure-prevention benefit while adding haematological and other toxicity [14], and a later randomised study specifically testing whether add-on phenytoin could prevent early seizures after supratentorial brain tumor surgery again found no advantage over standard care [15]. A broader trial of prophylactic anticonvulsants in brain tumour patients confirmed the absence of seizure benefit alongside a measurable decrement in patient-reported quality of life and more side effects in the treated group [16].

Table 1: Randomised trials and meta-analyses of prophylactic antiepileptic drugs in supratentorial tumor and craniotomy populations [12,13,14,15,16,17,18].				
Study	Year	Design	Agent(s)	Key finding
North et al.	1983	Double-blind RCT	Phenytoin	No reduction in seizures; more adverse effects
Lee et al.	1989	RCT	Anticonvulsants	No clear protective effect on early seizures

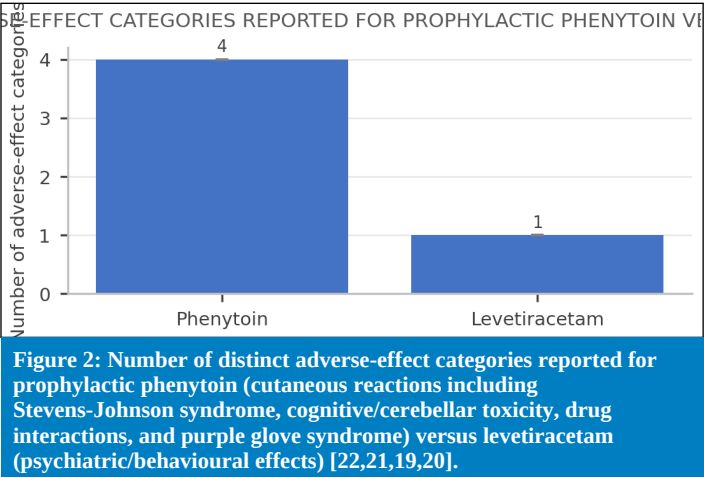
Study	Year	Design	Agent(s)	Key finding
Glantz et al.	1996	Placebo-controlled RCT	Divalproex sodium	No benefit; added haematologic toxicity
De Santis et al.	2002	RCT	Add-on phenytoin	No added benefit over standard care
Forsyth et al.	2003	RCT	Anticonvulsants	No benefit; worse quality of life, more side effects
Kuijlen et al.	1996	Meta-analysis	Phenytoin	No significant protective effect pooled across RCTs
Greenhalgh et al. (Cochrane)	2020	Systematic review	Various AEDs	Insufficient evidence to support routine prophylaxis

These individual trials are reinforced by synthesis-level evidence. A meta-analysis of prophylaxis used with supratentorial craniotomies found no significant protective effect of phenytoin across pooled randomised data [17], and the Cochrane systematic review of AEDs as prophylaxis for postcraniotomy seizures concluded that the available trials, though limited in number and quality, do not support a reduction in seizure occurrence with routine prophylaxis compared with placebo or no treatment [18]. Taken together, this body of evidence indicates that routinely administering prophylactic phenytoin or valproate to seizure-naïve patients undergoing supratentorial meningioma resection is unlikely to prevent seizures and carries an appreciable burden of avoidable adverse effects.

Choice of Agent: Phenytoin versus Levetiracetam

Where clinicians nonetheless elect to use short-course perioperative prophylaxis, comparative data favour levetiracetam over phenytoin on tolerability grounds, with broadly similar efficacy. A study comparing levetiracetam with phenytoin after supratentorial neurosurgery found comparable seizure control between agents, but fewer treatment-limiting side effects, such as rash and cognitive slowing, with levetiracetam [19]. A systematic review and meta-analysis focused specifically on prophylactic

levetiracetam in supratentorial brain tumour surgery corroborated this pattern, reporting seizure rates statistically indistinguishable from phenytoin alongside a more favourable safety profile and fewer severe adverse events [20].



This more favourable tolerability does not, however, come without cost. Levetiracetam carries a well-documented risk of psychiatric and behavioural adverse effects, including irritability, mood disturbance, and, rarely, frank psychosis, which can complicate postoperative recovery and must be weighed against its convenience [21]. Phenytoin, for its part, remains associated with cutaneous reactions ranging from mild rash to Stevens-Johnson syndrome, cerebellar and cognitive toxicity with sustained use, numerous drug interactions relevant to perioperative and oncological care, and, with intravenous administration, the rare but serious purple glove syndrome of limb oedema and discolouration at the infusion site [22]. Neither agent is free of risk, which strengthens rather than weakens the argument that any prophylactic AED use should be time-limited and reserved for situations of genuinely elevated risk rather than applied uniformly across an entire surgical population regardless of each patient's individual likelihood of seizure.

Guideline Recommendations and Clinical Practice

Society guidance has moved steadily away from routine prophylaxis. The AAN's original practice parameter recommended against continuing prophylactic AEDs beyond the immediate postoperative period in patients with newly diagnosed brain tumors who had not had a seizure, advising tapering within the first postoperative week in the absence of seizure activity [23]. The subsequent SNO/EANO practice guideline update reaffirmed this position with more contemporary evidence, explicitly recommending against routine seizure prophylaxis in seizure-naïve patients with newly diagnosed brain tumors, including around the time of craniotomy [24]. The Congress of Neurological Surgeons' evidence-based guideline, though framed around metastatic brain tumors, reached a concordant recommendation against routine prophylactic anticonvulsants beyond the immediate perioperative window in seizure-naïve patients, a position widely extrapolated to primary tumors including meningioma [25]. The EANO guideline dedicated specifically to meningioma likewise supports treating patients who have had a seizure rather than prophylactically treating all comers, consistent with the broader brain tumor literature [26].

Table 2: Society guideline recommendations on prophylactic antiepileptic drug use in newly diagnosed brain tumor and meningioma patients [23,24,25,26].			
Guideline (year)	Scope	Recommendation	Source
AAN practice parameter (2000)	Newly diagnosed brain tumors	Taper AED within first postoperative week if seizure-free	glantz2000
SNO/EANO update (2021)	Newly diagnosed brain tumors	Against routine prophylaxis in seizure-naïve patients	walbert2021
CNS guideline (2019)	Metastatic brain tumors	Against routine prophylaxis beyond immediate postoperative window	chen2019

Guideline (year)	Scope	Recommendation	Source
EANO meningioma guideline (2021)	Meningioma	Treat seizures when they occur rather than prophylax all patients	goldbrunner2021

In aggregate, these guidelines converge on a common framework: avoid routine, indefinite prophylactic AED use in seizure-naïve supratentorial meningioma patients; reserve any short perioperative course for individually judged high-risk situations, informed by the risk factors described above; discontinue promptly if no seizure occurs; and initiate standard antiepileptic treatment, rather than prophylaxis, in any patient who experiences a preoperative or postoperative seizure. This individualised approach reflects the balance between a modest, concentrated seizure risk in a recognisable subgroup and the consistent lack of benefit, plus real harm, from blanket prophylaxis.

Conclusion

Perioperative seizures in supratentorial meningioma surgery are neither rare nor inevitable: they cluster among patients with convexity or parasagittal tumors, peritumoral oedema, brain invasion, incomplete resection, and prior seizures, while patients without these features carry a comparatively low risk. Decades of randomised trials and meta-analyses of phenytoin and valproate prophylaxis, together with a Cochrane systematic review, have failed to show that routine AED prophylaxis reduces this risk, while documenting genuine drug-related harm. When prophylaxis is used, levetiracetam offers similar efficacy to phenytoin with a generally more favourable, though not risk-free, tolerability profile. Current AAN, SNO/EANO, CNS, and EANO-meningioma guidance therefore converges on an individualised, risk-stratified strategy rather than routine prophylaxis: identify high-risk patients using established predictors, limit any prophylactic course to the immediate

perioperative period, and treat seizures as they occur rather than pre-emptively medicating every patient undergoing supratentorial meningioma resection.

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