

Clinical Questions #4

*Editor's note:
This is the fourth
installment in a
series of "Clinical
Questions."
Readers are pre-
sented with a case
and clinical ques-
tion. An evidence-
based answer is
provided on a later
page. The answer
includes how the
evidence was found
and evaluated.*

Do Prophylactic Anticonvulsants in Patients with Brain Tumors Decrease the Incidence of Seizures?

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Patient

A 54-year-old male presents to an emergency department (ED) at an outside hospital with a 2-3 month history of worsening headaches, decreased visual acuity, and diplopia. A CT scan of the head shows two mass lesions. The ED physician requests transfer care to your facility. The patient has no previous history of seizures but the ED physician asks if you would like him to give the patient a loading dose of phenytoin prior to transfer for seizure prophylaxis.

Clinical Question

In patients with brain tumors, do prophylactic anticonvulsants decrease the rate of seizures?

How and where could you locate evidence to answer this question?

How would you treat this patient?

Turn the page for one possible approach.

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Suggested Approach for Clinical Question #4

1. Cochrane Database of Systematic Reviews (2nd Quarter 2005) using OVID interface:
 - a. Brain neoplasm
 - b. "brain metasta\$" (truncation symbol)
 - c. Anticonvulsants
 - d. Combine ([a] or [b]) and (c)
 - e. 1 pending systematic review
 - i. Tremont-Lukats, et al. Anti-epileptic drugs in preventing seizures in people with brain tumors. Cochrane Epilepsy Group. Cochrane Database of Systematic Reviews. 2, 2005.
2. Search all years of MEDLINE (1966 to June Week 3 2005) using Ovid Interface:
 - a. "exp Brain Neoplasms" (exploded MeSH Heading)
 - b. "brain metasta\$" (keyword)
 - c. "exp Anticonvulsants" (exploded MeSH Heading)
 - d. Combine ([a] or [b]) and (c) limited to English Language and Human Studies
 - e. "random\$" (keyword) Used to limit the results to randomized trials
 - f. Combine (d) and (e)
 - g. 37 studies:
 - i. 2 individual trials
 - ii. 1 systematic review: Servin JI, et al. seizure prophylaxis in patients with brain tumors: a meta-analysis.

Study Characteristics

- Systematic review and meta-analysis.
- Objective was to determine if antiepileptic drugs are beneficial in patients with brain tumors and no history of seizures.

Validity of Evidence

- Addresses a focused clinical question and includes appropriate inclusion and exclusion criteria.
- Includes only randomized controlled trials.
- Outlines an extensive search for all relevant trials including MEDLINE, EMBASE, CINAHL, the Cochrane Library and Best Evidence databases. Additional searches for relevant published abstracts in both English and non-English journals were also performed. There is no mention of searching for unpublished data.
- Assesses methodologic quality of individual trials. The authors evaluated certainty of seizure diagnosis, randomization method, allocation concealment, number of patients lost to follow up, serum anticonvulsant levels, length of follow up. However, the quality of each trial is not reported.
- The results were consistent from study to study with no heterogeneity between trials ($P=0.19$).
- Overall, this was a well done systematic review.

Results

- Five trials comprising 403 patients objectively diagnosed with a brain tumor met inclusion criteria.
- These trials included primary glial tumors, meningiomas and cerebral metastasis.
- Three of the 5 trials included patients who had undergone surgical debulking or resection of their disease.
- The anticonvulsants studied included phenobarbital, phenytoin and valproic acid.
- Odds ratio of new onset seizure with 95% confidence interval: 0.91 (0.45–1.83).
- No significant decrease in seizures in the subgroup analysis by tumor type or antiepileptic used.

Applying the Evidence to the Patient

- Our patient is similar to those in the studies and therefore we can expect to see similar results.
- The treatment option is definitely feasible for our patient.

Summary

The well-done systematic review included a moderate number of patients from randomized controlled trials with an objective diagnosis of a brain tumor. There were mild differences between the 5 studies used in the systematic review with patients in 3 of the studies undergoing surgical resection or debulking of their disease. There was no evidence of seizure prevention overall or in the subgroup analysis. Given the small number of patients in each subgroup, these results should be interpreted with caution. Known adverse effects with anticonvulsant therapy include severe rash (including Stevens-Johnson syndrome), hematologic effects, and drug-drug interactions. Therefore, we should be hesitant to place patients on these medications without a proven benefit. The relatively small number of patients in this meta-analysis means that larger scale studies could show a small clinical benefit from anticonvulsants.

Conclusion

There is no evidence that prophylactic anticonvulsant therapy decreases the incidence of seizures in patients with brain tumors and no history of seizures. The patient should not be started on phenytoin.

References

1. Sirven J, Wingerchuk D, Dratzkowski J, Lyons M, Zimmerman R. Seizure prophylaxis in patients with brain tumors: a meta-analysis. *Mayo Clinic Proc.* 2004;79(12):1489-1494.
2. Sackett DL. *Evidence-Based Medicine: How to Practice and Teach EBM.* 2nd ed. Churchill Livingstone; 2000.