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Efficacy and safety of prophylactic levetiracetam in patients with brain tumors : a meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None financial support.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 June 2023 and was last updated on 29 June 2023.

INTRODUCTION

Review question / Objective The aim of this meta-analysis is to evaluate the efficacy and safety of LEV for preventing seizures in adult brain tumor patients. Through the meta-analysis of the seizure rate and side effects of related studies, it is judged whether levetiracetam can prevent epilepsy in adult patients with brain tumors, and whether it is more effective and safe than other antiepileptic drugs.

Condition being studied Epilepsy is a common symptom in patients with brain tumors. Surgical resection of the tumor and combined drug therapy are often used to control epilepsy clinically. However, the prophylactic use of antiepileptic drugs in patients with brain tumors is still controversial. Moreover, previous studies in this field mostly focused on traditional antiepileptic drugs such as sodium valproate and phenytoin, but lacked analysis of new generation antiepileptic drugs such as levetiracetam. In order to systematically evaluate the preventive effect of levetiracetam on seizures and adverse drug reactions in patients with brain tumors, we summarized and meta-analyzed the relevant literature in the past 15 years to provide a certain reference value for clinical treatment consensus and guidelines.

METHODS

Participant or population Inclusion criteria for patients: Brain tumor patients over 18 years old who underwent craniotomy or biopsy , and LEV was given to prevent seizures. Patient under 18 years of age, pregnancy, breastfeeding, severe complications (including renal failure and liver

failure), and craniotomy for diseases other than brain tumors will be excluded of the study.

Intervention Articles that LEV administration as seizure prophylaxis in patients who underwent supratentorial craniotomy for brain tumor were eligilble for inclusion. Furthermore, studies comparing LEV administration to no antiepilptic drug, valproate, and phenytoin were also included.

Comparator Comparison of levetiracetam and other antiepileptic drugs(for example, VPA or PHT) for the prevention of seizures in patients with brain tumors.

Study designs to be included Randomized controlled trials studies, non-randomized studies, prospective cohort studies and retrospective studies.

Eligibility criteria Diagnostic criteria for seizures were based on clinical observations or EEG.Side effects of antiepileptic drugs included somnolence, nausea/vomiting, headache, insomnia or other rare side effect.

Information sources Embase®, PubMed®, Cochrane Library, Web of Science, CNKI.

Main outcome(s) Primary outcome measures were the efficacy and the safety of LEV. Efficacy was defined either by the appearance or not of seizures or the reduction in the incidence of seizures during the study period. Safety was defined by the reports of side effects (severe, moderate and zero), which were directly attributable to LEV. A secondary outcome measure was the tolerability of the specific regimen, defined by the discontinuation of the treatment due to side effects.

Quality assessment / Risk of bias analysis We adopted the Newcastle-Ottawa Scale (NOS), a general tool for literature quality evaluation to evaluate literature quality, mainly from three aspects: (1) selection of cases; (2) Comparability; (3) Evaluation of results; Full score is 9 point, more than 5 point means good quality. An assessment of reporting biases (such as publication bias) by constructing a funnel plot and using tests for funnel plot asymmetry was planned if there were at least ten studies included in the meta-analysis.

Strategy of data synthesis Binary outcomes were calculated as odds ratio (OR). Statistical heterogeneity among studies was evaluated using Cochran's Q test and Higgins I2 statistics. If I2 > 50% or $p < 0.10$ (indicating significant heterogeneity among studies), the data were combined using a random effects model.

Subgroup analysis According to the type of the control group, we make subgroup analysis of sources of heterogeneity（non use AED、VPA and PHT).

Sensitivity analysis By excluding one document one by one, the remaining documents (n-1) are merged and analyzed, and by observing the changes in the merged results, it is assessed whether the original Meta-analysis results have changed significantly due to the influence of certain studies, so as to determine whether the original Meta-analysis results are stable.

Country(ies) involved China.

Keywords brain tumour, levetiracetam, meta-analysis, prophylaxis, seizures.

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