Study Protocol

Assessing the therapeutic potential of dendritic cell vaccine in glioblastoma: a protocol for systematic review and meta-analysis

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Abstract

This study seeks to gather evidence-based information on the therapeutic effect of dendritic cell vaccines in treating glioblastoma. This protocol will follow the criteria of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guideline for 2020. In this review, we determined four primary central databases as sources of information: PubMed, Embase, Scopus and the Cochrane Central Register of Controlled Trials. Ethical approval for this study was unnecessary, as we already used published studies. Study findings will be published in journals and presented at conferences for broader dissemination.

Highlights

1. The most common and dangerous primary malignant brain tumor, glioblastomas (GBM), are still tricky and challenging to treat.
2. Even with multimodal treatment, victims’ median survival is just 15 months.
3. Active immunotherapy called dendritic cell vaccines (DCV) aims to trigger an anticancer immune system reaction.
4. Hundreds of GBM patients have been vaccinated in numerous DCV trials, which have confirmed the vaccine’s viability and safety.
5. This study aims to assess the rationalistic effect of dendritic cell vaccines for treating GBM.

INTRODUCTION

Rationale

The most common and dangerous primary malignant brain tumor, glioblastomas (GBM), are still tricky and challenging to treat. Even with multimodal treatment, victims’ median survival is just 15 months. Active immunotherapy called dendritic cell vaccines (DCV) aims to trigger an anticancer immune system reaction [1, 2].

Hundreds of GBM patients have been vaccinated in numerous DCV trials, which have confirmed the vaccine’s viability and safety. Many of these research results showed better survival following DCV and the activation of an anticancer immune response. However, a survival benefit was not shown in two randomized controlled studies. This makes one wonder if the hopeful idea behind DCV is genuine or if its full therapeutic potential has not yet been realized [1].

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OBJECTIVES
Primary objective
The primary aim is to assess the rationalistic effect of dendritic cell vaccines for treating GBM.

Secondary objectives
1. To significantly assess the therapeutic effects of dendritic cell vaccine in treating GBM.
2. To provide an overview of the dendritic cell vaccine’s preparation, administration and application.
3. To evaluate the effectiveness and safety of dendritic cell vaccines in treating GBM.
4. To evaluate the neurological functional recovery post-dendritic cell vaccine administration in the treatment of GBM.

MATERIALS AND METHODS
Period of study
From inception to the 15th of February 2024.

The population of study
Patients diagnosed with GBM.

Inclusion criteria
All observational studies: case-control and cohort studies and randomized and non-randomized controlled clinical trials describing the use of dendritic cell vaccine in treating GBM, and only articles reported in English will be included.

Exclusion criteria
Case reports, case series, abstract-only articles, letters to the editor, conference proceedings, review articles, articles with missing data in other languages and those reporting animal studies will be excluded. Studies describing the use of dendritic cell vaccines in non-GBM patients and other disease conditions will also be excluded.

Information source
Articles for our study will be sourced from PubMed, Embase, Scopus, Web of Science and Cochrane Central.

Search strategy


DATA MANAGEMENT
Study selection
The database literature search result will be downloaded and uploaded to the digital repository; Rayyan (ref) will conduct deduplication and an initial title and abstract screening by two blinded independent reviewers. Conflicts will be resolved through discussion between the review team, and if no consensus is reached, another independent author will adjudicate any conflict.

Table 1. PubMed electronic database search strategy of 5 July 2023

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Results</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>#3</td>
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<td>13:18:30</td>
</tr>
<tr>
<td>#1</td>
<td>Search: (therapeutic effect) AND (dendritic cell vaccine)) AND (glioblastoma)</td>
<td>43</td>
<td>13:15:34</td>
</tr>
</tbody>
</table>
The included articles will then undergo a full-text screening against the stated inclusion criteria, followed by a final screening to evaluate the risk of bias. A Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram will be used to depict the study’s selection process.

Data extraction
A standardized data extraction form to record the information from each study shall be used. Covidence, a software tool, may also facilitate data extraction and management. Information on the following aspects of each study will be extracted: authors, year, country, study design, sample size, population characteristics, intervention details, comparator details, outcome measures, follow-up duration, results and risk of bias assessment. Any missing or unclear data shall also be recorded and reported, and the original authors shall be contacted where needed be. Two independent reviewers shall perform data extraction and resolve discrepancies by discussing or consulting with a third reviewer.

CHARTING THE DATA
Measurement of effect
We will use the pooled hazard ratio for randomized clinical trials reporting on the event-to-time outcomes, relative risk or pooled mean difference to estimate the effect of dendritic cell vaccine (DCV) on the prognostic outcomes of patients with GBM.

Outcome and prioritization
Primary outcome
Mortality rate, survival rate and incidence of complications.

Secondary outcome
Pain scores, mean length of stay. If other secondary outcomes are identified.

Risk of bias in individual studies
The authors will independently assess the quality of studies based on the Newcastle–Ottawa Scale 10, a tool for assessing the risk of bias in observational studies.

DATA SYNTHESIS
The following data synthesis will be carried out:

1. Meta-analysis and forest graphs will be synthesized if the studies are clinically homogenous.
2. The scoping summary and table will be synthesized if the studies are clinically heterogeneous.

SUBGROUP ANALYSIS
In cases where we face significant heterogeneity, the outcomes shall be divided into categories, and a pooled subgroup analysis will be conducted to minimize the risk of bias.

PATIENT AND PUBLIC INVOLVEMENT
No patient was involved in the study, as we used already published studies.

STRENGTH OF BODY OF EVIDENCE
In recent research studies, dendritic cell vaccines have been explored for their therapeutic potential in treating GBM. These findings add to the growing evidence that supports the benefits of this treatment approach.

In a randomized clinical phase III trial found a significant improvement in overall survival among GBM patients treated with dendritic cell vaccines [3]. Similarly, a recent controlled clinical trial reported that patients with GBM who received a dendritic cell vaccine showed improved survival rates compared with those receiving standard care [4].

The preparation, administration and application of dendritic cell vaccine have a lot been well-documented in the literature [5]. The safety profile of these vaccines has been examined, with most studies reporting mild to moderate side effects mainly related to immune reactions [6].

However, the evidence regarding neurological functional recovery post-dendritic cell vaccine administration is still limited. More research is needed to evaluate this critical aspect of GBM treatment [7].

In conclusion, while there exists supporting evidence for the therapeutic efficacy of dendritic cell vaccines in the treatment of GBM it is essential to conduct well-designed randomized control studies and comprehensive systematic reviews to establish their safety and effectiveness. Further research is required to validate the potential of dendritic cell vaccines as a viable treatment option for GBM.

ETHICS AND DISSEMINATION
This systematic review of published articles on the therapeutic effect of dendritic cell vaccines for treating GBM is a novel approach to determining the breadth of the literature available on the subject. Therefore, as a secondary analysis, it will not require ethical approval. We also anticipate that the results of this study will reveal research gaps and more profound ideas on the subject. The findings will be published in journals and presented at conferences for broader dissemination.

LIMITATIONS
Despite the meticulous methods used in this systematic review and meta-analysis, some limitations must be addressed. First and foremost, a bias in papers published could occur because those with significant findings have a greater probability of being published compared with studies with insignificant findings. This could cause our analysis to overstate the dendritic cell vaccine’s therapeutic effect in treating GBM. In addition, relevant research. We may have missed some research that was only published in other languages, as we only reviewed studies published in English.

Furthermore, the studies included in this systematic review could be prone to bias, which could affect the result of our analysis.

CONFLICT OF INTEREST STATEMENT
None declared.

FUNDING
None declared.
AUTHORS’ CONTRIBUTION


REFERENCES


