INPLASY PROTOCOL

To cite: Liu et al. The efficacy and safety of butylphthalide combined with donepezil in the treatment of vascular dementia: A meta-analysis. Inplasy protocol 202310057. doi: 10.37766/inplasy2023.1.0057

Received: 18 January 2023

Published: 18 January 2023

Corresponding author:
Puiqing Liu

liupuqing508@163.com

Author Affiliation:
The Second Clinical Medical School of Zhejiang Chinese Medical University.

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

The efficacy and safety of butylphthalide combined with donepezil in the treatment of vascular dementia: A meta-analysis

Liu, PQ[1]; Chen, JW[2]; Chen, J[3]; Wang, XF[4]; Shou, ZX[5].

Review question / Objective: **The efficacy and safety of butylphthalide combined with donepezil in the treatment of vascular dementia: Ameta-analysis.**
Condition being studied: **Vascular dementia is the second most common cause of dementia and a major health concern worldwide, only after to Alzheimer's disease. As the increasing aging of the global population, the number of vascular dementia patients is expected to increase year by year, which will bring great economic burden to all countries in the world. In recent years, more and more published RCT studies have shown that butylphthalide can further improve behavioral ability and dementia symptoms in vascular dementia patients based on donepezil treatment. Our study aimed to systematically evaluate the efficacy and safety of butylphthalide combined with donepezil in the treatment of vascular dementia through meta-analysis, providing an objective and scientific reference for the clinical use of butylphthalide.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 January 2023 and was last updated on 18 January 2023 (registration number INPLASY202310057).

INTRODUCTION

Review question / Objective: **The efficacy and safety of butylphthalide combined with donepezil in the treatment of vascular dementia: Ameta-analysis**

Condition being studied: **Vascular dementia is the second most common cause of dementia and a major health concern worldwide, only after to Alzheimer's disease. As the increasing aging of the global population, the number of vascular dementia patients is expected to increase year by year, which will bring great economic burden to all countries in the world. In recent years, more and more published RCT studies have shown that**

butylphthalide can further improve behavioral ability and dementia symptoms in vascular dementia patients based on donepezil treatment. Our study aimed to systematically evaluate the efficacy and safety of butylphthalide combined with donepezil in the treatment of vascular dementia through meta-analysis, providing an objective and scientific reference for the clinical use of butylphthalide.

METHODS

Participant or population: The patients were diagnosed with Vascular Dementia according to Clinical Diagnostic Criteria of Vascular Dementia.

Intervention: Butylphthalide in combination with donepezil was the main intervention.

Comparator: Donepezil was the main comparator.

Study designs to be included: Randomized controlled trials will be included.

Eligibility criteria: (1) Patients: the patients were diagnosed with Vascular Dementia according to Clinical Diagnostic Criteria of Vascular Dementia. (2) Intervention: the experimental group patients were given donepezil tablets in combination with butylphthalide soft capsules 0.2g each time, 3 times a day; the control group patients were only given donepezil tablets, usually 5mg once every day (15mg for some severe patients in the study). There is no limit to the course of treatment, most of them about 3 months. And Other basic treatment measures were similar between experimental group and control group. (3) Outcomes: the primary outcomes included total effective rate and incidence of adverse events; the secondary outcomes included Mini-Mental State Examination (MMSE) score, ability of daily living (ADL) score, montreal cognitive assessment (MOCA) score, interleukin 6 (IL-6), tumor necrosis factor α (TNF-α), superoxide dismutase (SOD) and homocysteine (Hcy). (4) Study style: randomized controlled trials (RCTs), blind or not were included, including Chinese and English literature.

Information sources: Randomized controlled trials (RCTs) of butylphthalide combined with donepezil on vascular dementia were collected through PubMed, EMBASE, Cochrane Library, CNKI, VIP, WanFang and CBM databases. The retrieval time was from November 29, 2022.The search used a combination of subject words and free words, and traced the references of the included literature to supplement the acquisition of relevant literature by two reviewers independently from inception to November 29, 2022. Search terms included vascular dementia / vascular cognitive impairment, 3-n-butylphthalide, donepezil, randomized controlled trial/RCT.

Main outcome(s): The main outcomes included total effective rate and incidence of adverse events.

Additional outcome(s): Additional outcomes included Mini-Mental State Examination (MMSE) score, ability of daily living (ADL) score, montreal cognitive assessment (MOCA) score, interleukin 6 (IL-6), tumor necrosis factor α (TNF-α), superoxide dismutase (SOD) and homocysteine (Hcy).

Quality assessment / Risk of bias analysis: The bias risk assessment was carried out independently by two reviewers according to bias risk assessment tool of Cochrane Manual 5.1.0 version. And it was performed using the Revman5.4 software, including the items as following: (1) Random sequence generation, (2) Allocation concealment, (3) Blinding of participants and personnel, (4) Blinding of outcome assessment, (5) Incomplete outcome data, (6) Selective reporting, (7) Others. The results of bias risk assessment will be shown in a figure or graph indicating low, high or unclear.

Strategy of data synthesis: We used RevMan5.4 statistical software to perform the meta-analysis study. The binary variable outcomes were compared using

relative risk (RR), while continuous variable outcomes were compared using mean difference (MD), and all were expressed with 95% confidence interval (CI). The heterogeneity of the included studies were tested: If I2＜50% and P > 0.1, there is no heterogeneity. And the Fixed-Effect Model should be chosen for meta-analysis. If 50%≤I2≤75% and P＜0.1, there is mild to moderate heterogeneity. The heterogeneity analysis could be carried out to identify the source of heterogeneity. And the Random-Effect Model should be chosen for meta-analysis. If I2 > 75%, it indicated statistical heterogeneity existing among the studies, which made it inappropriate to do meta-analysis. In this situation, a descriptive analysis may be considered.

Subgroup analysis: We will consider subgroups such as course of treatment, donepezil dosage and severity of vascular dementia.

Sensitivity analysis: We will conduct the sensitivity analysis through excluding articles one by one to find the source of heterogeneity.

Country(ies) involved: China.

Keywords: butylphthalide, donepezil, vascular dementia, meta-analysis.

Contributions of each author:

Author 1 - Puqing Liu - search literature, assess literature quality, extract data and draft the manuscript.
Email: liupuqing508@163.com
Author 2 - Jingwen Chen - search literature, assess literature quality and extract data.
Email: jingwenahmu@163.com
Author 3 - Jun Chen - participate in discussion of study results.
Email: chenjun5869@163.com
Author 4 - Xuefeng Wang - guide Revman5.4 software operation and assist data analysis.
Email: wxfeng360@sina.com
Author 5 - Zhangxuan Shou - guide and support the implementation of this meta-analysis study.
Email: 20214021@zcmu.edu.cn

Support: This study was supported by grants from the provincial Natural Science Foundation of Zhejiang (LYY22H280001), Zhejiang Traditional Chinese Medicine Science and Technology Plan Project (2022ZB161) and Department of Healthcare in Zhejiang (2022482619).