INPLASY PROTOCOL

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None declared.

Vitamin D supplementation in the treatment of Myasthenia Gravis A protocol for a systematic review and meta-analysis

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Review question / Objective: **The patients should meet the internationally recognized diagnostic criteria for myasthenia gravis and be definitely diagnosed as myasthenia gravis, excluding MG patients caused by congenital, drug and other factors, as well as patients with serious primary diseases, autoimmune diseases or mental diseases. Patients are not restricted by race, region, gender, age, background, course of disease and other factors. We will focus on trials using vitamin D as an intervention at any dose and in any regimen (eg daily/ weekly/monthly intake). The control group was routinely given western medicine, including cholinesterase inhibitors, glucocorticoids, immunosuppressants, alone or in combination, or placebo. The intervention group was treated with vitamin D on the basis of western medicine treatment in the control group. The specific dosage form and dose were not limited, and the shortest course of treatment should be 4 weeks. Main outcome measures: (1) Quantitative score of myasthenia gravis (QMG); (2) Recurrence rate; (3) Effective. Secondary outcome measures: (1) The level of serum acetylcholine receptor antibody (AchRab); (2) The levels of inflammatory factors such as IL-6 and IL-10; (3) Clinical absolute score; (4) TCM syndrome score scale; (5) Quality of life score (QOL); (6) Incidence rate of adverse events. All randomized controlled trials (RCT) literatures from the establishment to September 2022 were retrieved and classified.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 September 2022 and was last updated on 30 September 2022 (registration number INPLASY202290129).

INTRODUCTION

Review question / Objective: **The patients should meet the internationally recognized diagnostic criteria for myasthenia gravis and be definitely diagnosed as myasthenia gravis, excluding MG patients caused by congenital, drug and other factors, as well as patients with serious primary diseases, autoimmune diseases or mental diseases.**

Patients are not restricted by race, region, gender, age, background, course of disease and other factors. We will focus on trials using vitamin D as an intervention at any dose and in any regimen (eg daily/ weekly/monthly intake). The control group was routinely given western medicine, including cholinesterase inhibitors, glucocorticoids, immunosuppressants, alone or in combination, or placebo. The intervention group was treated with vitamin D on the basis of western medicine treatment in the control group. The specific dosage form and dose were not limited, and the shortest course of treatment should be 4 weeks. Main outcome measures: (1) Quantitative score of myasthenia gravis (QMG); (2) Recurrence rate; (3) Effective. Secondary outcome measures: (1) The level of serum acetylcholine receptor antibody (AchRab); (2) The levels of inflammatory factors such as IL-6 and IL-10; (3) Clinical absolute score; (4) TCM syndrome score scale; (5) Quality of life score (QOL); (6) Incidence rate of adverse events. All randomized controlled trials (RCT) literatures from the establishment to September 2022 were retrieved and classified.

Condition being studied: Myasthenia gravis (MG) is an autoimmune disease related to the production of autoantibodies. It is mediated by antibodies against acetylcholine receptor (AChR), muscle specific kinase (MuSK) or other AChR related proteins in the postsynaptic muscle membrane, which interfere with the transmission of signals at the neuromuscular junction, resulting in clinical symptoms of skeletal muscle weakness and fatigue, leading to the occurrence and development of MG. At present, the incidence rate of Mg is increasing year by year. Vitamin D is a kind of vitamin with immune regulation effect. Research shows that with the continuous progress of MG severity, the vitamin D level of patients continues to decline. The purpose of this study was to systematically evaluate the efficacy and safety of vitamin D supplementation in the treatment of myasthenia gravis.

METHODS

Participant or population: The patients should meet the internationally recognized diagnostic criteria for myasthenia gravis and be definitely diagnosed as myasthenia gravis, excluding MG patients caused by congenital, drug and other factors, as well as patients with serious primary diseases, autoimmune diseases or mental diseases. Patients are not restricted by race, region, gender, age, background, course of disease and other factors.

Intervention: The intervention group was treated with vitamin D on the basis of western medicine treatment in the control group. The specific dosage form and dose were not limited, and the shortest course of treatment should be 4 weeks.

Comparator: Western medicine treatment.

Study designs to be included: RCT.

Eligibility criteria: 1. Articles that are inconsistent with the outcome indicators of this study.2. Articles for which the full text is not available and the author of the communication is still unable to obtain the relevant data and information.3. Articles in which the data is missing and the contact author is still unable to obtain complete data.4. Non-clinical randomized controlled trials, such as self-control, retrospective studies, reviews, etc.

Information sources: We will search from the following eight databases: PubMed, Cochrane Library, EMBASE, Web of Science, CNKI, Sinomed, Wanfang and Vip. All randomized controlled trials on the efficacy and safety of vitamin D supplementation in the treatment of myasthenia gravis from the establishment to September 2022 were retrieved. Search the medical subject title (MeSH), free text words, synonyms and related search terms of "vitamin D", "efficiency", "myasthenia gravis", "randomized controlled trial" and "placebo". In addition, where possible, RCT's standard search terms will be used additionally. There is no plan restriction in the search strategy to prevent ignoring

important research that is not correctly classified in their respective bibliographic databases. All databases will be searched from the beginning of the database without time limit.

Main outcome(s): (1) Quantitative score of myasthenia gravis (QMG); (2) Recurrence rate; (3) Effective.

Quality assessment / Risk of bias analysis: Cochrane risk of bias tool (RoB 2.0) will be conducted: randomization process, deviations from the intended interventions, missing outcome data, outcome measurements, selection of the reported results, and overall bias according to the three criteria of "low risk", "high risk" or "some concerns".

Strategy of data synthesis: Data will be statistically analyzed using RevMan 5.3 software. First, the results of a single study will be described. Next, hazard ratios and 95% confidence intervals (CI) for dichotomous data are calculated separately. The relative risk (RR) and its 95% confidence interval (CI) will be used as the dichotomous outcome variable for vitamin D efficacy and safety; the mean difference (MD) and its 95% confidence interval will be used as the continuous variable to differentiate between groups The resulting values were compared to describe the therapeutic effect of vitamin D. To assess clinical heterogeneity between studies, similarities between studies will be assessed, including clinical heterogeneity of study subjects, interventions, controls, and outcome measures. In order to evaluate the statistical heterogeneity between studies, the statistical heterogeneity will be judged according to the results of I2 test; Among them, $0<I2<50\%$ means that the heterogeneity is small, and the fixed effect model can be used to combine statistics; $50\%<I2<75\%$ indicates high heterogeneity; $I2>75\%$ indicates great heterogeneity. Cochrane risk of bias tool (RoB 2.0) will be conducted: randomization process, deviations from the intended interventions, missing outcome data, outcome measurements, selection of the reported results, and overall bias according to the three criteria of "low risk", "high risk" or "some concerns".

Subgroup analysis: To obtain reliable data, subgroup analyses will be performed with several different types of controls based on vitamin D dose, duration of intervention, and type of supplementation.

Sensitivity analysis: In order to investigate the stability of the results, we will conduct a sensitivity analysis of the results. When significant statistical heterogeneity was found, we excluded low-quality trials, replicated meta-analysis papers, studies with insufficient sample size and/or data that were included in the analysis one by one, then reanalyzed and pooled the data, and compared the re-obtained The difference between the effect and the original effect. In this way, we will be able to assess the impact of individual studies on the overall results, and whether the results are reliable.

Country(ies) involved: China.

Keywords: vitamin D supplementation, myasthenia gravis, protocol, systematic evaluation.

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