INPLASY

The impact of supplementing vitamin D through different methods on the prognosis of COVID-19 patients: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Piloting of the study selection process.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202450058

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 May 2024 and was last updated on 13 May 2024.

INTRODUCTION

Review question / Objective To analyze the impact of supplementing vitamin D to COVID-19 patients through different methods on their prognosis(mortality rate, ICU admission rate, length of hospital stay, and intubation rate).

Condition being studied Some studies and meta-analyses have suggested an association between low blood vitamin D levels and adverse outcomes in patients with novel coronavirus infection. but the research results on the use of vitamin D supplementation to improve outcomes in patients with COVID-19 infection are not clear.
The purpose of this review is to evaluate whether immediate supplementation with vitamin D upon hospital admission can improve the prognosis of COVID-19. It compares the differences in prognosis with different doses and administration regimens, aiming to explore rational strategies for administering vitamin D supplementation to COVID-19 patients.

METHODS

Search strategy Searches were conducted in PubMed, Embase, Web of Science, and Cochrane databases, with search dates ranging from inception to January 5, 2024. The search strategy followed the PICOS principles, primarily focusing on the study population, intervention methods, and research methodology. The search terms and keywords used were as follows:(COVID 19) OR“2019-nCoV Infection” OR”infection, 2019-nCoV” OR“SARS-CoV-2 Infection” OR“ SARS CoV 2 Infection” OR“2019 Novel Coronavirus Disease” OR“2019 Novel Coronavirus Infection” OR“COVID-19 Virus Infections” OR“infection, COVID-19 Virus” OR“Virus Infection, COVID-19” OR“Coronavirus Disease 2019” OR“Disease 2019, Coronavirus” OR“Coronavirus Disease 19” OR“Severe Acute Respiratory Syndrome

Coronavirus 2 Infection"OR"COVID-19 Virus Disease" OR"Disease, COVID-19 Virus"OR"Virus Disease, COVID-19"OR"SARS Coronavirus 2 Infection" OR"2019 nCoV Disease"OR"Disease, 2019-nCoV" OR"COVID-19 Pandemic" OR"Pandemic, COVID-19) AND"Vitamin D," "Calciol," "Vitamin D 3," "Vitamin D3," "Cholecalciferol," "25 Hydroxyvitamin D3," "Calcidiol," "25 Hydroxycholecalciferol," "Calcifediol," "Dedrogyl," "Hydropherol," "Calderol". AND"randomized controlled trial" OR "controlled clinical trial" OR "placebo" OR "randomly". Manual searches were conducted to supplement the research by retrieving bibliographies of relevant reviews and identified articles. Contact with study authors was made as necessary to obtain additional information.

Participant or population Participants: admitted patients aged ≥18 years with confirmed COVID-19 diagnosis.

Intervention Intervention: supplementation with vitamin D.

Comparator Comparison: no vitamin D supplementation or lower-dose supplementation.

Study designs to be included Randomized controlled trials and observational studies.

Eligibility criteria Exclusion criteria included reviews, simulation studies, animal studies, letters, conference papers, and case studies.

Information sources Searches were conducted in PubMed, Embase, Web of Science, and Cochrane databases, with search dates ranging from inception to January 5, 2024. The search strategy followed the PICOS principles, primarily focusing on the study population, intervention methods, and research methodology. The search terms and keywords used were as follows:(COVID 19) OR"2019-nCoV Infection" OR"infection, 2019-nCoV" OR"SARS-CoV-2 Infection" OR" SARS CoV 2 Infection" OR"2019 Novel Coronavirus Disease" OR"2019 Novel Coronavirus Infection" OR"COVID-19 Virus Infections" OR"infection, COVID-19 Virus" OR"Virus Infection, COVID-19" OR"Coronavirus Disease 2019" OR"Disease 2019, Coronavirus" OR"Coronavirus Disease 19" OR"Severe Acute Respiratory Syndrome Coronavirus 2 Infection"OR"COVID-19 Virus Disease" OR"Disease, COVID-19 Virus"OR"Virus Disease, COVID-19"OR"SARS Coronavirus 2 Infection" OR"2019 nCoV Disease"OR"Disease, 2019-nCoV" OR"COVID-19 Pandemic" OR"Pandemic, COVID-19) AND"Vitamin D," "Calciol," "Vitamin D 3," "Vitamin D3," "Cholecalciferol," "25 Hydroxyvitamin D3," "Calcidiol," "25 Hydroxycholecalciferol," "Calcifediol," "Dedrogyl," "Hydropherol," "Calderol". AND"randomized controlled trial" OR "controlled clinical trial" OR "placebo" OR "randomly" Manual searches were conducted to supplement the research by retrieving bibliographies of relevant reviews and identified articles. Contact with study authors was made as necessary to obtain additional information.

Main outcome(s) Mortality rate, ICU admission rate.

Additional outcome(s) Length of hospital stay, and intubation rate.

Data management Data extraction was performed independently by two researchers . Any discrepancies were resolved by referral to the third author, Zhang Xiangqun, when necessary. The following information was extracted from all eligible studies: first author's name, publication year, country of study, study design, patient characteristics, and clinical outcomes (mortality rate, ICU admission rate, length of hospital stay, and rate of endotracheal intubation). Data from included studies were entered into a dedicated report table using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). In case of missing data regarding the primary outcomes, we contacted the corresponding authors of the original studies.

Quality assessment / Risk of bias analysis Two independent Study participants assessed the literature's quality according to the quality assess ment criteria recommended by the Cochrane Collaboration for randomized controlled trials. According to the Cochrane Handbook, when including randomized controlled trials, the recommended tool is the revised version of the Cochrane tool, known as the Risk of Bias tool (RoB 2). The Rob 2 tool provides a framework for assessing the risk of bias for individual outcomes in any type of randomized trial. Evaluation criteria include random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases. Reviewers assess different studies based on the Cochrane Handbook. The risk of bias for each domain is categorized into three levels: "low risk," "some concerns," and "high risk." If all domains are assessed as low risk, the overall risk of bias is considered low. If some domains are assessed as "some concerns" and no domains are

assessed as high risk, the overall risk of bias is considered "some concerns." If at least one domain is assessed as high risk, the overall risk of bias is considered "high risk.

Strategy of data synthesis All analyses were conducted using Review Manager software version 5.4 (Nordic Cochrane Center, Cochrane Collaboration). A significance level of p 50%. If the effect size was represented by standardized mean differences (SMD) along with 95% confidence intervals (CI), the mean and standard deviation of quartile data were calculated using the provided formulas. Publication bias was assessed by constructing funnel plots of the effect size against standard error for each study. Sensitivity analysis was conducted by systematically excluding each study to assess the robustness of the results. Subgroup treatment effects were compared using Cochran's Q test and Higgins' I^2 statistic, with $p<0.05$ indicating statistical significance of differences. Detailed characteristics of the included studies are presented in Table 1.

Subgroup analysis Subgroup analysis was conducted based on the method of vitamin D supplementation in the intervention group, dividing it into single-dose and continuous-dose subgroups. The subgroup receiving vitamin D supplementation only once on the first day of admission was categorized as the single-dose group (number of doses = 1), while those receiving multiple doses after admission were categorized as the continuous-dose group (number of doses ≥ 2). Additionally, subgroups were categorized based on the total intake of vitamin D within 14 days of admission, dividing it into ≥100,000 IU group and <100,000 IU group.

Sensitivity analysis We conducted a sensitivity analysis, systematically assessing the impact of removing individual studies,and find that which single study exerted substantial influence on the overall results.

Country(ies) involved China (Emergency Medicine Clinical Research Center, Beijing Chao-Yang Hospital, No.5 Jingyuan Road, Shijingshan, Beijing 100043, China).

Keywords COVID-19, Vitamin D, prognosis, administration methods, dosage.

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