INPLASY PROTOCOL

To cite: Singh et al. Effectiveness of Vitamin B12 Supplementation on cognitive, motor & mood instability of Parkinson's disease patients on levodopa treatment :A Systematic review. Inplasy protocol 202320066. doi: 10.37766/inplasy2023.2.0066

Received: 15 February 2023

Published: 15 February 2023

Corresponding author:
Ruchi Singh

ruchi.physiology@aiimsbhopal.edu.in

Author Affiliation:
All India Institute of Medical sciences Bhopal.

Support: **NIL.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest: **None declared.**

Effectiveness of Vitamin B12 Supplementation on cognitive, motor & mood instability of Parkinson's disease patients on levodopa treatment: A Systematic review.

Singh, R[1]; Nair, A[2]; Rai, NK[3].

Review question / Objective: **The treatment of choice for patients of Parkinson's disease is levodopa. However, levodopa has been suggested to decrease Vit B12 level in these patients. Thus, the research question for this systematic review is whether vit B 12 supplementation in Parkinson's disease(PD) patients on treatment with levodopa improves vit B12 level effecting the Cognition, Motor functions and Mood instability among them in comparison to PD patients on levodopa treatment who are not supplemented with Vit B12.**
Condition being studied: **Parkinson disease is the progressive degeneration of dopaminergic neurons present within the substantia nigra that can lead to altered movements along with the prevalence of cognitive and mood instability as a result of dopamine(neurotransmitter) deficiency. The most effective treatment for the Parkinson's disease is the administration of levodopa, a dopamine precursor . Long term treatment with levodopa causes an increase in homocysteine levels and tissue deficiency of vitamin B12 and folate may occur. Vitamin B12 supplementation is administered as after management regime, in Parkinson patient on levodopa treatment . This study aims to conduct a systematic review, of studies , randomized control trials investigating the ability of vitamin B12 supplementation to enhances the recovery/reduce the decline, if any, of the symptoms of cognitive, motor, mood impairments associated with Parkinson's disease patient on levodopa treatment.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 February 2023 and was last updated on 15 February 2023 (registration number INPLASY202320066).

INTRODUCTION

Review question / Objective: **The treatment of choice for patients of Parkinson's disease is levodopa. However, levodopa has been suggested to decrease Vit B12 level in these patients. Thus, the research question for this systematic review is whether vit B 12 supplementation in Parkinson's disease(PD) patients on**

treatment with levodopa improves vit B12 level effecting the Cognition, Motor functions and Mood instability among them in comparison to PD patients on levodopa treatment who are not supplemented with Vit B12.

Rationale: The review intends to explore the effect of Vit B12 supplementation on the cognitive functions, motor functions and mood instability among PD patients on levodopa treatment. As, Vit B12 supplementation is a very feasible option to be supplemented in PD patients, if it could have a positive impact on their Motor function, cognition as well as mood, which could greatly improve their quality of life.

Condition being studied: Parkinson disease is the progressive degeneration of dopaminergic neurons present within the substantia nigra that can lead to altered movements along with the prevalence of cognitive and mood instability as a result of dopamine(neurotransmitter) deficiency. The most effective treatment for the Parkinson's disease is the administration of levodopa, a dopamine precursor . Long term treatment with levodopa causes an increase in homocysteine levels and tissue deficiency of vitamin B12 and folate may occur. Vitamin B12 supplementation is administered as after management regime, in Parkinson patient on levodopa treatment . This study aims to conduct a systematic review, of studies , randomized control trials investigating the ability of vitamin B12 supplementation to enhances the recovery/ reduce the decline, if any, of the symptoms of cognitive, motor, mood impairments associated with Parkinson's disease patient on levodopa treatment.

METHODS

Search strategy: Following search terms: “Vitamin b12 AND Parkinson”, (((parkinson) OR (parkinsonisms)) AND (b 12)) AND (polyneuropathy) “Parkinson's disease and vitamin B12 supplementation as intervention ”. Search strategy consisting of a combination of terms from medical subject headings (MeSH) and keywords in the title, abstract and text for the population, intervention, comparative and outcomes will be included.

Participant or population: INCLUSION CRITERIA:-Parkinson's Disease patients on treatment with levodopa will be studied in this review with following inclusion criteria- a) Diagnosis of Parkinson disease in patient must meets the diagnostic UK brain bank criteria and the H and Y scale. b)Prior to the intervention, no patient should be on vitamin supplementation. c) The patient must be over the age of 50years. d) Parkinson disease prevalence duration should be more than one year. e)The participants will include both males and/or females. .EXCLUSION CRITERIA:- Patient having any systemic illness or medical conditions such as diabetes,thyroidism and on drugs (such as thiazide diuretics, azathioprine, phenytoin, methotrexate) administration. Patients with undiagnosed Parkinson's disease and other neurological degenerative conditions.

Intervention: Vitamin B12 supplementation among patients of Parkinson's disease who are on treatment of Levodopa. Inclusion criteria for intervention group a) Patient's with diagnosed Parkinson disease receiving L-dopa treatment with intervention of Vitamin B12 Supplementation greater than (100ug dose).b)co-administration with vitamin B6 AND B9 Folic acid is also eligible. EXCLUSION CRITERIA:-a)Parkinson's disease Patient on treatment with levodopa but not have been administered vitamin B12supplementation as intervention.b) Vitamin B12 Supplementation less than (100ug dose) in Parkinson's disease patient being treated with levodopa. c)Patients with nutritional Vitamin B12 deficiency will be excluded.

Comparator: Parkinson's disease patients on levodopa treatment but without Vitamin B12 supplementation.

Study designs to be included: The following study designs that will be considered for inclusion: a)Randomized control trials (RCT),b)case control studies with intervention and follow-up.c)Studies with

baseline and follow up assessment. Exclusion criteria:- systematic review, review literature, case series non-controlled studies, quasi experimental studies andcross-sectional studies will be excluded.

Eligibility criteria: Studies which have compared the B12 level among Parkinson's disease patients with that of healthy controls will not be included, as the pathophysiology behind the reduction of B12 level among the two groups will not be same.

Information sources: Articles will be sourced from PubMed, Cochrane, Ovid, and Google Scholar Database. Search strategy will consist of a combination of terms from medical subject headings (MeSH) and keywords in the title, abstract and text for the population, intervention, comparator and outcomes. Only English-language articles with a full text will be considered. articles publication year till 2022 will be included. The main articles for the study must be RCT , CASE CONTROLS studies with follow-up planned comparative intervention. In addition, non-controlled studies, case studies, quasi-experimental studies and cross-sectional studies will be excluded. The studies that do not meet the requirement according to the inclusion and exclusion criteria will be excluded.

Main outcome(s): Primary outcomes :- Prespecified main and most important outcome of the review will be neurophysiological assessment for the detection and comparison of cognitive, motor, mood impairment . The assessment will be done by using UNIFIED PARKINSON'S DISEASE RATING SCALE (UPDRS) scale. UPDRS part 1, 2, 3 assessment will be done. Following conditions will be analyzed using UPDRS Part 1 MENTATION, BEHAVIOR AND MOOD such as Intellectual Impairment, Thought Disorder (Due to dementia or drug intoxication), Depression, Motivation/ Initiative and From part 2 which is ACTIVITIES OF DAILY LIVING following conditions of Falling (unrelated to freezing) , Freezing when walking , Walking , Sensory complaints related to parkinson's disease will be analyzed. and from Part 3- which is MOTOR EXAMINATION the condition of gait will be considered.

Additional outcome(s): Secondary outcome will be Bio -chemical assessment like analysis of homocysteine serum level and vitamin B12 serum level . Outcome measures must have been attained during baseline and follow up. Measures of effect for outcomes will be mean differences or standardized mean differences with 95% Confidence interval.

Data management: Selection against inclusion criteria will be performed following PICO, PICO inclusion and exclusion criteria will be specifically searched and included well defined. Researchers independently will search for all the RCT, and case controls studies conducted on vitamin B12 supplementation. databases like PubMed , Cochrane , CINAHL, Ovid will be included. Randomized controlled trial studies and case control studies with vitamin B12 supplementation as intervention will be referred as main articles . Addition to any of the outcomes of after intervention includes changes in cognitive-mental, behavior, mood and movement capacity. The table will be formed for synthesis data based on study characteristics (e.g. size of study, year of publication, conclusions). Heterogeneity will be assessed using subgroup analysis by Review Manager version 5.4 software.

Quality assessment / Risk of bias analysis: Risk of bias will be done with the help of Revised Cochrane risk of bias tool (ROB-2). and Revman review manager will be used .

Strategy of data synthesis: After following a strategical search , Revman review manger will be used will be used for further data synthesis, calculation of Risk of bias.

Subgroup analysis: Where possible, we will conduct subgroup analyses to explore possible source of heterogeneity for Main

outcomes and additional outcomes. Subgroup analyses will be performed to explore differences in effect sizes using the following characteristics: a) To determine after intervention changes of neurophysiological and biochemical outcomes during baseline and after follow up . b) qualitative analysis of homocysteine and vitamin B12 serum level assessment. c) based on duration of treatment.

Sensitivity analysis: Heterogeneity will be assessed using subgroup analysis by Review Manager version 5.4 software.

Language restriction: Articles in English language only will be considered for this review.

Country(ies) involved: India.

Keywords: Parkinson's Disease; Parkinson' disease patient on treatment with levodopa; Parkinson's disease patient on levodpa treatment with vitamin B12 supplementation.

Dissemination plans: yes, as a completed review.

Contributions of each author:

Author 1 - Ruchi Singh - Author 1 will independently search for the eligible studies in different search engines, will help author 2 two draft and will finally review the study.
Email: ruchi.physiology@aiimsbhopal.edu.in
Author 2 - Akhiya Nail - Author 2 will again independently search for the eligible studies and will make the first draft of the study.
Email: nairakhiya07@gmail.com
Author 3 - Nirendra Kumar Rai - Author 3 gave the concept of the study and will be responsible for any confusions in selection of studies, will critically review the drafts for final version.
Email: nirendrarai@gmail.com