INPLASY

Berberine and schizophrenia spectrum disorder: efficacy on symptoms and metabolic comorbidity – A systematic review and meta-analysis

INPLASY202450052

doi: 10.37766/inplasy2024.5.0052

Received: 11 May 2024

Published: 11 May 2024

Natale, A; Di Francesco, A; Canonico, S; Concero, C; Kirschner, M; Sabè, M; Rodolico, A; Sentissi, O; Petralia, A; Kaiser, S; Signorelli, MS.

Corresponding author:
Antimo Natale

antimo.natale@hug.ch

Author Affiliation:
Department of Clinical and Experimental Medicine, Section Psychiatry, University of Catania, Catania, Italy; Department of Psychiatry, Adult Psychiatry Service (APS), University Hospitals of Geneva (HUG), Geneva, Switzerland.

ADMINISTRATIVE INFORMATION

Support - No financial support.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202450052

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 May 2024 and was last updated on 11 May 2024.

INTRODUCTION

Review question / Objective The aim of this systematic review and meta-analysis is to evaluate the efficacy and acceptability of adjunctive berberine treatment for clinical symptoms in schizophrenia. It also intends to evaluate the efficacy of berberine in terms of efficacy and acceptability for the management of metabolic comorbidity in the same population.

Rationale Schizophrenia is a complex mental disorder characterized by a number of symptoms, including hallucinations, delusions, disorganized thinking, negative symptoms (such as motivational deficits, impaired emotional expressivity) and cognitive deficits. These symptoms, associated with metabolic complications, induced and not induced by treatments, have a very important impact on the quality of life and health of patients with schizophrenia. Therefore, there is an urgent need for effective and safe therapies that can treat all aspects of this complex disease.

Berberine, a natural alkaloid, has shown potential therapeutic effects on schizophrenia, including improvements in negative symptoms and cognitive function. In addition, berberine may have a protective effect against weight gain induced by antipsychotics, a common side effect of the treatment of schizophrenia.

Given the variety of studies and results, a meta-analysis of the effects of berberine on schizophrenia could provide a complete and balanced synthesis of the available evidence, as well as producing more robust results than a single primary study. This could help clarify the potential role of berberine in the treatment of schizophrenia and guide future research in this field.

Condition being studied This systematic review and meta-analysis addresses the possible effects of berberine in patients with schizophrenia

spectrum disorders. Individuals suffering from one of the conditions included in the spectrum display a wide range of symptomatology, including positive, negative, and cognitive symptoms. Positive symptoms include delusions and hallucinations, while negative symptoms include avolition, anhedonia, asociality, blunted affect, alogia. Cognitive symptoms include dysfunction in concentration, memory, and executive skills. Metabolic comorbidities are common in individuals with schizophrenia spectrum disorder, often linked to the side effects of antipsychotic medications. These medications, while effective in managing schizophrenia symptoms, can lead to weight gain, increased cholesterol and triglyceride levels, insulin resistance, and type 2 diabetes. These side effects can increase the risk of developing obesity, metabolic syndrome, and cardiovascular diseases.

METHODS

Search strategy We will conduct our searches through Pubmed, Cochrane CENTRAL and Scopus, using the following search string: (Berberine OR "Berberis vulgaris" OR "Berberis" OR "phytotherapy" OR "herbal medicine" OR “Phytotherapy”) AND ("Schizophrenia" OR "Psychotic Disorders" OR "Psychosis" OR "Schizoaffective Disorder" OR "Delusional Disorders" OR "Antipsychotic*").

Participant or population We will include adults (18 to 65 year old) who received a diagnosis of schizophrenia spectrum disorder (Schizophrenia, Schizophreniform Disorder, Schizoaffective Disorder, Delusional Disorder, Brief Psychotic Disorder, Psychotic Disorder Not Otherwise Specified).

Intervention Berberine as monotheraphy or add-on administration to other drugs, independently from route of administration.

Comparator None or placebo.

Study designs to be included Randomized and non-randomized clinical trials.

Eligibility criteria All the following criteria must be satisfied for inclusion:
1. Participants or population: We will include adults aged 18 to 65 who have received a diagnosis of a schizophrenia spectrum disorder, including schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, and psychotic disorder not otherwise specified.
2. Intervention: Studies focused on the use of Berberine, either as a monotherapy or as an add-on administration to other drugs. This will include any route of administration.
3. Comparator: Studies where the comparator is none, placebo, or active placebo.
4. Study design: We will include randomized and non-randomized clinical trials.
5. Clinical outcomes: Studies showing at least one of the following clinical results: assessment of positive, negative, cognitive symptoms; social and occupational functioning; quality of life; adherence to treatment; incidence of relapse; tolerability to treatment.
6. Metabolic outcomes: Studies that report at least one of the following metabolic outcomes: changes in body weight, changes in BMI (Body Mass Index), changes in fasting glucose levels, changes in fasting insulin levels, changes in lipid profile (total cholesterol, LDL, HDL, triglycerides), changes in leptin levels, changes in adiponectin levels.
7. Language: English, Italian, French and German studies only.

Information sources Electronic databases were undertaken using: Scopus; Pubmed and Cochrane CENTRAL.

Main outcome(s)
1. Positive Symptoms Change
2. Negative Symptoms Change
3. Cognitive Symptoms Change
4. Changes in Lipid Profile (total cholesterol, LDL, HDL, triglycerides)
5. Changes in BMI
6. Changes in Fasting Glucose Levels.

Additional outcome(s)
1. Changes in Body Weight
2. Changes in Fasting Insulin Levels
3. Changes in Leptin Levels
4. Changes in Adiponectin Levels
5. Response (As defined by primary studies)
6. Remission (As defined by primary studies)
7. Social and Occupational Functioning
8. Quality of Life
9. Adherence to Treatment
10. Incidence of Relapses
11. Treatment Tolerability.

Data management Data will be extracted in a relational database by two independent reviewer. If any discrepancy is present in extracted data, the reviewers will reach a final agreement.
If the two reviewers will not be able to resolve the disagreement a third reviewer will intervene in the final decision.

Quality assessment / Risk of bias analysis All the randomized-controlled studies included in our systematic review and meta-analysis will be evaluated through the application of the Risk of Bias 2 Tool, developed by Cochrane. The quality of non-randomized and non-controlled trials will be operated with the application of National Institutes of Health Quality Assessment Tool. Every study will be independently evaluated by two different authors (DFA, CS); any conflicts regarding the evaluations will be resolved by a more experienced author (NA).

Strategy of data synthesis The software to be utilized for data analysis will be later specified. For outcomes expressed with continuous data, the standardized mean difference will be computed. For outcomes expressed with binary data, such as response or remission, we will compute the odds ratio, relative risk, or risk difference, contingent on the manner in which the data is reported within the studies. Each effect size will be associated with a significance test (p-value calculation). Heterogeneity tests will be conducted for each outcome, which will include the calculation of Q, p, I^2, and Tau.

Subgroup analysis If suitable, we will produce subgroup analysis and/or sensitivity analysis according to the risk of bias among retreived studies.

Sensitivity analysis We do not anticipate conducting any sensitivity analysis.

Language restriction We will include English, Italian, French and German articles.

Country(ies) involved Italy; Switzerland.

Keywords Berberine; Schizophrenia Spectrum Disorders; Positive symptoms; Negative symtpoms; Cognitive symptoms; Metabolic syndrome.

Dissemination plans We plan to publish the present work in peer reviewed journals and present it in scientific conferences.

Contributions of each author

Author 1 - Antimo Natale.
Email: antimo.natale@hug.ch
Author 2 - Antonio Di Francesco.
Email: antonio.di.francesco@outlook.it
Author 3 - Salvatore Canonico.
Email: salvatore.canonico@hotmail.it
Author 4 - Carmen Concerto.
Email: c.concerto@policlinico.unict.it
Author 5 - Matthias Kirschner.
Email: matthias.kirschner@hug.ch
Author 6 - Michel Sabé.
Email: michel.sabe@hug.ch
Author 7 - Alessandro Rodolico.
Email: alessandro.rodolico@phd.studium.it
Author 8 - Othman Sentissi.
Email: o.sentissi@hug.ch
Author 9 - Antonino Petralia.
Email: petralia@unict.it
Author 10 - Stefan Kaiser.
Email: stefan.kaiser@hug.ch
Author 11 - Maria Salvina Signorelli
Email: maria.signorelli@unict.it