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Metabolic and clinical effect of alpha-lipoic acid administration in schizophrenic subjects stabilized with atypical antipsychotics: A 12-week, open-label, uncontrolled study

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ID: alphalipoic1

Background

Management and reduction of metabolic side effects remain a major concern when considering atypical antipsychotics for the treatment of schizophrenia. For example, olanzapine and clozapine are associated with the highest risk of metabolic complications, whereas quetiapine, risperidone, asenapine, and amisulpride can cause moderate metabolic alterations (Carli et al., 2021).
While there is a general consensus regarding routine monitoring of metabolic syndrome indices in patients receiving atypical antipsychotics, adherence to the guidelines is not common (Burghardt and Ellingrod, 2013) and no specific therapeutic interventions are available, meaning that metabolic complications in schizophrenic patients are treated as in the general population.
Alpha lipoid acid (ALA) is a natural substance commonly found in dietary components such as vegetables and meats, which is an essential cofactor of mitochondrial respiratory enzymes and is crucial for normal functioning of oxidative metabolism (Shay et al., 2009).
The therapeutic use of ALA in schizophrenia has recently been investigated in human populations and it seems to be a novel agent to treat antipsychotic-induced obesity (Kim et al., 2008).

This study aimed to evaluate the efficacy of adjunctive alpha lipoid acid (ALA) in a sample of schizophrenia patients receiving atypical antipsychotic therapy, to assess:

1. the efficacy of ALA on metabolic factors
2. its safety and potential therapeutic effects in a sample of schizophrenic patients in stable therapy with atypical antipsychotics.

Study design

12-week, open label, uncontrolled study. Alpha Lipoic Acid will be administrated in capsules at a fixed oral daily dose of 600 mg (Kim et al., 2008) for the entire duration of the study in addition to the atypical antipsychotic therapy. The drug dose will remain unchanged throughout the investigation

and no additional medications (anti-depressant/anticonvulsant/anxiolytic/anti-inflammatory) will be added to their drug regimen during the study.

Sample

Patients who meet DSM-5 criteria for schizophrenia, in stable atypical antipsychotic monotherapy.

Inclusion criteria

Patients with schizophrenia, aged between 18-60 years in stable therapy with antipychotics, (clozapine, olanzapine, quetiapine, or risperidone) for least 3 months.

Exclusion criteria

Treatment with more than one atypical antipsychotic, current treatment with insulin/oral hypoglycaemic/lipid-lowering agents, significant concomitant medical pathologies, organic brain disorders, history of alcohol or substance dependence (excluding nicotine), dementia, intellectual disability, and pregnancy/breastfeeding.

Methods

Patients will be recruited at the University of Messina, Psychiatric Unit. All the patients will provide written informed consent after a full explanation of the experimental design, according to the Declaration of Helsinki.

Patients will attend two visits: initial screening (day 0), and final visit (week 12). Standard laboratory methods will be used to determine outcome measures.

Primary outcome measures: fasting levels of glucose, glycated haemoglobin (Hb1c), total cholesterol, high-density lipoprotein (HDL) choleserol, triglycerides, and other outcome measures, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (γGT), creatine phosphokinase (CPK), uric acid, creatinine, azotaemia, and prolactinaemia. Moreover, a physical examination will be performed to measure systolic and diastolic blood pressure, heart rate, body weight, and body mass index (BMI). Electrocardiography (ECG) tracing will be performed to measure QT interval and QTc.

Secondary outcome measure: the assessment of psychopathologic symptoms using the Positive and Negative Schizophrenic Symptoms Scale (PANSS), (Kay et al., 1987).

Adverse effect monitoring

Adverse effects, either observed or spontaneously reported, will be recorded and classified for onset, duration, severity, and outcome. To monitor the adherence to the study protocol, weekly telephone calls during the study period will be carried out.

Study assessment

Study assessment	Baseline	12 weeks
Informed consent	x	
Medical history	x	
Lipid and Carbohydrate blood parameter measurement	x	x
Hepatic blood parameter measurement	x	x
Renal blood parameter measurement	x	x
Body mass index	x	x
Body weight	x	x
Blood pressure	x	x
Prolactinemia	x	x
Electrocardiography	x	x

Sample sizing and statistical methods for data analysis

A power and sample size estimation were conducted (G*Power 3.1.9.2.), and under the assumption of an effect size of 0.8, a significant level of 0.05 with a power of 0.80, a minimal sample size of 12 was determined.

Statistical tests will be selected based on the available data and the specific needs that emerged during the analysis. Continuous data will be expressed as mean (S.D), and the within-group differences between baseline and final tests will be analysed by the Wilcoxon rank-sum test for dependent samples. As for the magnitude of the treatment effect, effect size will be calculated based on Cohen's d statistic and values lower than 0.50, ranging from 0.50 to 0.79, and 0.80 or greater, will be considered small, moderate, and large, respectively.

The statistical analysis will be performed using the Statistical Package for the Social Sciences (SPSS) 25.0 software (SPSS Inc, Chicago, IL, USA).

References

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