PROSPERO International prospective register of systematic reviews

Pre- and post-treatment levels of plasma cytokines in drug-naive patients with first-episode psychosis: a meta-analysis

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Review question(s)
The aim of this meta-analysis will be to estimate the effect of antipsychotic treatment on plasma levels of candidate, relevant peripheral cytokines in drug-naive patients with first-episode psychosis.

Searches
We will search PubMed, Embase (via Ovid), Scopus and PsycINFO (via ProQuest) electronic databases for articles indexed up to May 2016.

No language restrictions will be set.

The search phrases will be adapted according to database-related index terms.

Types of study to be included
Longitudinal studies.

Condition or domain being studied
First-episode psychosis is defined by the first treatment contact, with no previous antipsychotic medication use, due to the occurrence of psychotic symptoms or a psychotic episode. Psychosis involves any diagnosis included in the schizophrenia disorder cluster. Schizophrenia and other psychotic disorders are severe mental disorders characterized by delusions, hallucinations, disorganized speech and behaviour, and other symptoms that cause poor clinical outcomes and severe impairment in psychosocial functioning. Aetiology of schizophrenic disorders remain not entirely elucidated. Among possible causes, immunological factors have been increasingly involved in the pathogenesis and course of schizophrenia. The inflammatory system may trigger or modulate the course of schizophrenic disorders. Modifications in cytokine levels in schizophrenia and related psychotic disorders have been repeatedly described. However, the effect of antipsychotics on cytokine levels in drug naive patients remains, incompletely explored yet.

Participants/ population
People suffering from first-episode psychosis never treated with antipsychotics (drug-naive).

Intervention(s), exposure(s)
Any antipsychotic treatment.

Comparator(s)/ control
Not applicable.

Context
We will include studies with a follow-up duration of at least 4 weeks, selecting adult, drug-naïve inpatients and/or outpatients with first-episode psychosis never previously treated with antipsychotics.

Outcome(s)

Primary outcomes

Pre- and post-treatment differences in plasma levels of cytokines.

Secondary outcomes

None.

Data extraction, (selection and coding)

We will perfom a preliminary screening based on titles and abstracts, in order to include potentially relevant articles. After the first screening, studies will be retrieved in full text to check eligibility according to our inclusion/exclusion criteria. We have developed a sheet for the extraction of the following information from each included study: year of publication; country; study design; inclusion criteria; setting; sample size; mean age; percentages of men and women; diagnostic methods for first episode psychosis; means with standard deviations of cytokines values, pre- and post-treatment. If raw data are not reported, we will contact the corresponding author to obtain this information

Risk of bias (quality) assessment

We will evaluate selection and information bias, as well as potential sources of indirectness, by consideration of whether: (i) a standardized diagnostic interview (e.g., SCID) has been used to confirm diagnosis for subjects included the study, (ii) subjects with comorbid alcohol / substance use disorders have been excluded, (iii) a standard dose of a single antipsychotic, rather than mixed and heterogeneous treatments, has been tested.

Strategy for data synthesis

Pre- and post-treatment plasma cytokines mean values, with relevant standard deviations, will be extracted from each included study. The pooled analyses will be based on pre- and post-treatment standardized mean differences (Hedges' g) with related 95% confidence intervals. Pooled estimates, obtained by weighting each study according to the random effects model, will be carried out for those cytokines with data available from at-least three different samples. We will assess heterogeneity by using the I-squared index. For those analyses including at least 10 studies, Egger's test will be used to estimate the risk of publication bias.

Analysis of subgroups or subsets

We will perform appropriate meta-regression, sensitivity and/or subgroup analyses in order to test potential effect size variations due to relevant characteristics of individual studies, such as age, gender, follow-up duration, Positive and Negative Syndrome Scale (PANSS) scores, and tested antipsychotic agents.

Dissemination plans

A comprehensive dissemination strategy will be implemented at the conclusion of this review. The full manuscript will be submitted for publication to a peer-reviewed journal for appropriate academic and clinical audiences. Findings of this meta-analysis will be presented in scientific sessions of both national and international congresses. The target audience for this work will be psychiatrists and mental health professionals.

Contact details for further information

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Not applicable

Conflicts of interest
None known

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English

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Italy

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Subject indexing assigned by CRD

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Antipsychotic Agents; Cytokines; Humans; Plasma; Psychotic Disorders; Treatment Outcome

Stage of review
Ongoing

Date of registration in PROSPERO
18 April 2016

Date of publication of this revision
18 April 2016

Stage of review at time of this submission	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No