Protocol

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Systematic review of systematic reviews on the efficacy of drug treatment and psychotherapy for psychiatric disorders

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1. Background

Due to the implementation of new drugs and psychological treatments every year, medical knowledge in psychiatry has grown in exponential ways during last decades. Currently, there are more than 11000 controlled trials currently summarized in the Cochrane schizophrenia group's register (1). Therefore, it is nearly impossible for someone, who is not specialized in a particular medical field, to stay updated with the development of the newest treatments/trends and modalities. The last two decades have therefore witnessed an increasing amount of systematic reviews and meta-analyses that attempted to summarize the results of single trials and are a valuable tool to help clinicians to choose the best between different treatment options. There are so many systematic reviews in the field of psychiatry these days, that it is time to present an overview on how efficacious the major treatments in psychiatry are. This appears to be important, because the efficacy of many psychotropic drugs – e.g. the use of antidepressants for major depressive disorder (2), cholinesterase inhibitors for Alzheimer's disease (3) or even maintenance treatment with antipsychotics (4) – has recently been questioned. So has the effectiveness of psychotherapeutic treatments, in particular psychodynamic approaches. Moreover, there is a debate in the field of psychiatry as to whether patients should be treated with medication or rather with psychotherapy. In this context an overview of systematic reviews on the efficacy of psychotropic drugs and the major psychotherapeutic treatments for psychiatric disorders would be useful, but to the best of our knowledge does not exist. Such a review will provide an overview for clinicians, patients and policy makers as to what the state of the art in psychiatry is, how drug treatment and psychotherapy should be balanced and in which direction the field should go in the near future.

2. Objectives

The objective is to develop a systematic review of systematic reviews on the efficacy of drug treatment and psychotherapy for psychiatric disorders.

3. Method

3.1 Criteria for considering studies for this review

3.1.1 Types of studies

Systematic reviews using meta-analytical techniques to analyze the effect of psychotherapy, pharmacotherapy or combination therapy in studies dealing with major psychiatric disorders as listed below. Eligible comparisons are drugs versus placebo/no treatment , psychotherapy versus placebo/no treatment (e.g. waiting list/treatment as usual), pharmacotherapy versus psychotherapy or combination of psychotherapy and pharmacotherapy in comparison with either therapy alone, published in journals with peer-reviewed process. Studies have to include sampled population in which a primary diagnosis of a psychiatric disorder was defined by any diagnostic criteria. Languages are restricted to English, German, French and Spanish. No restrictions concerning year of publication are applied. Systematic reviews have to include at least one randomized controlled trial (RCT).

Inclusion Criteria:

- Systematic reviews with meta-analyses including studies in randomized-controlled-trial design
- Primary therapies (antipsychotic therapies and no benzodiazepines for schizophrenia) and best established psychotherapies (usually cognitive-behavior therapy (CBT) or psychodynamic approaches)
- Participants between 18-65, except
    - Participants with Dementia
    - Participants with Attention-deficit/hyperactivity disorder (ADHD)
- Monotherapy (e.g. not antidepressant + mood stabilizer)
- Meta-analyses including psychotherapy or pharmacotherapy compared to placebo, waitlist, control group or treatment as usual
- Meta-analyses comparing psychotherapy with pharmacotherapy

- Combination of psychotherapy and pharmacotherapy in comparison with either therapy alone (e.g. combined psychotherapy plus antidepressants for panic disorder)
- Meta-analyses dealing with acute treatment or maintenance treatment will be eligible

Exclusion criteria:

- Children <18 or old people >65
- Systematic reviews without meta-analysis
- Before versus after effect sizes in contrast to between interventions effect sizes
- Special subgroups (e.g. treatment of therapy refractory schizophrenia, primary care patients, elderly)
- Meta-analyses dealing with psychiatric comorbidities (depression and substance abuse) or somatic comorbidities (e.g. depression in cancer patients)
- Special and not commonly used therapy strategies (e.g. acceptance and commitment therapy)
- Group therapy only
- Incomplete presentation of results and missing data not calculable

3.1.2 Types of diseases

Two authors (MH and SL) identified common psychiatric diseases by reviewing the International Classification of Diseases 10 (5) and DSM-IV manuals (6) for disease classes and their subgroups. They chose broad disease categories, e.g. schizophrenia in general, rather than subtypes such as delusional disorder or schizoaffective disorder. The following disorders and their associated sub-categories were selected:

1. Delirium, Dementia, and Amnestic and Other Cognitive Disorders:
    1.1 Dementia of the Alzheimer´s Type
    1.2 Vascular dementia
2. Substance-Related Disorders
    2.1 Alcohol dependence
    2.2 Heroin dependence

- 2.3 Cannabis dependence
- 2.4 Amphetamine dependence
- 2.5 Cocaine dependence
- 2.6 Sedatives dependence

3. Schizophrenia and Other Psychotic Disorders
   - 3.1 Schizophrenia
   - 3.2 Schizoaffective disorder
   - 3.3 Delusional disorder
4. Mood Disorders
   - 4.1 Major depressive disorder
   - 4.2 Bipolar disorder
   - 4.3 Dysthymic disorder
5. Anxiety Disorders
   - 5.1 Panic disorder
   - 5.2 Specific phobia
   - 5.3 Social phobia
   - 5.4 Obsessive-compulsive disorder
   - 5.5 Generalized anxiety disorder
   - 5.6 Post-traumatic stress disorder
6. Somatoform Disorders
7. Eating Disorders
   - 7.1 Anorexia Nervosa
   - 7.2 Bulimia Nervosa
   - 7.3 Eating disorder not otherwise specified (e.g. Binge Eating)
8. Sleep Disorders – Primary Insomnia
9. Impulse-Control-Disorders
10. Adjustment Disorders
11. Personality Disorders
12. Disorders usually first diagnosed in Infacy, Childhood or Adolesence
    - 12.1 Pervasive delevopmental disorders
    - 12.2 Attention-deficit and disruptive behavior disorders

Nicotine dependence is very frequent but we did not categorize it as a psychiatric disorder.

3.1.3 Types of interventions

1. Pharmacotherapies

The primary pharmacotherapies for the respective disorders. e.g. antidepressants or benzodiazepines for panic disorder, no experimental/non standard treatments (e.g. transcranial magnetic stimulation or antipsychotic drugs for panic) and also no augmentation strategies (e.g. antipsychotic drugs added to antidepressants for panic disorder).

2. Psychotherapies

Focus on general cognitive behavioral and psychodynamic approaches, unless other treatments were are the standard treatments (e.g. cognitive training for dementia). Comparisons placebo, no specific treatment including waiting list for psychotherapy.

3.1.3 Types of outcome measures

Acute treatment

Primary, global efficacy outcomes for the disorders. Not necessarily the primary ones in the respective reviews. For example, the Beck Depression Inventory (BDI) (7) is the major measurement scale for depression, but if a review defined the primary outcome as drop-out due to inefficacy, then we would still extract the BDI. Not specific domains such as antipsychotics for aggression in schizophrenia and not adverse events as this would go beyond the scope of the review.

Maintentenance treatment

Relapse or deterioration as defined by the original authors

Additional data

Additionally, we extracted the number of studies included in the meta-analysis, number of participants, mean duration, number of sessions (psychotherapy only) date of last search, assessment of heterogeneity, study quality and publication bias.

Moderator variables

- Publication year
- Effects in placebo groups compared to waitlists (psychotherapy only)
- Intention-to- treat analysis versus completers only

3.2 Search methods for identification of studies

3.2.1 Data Sources

The following databases were searched from inception:
Pubmed, EMBASE, and Psycinfo. Additionally we manually searched the Cochrane Library.
Included articles were scanned for cross-references and retrieved if suitable and not found before.

3.2.2 Search Strategy

Search terms were meta-analy* OR metaanaly* OR systematic review* combined with Medical Subject Heading Terms (MESH) and text words concerning the particular disease. We used broad search terms (e.g. anxiety disorder to look for generalized anxiety disorders) to minimize the possibility to miss relevant articles. The results of the individual data bases were then transferred to Endnote (8) and duplicates were eliminated. A flowchart according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) (9) will be published in the final publication.

3.3 Data collection and analysis

3.3.1 Selection of studies

Titles and abstracts of the results were screened for relevance and suitability by two independent reviewers. If necessary, disagreements were resolved by a third reviewer. Included articles were then retrieved in full text and assessed by using our inclusion and exclusion criteria. We focused on all patients rather than subgroups (e.g. elderly) and on drug classes (e.g. selective serotonine reuptake inhibitors) rather than single drugs.

3.3.2 Data extraction and management

1. Included diseases

Decisions were made by consensus of the two reviewers.

2. Extraction

Two review authors independently extracted data from included studies. Again, any disagreement was discussed with a third member of the review team, decisions documented and, if necessary, authors of studies were contacted for clarification.

3. Management

Data were extracted onto simple forms

3.3.3 Measures of treatment effect

Whenever calculated we used data from intent-to-treat analysis.
If studies with multiple control or treating groups reported results of comparisons with placebo, waiting list and control group separately we used all to compare the effect sizes between different controls.

1. Dichotomous data

For binary outcomes, such as responders on the clinical global impression scale (CGI), we extracted the responder percentage in drug and placebo group the risk ratio (RR) and its 95% confidence interval (CI). If no RR was reported we extracted the odds ratio (OR). Additionally we extracted the absolute risk or response difference (ARD), the relative risk reduction (RRR) and number-needed-to-treat (NNT) based on risk in control group.

2. Continuous Data

For continuous data (rating scales like positive and negative syndrome scale in schizophrenia (PANSS)(10) we extracted both the mean difference (MD) and standardised mean difference (SMD) between groups after the intervention and at follow-up. SMD is difference in means (DM) divided by pooled standard deviation, expressing DM in standard deviation units. There are various modifications of the general form (e.g. Cohens d (11), Hedges g (12), which usually yield similar results. MD keeps the original units and is intuitively to understand, if you know the original scale (e.g. kg for body weight).
SMD is useful when in the single studies of a meta-analysis different instruments are used to measure the same concept (e.g. two depression scales) or if the original unit is difficult to intuitively interpret (e.g. MD in PANSS).

3.4 Dealing with missing data

In case no data was obtained we transformed the existing data to our five standard parameters (WMD/SMD/ARD/RRR/RR/NNT), or even re-calculated meta-analyses by entering single study results using Review Manager 5.0.22 (13) or Comprehensive Meta-Analysis version 2 (14) . If data was not shown as responder (e.g. rates of non-responders), we always recalculated and presented it that way.

3.5 Assessment of reporting bias and study quality

The individual reviews were checked for reporting any methods of bias assessment (e.g. funnel plot, fail safe, etc.).
Quality assessment was done using the AMSTAR (assessment of systematic reviews) (15) Score an 11-item checklist.

3.6 Data synthesis

We used fixed or random effects model, as done by the original authors.

4. Material

Endnote X4 (8)

Comprehensive Meta-analysis 2 (14)

Review Manager 5.0 (13)

Excel 2007 (16)

5. References

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