Meta-analysis of cognitive behavioral therapy for depression in children

PROTOCOL

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BACKGROUD

Depression ranks as one of the most disabling diseases worldwide as measured by its impact on Quality of Life (QOL).[1] The lifetime prevalence of depression in preschool children is about 1%,and in school children about 3%.[2] The average duration of a major depressive episode in children has been estimated at six to nine months.[3] Compared with diagnosis of adults, diagnosis of depression in children is more often missed[4] and which led to a more severe effect on children, because of the impact upon their academic and social development. Depressed children are linked to increased risk of psychological and physiological ill-health in the future, suicide attempts, and social adjustment problems.[5,6] Without treatment, both depression and subclinical depressive symptoms may progress into chronic depression or others more severe condition.[7] Thus, the extent, impact, and long-term sequelae of children depression highlight the need for effective treatment.

In the past two decades, two broad categories of treatment have been used to treat this population; pharmacotherapy[eg, tricyclic antidepressants(TCAs), and serotonin selective reuptake inhibitors(SSRIs)] and psychotherapy. Previous study have shown a small but significant increased risk of suicide for those taking SSRIs compared with placebo.[8] In September 2004, the FDA has cautioned practitioners in the use of SSRIs in children. And TCAs are unlikely benefit in the treatment of depression in pre pubertal children.[9,10] Meanwhile, a number of structures psychosocial treatment are administered for depression in children, such as cognitive-behavioural therapy (CBT), interpersonal therapy (IPT). As we know, CBT is the most studied structures psychosocial intervention for the treatment of depression in children and adolescents, with more than 80% of published psychotherapy studies examing the effects of CBT protocols.[11] Some randomized controlled trials (RCTs) have examined the efficacy of CBT.[12-14] Our previous network meta-analyses which included 52 RCTs of psychotherapies for depression in children and adolescents found that only IPT

and CBT are significantly more beneficial than most control condition at post-treatment and at follow-up, however, subgroup analyses showed that IPT and CBT were less robust effects in studies on children with depression.[15] So far, almost systematic reviews or meta-analysis which conducted to validate the efficacy of psychotherapeutic are based on both children and adolescents.[12,16,17] Importantly, most guidelines and recommendations for adolescents and younger children are based primarily on treatment results for adolescents.[13] That is reasonable to believe that the effect is not equal for younger children: symptoms, cognitive development, and the included treatment components differ between children and adolesents.[11,14,18,19] Therefore, it is important to analyse cognitive-behavioural therapy use in children separately from adults and adolescents.

To further improve the management for depression in children, we will conduct a systematic review and meta-analysis to evaluate the efficacy and acceptability of the use of cognitive-behavioural therapy for children depression.

Methods

Criteria for included studies

Types of studies

Any relevant randomized controlled trials (RCTs) including cluster RCTs will be included. For trials that have a crossover design, only the results from the first randomization period will be considered. Quasi-randomized trials (such as those allocating by using alternate days of the week) will be excluded.

Types of participants

Children should be no more than 13 years old when they initially participated in the primary studies. The following criteria to identify the participants will be applied in our study: (1) major depression, minor or intermittent depression, or dysthymia as diagnosed according to standardised criteria such as ICD-9,[20] ICD-10,[21] DSM-III,[22] DSM-III-R,[23] DSM-IV,[24] DSM-V,[25] Research Diagnostic Criteria [26]and Feighner criteria,[27] (2) depressive status,

defined as scoring above a certain cut-off on a depression rating scale, such as the Hamilton Depression Rating Scale (HAMD),[28] Children 's Depression Inventor y (CDI),[29] Beck depression inventory (BDI),[30] Center for Epidemiologic Study Depression Scale(CES-D),[31]Children 's Depression Rating Scale (CDRS) [32]or Children's Depression Rating Scale-Revised (CDRS-R).[33] Trials where adults and children or adolescents are treated will be eligible for inclusion, if data on the children or adolescents could be extracted separately or obtained from trial authors. The studies where participants had comorbid secondary medical or other mental health conditions will not be excluded; however, participants with a secondary diagnosis of Axis I psychiatric disorders (eg, schizophrenia and bipolar disorder) will be excluded because the effectiveness of psychotherapy might be affected by these comorbidities. Besides, studies in which participants have a diagnosis of resistant depression or psychotic depression will be excluded.

Types of interventions

RCTs comparing cognitive-behavioural therapy with the control conditions for depression in children will be included. For control conditions, waiting-list control (WL), non-treatment control(NT), treatment as usual (TAU) and psychological placebo(PBO) will be included. NT is a control condition in which the participants receive no active treatment during the study and in which they do not expect to receive such after the study is over. However, participants in WL do not receive active treatment during the study but are forewarned that they can receive one after the study period is over. PBO is a control condition that is designed by the researchers to be inactive and non-therapeutic, but which includes enough of the appearance of an active therapy (for example, seeing a therapist for sessions in an office) that patients are expected to perceive it as active psychotherapy. In TAU, sometimes called "usual care," patients receive the intervention that they would have received if the study had never taken place.

Types of outcome measures

Efficacy outcome

1. The primary outcome of efficacy will mean overall change in the total score in continuous depression severity scales from baseline to post-treatment and from baseline to the end of follow-up, which will be assessed in the first instance by change in HRDS. If data are not available, we will use change in CDI or BDI and then other depressive rating scales.

2. Secondary outcome of efficacy will be the proportion of patients who respond to treatment, which is defined as substantial overall improvement from baseline as defined by the original investigators, such as more than a 50% reduction on a depression continuous measure [ie, '1=very much improved' or '2=Much improved' according to the Clinical Global Improvement (CGI) Scale or other criteria].[31] When'response ' is not reported, we will use 'remission' if available. Remission is defined as a reduction to the normal range (such as HRSD score ≤9, BDI score ≤10, CDI ≤12) and variably across studies.[34]

Overall acceptability

All-cause discontinuation as a measure of treatment acceptability is defined as the proportion of patients who drop out for any reason.

Search strategy

All published, unpublished and ongoing RCTs that compared cognitive-behavioural therapy with the control conditions in the treatment of depression in children will be identified. We will identify relevant trials from systematic searches in the following electronic databases: PubMed, Embase, CENTRAL(the Cochrane Central Register of Controlled Trials), Web of Science, PsycINFO, CINAHL and LiLACS. A comprehensive search of unpublished theses and dissertations via ProQuest Dissertation Abstracts will be completed. We will search clinicaltrials.gov for ongoing trial registers. We will also check relevant reports on the US Food and Drug Administration (FDA) website, the WHO's trial portal, and hand-search major

psychiatric and medical journals. The search dead line will be from inception up to 2015. No language restrictions will be applied. Additional relevant studies will be obtained by scanning reference lists of trials identified in the initial searches and relevant review papers. In addition, all relevant authors will be contacted to supplement incomplete information.

Study selection and data extraction

Selection of trials

Titles and abstracts of reference s identified by the electronic search strategies described above will be independently examined by two reviewers .If both reviewers judge that the trial does not meet eligibility criteria, we will exclude it. Then we will obtain the full texts of all remaining articles and determine whether to include them by the same eligibility criteria. Besides, the references of relevant review papers and included trials will be checked. Any disagreement will be resolved by consensus between the two reviewers and, if need be, with another reviewer.

Quality assessment

The study quality assessment will refer to the Cochrane criteria with assess risk of bias as ‘ low risk ’, ‘ unclear risk’ or ‘ high risk ’: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants, personnel and outcome assessors; (4) incomplete outcome data reported; (5) selective outcome reporting; and (6) other sources of bias. Any disagreement will be resolved by consensus between two raters and, if need be, with another reviewer.

Data extraction

Two independent reviewers will extract the data from the original reports using standardized data extraction forms, which include study characteristics (such as first listed author, publication year, journal, country, institution and sponsor), patient characteristics (such as diagnostic criteria for depression and the number of patients),intervention details (such as

session of treatment, the duration of treatment, treatment setting and pattern) and outcome measures (such as acute treatment outcomes and follow-up outcomes). Any disagreements will be resolved by a third review author.

Statistical analysis

Pairwise meta-analyses will be performed using Review Manager (V.5.3). Using the random-effects model when significant heterogeneity existed or a fixed-effects model when no significant heterogeneity existed. Heterogeneity of treatment effects across studies will be assessed by I^2 and the Q-statistic test.[35] A I^2 value of 25% indicates low heterogeneity, and larger values show increasing heterogeneity, with 50% as moderate, and 75% as high heterogeneity. The pooled estimates of standardized mean difference (SMD) with 95% CIs will be calculated for the continuous outcomes, and odds ratios (OR) with 95% CIs will be calculated for the dichotomous outcomes. Publication bias will be examined with the funnel plot method, and Egger's regression asymmetry test.[36]

Subgroup analyses will be conducted to examine whether effect estimates would be influenced by the type of control conditions (WL, NT ,TAU, or PBO), comorbid (with or without), and number of sessions planned (<10 vs. ≥10 sessions). We will perform sensitivity analysis by excluding studies with parental involvement.

Role of the funding source

No company will be involved in the study design, data collection, data analysis, data interpretation, writing of the report, or in the decision to submit the report for publication.

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