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[Intervention Review]

Antidepressants for the treatment of depression in people with cancer

Giovanni Ostuzzi[1], Faith Matcham[2], Sarah Dauchy[3], Corrado Barbui[4], Matthew Hotopf[2]

[1]Department of Neuroscience, Biomedicine and Movement Sciences, Section of Psychiatry, University of Verona, Verona, Italy. [2]Department of Psychological Medicine, The Institute of Psychiatry, King's College London, London, UK. [3]Chef du Département Interdisciplinaire de Soins de Support, Gustave Roussy, Paris, France. [4]Department of Neuroscience, Biomedicine and Movement Sciences, Section of Psychiatry, University of Verona, Verona, Italy

Contact: Giovanni Ostuzzi, Department of Neuroscience, Biomedicine and Movement Sciences, Section of Psychiatry, University of Verona, Policlinico "GB Rossi", Piazzale L.A. Scuro, 10, Verona, 37134, Italy. giovanni.ostuzzi@gmail.com.

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ABSTRACT

Background

Major depression and other depressive conditions are common in people with cancer. These conditions are not easily detectable in clinical practice, due to the overlap between medical and psychiatric symptoms, as described by diagnostic manuals such as the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) and *International Classification of Diseases* (*ICD*). Moreover, it is particularly challenging to distinguish between pathological and normal reactions to such a severe illness. Depressive symptoms, even in subthreshold manifestations, have been shown to have a negative impact in terms of quality of life, compliance with anti-cancer treatment, suicide risk and likely even the mortality rate for the cancer itself. Randomised controlled trials (RCTs) on the efficacy, tolerability and acceptability of antidepressants in this population are few and often report conflicting results.

Objectives

To assess the efficacy, tolerability and acceptability of antidepressants for treating depressive symptoms in adults (aged 18 years or older) with cancer (any site and stage).

Search methods

We searched the following electronic bibliographic databases: the Cochrane Central Register of Controlled Trials (CENTRAL 2017, Issue 6), MEDLINE Ovid (1946 to June week 4 2017), Embase Ovid (1980 to 2017 week 27) and PsycINFO Ovid (1987 to July week 4 2017). We additionally handsearched the trial databases of the most relevant national, international and pharmaceutical company trial registers and drug-approving agencies for published, unpublished and ongoing controlled trials.

Selection criteria

We included RCTs comparing antidepressants versus placebo, or antidepressants versus other antidepressants, in adults (aged 18 years or above) with any primary diagnosis of cancer and depression (including major depressive disorder, adjustment disorder, dysthymic disorder or depressive symptoms in the absence of a formal diagnosis).

Data collection and analysis

Two review authors independently checked eligibility and extracted data using a form specifically designed for the aims of this review. The two authors compared the data extracted and then entered data into Review Manager 5 using a double-entry procedure. Information extracted included study and participant characteristics, intervention details, outcome measures for each time point of interest, cost analysis and sponsorship by a drug company. We used the standard methodological procedures expected by Cochrane.

Main results

We retrieved a total of 10 studies (885 participants), seven of which contributed to the meta-analysis for the primary outcome. Four of these compared antidepressants and placebo, two compared two antidepressants, and one three-armed study compared two antidepressants and placebo. In this update we included one additional unpublished study. These new data contributed to the secondary analysis, while the results of the primary analysis remained unchanged.

For acute-phase treatment response (6 to 12 weeks), we found no difference between antidepressants as a class and placebo on symptoms of depression measured both as a continuous outcome (standardised mean difference (SMD) −0.45, 95% confidence interval (CI) −1.01 to 0.11, five RCTs, 266 participants; very low certainty evidence) and as a proportion of people who had depression at the end of the study (risk ratio (RR) 0.82, 95% CI 0.62 to 1.08, five RCTs, 417 participants; very low certainty evidence). No trials reported data on follow-up response (more than 12 weeks). In head-to-head comparisons we only retrieved data for selective serotonin reuptake inhibitors (SSRIs) versus tricyclic antidepressants, showing no difference between these two classes (SMD −0.08, 95% CI −0.34 to 0.18, three RCTs, 237 participants; very low certainty evidence). No clear evidence of a beneficial effect of antidepressants versus either placebo or other antidepressants emerged from our analyses of the secondary efficacy outcomes (dichotomous outcome, response at 6 to 12 weeks, very low certainty evidence). In terms of dropouts due to any cause, we found no difference between antidepressants as a class compared with placebo (RR 0.85, 95% CI 0.52 to 1.38, seven RCTs, 479 participants; very low certainty evidence), and between SSRIs and tricyclic antidepressants (RR 0.83, 95% CI 0.53 to 1.30, three RCTs, 237 participants). We downgraded the certainty (quality) of the evidence because the included studies were at an unclear or high risk of bias due to poor reporting, imprecision arising from small sample sizes and wide confidence intervals, and inconsistency due to statistical or clinical heterogeneity.

Authors' conclusions

Despite the impact of depression on people with cancer, the available studies were very few and of low quality. This review found very low certainty evidence for the effects of these drugs compared with placebo. On the basis of these results, clear implications for practice cannot be deduced. The use of antidepressants in people with cancer should be considered on an individual basis and, considering the lack of head-to-head data, the choice of which agent to prescribe may be based on the data on antidepressant efficacy in the general population of individuals with major depression, also taking into account that data on medically ill patients suggest a positive safety profile for the SSRIs. To better inform clinical practice, there is an urgent need for large, simple, randomised, pragmatic trials comparing commonly used antidepressants versus placebo in people with cancer who have depressive symptoms, with or without a formal diagnosis of a depressive disorder.

PLAIN LANGUAGE SUMMARY

Antidepressants for the treatment of depression in people with cancer

The issue

Depressive states are frequent among people suffering from cancer. Often depressive symptoms are a normal reaction or a direct effect of such a severe and life-threatening illness. It is therefore not easy to establish when depressive symptoms become a proper disorder and need to be treated with drugs. Current scientific literature reveals that depressive symptoms, even when mild, can have a relevant impact on the course of cancer, reducing people's overall quality of life and affecting their compliance with anti-cancer treatment, as well as possibly increasing the likelihood of death.

The aim of the review

It is important to assess the possible beneficial role of antidepressants in adults (aged 18 years or above) with cancer. The aim of this review is to assess the efficacy and acceptability of antidepressants for treating depressive symptoms in patients with cancer at any site and stage.

What are the main findings?

We systematically reviewed ten studies assessing the efficacy of antidepressants, for a total of 885 participants. The evidence is current to 3 July 2017. Due to the small number of people in the studies, and issues with how the studies reported what was done, there is uncertainty over whether antidepressants were better than placebo in terms of depressive symptoms after 6 to 12 weeks of treatment. We did not have enough evidence to determine how well antidepressants were tolerated in comparison with placebo. Our results did not show whether any particular antidepressant was better than any other in terms of both beneficial and harmful effects. To better inform clinical practice, we need large studies which randomly assign people to different treatments. Currently, we cannot draw reliable conclusions about the effects of antidepressants on depression in people with cancer.

Certainty of the evidence

The certainty of the evidence was very low because of a lack of information about how the studies were designed, low numbers of people in the analysis of results, and differences between the characteristics of the studies and their results.

What are the conclusions?

Despite the impact of depression on people with cancer, the available studies were very few and of low quality. This review found very low certainty evidence for the effects of these drugs compared with placebo.