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[Intervention Review]

Fluoxetine versus other types of pharmacotherapy for depression

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ABSTRACT

Background

Depression is common in primary care and it is associated with marked personal, social and economic morbidity, and creates significant demands on service providers in terms of workload. Treatment is predominantly pharmaceutical or psychological. Fluoxetine, the first of a group of antidepressant (AD) agents known as selective serotonin reuptake inhibitors (SSRIs), has been studied in many randomised controlled trials (RCTs) in comparison with tricyclic (TCA), heterocyclic and related ADs, and other SSRIs. These comparative studies provided contrasting findings. In addition, systematic reviews of RCTs have always considered the SSRIs as a group, and evidence applicable to this group of drugs might not be applicable to fluoxetine alone. The present systematic review assessed the efficacy and tolerability profile of fluoxetine in comparison with TCAs, SSRIs and newer agents.

Objectives

To determine the efficacy of fluoxetine, compared with other ADs, in alleviating the acute symptoms of depression, and to review its acceptability.

Search methods

Relevant studies were located by searching the Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR), the Cochrane Central Register of Controlled Trials (CENTRAL), Medline (1966-2004) and Embase (1974-2004). Non-English language articles were included.

Selection criteria

Only RCTs were included. For trials which have a crossover design only results from the first randomisation period were considered.

Data collection and analysis

Data were independently extracted by two reviewers using a standard form. Responders to treatment were calculated on an intentionto-treat basis: drop-outs were always included in this analysis. When data on drop-outs were carried forward and included in the efficacy evaluation, they were analysed according to the primary studies; when dropouts were excluded from any assessment in the primary studies, they were considered as treatment failures. Scores from continuous outcomes were analysed including patients with a final assessment or with the last observation carried forward. Tolerability data were analysed by calculating the proportion of patients who Trusted evidence. Informed decisions. Better health.

failed to complete the study and who experienced adverse reactions out of the total number of randomised patients. The primary analyses used a fixed effects approach, and presented Peto Odds Ratio (Peto OR) and Standardised Mean Difference (SMD).

Main results

On a dichotomous outcome fluoxetine was less effective than dothiepin (Peto OR: 2.09, 95% CI 1.08 to 4.05), sertraline (Peto OR: 1.40, 95% CI 1.11 to 1.76), mirtazapine (Peto OR: 1.64, 95% CI 1.01 to 2.65) and venlafaxine (Peto OR: 1.40, 95% CI 1.15 to 1.70). On a continuous outcome, fluoxetine was more effective than ABT-200 (Standardised Mean Difference (SMD) random effects: - 1.85, 95% CI - 2.25 to - 1.45) and milnacipran (SMD random effects: - 0.38, 95% CI - 0.71 to - 0.06); conversely, it was less effective than venlafaxine (SMD random effect: 0.11, 95% CI 0.00 to 0.23), however these figures were of borderline statistical significance.

Fluoxetine was better tolerated than TCAs considered as a group (Peto OR: 0.78, 95% CI 0.68 to 0.89), and was better tolerated in comparison with individual ADs, in particular than amitriptyline (Peto OR: 0.64, 95% CI 0.47 to 0.85) and imipramine (Peto OR: 0.79, 95% CI 0.63 to 0.99), and among newer ADs than ABT-200 (Peto OR: 0.21, 95% CI 0.10 to 0.41), pramipexole (Peto OR: 0.20, 95% CI 0.08 to 0.47) and reboxetine (Peto OR: 0.61, 95% CI 0.40 to 0.94).

Authors' conclusions

There are statistically significant differences in terms of efficacy and tolerability between fluoxetine and certain ADs, but the clinical meaning of these differences is uncertain, and no definitive implications for clinical practice can be drawn. From a clinical point of view the analysis of antidepressants' safety profile (adverse effect and suicide risk) remains of crucial importance and more reliable data about these outcomes are needed. Waiting for more robust evidence, treatment decisions should be based on considerations of clinical history, drug toxicity, patient acceptability, and cost. We need for large, pragmatic trials, enrolling heterogeneous populations of patients with depression to generate clinically relevant information on the benefits and harms of competitive pharmacological options. A meta-analysis of individual patient data from the randomised trials is clearly necessary.

PLAIN LANGUAGE SUMMARY

Fluoxetine compared with other antidepressants for depression

The efficacy and tolerability of fluoxetine was compared to other antidepressants (tricyclics, heterocyclics and newer antidepressants) for the acute treatment of depressive illness. One hundred thirty-two randomised controlled trials were identified. Pooling the results from the trials, statistically significant differences in efficacy and in tolerability were found between fluoxetine and some antidepressants. However, it is difficult to draw clear clinically meaningful conclusions and more reliable data about antidepressants' safety profile are needed. Without more robust evidence, the researchers suggest that treatment decisions are to be based on considerations of drug toxicity, patient acceptability, and cost.