Citalopram and Fluoxetine in Major Depression
Comparison of Two Clinical Trials in a Psychiatrist Setting and in General Practice

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Summary

Two studies carried out in France compared citalopram with fluoxetine 20mg daily in the treatment of major depression (DSM-III-R). One of the studies was carried out in a psychiatrist setting (citalopram 40mg daily) and the other in a general practice setting (citalopram 20mg daily). Both studies showed a significant improvement in the mean primary and secondary efficacy variables (MADRS and HDRS) without any difference between the two treatment groups. In the general practice study, the onset of recovery was greater in the citalopram group after 2 weeks. In this population, citalopram was superior to fluoxetine in patients not receiving concomitant anxiolytics/hypnotics. The incidence of adverse events was comparable in both groups. A higher frequency of vomiting was observed at initiation of the 40mg citalopram treatment, but disappeared afterwards.

Depression is a chronic, recurrent disorder and as such requires long-term treatment with drugs that have a low incidence of adverse effects. Traditional tricyclic antidepressant drugs are now being replaced by the new selective serotonin reuptake inhibitors (SSRIs), which have minimal psychomotor effects, anticholinergic adverse effects, problems of weight gain, and cardiotoxicity. Neurochemical and behavioural studies in laboratory animals have demonstrated that citalopram is the most selective serotonin reuptake inhibitor yet developed with negligible effects upon other transmitter substances and minimal affinity for either histamine or muscarine receptors. The antidepressant efficacy of citalopram has been well documented in clinical trials. Citalopram has fewer adverse effects than the classical tricyclic antidepressants, especially with
regard to those of anticholinergic origin. Indeed, phase II and III clinical trials involving more than 3,000 patients have shown citalopram to be an effective and well tolerated antidepressant drug.

Recently, a trial that compared citalopram at two dosage levels (20 to 30 mg and 40 to 60 mg daily) with imipramine (100 to 150 mg daily) in a general practice setting has been completed. This study did not show any difference in efficacy between imipramine and citalopram at both dosage levels, an outcome consistent with those of other studies that have illustrated citalopram to be as efficacious as the tricyclic antidepressants. However, the imipramine-treated patients reported a higher frequency of adverse events, especially anticholinergic type events, than did the citalopram-treated groups.

As the efficacy of citalopram compared with the tricyclic antidepressants has been well established, it was of interest to compare citalopram with another SSRI, e.g., fluoxetine. Fluoxetine is an SSRI that has a widespread use worldwide. It has a pharmacological profile that is similar to that of citalopram. This paper describes the results of two trials that compared citalopram and fluoxetine with regard to their efficacy and tolerability in patients with major depression within a specialist psychiatric setting (the psychiatrist trial) or in a general practice setting (the GP trial).

Patients and Methods

Study Participants

Patients from throughout France were recruited for the trials. In one trial they were seen and treated by psychiatrists, either as inpatients or as outpatients. In the other they were seen and treated by general practitioners.

The following inclusion criteria were used: patients of either gender, aged between 18 and 65 years (psychiatrist trial) or 18 to 70 years (GP trial), who had fulfilled the DSM-III-R criteria for a major depressive disorder (both trials) or a bipolar disorder (psychiatrist trial only). The severity of the depression should correspond to a total score of 25 or more (psychiatrist trial) or 22 or more (GP trial) on the Montgomery-Åsberg Depression Rating Scale (MADRS). All patients gave their signed, informed consent to participate.

Exclusion criteria were pregnancy, lactation, failure to use an acceptable contraceptive method, or known drug or alcohol abuse within the last year. Patients with severe somatic, neurological or psychiatric diseases, those who had been treated with MAO inhibitors within the 2 weeks prior to entry into the trial or were hypersensitive to the test drugs, and patients who were at risk of suicide were also excluded.

Study Design

The protocols for both clinical settings were similar, the main differences being the daily dose and the quantitative inclusion criterion.

Both trials were double-blind, multicentre, fixed-dose, parallel-group comparison studies. Citalopram was administered as tablets containing citalopram hydrobromide corresponding to 40 mg (psychiatrist trial) or 20 mg (GP trial) citalopram base, while fluoxetine was given as capsules containing 20 mg fluoxetine hydrochloride in both trials. Because of the different appearances of the two drugs, the ‘double-dummy’ principle was used to blind the studies.

The daily dose of fluoxetine was the same in both trials (20 mg), which was based on the recommendations from the manufacturer (Eli Lilly) and the literature. In the psychiatrist trial the daily dose of citalopram was 40 mg, which was based on the information available from clinical trials at that moment. In the GP trial, designed later on, the daily dose of citalopram was 20 mg, which was based on data on file showing that this was the minimum effective dose.

Following screening for eligibility (first visit), patients entered a 4- to 7-day washout period during which all previous antidepressants were stopped. Patients having received MAO inhibitors during the 2 weeks preceding inclusion could not enter the study. Patients showing more than 20%