

## Efficacy of citalopram in anorexia nervosa: a pilot study

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### Abstract

**Introduction:** Anorexia nervosa (AN) still lacks a defined treatment. Since fluoxetine proved effective in weight-restored anorexics, this pilot study evaluates the efficacy of another SSRI, citalopram, in restricting-type AN. **Experimental procedures:** Fifty-two female anorectic outpatients were randomized in the citalopram ( $n=26$ ) and waiting list ( $n=26$ ) as a control group. Efficacy was assessed using Eating Disorder Inventory-2, Eating Disorder Inventory-Symptom Checklist, State-Trait Anger Expression Inventory, Beck Depression Inventory, Symptom Checklist-90 and Structured Clinical Interview for DSM-IV Axis II Disorders. **Results:** Thirteen patients dropped-out, thus 19 patients received citalopram and 20 remained in the control group. After 3 months of treatment, the citalopram group showed a decrease on BDI and SCL-90 Depression subscale and an improvement of baseline obsessive compulsive features on SCL-90, EDI-2 impulsiveness and Trait-anger on STAXI. Weight gain was similar in the two groups. **Discussion:** These preliminary results support the efficacy of citalopram in anorexics. Citalopram seems to improve depression, obsessive–compulsive symptoms, impulsiveness and Trait-anger.

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### 1. Introduction

Anorexia nervosa (AN) is a complex disorder that occurs predominantly in young women (American Psychiatric Association, 1994). It is believed to be determined by many factors but its etiology is uncertain. As a consequence there is still no proven or unequivocal treatment for this disorder (Ferguson et al., 1999; Herzog et al., 1992). According to some authors (Jimerson et al., 1996) adjunctive pharmacotherapy in the treatment of hospitalized patients has few benefits. Other authors have reported as useful clomipramine (Crisp et al., 1987), cyproheptadine hydrochloride (Halmi et al., 1986; Goldberg et al., 1979; Vigersky and Loriaux, 1977) and monoamine oxidase inhibitors (Johnson et al., 1983; Hudson et al., 1985).

Recently, numerous studies using selective serotonin reuptake inhibitors (SSRIs) have been conducted, but the

results are inconsistent. Strober et al. (1997) demonstrated that fluoxetine, in addition to other therapies, did not significantly improve outcome. An open-trial study has, however, demonstrated the effectiveness of fluoxetine on weight, obsessive thoughts, and depression (Gwirtsman et al., 1990). Further studies to explain these different results suggested that the effectiveness of fluoxetine depends on the clinical condition of the patient. Kaye and co-workers found that in weight-restored AN patients fluoxetine improved outcome and reduced relapse (Kaye et al., 1991; Kaye, 1997). Attia et al. (1998) demonstrated the ineffectiveness of fluoxetine in underweight patients. A retrospective study further demonstrated that all SSRIs are ineffective in malnourished underweight patients with AN (Ferguson et al., 1999). This hypothesis is also supported in a review by Kaye et al. (1999). It is as yet unclear whether fluoxetine or other SSRIs can be used before complete weight restoration as it is difficult to derive consistent responses from the above-mentioned studies.

Until recently only a few reports in the literature have

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discussed the use of other SSRIs in the treatment of AN (Calandra et al., 1999; Raitasuo et al., 1998; Bergh et al., 1996). Further explorations are justified because these compounds are known to influence the depressive and obsessive aspects of AN, which are extremely important from clinical and genetic viewpoints (Lilenfeld et al., 1997; Casper, 1990; Kaye et al., 1998; Collier et al., 1997; Enoch et al., 1998). Besides, as demonstrated by studies on the cerebrospinal fluid 5-hydroxyindoleacetic acid (5-HIAA) factor (Kaye et al., 1998) and on the temperamental trait Harm Avoidance (Cloninger et al., 1993; Fassino et al., in press), some pathological behaviors common in AN could be linked to serotonergic activity.

Citalopram is the most recent SSRI. It is characterised by a more selective pharmacological profile with respect to other compounds of this class, and it is safe (Bezchlibnyk-Butler et al., 2000; Tan and Levin, 1999; Feighner and Overo, 1999).

The aim of this pilot study was to examine the efficacy of citalopram in the treatment of outpatients suffering from restricting-type AN. Primary outcome measures were eating symptoms and psychopathological symptoms were considered. Moreover, one objective was to verify whether changes noted after pharmacological treatment are independent from possibly confounding variables such as age, years of disease, body mass index (BMI), and personality disorders.

## 2. Experimental procedures

### 2.1. Study design

A prospective, randomized, controlled study of the efficacy of citalopram in outpatients with restricting-type AN. The control group comprised restricting-type AN outpatients receiving no drug treatment (waiting list). The study was conducted in accordance with the Helsinki declaration. Written informed consent was obtained from all patients prior to enrolment.

### 2.2. Patient selection and procedures

Subjects were recruited from the anorectic outpatient population of the Centre for Eating Disorders, Turin University from 1 September 1998 to 1 September 2000. The inclusion criteria were: diagnosis of restricting-type AN, age 16–35 years and not being under psychopharmacological therapy during the month preceding the beginning of the study (6 weeks if the drug was fluoxetine) or estrogen–progesterone therapy. The exclusion criteria were a psychiatric comorbidity and known sensitivity to citalopram.

All patients meeting the inclusion criteria were enrolled into the study after diagnostic assessment. All eligible patients were included on a waiting list to receive an

integrated treatment (dietary and psychiatric treatment), which represents the usual practice at the Centre for Eating Disorders (Fassino et al., 1998). Using a random allocation, the patients were divided in two groups: treatment group (citalopram therapy) and control group (waiting list without drug therapy).

Dosage and possible side effects of treatment were explained to the patients in the citalopram group. The study treatment was provided free of charge. Citalopram was administered after the evening meal, starting at 10 mg/day and increased to 20 mg/day after 6 days of therapy for at least 12 weeks. The patients in the control group did not receive citalopram but were followed by a periodic clinical assessment and test administration, in the same way as for the citalopram group. The only other psychoactive treatment allowed (in four patients) was lorazepam (up to 4 mg/day), if needed for control of anxiety, agitation, or insomnia.

### 2.3. Study assessments

Two psychometric tests were used for the evaluation of Eating Disorder (ED) and four instruments for the evaluation of psychopathological traits. Eating Disorder evaluation involved the Eating Disorder Inventory-2 (EDI-2) to investigate the psychological traits typical of this disorder (Drive for Thinness, Bulimia, Body Dissatisfaction, Ineffectiveness, Perfectionism, Interpersonal Distrust, Interceptive Awareness, Maturity Fears, Asceticism, Impulse Regulation, Social Insecurity) and the Eating Disorder Inventory-Symptom Checklist (EDI-SC) to evaluate frequency and features of the basic behaviors of ED (Garner, 1991).

Psychopathological traits were assessed using the State-Trait Anger Expression Inventory (STAXI) for the assessment of the experience and expression of anger (Spielberger, 1983); the Beck Depression Inventory, simplified version of 13 items (BDI) (Beck, 1978); the Hopkins Symptom Checklist (SCL-90) (Derogatis, 1977), and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) (First et al., 1995). During the first assessment (T0) all patients were interviewed to collect medical, psychiatric, and pharmacological history.

In all patients body weight, eating behavior, and psychopathological symptoms were evaluated at baseline and on days 14, 28, 41, 46, 70, and 84. In the patients in the citalopram group, possible side effects were also evaluated. EDI-2, EDI-SC, BDI, and STAXI were administered at baseline and on days 28, 56, and 84. SCID-2 was administered at baseline and completed with the interview on day 4 or 5. The SCL-90 was administered at baseline and on day 84.

### 2.4. Statistical analysis

To evaluate the benefit of citalopram on the treatment of AN, only measures observed at baseline and at time T3

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