Mirtazapine plus citalopram has short term but not longer term benefits over citalopram alone for the symptoms of obsessive compulsive disorder

Pallanti S, Quercioli L, Bruscoli M. Response acceleration with mirtazapine augmentation of citalopram in obsessive-compulsive disorder patients without comorbid depression: a pilot study. *J Clin Psychiatry* 2004;**65**:1394–9.

Q Does mirtazapine plus citalopram improve symptoms of obsessive compulsive disorder more than citalopram alone?

METHODS

Design: Randomised controlled trial.

Allocation: Concealed.

Blinding: Single blind (participants blinded; unclear if assessors were blinded to treatment).

Follow up period: 12 weeks.

Setting: Two medical centres in Italy and New York from November 2001 to July 2003.

Patients: 49 people (mean age 29.4 years) with DSM-IV obsessive compulsive disorder (OCD) without comorbid depression. Inclusions: moderately severe OCD symptoms (Clinical Global Impression (CGI) scale) for more than 1 year; no previous treatment with selective serotonin reuptake inhibitors; prior treatment with behavioural therapy, benzodiazepines, or antipsychotics only. Main exclusions: psychotic or organic mental disorders; mental retardation; developmental disabilities; comorbid depression; substance abuse; history of bipolar I or II disorders; personality disorder; pregnancy; Tourette's syndrome.

Intervention: Citalopram (40–80 mg/day) plus placebo, or citalopram plus mirtazapine (15–30 mg/day).

Outcomes: OCD symptoms (Yale Brown Obsessive Compulsive Scale (YBOCS) score).

Patient follow up: 92% of participants completed the trial.

MAIN RESULTS

At 4 weeks, citalopram plus mirtazapine significantly reduced OCD symptoms compared with citalopram plus placebo, although there was no significant difference between groups at 12 weeks (mean reduction in YBOCS scores at 4 weeks: 4.0 with citalopram plus placebo *v* 12.7 with citalopram plus mirtazapine, $p < 0.001$; mean reduction in YBOCS scores at 12 weeks: 17.3 with citalopram plus placebo *v* 19.7 with citalopram plus mirtazapine, not significant).

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CONCLUSIONS

At 4 weeks, citalopram plus mirtazapine improves OCD symptoms compared with citalopram plus placebo, but there are no additional benefits at 12 weeks.

Commentary

Selective serotonin reuptake inhibitors (SSRIs) are widely used in the treatment of depression and obsessive compulsive disorder (OCD). However, their clinical use is limited by a delayed onset of therapeutic action (in particular in OCD) and the occurrence of undesired side effects such as nausea, vomiting, agitation, insomnia, and sexual dysfunction.

For several theoretical reasons, augmentation of SSRI treatment with mirtazapine may provide a clinical benefit. Mirtazapine enhances serotonergic neurotransmission by increasing the serotonergic cell firing and by blocking presynaptic α_2 -adrenergic heteroreceptors at the serotonergic nerve terminals. In contrast with SSRIs, this mechanism of action does not require a time dependent desensitisation of receptors and may explain, in part, the finding of an earlier onset of action of mirtazapine in depression compared with SSRIs.¹ Since the therapeutic effects of mirtazapine are thought to be mediated via 5HT_{1A} receptors whereas 5HT₂ and 5HT₃ receptors are blocked, the typical side effects found with SSRIs are avoided. Moreover, mirtazapine has been demonstrated to be an acute inhibitor of cortisol secretion both in healthy people² and in people with depression.³ A rapid normalisation of hypothalamic–pituitary–adrenocortical hyperactivity after administration of mirtazapine may also play a role in the presumed early onset of action in depression.

Indeed, Pallanti *et al* found an acceleration of clinical improvement and lower rates of side effects in OCD patients if citalopram was combined with mirtazapine. This finding is of clinical importance since successful pharmacotherapy in OCD patients often takes quite a long time, requires high doses of SSRIs and is therefore associated with relatively high frequencies of side effects. However, the main criticism of Pallanti *et al*'s study is the single blind design and the absence of blinded ratings of outcomes. To confirm the result further double blind, placebo controlled studies are needed.

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