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ADDITION OF A SELECTIVE 5-HT$_{2A}$/D$_4$ ANTAGONIST ACCELERATES THE ANTIDEPRESSANT EFFECTS OF CITALOPRAM

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Objectives: Improvement in symptoms of depression is typically delayed with antidepressant treatment. Pipamperone (PIP) at low doses acts as a highly selective 5HT$_{2A}$/D$_4$ receptor antagonist. The purpose of this study was to investigate whether the addition of PIP to the SSRI citalopram (CIT) would increase the rate of resolution of depressive symptoms.

Methods: This was an 8-week, double-blind, parallel-group, single-dummy study in patients with MDD who received either CIT 40 mg daily or PIP 5 mg bid plus CIT 40 mg daily (PIPCIT).

Results: The mean total MADRS score (±SD) of the 165 patients (81% women; mean age, 40 y) was 32.6±5.5. More CIT than PIPCIT patients discontinued treatment in the first 4 weeks [15 (18%) vs 3 (4%); P=0.003]. Reductions in mean total MADRS scores were significantly (ITT LOCF) larger in patients receiving PIPCIT after 1 week [-6.42±6.18 vs -3.99±5.15; P=0.007] and 4 weeks [-15.06±8.48 vs -12.11±8.30; P=0.025] compared with those receiving CIT alone. Significant differences in favor of PIPCIT were observed in MADRS items “reduced sleep,” “reduced appetite,” “concentration difficulties,” and “pessimistic thoughts.” Mean CGI-I scores were also improved after 1 week of PIPCIT [3.09±0.85 vs. 3.47±0.72; P=0.002]. There were no significant differences observed at 8 weeks. No additional, clinically significant adverse events were noted in the PIPCIT group.

Conclusions: A low dose of PIP added to CIT provided superior antidepressant effects and less discontinuations compared with CIT alone during the first 4 weeks of treatment, and especially in the first week, at apparently no tolerability/safety cost.

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