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ORIGINAL ARTICLE

Antidepressant monotherapy compared with combinations of antidepressants in the treatment of resistant depressive patients: A randomized, open-label study

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Abstract

Objective. This randomized, 6-week, open-label study compared efficacy of CAD and antidepressant monotherapies (ADM) that had been chosen according to clinical judgment of the attending psychiatrist. *Methods.* A total of 60 inpatients (intent-to-treat analysis) with depressive disorder (≥ 1 unsuccessful antidepressant treatment) were randomly assigned to the interventions. The responders who completed the acute phase of study, were evaluated for relapse within 2 months of follow-up treatment. The primary outcome measure was change in the Montgomery–Åsberg Depression Rating Scale (MADRS) and response was defined as a ≥ 50% reduction of MADRS score. *Results.* Mean changes in total MADRS score from baseline to week 6 for patients in both treatment modalities were not different (ADM = 13.2 ± 8.6 points; CAD = 14.5 ± 9.5 points; $P = 0.58$). The analysis of covariance performed for significantly higher value of imipramine equivalent dose in CAD group showed only a non-significant between-group difference for total MADRS change ($P = 0.17$). There were also no differences between groups in response rate (ADM = 48%; CAD = 58%) and number of drop-outs in acute treatment as well as proportion of responders' relapses in the follow-up. *Conclusions.* Both treatment modalities produced clinically relevant reduction of depressive symptomatology in acute treatment of patients with resistant depression and their effect was comparable.

Key Words: *Resistant depression, treatment, antidepressant monotherapy, combination of antidepressants*

Introduction

Major depressive disorder (MDD) is a chronic, recurrent illness associated with significant morbidity and mortality. Despite recent progress in psychopharmacology and treatment possibilities many (about 30%) patients do not respond to standard antidepressant monotherapy (ADM) [1,2]. The most frequent pharmacological methods to manage resistant depression are switching antidepressants (ADs), augmentation of ADs with various compounds (second-generation antipsychotics, triiodothyronine, lithium, pindolol, buspirone, etc.), and combinations of two distinctly different ADs. However, there is no clear consensus in current guidelines of treatment which strategy should be preferred [3–5]. Antidepressant combination (CAD) is an often used strategy to overcome resistance to treatment in current clinical practice [6,7]. A combination of ADs might increase the number of patients who could benefit from treatment [8,9]. Synergy between various mechanisms of action might affect a wider range of neurotransmitter or neuromodulator systems that might lead to faster onset of action and potential avoidance of side effects [10,11]. There are plenty of possible combinations but the evidence supporting their efficacy ranges from nothing or case reports to randomized clinical trials [12–14]. CAD can be applied in two different approaches: (1) Continuing the first AD and adding the second one, (2) combining two new ADs from the initiation of treatment. Several double-blind studies demonstrated higher efficacy

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