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Original Research

Do depressed patients on adjunctive atypical antipsychotics demonstrate a better quality of life compared to those on antidepressants only? A comparative cross-sectional study of a nationally representative sample of the US population

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Abstract

Background: The adjunctive use of some atypical antipsychotics (AAPs) has been popular for patients with treatment-resistant depression. However, little is known about the impact of these agents on patients' Health-related quality of life (HRQoL).

Objectives: The objective of this study is to examine the impact of the adjunctive AAPs use on HRQoL among users of antidepressants with self-reported depression.

Methods: Patients with depression (ICD-9-CM: 296, 300, and 311), and to have used the given AAPs and/or antidepressants for at least a year, were identified in the Medical Expenditure Panel Survey of 2008–2011. The patients were classified into users of adjunctive AAPs (i.e., antidepressants plus AAPs) and users of antidepressants only. Adjusted multivariate linear regression analyses were conducted to examine the association between the utilization of AAPs and HRQoL measure.[c]

Results: A total of 3638 participants who met the inclusion criteria were identified (306 on AAPs vs. 3332 on antidepressants only). The study subjects were $\geq$18 years, predominately White (91.9%) and female (71%). The AAPs utilization was not associated with higher scores in the Physical Component Summary (PCS-12) of the Short Form Health Survey (SF-12v2) (β = 1.542, 95% CI = −0.0142 to 3.0977, P = 0.0521). Rather, it was negatively associated with the Mental Component Summary (MCS-12) scores of the SF-12v2 (β = −1.5537, 95% CI = −3.0247 to −0.0827, P = 0.0385).

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[c] Socio-demographics, Charlson Comorbidity Index, Satisfaction with the Quality of Health Care, Patient Health Questionniare-2 (PHQ-2) scores, and number of prescription medications associated with depression were controlled for.

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Conclusions: The utilization of AAPs was not associated with higher scores of HRQoL. The findings of this study should underscore the need to consider other treatment options as add-on therapy for depression before resorting to AAPs.

Keywords: Health-related quality of life (HRQoL); Atypical antipsychotic agents (AAPs); Antidepressants (ATDs); Short Form Health Survey-12 version two (SF-12v2); Physical Component Summary-12 (PCS-12); Mental Component Summary-12 (MCS-12)

Introduction

The advent of antipsychotic agents in the late 1950s has revolutionized the treatment of psychiatric disorders. The first generation of these medications (FGAs), which are also known as typical antipsychotics, were mainly indicated for schizophrenia and bipolar disorders, and were found to be effective. However, the typical antipsychotics were largely replaced in the last two decades by the newer atypical agents (AAPs), also known as second generation antipsychotics (SGAs), given their favorable adverse effects profiles over their predecessors .[1,2] All atypical antipsychotics possess serotonin-2 receptor blockade activity and some have norepinephrine reuptake inhibition properties. Furthermore, some atypical antipsychotic agents have histamine-1 (H_1) receptor antagonism properties.[3] Taken altogether, these properties made these agents attractive for psychiatrists to include them in their prescribing lists for patients with different depressive disorders.[4]

As many as 40% of patients with depression reportedly fail to respond to conventional therapy, which mostly consists of a single antidepressant agent at an adequate dose and duration.[5–7] This is in line with the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial's findings, which is regarded as the gold standard for non-psychotic depressive disorders treatment.[8] Therefore, the American Psychiatric Association practice guidelines recommend that patient on a certain antidepressant who failed to have an adequate response after an adequate period of time should be switched to different antidepressants.[9] However, if the patient partially responded to the initial treatment, clinicians can either titer up the dose till the patient responds, add another antidepressant to the patient's treatment regimen or consider augmenting the antidepressant effect of the initial agent using different therapeutic agents (i.e. lithium, atypical antipsychotics, buspirone).[8–10]

Thus, patients with treatment-resistant depression (TRD), those who have not responded to one or more antidepressant(s), become candidates for adjunctive drug therapies of their depression.[11] Although atypical antipsychotics were not originally indicated for depression treatment, the off-label use of some of these agents to treat both minor and major non-psychotic depression is common.[12] The atypical antipsychotics are increasingly being used to treat depression especially after several randomized controlled trials have showed their superiority over placebo as an adjunctive therapy for patients with TRD.[10,13–16] Hence, the American Psychiatric Association has included AAPs in their treatment guidelines for non-psychotic depressive disorders as an adjunctive therapy.[9] However, it is important to note that only some and not all atypical antipsychotic agents are recommended as an adjunctive therapy for TRD. Aripiprazole, olanzapine/fluoxetine combination [OFC], and quetiapine have received FDA approvals for the adjunctive treatment of Major Depressive Disorder (MDD).[3,17] Furthermore, quetiapine has received an approval from the FDA for bipolar depression treatment as single-agent therapy.[18,19] However, other atypical antipsychotic agents such as risperidone and ziprasidone are used in practice as adjunctive therapy to manage TRD despite the fact that they are not approved yet by the FDA.[14,20–23] While the adjunctive use of AAPs has resulted in a slight but significant reduction in the observer-rated depressive symptoms, there is a lack of benefit with regard to patient reported outcomes (PROs) (i.e. quality of life, functional impairment, and patient-rated depressive symptoms).[16] PROs such as the quality of life is significantly associated with validated measures of depressive symptoms such as Hamilton Rating Scale for Depression and the Beck Depression Inventory.[24] The severity of depression is inversely