Adverse Effects of Second-Generation Antipsychotics as Adjuncts to Antidepressants

Are the Risks Worth the Benefits?

Michael E. Thase, MD

KEYWORDS

• Adverse effects • Second-generation antipsychotics • Adjunctive therapy • Risks • Benefits

KEY POINTS

- Using attrition due to adverse effects as the indicator of harm, the number needed to harm in short-term clinical trials ranges from 8 to 20 (ie, 5% to 12% risk differences in attrition).
- There are meaningful differences in the incidence of specific adverse effects, with akathisia more common with aripiprazole, sedation more common with quetiapine extended release, and weight gain more common with olanzapine.
- Duration of therapy is an important determinant of longer-term risks, and careful monitoring of weight and related metabolic parameters is indicated during continuation pharmacotherapy; cases of tardive dyskinesia have been observed within the first year of continued adjunctive second-generation antipsychotics (SGA) therapy.
- Although the benefits of adjunctive therapy with SGAs can be considerable, treatment with these adjuncts appears most indicated for depressed patients who are unlikely to respond to alternate strategies and for whom the rapidity of benefit (eg, inpatient status, marked impairment, or worsening symptom severity) justifies the several risks.

Financial Disclosure: During the last 3 years, Dr M.E. Thase reports earning fees as a consultant to Alkermes, Allergan, AstraZeneca, Avenir, Aventis, Bristol-Myers Squibb, Cerecor, Eli Lilly & Co, Forest Laboratories, Gerson Lehman Group, GlaxoSmithKline, Guidepoint Global, Janssen (Johnson & Johnson), H. Lundbeck A/S, MedAvante, Inc, Merck, Naurex, Neuronetics Inc, Novartis, Otsuka, Nestle (PamLab), Pfizer, Roche Inc, Shire US Inc, Sunovion, and Takeda. During the same timeframe, he has received research grants from Agency for Healthcare Research and Quality, Alkermes, AstraZeneca, Assurex, Avenir, Eli Lilly & Co, Forest Pharmaceuticals, GlaxoSmithKline, Janssen (Johnson & Johnson), the National Institute of Mental Health, Otsuka Pharmaceuticals, Pharmaneuroboost, Roche, and Takeda. Dr M.E. Thase's spouse is an employee of Peloton Advantage, which does business with several pharmaceutical companies.

Mood and Anxiety Treatment and Research Program, Perelman School of Medicine, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104-3309, USA
E-mail address: thase@mail.med.upenn.edu

Psychiatr Clin N Am 39 (2016) 477–486
http://dx.doi.org/10.1016/j.psc.2016.04.008 **psych.theclinics.com**
0193-953X/16/$ – see front matter © 2016 Elsevier Inc. All rights reserved.

INTRODUCTION

Major depressive disorder (MDD) is one of the world's great public health problems and, until recently, development of safe and effective novel antidepressant medications was one of the top priorities of the pharmaceutical industry. These efforts have led to development of several newer classes of medications that have largely supplanted older standards, including "classic" drugs such as the tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs), as the antidepressants of first choice throughout most of the economically developed world. However, the advantages of the newer medications over the TCAs and MAOIs were in areas such as ease of use, tolerability, and safety in overdose, not efficacy. The newer antidepressants are, in fact, either no more effective or slightly less so than the older standards. As the use of antidepressants has skyrocketed since the introduction of fluoxetine in late 1987 ushered in the modern era of antidepressant therapy, so too has the problem of antidepressant nonresponse. This problem is mammoth in scope, because as many as 10% of the adult US population now take antidepressants and only about one-half of the depressed patients who begin pharmacotherapy will experience at least a 50% reduction in symptom intensity (ie, a minimal definition of response) after 6 to 8 weeks of therapy with an adequate dose of medication.[1] There is evidence that the problem of antidepressant nonresponse grows progressively as the number of failed treatment trials mounts. For example, about 60% of those who continue on for a second course of treatment will not respond, and after 4 trials, about 30% of patients will still be depressed.[1] Patients who have not responded to 2 sequential, adequate courses of antidepressant medication are considered by some experts and regulatory guidelines alike to meet the minimum definition of treatment-resistant depression (TRD).[2] In one large-scale study known as Sequenced Treatments Alternatives to Relieve Depression (STAR*D),[1] for example, patients who had not responded to 2 trials of newer-generation antidepressants had less than a 20% chance of remission with subsequent monotherapy trials with 2 of the old favorites, the TCA nortriptyline and the MAOI tranylcypromine. Because patients with TRD account for a disproportionately large share of the burden/disability associated with MDD,[3] developing safe and effective strategies for them represents one of the most important topics in psychiatric therapeutics. It is within this context that adjunctive therapy with second-generation antipsychotics (SGA) has emerged as one of the leading options for patients with TRD. This article considers the benefits of adjunctive SGA therapy as well as the risks.

OVERVIEW OF TREATMENT-RESISTANT DEPRESSION

Although clinicians often think about TRD as a categorical entity (ie, either you meet the criteria or you do not), patients' histories and patterns of response and nonresponse vary dramatically across several dimensions. At the most superficial level, it seems unlikely that someone who has not responded to two 6-week courses of selective serotonin reuptake inhibitor (SSRI) therapy at minimum doses has the same prognosis as someone who has not responded to 12 months of continuous therapy with 4 different classes of medication. Conversely, although clinicians often consider electroconvulsive therapy (ECT) to be the sine qua non of biological therapies for severe depression, it is unlikely that this venerable treatment, which is more intensive, invasive, and costly than most other strategies, would be considered the most appropriate option for the first patient described above, but many would agree that it is a reasonable next step for the second patient. Similar

Download English Version:

https://daneshyari.com/en/article/4188951

Download Persian Version:

https://daneshyari.com/article/4188951

Daneshyari.com