Trend Watch

Real-world Data on Atypical Antipsychotic Medication Side Effects

by Elisa Cascade; Amir H. Kalali, MD; Sagar Mehra; and Jonathan M. Meyer, MD

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ABSTRACT

In this article, we provide information on patient-reported side effects from a cross-section of real-world patients. Specifically, data on side effects were tabulated for patients taking at least one of the following atypical antipsychotic medications: aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone. Approximately 54 percent of the 353 respondents reported having experienced a side effect as a result of taking an atypical antipsychotic medication. Most common side effects mentioned included the following: weight gain/hunger, tiredness/lethargy, and lack of coordination/muscle problems, such as tenderness, twitches, and tremors. Of those experiencing a side effect, less than 25 percent reported this side effect to their physician.

KEY WORDS

Aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone, atypical antipsychotic, side effect, self report, schizophrenia

INTRODUCTION

Recognizing that time for patient care is limited, it is important for practicing physicians to understand which issues to prioritize in their interactions with patients and caregivers. In this article, we provide information on patient-reported side effects from a cross-section of real-world patients.

METHODS

iGuard.org, a medication monitoring service, randomly surveys enrolled members on a continuous basis to obtain data on treatment satisfaction, efficacy, and side effects using a validated patient-reported outcomes instrument called the Treatment Satisfaction Questionnaire for Medications (TSQM). Data on side effects were tabulated for patients taking at least one of the following atypical antipsychotic medications: aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone.

RESULTS

Fifty-four percent of the 353 iGuard.org members who completed a survey reported having experienced a side effect as a result of taking an atypical antipsychotic medication. Figure 1 displays the

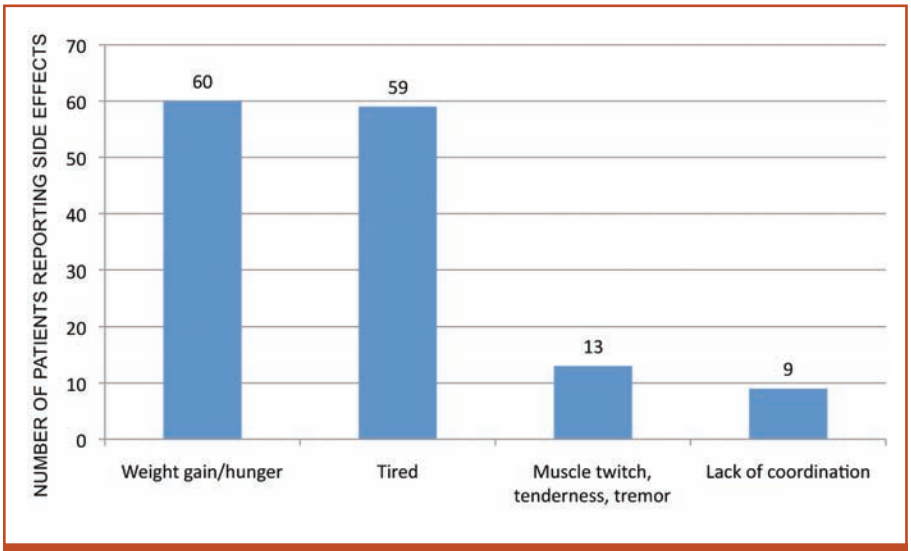

FIGURE 1. Most commonly mentioned side effects (n=172 patients listing at least 1 side effect)
All other mentions are <5% prevalence.
SOURCE: Analysis of www.iGuard.org data for aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone

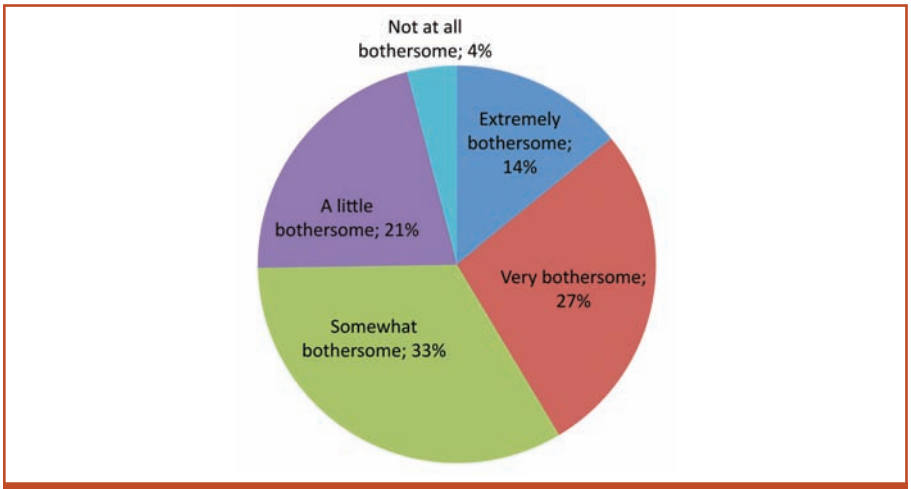

FIGURE 2. Impact of side effects
SOURCE: Analysis of www.iGuard.org data for aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone

most commonly mentioned side effects. As seen in Figure 1, of the 172 patients who listed at least one side effect, 30 to 35 percent of patients reported weight gain/always hungry and/or tiredness/lethargy. Lack of coordination and muscle problems, such as twitches, tenderness, or tremors, were also mentioned by 5 to 10 percent of patients.

Forty-one percent of these patients experiencing a side effect with their atypical antipsychotic medication indicated that the side effects were very bothersome or extremely bothersome (Figure 2). As seen in Figure 3, however, only approximately 25 percent of those individuals experiencing side effects reported them to their physicians.

EXPERT COMMENTARY

by Jonathan M. Meyer, MD

The literature on antipsychotic-related adverse effects has evolved significantly in the past decade from a focus on the incidence of individual complaints to a more holistic concern over global patient impact. Included in this enlarged perspective is the role of side-effect burden on medication adherence and resultant psychiatric outcomes. This relationship between psychiatric course and medication-related side effects is seen most clearly with weight gain. Using body mass index (BMI) as a proxy measure, Fagiolini[1] published longitudinal data from a bipolar sample (n=125) demonstrating that subjects with obesity had shorter time to recurrence of symptoms than subjects without obesity (log rank $\bar{}2=5.54$, df=1, $p<0.02$). Weiden et al[2] subsequently examined self-reported antipsychotic adherence over the prior 30 days in a sample of 249 patients with schizophrenia, stratified by BMI category (normal, overweight, obese). While 26 percent of normal BMI subjects reported recent nonadherence, this rate increased to 39 percent for the overweight group, and 47 percent in the obese cohort (Figure 4).

Given this relationship between psychiatric outcomes and adverse effects, the iGuard data raise three important issues:

1. Antipsychotic-related side effects continue to be highly prevalent among atypical antipsychotic exposed patients.
2. Antipsychotic side effects cause significant distress.
3. The extent of patient distress and concern from antipsychotic adverse effects is significantly underreported to treating physicians.

Obesity in general and treatment-emergent weight gain in particular are major clinical problems for individuals who are severely mentally ill. Medication-related weight gain and hunger are directly related to antipsychotic affinity for histamine H_1 receptors and blockade of hypothalamic sites regulating satiety.[3,4] Despite the fact that several of the surveyed antipsychotics have modest H_1 affinity, weight gain was a significant problem in the iGuard sample, with a prevalence (60%) nearly identical to that reported in a 2001 survey of 99 patients with schizophrenia (59%).[5] Moreover, the 2001 study found that 64 percent of patients with weight gain complaints reported moderate to severe distress due to weight gain. The high level of subjective distress from weight gain has been reported elsewhere[6] and helps explain why patients may choose to forego effective treatments, a finding seen in the national Institute of Mental Health (NIMH)-sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Schizophrenia trial. Despite the fact that olanzapine was superior to other treatments on time to all cause discontinuation in Phase 1, olanzapine had the numerically highest drop out rate due to adverse effects (18% vs. 10–15% for all other agents in phase 1), primarily due to weight gain.[7] The iGuard data and the Weiden 2004 paper raise the concern that if the distress from antipsychotic-induced weight gain is not directly communicated to physicians, it may be manifested as medication nonadherence.

Consistent with the reduced incidence of acute extrapyramidal adverse effects with atypical antipsychotics (compared to older, potent dopamine D_2 antagonists), neurological complaints in the iGuard survey are minimal, especially when compared to the 2001 schizophrenia survey data;[5] however, fatigue (tiredness/lethargy) has emerged as a subjective concern on par with weight gain. Tiredness is a composite outcome measure reflecting the effects of central H_1 and muscarinic antagonism, with additive impact from α_1-adrenergic and D_2 blockade. As expected from their receptor affinities, olanzapine and quetiapine have significant clinical signals for sedation or somnolence, but the data presented here indicate that clinicians may be overlooking these issues among users of other antipsychotics that are, in theory, nonsedating. Lastly, it is surprising that sexual adverse effects were not on the iGuard list of

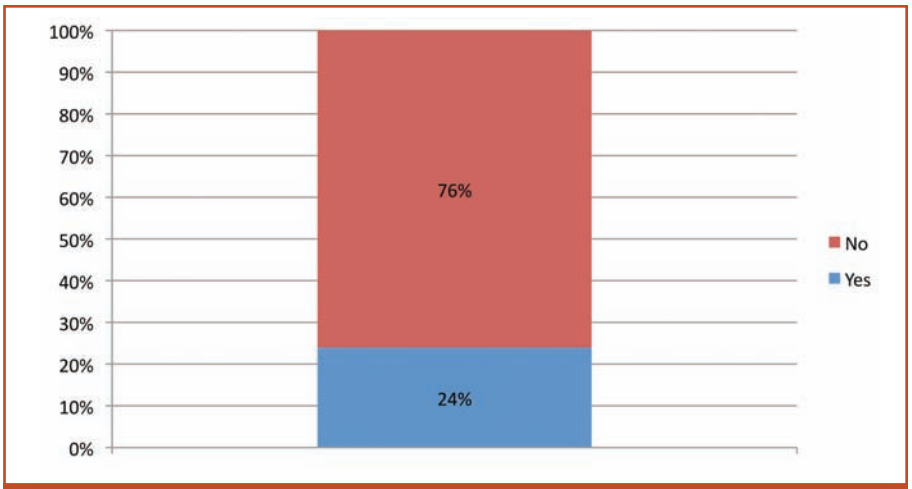

FIGURE 3. Patients reporting side effects to their physician
SOURCE: Analysis of www.iGuard.org data for aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone

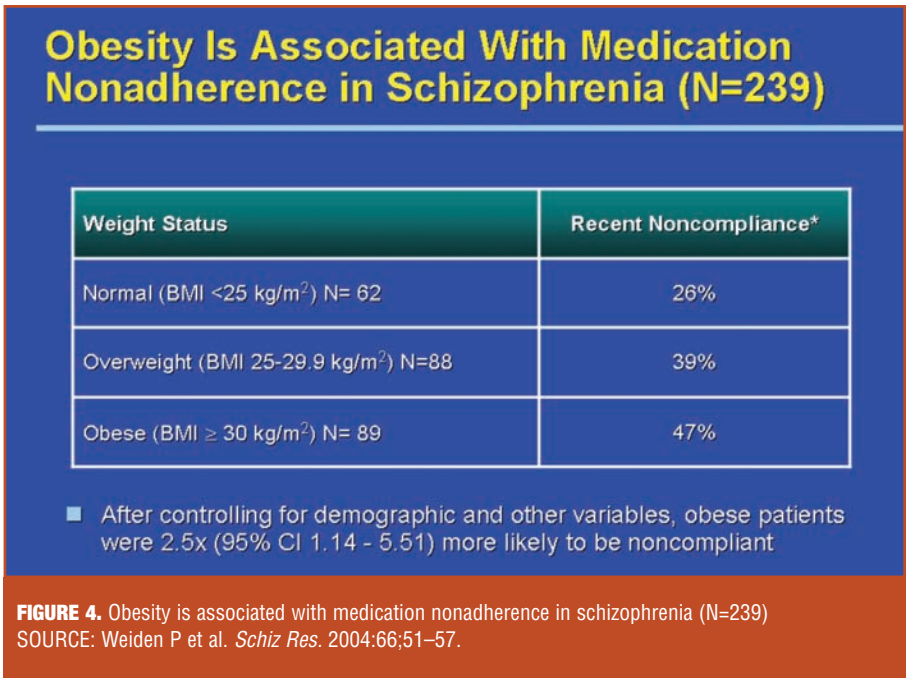

FIGURE 4. Obesity is associated with medication nonadherence in schizophrenia (N=239)
SOURCE: Weiden P et al. *Schiz Res.* 2004:66;51–57.

common side effects (i.e., ≥5%). This may represent a distinct pattern with respect to the adverse effect profiles of newer antipsychotics, but may also represent methodological or sampling issues with respect to the conduct of the survey. Clinicians should be mindful that as recently as 2001, 39 percent of the 99 schizophrenia subjects surveyed experienced antipsychotic-related sexual complaints, of whom 79 percent reported moderate-to-severe distress.[5] Sexual issues in the severely mentally ill are commonly overlooked and significantly underreported,[8] so the absence of self-reported sexual adverse effects from antipsychotic treatment, even with an anonymous survey, should not lead the assumption that these issues do not exist.

The overarching theme from this iGuard survey is that patients continue to suffer from significant antipsychotic-related side effects, but suffer silently. Whether the underreporting of antipsychotic adverse effects is the product of disease-related factors (e.g., negative symptoms of schizophrenia) or systemic variables (e.g., limited physician contact time, perceived lack of clinician interest by the patient), these results emphasize the need for directed inquiry regarding the existence of side effects and level of patient distress. Such discussions build patient rapport and are consonant with the Shared Decision Making model designed to promote patient participation in treatment decisions, and improve treatment outcomes.[9]

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