Detecting and Managing Adverse Effects of Antipsychotic Medications

Current State of Play

Donna Ames, MD[a,b,*], Sian M. Carr-Lopez, PharmD[c,d], Mary A. Gutierrez, PharmD, BCPP[e], Joseph M. Pierre, MD[f,g], Jennifer A. Rosen, PharmD, BCPP[h,i,j], Susan Shakib, PharmD, BCPS[k,l], Lynn M. Yudofsky, MD[m]

KEYWORDS

• Antipsychotic medication • Adverse effects • First-generation antipsychotics • Second-generation antipsychotics • Weight gain • Hyperlipidemia • QT prolongation • Hyperprolactinemia

KEY POINTS

- This review provides a summary of the most recent evidence of the adverse effects profiles of each of the currently available antipsychotic medications.
- This article reviews the relative propensity for certain antipsychotics to induce weight gain, diabetes, hyperlipidemia (HLP), cardiac side effects, sudden death, sexual side effects, and osteoporosis.

Continued

[a] Department of Psychiatry, Psychosocial Rehabilitation and Recovery Center, West Los Angeles Veterans Affairs Medical Center, 11301 Wilshire Boulevard, Los Angeles, CA 90073, USA; [b] David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue, Los Angeles, CA 90095, USA; [c] Pharmacy Service, Veterans Affairs Northern California Health Care System, 10535 Hospital Way, Mather, CA 95655, USA; [d] Department of Pharmacy Practice, University of the Pacific, 3601 Pacific Avenue, Stockton, CA 95211, USA; [e] Chapman University School of Pharmacy, 9401 Jeronimo Road, Irvine, CA 92618, USA; [f] Schizophrenia Treatment Unit, West Los Angeles VA Medical Center, Los Angeles, CA 90073, USA; [g] Department of Psychiatry & Biobehavioral Sciences, David Geffen School of Medicine at UCLA, 10833 Le Conte Avenue, Los Angeles, CA 90095, USA; [h] Department of Pharmacy, Veterans Affairs Northern California Healthcare System, 150 Muir Road, Martinez, CA 94553, USA; [i] University of the Pacific School of Pharmacy, 3601 Pacific Avenue, Stockton, CA 95211, USA; [j] University of Southern California School of Pharmacy, 1985 Zonal Avenue, Los Angeles, CA 90089, USA; [k] Thomas J. Long School of Pharmacy & Health Sciences, University of the Pacific 3601 Pacific Avenue, Stockton, CA 95211, USA; [l] Department of Pharmacy, Veterans Affairs Long Beach Healthcare System, 5901 East 7th Street, Long Beach, CA 90822, USA; [m] Semel Institute for Neuroscience & Human Behavior, UCLA, 760 Westwood Plaza, Suite C8-193, Los Angeles, CA 90024, USA
* Corresponding author.
E-mail address: Donna.ames@va.gov

Psychiatr Clin N Am 39 (2016) 275–311
http://dx.doi.org/10.1016/j.psc.2016.01.008 **psych.theclinics.com**
0193-953X/16/$ – see front matter Published by Elsevier Inc.

Continued

- Readers will learn about appropriate clinical approaches to recognizing, monitoring and mitigating adverse effects.
- Guidelines for appropriate monitoring of these medications' adverse effects are presented.

INTRODUCTION

Antipsychotic drugs (APDs) are some of the most frequently prescribed medications, not only for psychotic disorders and symptoms but also for a wide range of both on-label and off-label indications, including affective disorders, anxiety disorders, behavioral disturbances, and insomnia. Because second-generation APDs (SGAs) have largely replaced first-generation APDs (FGAs) as first-line options due to their substantially decreased risk of extrapyramidal side effects, attention has shifted to other clinically concerning adverse events associated with APD therapy. The focus of this article is to update the authors' previous review[1] of the nonextrapyramidal side effects associated with SGAs, including weight gain, diabetes, HLP, cardiac side effects, mortality risk, hyperprolactinemia (hPRL), sexual side effects, and osteoporosis. Issues surrounding diagnosis and monitoring as well as clinical management are addressed.

WEIGHT GAIN

Relative to the general population, treatment-naïve patients with schizophrenia and bipolar disorder have a higher prevalence of obesity and being overweight.[2,3] Nonetheless, controlled clinical trials have consistently demonstrated greater degrees of weight gain during treatment with APDs compared with placebo, although individual differences in relative weight gain exist between medications. Weight gain and obesity are concerning due to an associated decrease in medication adherence and an increase in the risk of cardiovascular disease.[2,4] This is especially concerning among those with severe mental illnesses (SMIs), who seem at significantly higher risk for cardiovascular morbidity and mortality, which is the most common cause of death in this population.[2,4]

Mechanisms

The precise mechanism underlying APD-induced weight gain is not fully understood. Several theoretic mechanisms have been postulated involving neurochemical mechanisms that result in imbalances between energy intake and expenditure.[5,6] It has been speculated that APD-induced weight gain may involve antagonism of histamine H_1 and serotonin 2C receptors[5,7,8] inasmuch as brain serotonin seems to play a role in influencing satiety and hunger, whereas the histaminergic system affects food intake and energy regulation.[9] It has been speculated that APD-induced weight gain may involve antagonism of histaminergic H1 and serotonin 2C receptors.[10]

Available clinical evidence suggests that APD-induced weight gain may arise from an increase in appetite and food intake, in conjunction with delayed signaling of satiety.[11,12] A 6-week double-blind randomized controlled trial (RCT) comparing the eating behavior of patients taking CLZ and OLZ revealed an increase in food cravings and binge eating over time for both medications.[13] Between the 2 treatment groups, food cravings and binge eating were more frequent with OLZ (48.9% and 16.7%, respectively) relative to CLZ (23.3% and 8.9%, respectively). These results suggest that APDs influence feeding behaviors that contribute to weight gain.