Letters to the Editor

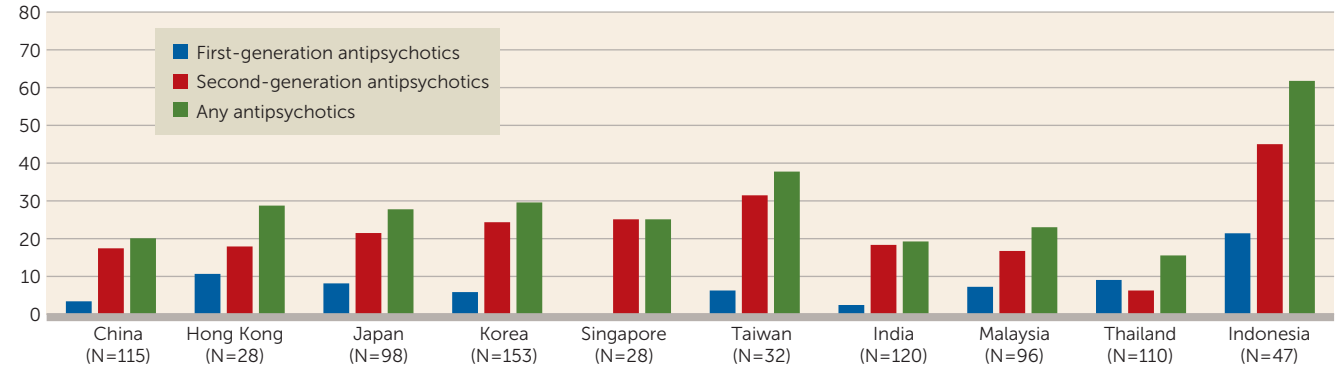
Adjunctive Antipsychotic Prescriptions for Outpatients with Depressive Disorders in Asia: The Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) Study

TO THE EDITOR: Augmenting treatment with antidepressants with second-generation antipsychotics for partial- and nonresponders to first treatment and for psychotic depression is recommended on the basis of excellent evidence by most pharmacological treatment guidelines for depressive disorders (1). The data from the Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) study include information on pharmacological treatment for outpatients with depressive disorders over the period March to June 2013 in 10 Asian countries: China, Hong Kong, Japan, Korea, Singapore, Taiwan, India, Malaysia, Thailand, and Indonesia (2). A total of 827 outpatients, aged from 18 to 80 years and diagnosed with depressive episode (F32) or recurrent depressive disorder (F33) according to ICD-10, were enrolled.

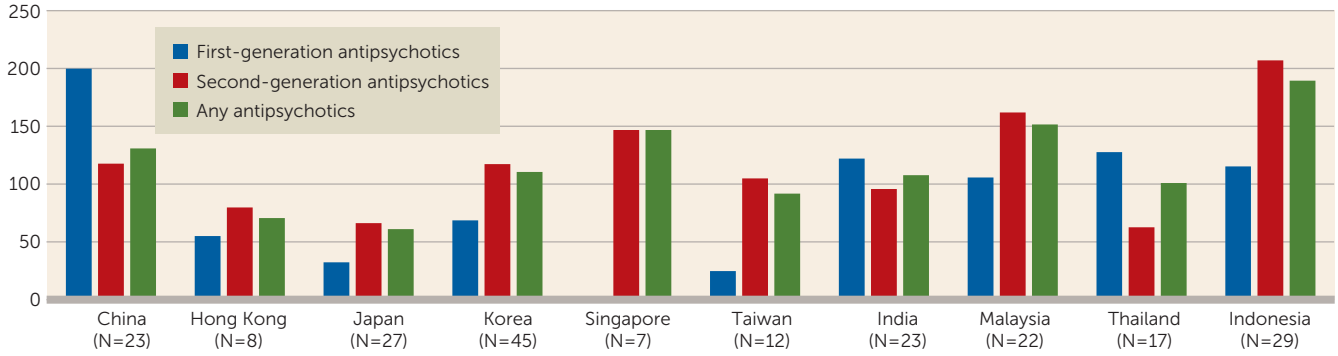
The average antipsychotic prescription rate in these depressed outpatients in Asia was 25.8% (N=213). As shown in Figure 1A, there was a tendency for the percentage prescription of second-generation antipsychotics to be greater than that of first-generation antipsychotics in all countries/regions, and the percentage of depressed outpatients receiving any antipsychotic ranged from 15.5% (Thailand) to 61.3% (Indonesia). The percentage of prescriptions for adjunctive antipsychotics in Indonesia was much greater than in any other country/region ($\chi^2=46.652$, $p<0.0001$). The percentage of depressed outpatients receiving second-generation antipsychotics ranged from 6.3% (Thailand) to 44.7% (Indonesia), compared with 0.0% (Singapore) to 21.3% (Indonesia) for first-generation antipsychotics. As shown in Figure 1B, the average chlorpromazine-equivalent dose for depressed outpatients prescribed with antipsychotics ranged from 61.2 mg (Japan) to 189.8 mg (Indonesia). Especially, the chlorpromazine-equivalent dose for depressed outpatients in Indonesia was greater than that in the other countries ($F=2.908$, $p=0.003$). More specifically, the average chlorpromazine-equivalent

FIGURE 1. Adjunctive Antipsychotic Prescriptions for Outpatients with Depressive Disorders in 10 Asian Countries

A. Percentage (%) of depressed patients receiving antipsychotics



B. Average chlorpromazine-equivalent dosage (mg) for depressed patients receiving antipsychotics



doses for depressed outpatients prescribed first- and second-generation antipsychotics ranged from 25.0 mg (Taiwan) to 200.0 mg (China) and from 62.6 mg (Thailand) to 207.1 mg (Indonesia), respectively.

A cohort study of depression in individuals ages 18 to 64 in Florida Medicaid (1996–2005) revealed a 10-year trend in which the percentage of adjunctive antipsychotic use rose from 25.9% to 41.9% (3). The results of the present study suggest that the percentages of adjunctive antipsychotic prescriptions in the 10 Asian countries, excluding Indonesia, are somewhat lower than in the United States. Higher percentage and average chlorpromazine-equivalent dose of adjunctive antipsychotic prescription in outpatients with depression in Indonesia can be influenced by greater prevalence of psychotic symptoms and uncontrolled behaviors and economic advantages for antidepressants. Moreover, international differences in clinical manifestations of depressive disorder can be attributed to the pathofacilitative or pathoreactive effects of specific cultures (4). In addition, adjunctive antipsychotic prescriptions for depressed outpatients can be influenced by psychopathology, cultural effects, clinical practice guidelines, national insurance systems, clinicians' preferences, and other factors. To understand the pattern of antipsychotic supplementation for depressed outpatients in Asia, a further study identifying the most important contributing factors is needed.

REFERENCES

1. Han C, Wang SM, Kato M, et al: Second-generation antipsychotics in the treatment of major depressive disorder: current evidence. Expert Rev Neurother 2013; 13:851–870
2. Park SC, Lee MS, Shinfuku N, et al: Gender differences in depressive symptom profiles and patterns of psychotropic drug usage in Asian patients with depression: findings from the Research on Asian Psychotropic Prescription Patterns for Antidepressants study. Aust N Z Psychiatry 2015 March 31. pii: 0004867415579464.
3. Fullerton CA, Busch AB, Normand SLT, et al: Ten-year trends in quality of care and spending for depression: 1996 through 2005. Arch Gen Psychiatry 2011; 68:1218–1226
4. Tseng W-S: Culture and psychopathology: general view, in Textbook of Cultural Psychiatry. Edited by Bhugra D, Bhui K. Cambridge, England, Cambridge University Press, 2007, pp 95–112

Seon-Cheol Park, M.D., Ph.D.
Naotaka Shinfuku, M.D., Ph.D.
Margarita M. Maramis, M.D.
Min-Soo Lee, M.D., Ph.D.
Yong Chon Park, M.D., Ph.D.

From the Department of Psychiatry, Yong-In Mental Hospital, Yongin, South Korea; the Department of Social Welfare, School of Human Sciences, Seinan Gakuin University, Fukuoka, Japan; the Department of Psychiatry, Faculty of Medicine, University of Airlangga / Dr. Soetomo General Hospital, Surabaya, Indonesia; the Department of Psychiatry, Korea University College of Medicine, Seoul, South Korea; and the Department of Psychiatry, Hanyang University College of Medicine, Seoul, South Korea.

The authors report no financial relationships with commercial interests.

This letter was accepted for publication in May 2015.

Am J Psychiatry 2015; 172:684–685; doi: 10.1176/appi.ajp.2015.14121590

Gluten-Free Diet Regimens and Psychiatric Symptoms

TO THE EDITOR: The article by William W. Eaton, Ph.D., and colleagues (1), published in the March 2015 issue of the *Journal*, described the case of an adolescent with complex autoimmune illness, whose psychotic symptoms were found to significantly improve after a gluten-free diet and pharmacological treatment with antidepressant and antipsychotic medication. The authors discussed possible mechanisms implied in patient's response to the gluten-free diet, arguing for immunological abnormalities and neuroinflammatory processes that may have played a role in the pathogenesis of schizophrenia and autoimmune conditions.

The patient had two previous diagnoses of major depressive disorder with psychotic features, and the family had a history of affective disorder, with both parents having a history of seasonal affective disorder and two grandparents having experienced bouts of depression. In addition, the patient was treated with low dosages of antipsychotics (previously 5 mg/day of aripiprazole, afterward 1.5 mg/day of risperidone) along with antidepressants (previously 10 mg/day of escitalopram, afterward 150 mg/day of venlafaxine). Taken as a whole, these elements suggest the possibility of an affective diathesis rather than schizophrenia. This diagnostic interpretation would not disconfirm the presence of interplaying immunoinflammatory patterns underlying the genesis of complex autoimmune and psychiatric conditions, like major depressive disorder, as these have been consistently reported (2) along with a positive response following a gluten-free diet in depressed patients (3).

The patient's gluten sensitization does not conform to a recognized gluten-related disorder subtype. However, celiac disease is suggested by the presence of anti-gliadin antibodies and the relevant autoimmune family history (unfortunately, human leukocyte antigen typing and duodenal histology are unknown), while positivity to specific immunoglobulin E underlines a possible Th2 allergic pathway. Neurological and mood alterations of various severity have been widely reported in all gluten-related disorders, as possible extraintestinal symptoms improving during a gluten-free dietetic regimen. Ultimately, on the basis of the current knowledge and the absence of gluten-free diet side effects, dietotherapy should be further investigated in addition to current pharmacological treatments (4, 5).

REFERENCES

1. Eaton WW, Chen LY, Dohan FC Jr, et al: Improvement in psychotic symptoms after a gluten-free diet in a boy with complex autoimmune illness. Am J Psychiatry 2015; 172:219–221
2. Anderson G, Maes M: Oxidative/nitrosative stress and immunoinflammatory pathways in depression: treatment implications. Curr Pharm Des 2014; 20:3812–3847
3. Carr AC: Depressed mood associated with gluten sensitivity: resolution of symptoms with a gluten-free diet. N Z Med J 2012; 125:81–82
4. Peters SL, Biesiekierski JR, Yelland GW, et al: Randomised clinical trial: gluten may cause depression in subjects with non-coeliac gluten