Drs Chan and Gau Reply

To the Editor: We appreciate the comments made by Suzuki et al regarding our recently published article.[1] We provide our response to each of their comments as follows.

Citing the potential problem of withdrawal TD, Suzuki et al questioned the necessity of an antipsychotic washout period in our study because it focused on tardive dyskinesia (TD) rather than psychotic symptoms. However, the aim of our study was to investigate differential effects of 2 antipsychotics on the severity of TD. A study design without a washout period would result in a carryover effect, preventing us from knowing whether the change in TD severity was due to the effect of previous medication or new study medication, especially in the initial study period. In fact, many studies examining TD in patients with schizophrenia had a much longer washout period than our study to prevent carryover effect.[2,3]

We agree that the generalizability of our results is limited to patients with more severe TD. One of the inclusion criteria of our study was a severity of TD of no less than a moderate degree.[1] Hence, schizophrenia patients with existing mild or questionable TD were not included in our study population, and the results are not intended to be applied to commonly encountered patients with schizophrenia.

Suzuki et al suggested that most of the patients could have been treated in the absence of anticholinergics to avoid the confounding effects of anticholinergics. However, the role of anticholinergics and cholinergics in the risk and severity of TD has been unclear.[4,5] Moreover, withdrawal of the use of anticholinergics in patients who underwent antipsychotic treatment to prevent the possible effect of anticholinergics on study results may pose ethical problems and may influence the motivation of schizophrenia patients to participate in the study. This is particularly a problem for risperidone, which has a higher dopamine D_2 receptor blockade profile and higher risks of extrapyramidal side effects.[6]

The changes in Abnormal Involuntary Movement Scale (AIMS) total score for study completers from baseline to endpoint in the risperidone group (n = 21) and the olanzapine group (n = 23) were -9.0 ± 7.1 and -7.8 ± 8.1, respectively. The degree of AIMS total score reduction in study completers was slightly higher than in the last-observation-carried-forward (LOCF) analysis. This is compatible with the general concept that analysis of study completers will overestimate the effects of study medications because study completers are more likely to represent the patients with better efficacy and fewer adverse events. The results of statistical analyses of group difference were similar, regardless of whether LOCF analysis or compliance analysis with completers only was used. The details of the latter analysis will be provided upon request.

Suzuki et al cited some references regarding prohibition of use of anticholinergics during the study period and the incidences of TD across different antipsychotic treatments and tried to apply the results in those papers to our work. However, those references were not related to schizophrenia patients with existing TD, and patients with and without existing TD may be completely different populations. To apply the results seen in a population without TD to a population with TD is questionable. Due to ethical concerns, our study design did not include a control group treated with first-generation antipsychotics. Hence, we cannot make a comparison between the effects of first- and second-generation antipsychotics in schizophrenia patients with existing TD.

REFERENCES

1. Chan HY, Chiang SC, Chang CJ, et al. A randomized controlled trial of risperidone and olanzapine for schizophrenic patients with neuroleptic-induced tardive dyskinesia. *J Clin Psychiatry*. 2010;71(9):1226–1233.
2. Bai YM, Yu SC, Lin CC. Risperidone for severe tardive dyskinesia: a 12-week randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. 2003;64(11):1342–1348.
3. Emsley R, Turner HJ, Schronen J, et al. A single-blind, randomized trial comparing quetiapine and haloperidol in the treatment of tardive dyskinesia. *J Clin Psychiatry*. 2004;65(5):696–701.
4. Soares KV, McGrath JJ. Anticholinergic medication for neuroleptic-induced tardive dyskinesia. *Cochrane Database Syst Rev*. 2000;(2):CD000204.
5. Tammenmaa IA, McGrath JJ, Sailas E, et al. Cholinergic medication for neuroleptic-induced tardive dyskinesia. *Cochrane Database Syst Rev*. 2002;(3):CD000207.
6. Kapur S, Zipursky RB, Remington G. Clinical and theoretical implications of 5-HT_2 and D_2 receptor occupancy of clozapine, risperidone, and olanzapine in schizophrenia. *Am J Psychiatry*. 1999;156(2):286–293.

Hung-Yu Chan, MD, PhD
jan30@seed.net.tw
Susan S.-F. Gau, MD, PhD

Author affiliations: Taoyuan Mental Hospital, Taoyuan County; and Department of Psychology, Chung Yuan Christian University, Chung-Li (Dr Chan); National Taiwan University Hospital, Taipei (both authors); and National Taiwan University College of Medicine, Taipei (Dr Gau), Taiwan.

Potential conflicts of interest: **Dr Chan** has received speech honoraria from Astellas, AstraZeneca, Eli Lilly, Janssen, Otsuka, Pfizer, and Sanofi Aventis. **Dr Gau** declares no conflicts of interest. ***Funding/support:*** None reported.
doi:10.4088/JCP.10lr06261ayel