Treating the behavioral and psychological symptoms of senile dementia with antipsychotic drugs

Shifu Xiao

Most elderly patients with dementia have behavioral and psychological symptoms that co-occur with the characteristic cognitive impairment and social dysfunction; these symptoms are often referred to by the acronym BPSD (Behavioral and Psychological Symptoms of Dementia). In fact, the very first case of Alzheimer’s Disease reported (by Alzheimer in 1906) had hallucinations, delusions and aggressive behavior in addition to cognitive impairment[1]. In fronto-temporal dementia and Lewy Body Dementia the behavioral and psychological symptoms are quite prominent and often become the primary focus of clinical treatment[2,3]. Cross-sectional studies report BPSD in 50%-90% of all patients with dementia; 30%-50% have hallucinations, 30%-80% have delusions, 30%-40% have depression, and 30%-70% have other abnormal behaviors[4-6]. And long-term follow-up studies find that almost all patients with dementia manifest BPSD at some point during the course of their illness[6]. BPSD can exacerbate the cognitive and social dysfunction of dementia leading to a decreased quality of life for both the patient and the caregiver, more frequent hospitalization or chronic institutionalization, and, thus, a higher burden of illness.

There is an ongoing controversy about the role of antipsychotic medications in the management of BPSD[7,8]. Previous studies had found that antipsychotic medications were effective in the management of BPSD but over the last decade several studies have reported increased rates of severe adverse events and death among patients with dementia who are treated with antipsychotic medications[9,10]. A meta-analysis of 17 studies[9] found a 1.5-1.7-fold increase in mortality in patients with dementia who were treated with atypical antipsychotic medications versus those treated with placebo; a total of 4.2% died in the atypical antipsychotic group versus 2.6% in the placebo group, primarily from cardiovascular events and respiratory infections. Responding to these new findings, in 2005 the Food and Drug Administration in the United States required the addition of a black-box warning to the instructions for the use of atypical antipsychotic medications.

Typical antipsychotic drugs are also associated with increased mortality in patients with BPSD: a retrospective study[11] of 22,890 cases over 65 years of age using typical antipsychotic medications found a 1.37-fold increase in mortality. The authors of this study estimated that replacing typical with atypical medications would increase mortality by 7%. The large CATIE-AD study of Alzheimer’s Disease patients supported by the National Institute of Mental Health in the United States[12] concluded that the treatment benefit of using antipsychotic medications in patients with dementia is offset by the adverse effects and that there were no significant differences in efficacy or tolerability between the different types of antipsychotic medications.

Currently, the management of BPSD is NOT one of the approved indications for antipsychotic medications. However, in routine clinical care antipsychotic medications are often used for conditions not listed in the indications. For example, widely-used treatment guidelines for dementia in the United States[9], the European Union[10] and China[13] recommend the judicious use of atypical antipsychotic medications if the symptoms are severe or endanger the safety of the patient or others. In this situation the recommended starting doses are usually 1/3 to 1/2 of the standard adult dosage, the final target dose should be as low as possible, and the patient’s response and side-effects need to be carefully monitored. The risk-benefit ratios for continuing low maintenance doses of antipsychotic medication versus gradually stopping the medication after the behavioral and psychological symptoms have been controlled are, as yet, unclear, so clinicians must rely on their clinical judgment about whether and when to stop the medication.
Given the very real danger of serious complications or death, more long-term follow-up studies of the management of the BPSD are urgently needed to give clinicians guidance about how best to serve their patients with dementia who have associated behavioral or psychological symptoms.

References
肺部感染等严重不良事件。2005年美国FDA要求在非典型抗精神病药的说明书上以黑框警示。


参考文献

(此处略，与英文版中的相同，见第377页)