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Thiothixene in the Management of Delirium: A Case Series

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Background: *Pharmacologic strategies are often required to help manage agitated patients with delirium. First-and second-generation antipsychotic medications (such as haloperidol, quetiapine, and olanzapine) are commonly used.* **Objective:** *On the psychiatric consultation service in our hospital, thiothixene has been used based on its favorable potency, sedative, and cost profiles. Little has been written about the utility of this drug for management of delirium.* **Methods:** *We reviewed our experience with thiothixene in this setting using pharmacy records to identify patients who received at least 1 dose between July 2011 and March 2014. We scrutinized the relevant medical records (n = 111) and recorded the following data: age, sex, medical diagnoses, signs and symptoms of delirium, dosing of thiothixene, and response to thiothixene in terms of both apparent benefit as well as side effects.* **Results:** *Resolution or improvement was documented in 78% of patients and good tolerability in 82% of patients.* **Conclusions:** *Although further data from a randomized, controlled trial would be ideal, our experience suggests that thiothixene could be a safe and effective pharmacologic treatment for agitation and psychosis due to delirium.*

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INTRODUCTION

Delirium with agitation is commonly encountered on hospital psychiatry consultation services. Pharmacologic strategies are often required to help manage such patients.[1] Although the exact pathophysiology of delirium has yet to be fully elucidated, many hypotheses have been proposed, including deficiency in the cholinergic system as well as hyperactivity in the dopaminergic system.[2,3] Dopamine antagonists are recommended in various guidelines.[4,5] Although more well-conducted trials have been performed in the past decade, there are still limited data that identify a specific agent as the treatment of choice in the management of delirium.[6] Thus, antipsychotic selection is based on clinical factors such as target symptoms, side effect profile, and available routes of administration. Our hospital psychiatric consultation service at the Mayo Clinic has used thiothixene, a mid- to high-potency first-generation antipsychotic, for management of delirium. Compared with haloperidol, thiothixene has mild sedative effects, which we postulate to be clinically beneficial for reducing agitation and improving sleep.[7] As there are limited data available regarding thiothixene use for the management of delirium, we describe our experience using it.

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We believe that thiothixene is an effective and well-tolerated treatment for agitation in patients with delirium.

METHOD

This project was approved by the Mayo Clinic Institutional Review Board. Pharmacy records were obtained to identify patients who were dispensed at least 1 dose of thiothixene between July 2011 and March 2014. Only those patients given a diagnosis of delirium and for whom thiothixene was specifically administered for delirium were included. The diagnosis of delirium was recorded by either the psychiatric consultant who saw the patient or the primary service team personnel. The medical records were reviewed by personnel familiar with the diagnosis of delirium, and patients who received thiothixene for reasons other than delirium were excluded (e.g., schizophrenia, schizoaffective disorder, bipolar disorder, or dementia with agitation). We scrutinized the relevant medical records to record age, sex, medical diagnoses, and the signs and symptoms of delirium. Dose and duration of thiothixene use, documented response, potential side effects, and data regarding other antipsychotics that were administered while the patient was receiving thiothixene were also collected. Given the nature of this study, descriptive statistics were used to describe outcome variables as means with standard deviations or proportions where appropriate.

RESULTS

Tables 1–4 provide relevant characteristics of the patients and outcomes. In total, 111 patients were identified as having received thiothixene for the management of delirium during the study period. The mean age (±standard deviation [SD]) of these patients was 67.5 ± 13.3 years, and 63% were men. Patients had been admitted to a wide variety of hospital services, but critically ill patients represented a small number (8.1%) of the sample (Table 1). Most patients (93%) had symptoms characteristic of hyperactive or mixed-type delirium, with only 7% of patients specifically noted to have a hypoactive delirium.

The average daily dose (±SD) of thiothixene was 6.9 ± 4.6 mg. The mean maximum dose (±SD) of thiothixene received by any patient was 9.4 ± 6.8 mg. Based on review of medical record notes, 78% demonstrated improvement of symptoms associated with delirium, most commonly behavioral agitation, while thiothixene was used (Table 2). Only 13% demonstrated no benefit as stated in the medical record. Monotherapy with thiothixene was found in 76.5% of patients. At least 1 dose of another antipsychotic was given during a course of thiothixene therapy in 23.5% of patients (Table 3). The majority of concomitant use involved haloperidol (15 patients), chiefly owing to its ability to be given parenterally. Thiothixene was continued after hospitalization in 48% of the patients who either received specific instructions for a taper or were advised to have a provider assess the need for the agent at follow-up. For those patients in whom thiothixene was not continued on discharge, the average duration of therapy was 5.4 ± 4.4 days. Table 4 lists possible adverse effects of thiothixene, demonstrating that thiothixene appears to have been well tolerated in this medically complicated sample.

TABLE 1. Demographic Data

Patient characteristic	Result
Age, y ± SD	67.5 ± 13.3
Sex, male (%)	63%
Floor type (*n*, %)	General—103 (93%) ICU—9 (8.1%)
Service type (*n*, %)	Cardiology—5 (4.5%) Critical care unit—9 (8.1%) General medicine—41 (37%) Hematology/oncology—6 (5.4%) Neurology—6 (5.4%) Respiratory—4 (3.6%) Surgical—31 (27.9%) Transplant—9 (8.1%)

ICU = intensive care unit; SD = standard deviation.

DISCUSSION

There are no Federal Food Drug Administration–approved pharmacologic agents for the management of delirium, but antipsychotics are most commonly used.[8]

TABLE 2. Documented Effectiveness of Thiothixene

Documented effect described	Result, *n* (%)
Resolution/improvement	87 (78)
Minimal improvement	8 (7)
No benefit	14 (13)
Not documented/unknown	2 (2)