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Original Research Reports

Mirtazapine for Symptomatic Relief on a Psychiatric Consultation Service: A Case Series

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Background: *With a complex pharmacologic profile, mirtazapine may promote sleep, stimulate appetite, improve nausea, and reduce pain. Some practitioners working on the Mayo Clinic inpatient psychiatric consultation/liaison service have recommended mirtazapine in medically ill patients with or without formal psychiatric comorbidity to target these symptoms.* **Objective:** *To assess the success of this practice, we conducted a retrospective chart review covering a 4.5-year period.* **Methods:** *For patients recommended to start mirtazapine, global improvement in specific symptoms and suspected side effects were recorded.* **Results:** *During the study period, 528 medically ill patients started mirtazapine following a recommendation from the psychiatric consultation service. In total, 475 patients were provided mirtazapine to specifically target sleep, nausea, pain, or appetite. There was documented improvement in these symptoms for 37.7%, 37.0%, 36.4%, and 23.5% of the patients, respectively. These rates of improvement are conservative for the 229 patients without documented response, i.e., 48% of the patients who were given the medication for a somatic symptom were counted as having no improvement. Commonly documented adverse effects were daytime sedation (5.3%), worsening mental status (2.3%), and nightmares (1%).* **Conclusions:** *Despite the limitations of this retrospective, qualitative study, these data confirm that mirtazapine is generally well tolerated and can provide at least short-term relief of certain symptoms in medically ill patients. Controlled trials are needed to assess these benefits more systematically, and it is not clear how long mirtazapine should be used for these symptoms.*

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Key words: Consultation Liaison Psychiatry, antidepressants, psychopharmacology, sleep, nausea, appetite, pain.

INTRODUCTION

As mirtazapine carries a single Food and Drug Administration-approved indication for major depressive disorder, practitioners may not recognize mirtazapine's potential to provide benefit in managing somatic symptoms. Outside psychiatric use, mirtazapine has gained attention in the oncology literature as possessing beneficial properties for nausea and appetite stimulation.[1] Mirtazapine possesses complex neuropharmacologic actions, which may explain its possible usage for a number of symptoms. Mirtazapine acts as a histamine-$_1$ receptor (H_1) antagonist

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and 5-HT_{2C} receptor antagonist, which may help improve appetite and sleep. The binding affinity to the serotonin-$_3$ receptor (5-HT_3) is similar to that of ondansetron and other medications in the same class, making a notable antiemetic.[1] Action at the alpha adrenergic-$_2$ receptor (alpha-$_2$) plus 5-HT_{1A} agonism has led to studies evaluating mirtazapine to attenuate pain.[2] Despite the potential benefits of mirtazapine on somatic symptoms, randomized, placebo-controlled trials are lacking in the literature, with data supporting its use limited to small open-label studies or retrospective reports. Given the paucity of data, we sought to describe the use of mirtazapine as recommended by our psychiatric consultation/liaison service. Our primary goal was to assess the effectiveness of mirtazapine for symptomatic treatment of pain, nausea, low appetite, or insomnia. We did not attempt to assess its antidepressant activity as it is already approved for that purpose.

METHODS

This project was approved by the Mayo Clinic Institutional Review Board. Pharmacy records were obtained from the dates of January 1, 2010–June 30, 2015, to identify patients in a nonpsychiatric inpatient setting who were dispensed at least 1 dose of mirtazapine during hospitalization. We reviewed the relevant medical records for age, sex, reason for hospitalization, psychiatric diagnoses, and symptoms targeted by mirtazapine. Initial and final dose at dismissal, documented response, potential adverse effects, and concomitant psychotropics were also recorded. Patients were excluded if they had mirtazapine documented as an outpatient medication before admission, if psychiatry was not consulted, if mirtazapine was initiated before psychiatric consultation, or if mirtazapine was not administered to the patient. Given the nature of this retrospective evaluation, descriptive statistics were used to describe outcome variables as means with standard deviations or proportions where appropriate.

RESULTS

Pharmacy records revealed that 3954 individual patients were dispensed mirtazapine during the 4.5-year study period. Screening these records yielded a total of 528 patients with a psychiatric consult specifically recommending mirtazapine. In this cohort of patients, the mean age (+ standard deviation [SD]) was 60.8 + 17.3 years and 54% of them were male. Mirtazapine was initiated at a mean dose of 9.6 + 3.5 mg and titrated to a mean maximal dose of 12.3 + 6.2 mg. Patients treated on a wide variety of medical services (Table 1) received mirtazapine for 1 of 3 documented reasons: (1) solely for mood or anxiety (n = 53), (2) mood or anxiety plus one or more somatic symptoms (i.e., sleep, appetite, nausea, and pain) (n = 340), or (3) one or more somatic symptoms without a diagnosis of comorbid depression or anxiety (n = 135). Thus, 475 patients received mirtazapine to target at least 1 somatic symptom.

TABLE 1. Primary Service Type (n = 528).

Service Type	N = (%)
BMT/Transplant	63 (11.9)
Cardiac	34 (6.5)
Critical Care	27 (5.1)
Gastroenterology	15 (2.8)
Hematology/Oncology	29 (5.5)
Medical	148 (28)
Neurology	23 (4.4)
PMR	21 (4)
Surgical	168 (31.8)

The 475 patients were often started on mirtazapine for multiple proposed benefits. The most common target symptom documented was insomnia, for which 432 (90.1%) patients received mirtazapine. The other documented rationales for mirtazapine included appetite stimulation, nausea, and pain in 251 (52.8%), 46 (9.7%), and 46 (4.6%) patients, respectively. Supplementary rationales included the smaller effect on the corrected QT interval compared with another prescribed antidepressant, favorable use in the setting of hyponatremia compared with selective serotonin reuptake inhibitors, less risk of sexual side effects, selection over a selective serotonin reuptake inhibitor or tricyclic in the setting of gastrointestinal bleeding, availability as an orally-disintegrating tablet, minimal drug-drug interactions, cost, rapid onset of action, anxiolytic effects, and low abuse potential. It was difficult to characterize the response to mirtazapine for a specific target symptom due to poor documentation in many cases. Any improvement of a somatic symptom or a lack of benefit related to mirtazapine was documented in only 246 of 475 patients. Of the 432 patients given mirtazapine for sleep, 163 (37.7%) patients had documented improvement. Nausea reduction was reported in 17 (37.0%) of 46 patients, and improved