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Case report

Atypical antipsychotics in the treatment of fibromyalgia: a case series with olanzapine

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Abstract

Fibromyalgia is a common and disabling chronic pain syndrome. Although a wide array of symptomatic pharmacological treatments has been used to treat this condition, only modest results have been obtained. Olanzapine has been proven effective in some chronic pain conditions. The authors present a case series of patients suffering from fibromyalgia who received olanzapine as add-on therapy during a 3-month period. Olanzapine (2.5–20.0 mg/day) was administered to 25 consecutive patients (24 females, 1 male) meeting the American College of Rheumatology diagnostic criteria for fibromyalgia, and who were receiving nonsteroidal anti-inflammatory drugs (NSAIDs; 68%), benzodiazepines/zolpidem (48%), antidepressants (32%), and cyclobenzaprine (4%), either alone or in combination. Overall, 6 of the 14 patients (43%) who completed the 12-week trial reported to be much or very much improved ('responders'), according to the Clinical Global Impression (CGI) scale and 7 of them (50%) reported a good or very good sense of well-being. Olanzapine's modal dose among responders was 10.0 mg/day. It was discontinued in 11 patients (44%) due to adverse reactions, most commonly weight gain (n=5, 20%). Our preliminary findings suggest a possible role for olanzapine in treating fibromyalgia. Unfortunately, the beneficial outcome of olanzapine was largely obscured by its poor tolerability, which could be explained by the greater propensity of patients with fibromyalgia to adverse drug reactions, and the greater risk of antipsychotic-induced weight gain among women. Whether other atypical antipsychotics will provide similar symptomatic relief, while showing a better tolerability profile than olanzapine in patients with fibromyalgia, should be further investigated.

Keywords: Antipsychotics; Chronic pain; Fibromyalgia; Neuroleptics; Olanzapine

1. Introduction

Fibromyalgia is a common chronic pain syndrome characterized by widespread musculoskeletal pain, tenderness, stiffness, fatigue, nonrestorative sleep and mood disturbances (Wolfe et al., 1990; Goldenberg, 1999). Since its pathophysiology remains unclear, pharmacological treatment is largely empiric and symptomatic (Barkhuizen, 2002).

Although no medication is currently approved specifically for this condition, and only modest results have been documented with pharmacological interventions, a broad array of medications has been used to treat fibromyalgia. This includes analgesics (from nonsteroidal anti-inflammatory drugs (NSAIDs) to opioids), antidepressants, anxiolytics, sleep aids, muscle relaxants, trigger point injections and less conventional treatment approaches, such as ademetionine, growth hormones, pramipexole, *N*-methyl-D-aspartate (NMDA) antagonists and 5-HT3 antagonists

Abbreviations: CGI, Clinical Global Impression; NMDA, *N*-methyl-D-aspartate; NSAIDs, nonsteroidal anti-inflammatory drugs.

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among others (Pridmore and Rosa, 2001; Barkhuizen, 2002; Forseth and Gran, 2002).

Fibromyalgia patients have shown increased prolactine levels after buspirone challenge which has been attributed to a hypersensitivity of dopaminergic D_2 receptors (Malt et al., 2003). This finding suggests that drugs with antagonistic D_2 receptors properties could be of potential benefit in fibromyalgia management.

Some preclinical studies and anecdotal clinical reports suggest that atypical antipsychotics may have analgesic properties (Pridmore et al., 2003). Among them, olanzapine has shown analgesic properties in animal models (Schreiber et al., 1999) and has been employed in the treatment of cancer pain (Khojainova et al., 2002). Regarding fibromyalgia, a significant decrease in pain and marked improvement in daily functioning have been reported in two selected patients with fibromyalgia treated with olanzapine (Kiser et al., 2001). This drug has also been successfully used to treat chronic daily headaches (Silberstein et al., 2002), a condition which has a high comorbidity with fibromyalgia (Nicolodi and Sicuteri, 1996).

We present a case series of patients suffering from fibromyalgia who received olanzapine as add-on therapy during a 3-month period.

2. Methods

2.1. Patients

Olanzapine was administered to 25 consecutive patients (24 females, 1 male) with a mean age of 47 years (ranging from 20 to 67). All of them met the American College of Rheumatology diagnostic criteria for fibromyalgia (Wolfe et al., 1990) and gave their informed consent to participate in this case series study. Patients' associated conditions and fibromyalgia medications they were receiving are shown in Table 1.

Table 1
Patients' clinical characteristics

Clinical characteristic	*N* (%)
Associated conditions	
Morning stiffness	24 (96)
Fatigue	24 (96)
Disordered sleep	23 (92)
Temporomandibular joint dysfunction	21 (84)
Primary headache	18 (72)
Irritable bowel syndrome	3 (12)
Current fibromyalgia medications	
NSAIDs	17 (68)
Benzodiazepines/zolpidem	12 (48)
Antidepressants	8 (32)
Cyclobenzaprine	1 (4)

Table 2
Clinical outcomes in 25 patients with fibromyalgia receiving adjuvant olanzapine treatment

	Baseline	Week 4	Week 8	Week 12
Clinical Global Impression				
Much/very much improved ('Responders'), *n* (%)[a]	NA	6 (27.3)	8 (47.1)	6 (42.9)
Mildly improved, *n* (%)[a]	NA	12 (54.5)	6 (35.3)	7 (50.0)
Overall sense of well-being				
Good/very good, *n* (%)[a]	3 (12)	8 (36.4)	10 (58.8)	7 (50.0)
Responders' dosage				
2.5 mg/day	NA	*n*=0	*n*=1	*n*=0
5.0 mg/day	NA	*n*=0	*n*=1	*n*=1
7.5 mg/day	NA	*n*=1	*n*=0	*n*=0
10.0 mg/day	NA	*n*=5	*n*=5	*n*=3
12.5 mg/day	NA	*n*=0	*n*=0	*n*=1
20.0 mg/day	NA	*n*=0	*n*=1	*n*=1
Observed cases, *n*	25	22	17	14

NA=not applicable.
[a] Percentages calculated on the observed cases at each visit.

2.2. Study treatment

Olanzapine was added to patients' original drug regimen at an initial dose of 2.5 mg/day. Weekly dose adjustments upward were made in 2.5-mg increments until a dose of 10 mg/day was reached, and additional dose adjustments were subsequently made according to therapeutic response and tolerability.

2.3. Assessments

Patients' evaluations were scheduled at the end of weeks 4, 8 and 12. Drug effectiveness was assessed using the Clinical Global Impression (CGI) improvement scale (Guy, 1976) and a five-item *likert* scale for evaluating overall sense of well-being. Emerging adverse reactions to treatment were collected in every visit.

2.4. Data analysis

Due to the non-comparative design, only a descriptive analysis has been employed. The mean and range were calculated for the quantitative variables, and the frequency and percentage for the qualitative variables.

3. Results

CGI response rates (i.e. the proportion of patients who were rated as 'very much' or 'much' improved), number and percentage of patients with mild improvement, number and percentage of patients who were rated 'very good' or 'good' on the general well-being scale, and dosage for CGI responders, for each visit of observed cases, are presented in Table 2. Overall, 6 of the 14