Intramuscular olanzapine in patients with borderline personality disorder: an observational study in an emergency room☆

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Abstract

Objective: Despite the frequency of borderline personality disorder (BPD) in patients with acute agitation in emergency departments (EDs), there are few data about the use of intramuscular (IM) psychotropics in those patients. This is the first open-label study with olanzapine in this setting.

Method: Measures were collected prospectively for patients with acute agitation in ED. Consent was obtained subsequently and diagnosis ascertained using the Structured Clinical Interview for DSM-IV. A group of 25 patients with severe agitation and BPD received olanzapine 10 mg IM. Efficacy and safety data are available at baseline, 2 h postinjection and at discharge.

Results: Significant reductions of agitation associated with good tolerance were observed 2 h after the first IM olanzapine. Sixteen percent of patients required a second IM olanzapine.

Conclusions: Randomized, placebo-controlled studies are needed to confirm the efficacy of IM olanzapine in patients with acute agitation and BPD.

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1. Introduction

Management of psychomotor agitation raises nosological, diagnostic, legal, ethical and even logistical questions for an emergency department (ED) [1]. Historically, little attention was paid to diagnosis in the management of agitation as few choices were available. There are now more alternatives, but still little data concerning the newer intramuscular (IM) psychotropics in patients with severe agitation in emergency settings [1,2]. In spite of the high frequency of borderline personality disorder (BPD) in patients with agitation in the ED, 25% according to one recent letter [3], there are good data only for patients with schizophrenia or bipolar disorders.

The only published report concerning patients with BPD requiring IM psychotropic medication is a letter describing a series of 13 patients who received IM olanzapine (OLZ) and 7 who received IM ziprasidone in an emergency setting [3]. There is also a larger sample of patients treated with IM ziprasidone in an emergency setting, but no data on diagnosis are available [4].

Oral typical antipsychotics are increasingly used in clinical practice in the management of BPD and a small but growing body of literature supports their efficacy [5,6]. All of the available data reported positive effects of OLZ [7,8], clozapine, quetiapine and risperidone in patients with BPD, especially if patients have psychotic-like, impulsive or suicidal symptoms [6]. Although concerns about worsening of aggressive behavior with benzodiazepines in BPD derive primarily from studies of longer term use [1], IM OLZ would also seem to be a logical choice in this population,
given its rapid onset and favorable side-effect profile [2,9,10]. Accordingly, we began to use IM OLZ routinely in the ED for patients with BPD and acute agitation who refused oral medication.

2. Method

A prospective observational study of the safety and efficacy of IM psychotropic medication in patients with acute agitation was conducted in the ED of a regional hospital in Belgium.

Consistent with local clinical policy, all patients with suspected BPD and agitation who refused oral medication received 10 mg IM OLZ monotherapy. The decision to administer an IM injection was made by one of the regular staff, independent of the investigators. A second IM administration was allowed at least 2 h after the first IM. The exclusion criteria were alcohol or drug abuse or dependence, pregnancy, unstable diabetes or known intolerance to OLZ. There is no psychotropic medication in Belgium with an official indication for IM sedation in BPD. As a result, the ethics committee required that preliminary safety data be obtained before a placebo-controlled study could be performed. As there was no alteration of patient care, the local ethics committee agreed that consent to use the data could be obtained after resolution of the psychomotor agitation. After informed consent was obtained, all the data could be obtained before a placebo-controlled study could be performed.

A cohort of 25 patients were determined to have BPD and these form the basis for this report. This represents 25% of the total population with any diagnosis treated with OLZ IM. Patients with schizophrenia, schizophreniform disorder and bipolar disorder are the subject of a separate report. Two patients refused consent, and, as a result, their SCID diagnosis could not be determined and their data could not be utilized.

An investigator not involved with the direct care of the patient assessed patients for the level of agitation and for side effects. Agitation was assessed at entry, 2 h after the first 10 mg OLZ IM administration and 12–24 h after the first injection. Measures included the Positive and Negative Syndrome Scale Excited Component (PANSS-EC: tension, uncooperativeness, hostility, poor impulse control, and excitement), Agitated Behavior Scale (ABS) and Clinical Global Impression–Severity (CGI-S). Vital signs and adverse effects were assessed at the same intervals. Movement disorders were assessed using the Barnes Akathisia Global Score (BAS) and Simpson-Angus Extrapyramidal Effects Scale (SAS).

Student’s t-test for paired samples was used to compare changes in PANSS-EC, ABS and CGI-S scores, and blood pressures and cardiac frequency from baseline to 2 h after IM injection and at discharge.

3. Results

The study population was composed of 19 females and 6 males. The mean age was 33.48 ± 8.65 years. Due to the severity of the agitation, physical restraint was required in 20 patients (80%). Four patients (16%) required a second 5 mg OLZ IM, 2 h following the first IM, and one patient required a third 5 mg OLZ IM after the first 12 h.

There were statistically significant reductions in PANSS-EC, ABS and CGI scores 2 h after the first IM (Fig. 1). The mean baseline PANSS-EC score was 25.96 ± 3.1, which declined to 10.4 ± 5.9 (P < 0.001; t = 13.2) 2 h after the first 10 mg OLZ IM and to 8.5 ± 3.0 (P = 0.1578; t = −1.6) at discharge. The decline in ABS score was similar: 34.52 ± 5.1 at entry to 18.6 ± 4.5 (P < 0.001; t = 17.7) 2 h after the first IM injection and 16.64 ± 3.0 (P = 0.0765; t = −2.2) at discharge. The CGI score declined from 5.16 ± 0.5 at entry to 3.04 ± 1.3 (P < 0.001; t = 8.2) 2 h after the first IM and to 2.84 ± 0.7 (P = 0.5015; t = −0.7692) at discharge.

There was a reduction in blood pressure (systolic/diastolic, mm Hg) from 136.4 ± 11.7/86.4 ± 7.9 at entry to 123.28 ± 9.3/78 ± 8.5 two hours after the first IM injection and to 123.4 ± 8.5/79.2 ± 7.59 at discharge. The pulse rate diminished also from 93.84 ± 9.4 at entry to 81.48 ± 6.7 two hours after the first IM injection and to 80.36 ± 6.09 at discharge. Those reductions are statistically significant when comparing the entry with 2 h after IM injection for systolic (P = 0.001; t = 7.1) and diastolic (P = 0.007; t = 4.9) blood pressures, as well as for the pulse rate (P < 0.001; t = 9.2). One patient had an asymptomatic reduction of 25 mm Hg in systolic (160 mm Hg at entry) and 20 mm Hg in diastolic blood pressure (100 mm Hg at entry), with a pulse rate varying from 105 to 90 per minute. There were no complaints of dizziness or other spontaneously reported adverse effects. There was no statistically significant increase in SAS and BAS scores.

4. Discussion

In the absence of adequate studies directed at this population, there has been no consensus as to the appropriate
management of agitation in patients with personality disorders. Parenteral benzodiazepines, antipsychotics and combinations have all been used, although none of these has a first-line rating using expert consensus methods [1].

This prospective observational study suggests good effectiveness (efficacy with few side effects) of monotherapy with 10 mg IM OLZ in patients with BPD and acute agitation in an ED. These findings are consistent with data from a recent letter with a smaller sample and less safety data [3].

The significant reductions in agitation observed in this study 2 h after monotherapy with 10 mg IM of OLZ are larger than those reported for consented patients with schizophrenia or bipolar disorders in clinical trials: PANSS-EC score change, −15.5 (this study) vs. −9 [9,10]. This may be related to higher entry scores, e.g., the entry PANSS-EC score in this study was 25.9 vs. 18.5 in randomized placebo-controlled studies [9,10]. However, this may also be related to the lack of a placebo control [11].

Interestingly, this study did not find a significant improvement between the 2-h time point and discharge 12–24 h later, as was found in placebo-controlled trials in schizophrenia and bipolar disorder. A floor effect may account for this or the mix of 12- and 24-h observation periods. The rate of 16% of patients requiring a second IM OLZ is similar to that of patients with schizophrenia receiving benzodiazepines after IM OLZ in a randomized study: haloperidol (15%) and placebo (39%) [2]. It is also possible that the neurobiology of the disorders is different, and agitation may be slower to respond when arousal occurs in the setting of psychosis or mania.

The safety data here are similar to that reported by the manufacturer to European and American regulators. Recently, the manufacturer has also presented data on spontaneously reported adverse events for approximately 278,600 exposures in the first year post marketing [12]. The absence of clinically significant extrapyramidal and cardiovascular side effects is promising, but considering the statistically significant reduction in systolic and diastolic blood pressure and pulse, vital signs should be checked especially in the first 2 h post injection, and combinations with benzodiazepines are not recommended [1].

The major strength of this study is that it included all patients with consent and diagnosis obtained subsequently, resulting in a more representative and generalizable sample. The age of our subjects, 33.48±8.65 years, is similar to that reported in two randomized trials in this population, 31.7 and 29.3 years [13,14]. The preponderance of females is also typical.

Placebo response in similar studies has been low [15]. Nevertheless, the lack of a control group is a limitation: the effects of antipsychotics appeared twice as large in studies with an active control as in studies with a placebo control group [11]. Although the five-item PANSS-EC is commonly used, principal component analysis has found that the tension item is not highly correlated with the other items in this scale [16].

Finally, safety data in a relatively unselected population are also needed. However, because of the small sample size, the findings here should be interpreted cautiously. Randomized placebo-controlled studies assessing more severely disturbed patients with various conditions with and without substance use are still needed in order to clarify the guidelines for managing severe agitation in the ED.

References