Intramuscular Ziprasidone, 2 mg Versus 10 mg, in the Short-Term Management of Agitated Psychotic Patients

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Background: There is a clear need for effective, well-tolerated intramuscular (i.m.) agents for the acute control of agitated psychotic patients. Currently used agents, including conventional antipsychotics and/or benzodiazepines, may be associated with distressing side effects such as extrapyramidal side effects and excessive sedation.

Objective: The objective of this study was to evaluate the efficacy and tolerability of the rapid-acting i.m. formulation of the novel antipsychotic ziprasidone in the treatment of inpatients with psychosis and acute agitation (DSM-IV diagnoses).

Method: In a 24-hour, double-blind, fixed-dose clinical trial, patients were randomly assigned to receive up to 4 injections (every 2 hours p.r.n.) of 2 mg (N = 54) or 10 mg (N = 63) of ziprasidone i.m. The Behavioral Activity Rating Scale measured behavioral symptoms at baseline and the response to treatment up to 4 hours after the first i.m. injection.

Results: Ziprasidone i.m., 10 mg, rapidly reduced symptoms of acute agitation and was significantly more effective ($p < .01$) than the 2-mg dose up to 4 hours after the first injection. Patients were calmed but not excessively sedated, and over half were classed as responders 2 hours after the 10-mg dose. No acute dystonia or behavioral disinhibition was reported. One patient who received the 10-mg dose experienced the extrapyramidal side effect akathisia.

Conclusion: Ziprasidone i.m., 10 mg, is rapidly effective and well tolerated in the short-term management of the agitated psychotic patient. Comparison with a study of identical design comparing 2-mg with 20-mg doses in patients with similar levels of psychopathology suggests that efficacy with 10 mg or 20 mg of ziprasidone i.m. is significant and dose related.

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The phasic nature of psychotic disorders, particularly schizophrenia, in which florid episodes, acute agitation, and worsening hallucinations are superimposed over the chronic course, results in a high proportion of sufferers requiring emergency intervention numerous times during the course of their illness. Although novel antipsychotics are increasingly regarded as first-line agents in the management of schizophrenia,[1] the short-term pharmacologic treatment of episodes of acute psychotic agitation is still limited to intramuscular (i.m.) administration of conventional antipsychotics and benzodiazepines.[2] Not only are patients with psychotic disorders who require emergency i.m. treatment still at risk of adverse effects of these agents during critical phases of their illness, but initiation of novel antipsychotics may be delayed.

Ziprasidone is the first novel antipsychotic to enter large-scale clinical development as a rapid-acting i.m. formulation for the acute control and short-term management of the agitated psychotic patient. The unique pharmacology of ziprasidone differentiates it from available antipsychotics[3,4] and predicts a broad spectrum of clinical activity with favorable tolerability in the treatment of psychotic disorders. Well-controlled clinical trials have dem-

onstrated the effectiveness of oral ziprasidone in treating a broad range of symptoms in patients with schizophrenia, both in the short-term treatment of the acutely ill[5–8] as well as in the longer-term treatment of negative symptoms in stable, chronically ill patients.[9,10] In addition, oral ziprasidone is well tolerated. It is not associated with sustained hyperprolactinemia, excessive sedation, or weight gain and has a very low liability for extrapyramidal side effects.[5,7,10,11]

A pilot study[12] of ziprasidone i.m. demonstrated that it substantially reduced psychomotor agitation in patients with acute psychosis, who became calm, rousable, and lucid after being treated. Additionally, as predicted, it was very well tolerated and not associated with movement disorders such as acute dystonia or parkinsonism.[12] While ziprasidone i.m. reduced symptoms, particularly at doses of 10 and 20 mg and with some evidence of symptom reduction at lower doses, it was not excessively sedating, and the transition from i.m. treatment to oral treatment was smooth and uneventful. Thus, a large-scale clinical development program for ziprasidone i.m. was initiated. Here we report the results of a prospective, double-blind, randomized, multicenter study comparing fixed doses of 2 mg of ziprasidone i.m. and 10 mg of ziprasidone i.m. in the treatment of patients with psychosis and acute agitation for up to 24 hours.

PATIENTS AND METHOD

Patients

Inpatients aged 18 years and over with a primary diagnosis of schizophrenia, schizoaffective disorder, bipolar disorder with psychotic features, delusional disorder, or psychotic disorder not otherwise specified (DSM-IV)[13] were enrolled at 17 centers in the United States. The patients had been recently admitted to hospital and had acute agitation associated with their underlying psychotic disorder. Patients were required to have a score of at least 3 (mild) at screening (no more than 72 hours before the first dose) and at baseline (no more than 4 hours before the first dose) on at least 3 of the following items of the Positive and Negative Syndrome Scale for schizophrenia (PANSS)[14]: anxiety, tension, hostility, or excitement.

Patients were excluded if they had DSM-IV–defined substance abuse/dependence in the 2 months before the study or substance-induced psychosis on entry, although patients with a positive urine test for cannabinoids or benzodiazepines were admitted at the investigator's discretion. Patients were also excluded if they had a known or suspected history of alcohol abuse, were at imminent risk of suicide in the opinion of the investigator, had a clinically significant electrocardiogram (ECG) abnormality, abnormal laboratory test findings, or medical illness. Patients were also excluded if they had received clozapine within the last 12 weeks or an investigational drug in the last 4 weeks or if they had ever received ziprasidone in another clinical trial.

Women of childbearing potential were included only after a serum pregnancy test confirmed they were not pregnant and if they were using reliable contraception. All patients enrolled were competent to give written informed consent after a thorough explanation of procedures and possible adverse effects was given. The Institutional Review Board at each center approved the study.

Treatment

Prestudy antipsychotic treatment was not administered during the 24-hour study period. Patients were randomly assigned to receive 2 mg or 10 mg of ziprasidone i.m. After the initial dose, up to 3 identical, additional doses could be administered a minimum of 2 hours apart (maximum of 4 doses in the 24-hour period) at the discretion of the investigator. The volume of both the 10- and 2-mg doses was 0.5 mL. Injections could be given in the buttocks or the upper arm. The 2-mg dose contained the same concentration of the solubilizing excipient, sulfobutylether β-cyclodextrin, as the 10-mg dose. Injections were prepared by an unblinded third party and were visually indistinguishable. Antipsychotic treatment was withdrawn after patients fulfilled screening criteria (4–72 hours before first dose of ziprasidone i.m.). Lorazepam (up to 8 mg/day) for agitation and temazepam for insomnia (up to 30 mg at night) were allowed between screening and up to 4 hours before the baseline assessment. These drugs were not allowed in the 4 hours before the baseline assessment or immediately after, but were permitted during the 24-hour study period if needed. Benztropine for extrapyramidal side effects and propranolol for akathisia were allowed during the study if clinically necessary, but were not permitted as a prophylactic treatment.

Efficacy and Safety Assessments

Baseline assessments were performed no more than 4 hours before the first ziprasidone injection. The study endpoint was defined as either 6 hours after the administration of the last dose or the end of the 24-hour treatment period, whichever was later, or the time of early termination. Trained investigators used the validated, 7-point Behavioral Activity Rating Scale (BARS)[15] to rate patients as follows: 1 = difficult or unable to rouse; 2 = asleep but responds normally to verbal or physical contact; 3 = drowsy, appears sedated; 4 = quiet and awake (normal level of activity); 5 = signs of overt (physical or verbal) activity, calms down with instructions; 6 = extremely or continuously active, not requiring restraint; and 7 = violent, requires restraint. The BARS was rated immediately before each dose; 15, 30, 45, 60, 90, and 120 minutes after each dose; and hourly until the next dose or, if no subsequent dose was given, at endpoint. Interrater reliability on the BARS was established during training sessions.[15]

The Clinical Global Impressions-Severity of Illness scale (CGI-S), ranging from 1 (normal, not at all ill) to 7 (the most extremely ill),[16] and the PANSS were rated at screening, baseline, 4 hours after the first dose, and at endpoint. The CGI-Improvement scale (CGI-I), ranging from 1 (very much improved) to 7 (very much worse) compared with baseline was rated 4 hours after the first dose and at endpoint. All patients were rated at 4 hours after the first dose even if they had received a second dose between 2 and 4 hours.

All observed or volunteered adverse events were recorded and classified according to COSTART. The investigator also rated the severity of adverse events and their likely relationship with treatment. Extrapyramidal symptoms (EPS) were further assessed using the Barnes Akathisia Scale[17] and the Simpson-Angus Scales[18] at screening, at baseline, 1 hour after the first injection, and at endpoint. Laboratory examinations were carried out at screening and at endpoint. Blood pressure and pulse rate were measured, both sitting and standing, at screening, before each ziprasidone i.m. dose, 30 and 60 minutes after each dose, and at endpoint. An ECG was also obtained at screening, baseline, and endpoint.

Data Analysis

Efficacy analyses were performed on pooled data from all patients in each treatment group who received at least 1 dose of ziprasidone i.m. Mean BARS scores were calculated in each group up to 4 hours after the first dose and compared between groups at each assessment using analysis of covariance (ANCOVA) with fixed effect terms for center and treatment. The primary endpoint for the comparison of mean BARS scores was 2 hours after the first dose. Mean scores at 3 and 4 hours after the first dose in patients who had not received a second dose by each of these timepoints were also compared. The percentage of patients classified as BARS responders, defined a priori as having ≥ 2-point reduction in BARS, was calculated for each postdose assessment. The mean area under the curve (AUC) of the BARS from 0 to 2 hours and 0 to 4 hours after the first injection was also compared between treatment groups using ANCOVA. The AUC BARS at 0 to 4 hours excluded patients who received a second injection before 4 hours. The PANSS agitation items score comprised the sum of the anxiety, tension, hostility, and excitement item scores. The mean change from baseline at 4 hours for all patients in the PANSS total score, PANSS agitation items, and CGI-S scores and the mean CGI-I were compared between groups. All statistical tests were 2-sided, and p values, derived using the Student t test, were considered significant at $< .05$. No formal statistical analyses of tolerability and safety assessments or concomitant medication usage were undertaken.

In addition to the primary analysis of the data described above, the treatment effect for the mean AUC of the BARS at 0 to 2 and 0 to 4 hours after first dose of 10 mg compared with 2 mg was calculated. The treatment effect for 10 mg of ziprasidone i.m. was compared with the treatment effect for 20 mg of ziprasidone i.m. that was determined in an identical study[19] comparing the 20-mg i.m. dose (N = 41) with a 2-mg dose (N = 38). The 20-mg study[19] was of identical design, utilized the same protocol, and was conducted in patients with very similar baseline characteristics and baseline BARS scores to those in the present study.

Table 1. Baseline Efficacy Variables[a]

	Ziprasidone i.m. 2 mg (N = 54)		Ziprasidone i.m. 10 mg (N = 63)	
Scale	Mean	SD	Mean	SD
BARS	4.65	0.65	4.79	0.57
PANSS total	89.4	18.8	90.0	20.2
PANSS agitation items	14.9	2.7	15.0	3.3
CGI-S	4.2	0.9	4.4	0.9

[a]Abbreviations: BARS = Behavioral Activity Rating Scale, CGI-S = Clinical Global Impressions-Severity of Illness scale, PANSS = Positive and Negative Syndrome Scale.

RESULTS

Patients and Treatment

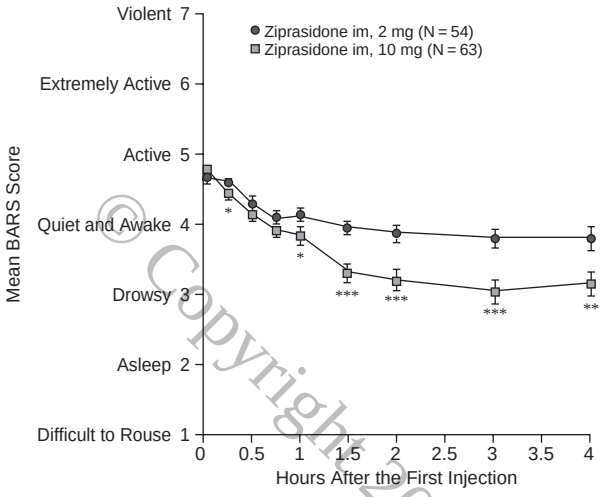
A total of 143 patients were screened, and 117 were randomly assigned to either 2 mg (N = 54) or 10 mg (N = 63) of ziprasidone i.m. The baseline characteristics in both treatment groups were similar. Approximately half had schizophrenia and one third had schizoaffective disorder as the underlying psychotic disorder. Approximately two thirds of the patients were men, 60% of the patients were white, and the mean age was 32.9 years (range, 18–76 years). Two thirds of the patients entered had received antipsychotic treatment in the 48 hours before screening, and baseline psychopathology was similar in both groups (Table 1).

In the group receiving 2 mg of ziprasidone i.m., 13 (24.1%) received 1 injection, 18 (33.3%) received 2 injections, 10 (18.5%) received 3 injections, and 13 (24.1%) received 4 injections during the 24-hour study period. In the 10-mg group, the corresponding numbers of patients were 23 (36.5%), 21 (33.3%), 10 (15.9%), and 9 (14.3%).

Two patients from each group discontinued before the end of the 24-hour study period. One patient, treated for preexisting hypertension, discontinued 2 mg of ziprasidone i.m. because hypertension increased (220/110 mm Hg) 7.5 hours after the first dose; this was classed as a serious adverse event. The other discontinued the 2-mg dose for reasons unrelated to treatment. One patient discontinued 10 mg of ziprasidone i.m. with diarrhea, akathisia, and nausea, and the other with disruptive behavior and agitation.

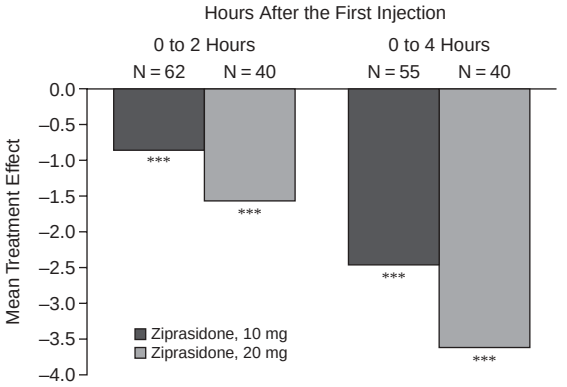
Concomitant lorazepam was taken by 7 patients in the 2-mg group and 6 in the 10-mg group at some time during

Figure 1. Mean (SE) Behavioral Activity Rating Scale (BARS) Score 0 to 4 Hours After the First Injection (all patients)[a]



[a]In the 2-mg group at baseline, N = 54; at 2 hours, N = 54; and at 4 hours, N = 45. In the 10-mg group at baseline, N = 63; at 2 hours, N = 62; and at 4 hours, N = 55.
*p < .05 vs. 2 mg. **p < .01 vs. 2 mg. ***p ≤ .001 vs. 2 mg.

Figure 2. Comparison of Treatment Effects for the Area Under the Curve of the Behavioral Activity Rating Scale From 0 to 2 Hours and 0 to 4 Hours After the First Injection for Ziprasidone, 10 mg and 20 mg[a]



[a]K.R.R., data on file, Pfizer Inc, Oct. 1997.
***p < .001 vs. 2 mg.

the 24 hours of the study, fewer than were taking lorazepam at baseline (11 and 12, respectively). Three patients in each group took temazepam for insomnia. Concomitant benztropine was taken at some time during the 24 hours of the study by 8 patients (14.8%) in the 2-mg group and 6 (9.5%) in the 10-mg group, a reduction compared with the 12 (22.2%) and 11 (17.5%), respectively, who were taking benztropine at the baseline assessment.

Efficacy

Ziprasidone i.m., 10 mg, was associated with a significantly lower mean BARS score than 2 mg of ziprasidone i.m. 15 minutes after the first injection ($p < .05$) (Figure 1). Mean BARS scores continued to decrease in the 10-mg group until 2 hours after the first dose and were significantly ($p < .05$) lower than the 2-mg group at all timepoints up to 2 hours except for 30 and 45 minutes. The mean BARS scores for those patients with 3- and 4-hour assessments after the first dose were also significantly lower in the 10-mg group compared with the 2-mg group ($p < .01$), and in both dose groups the mean scores were similar to those at the 2-hour assessment. After the small initial reduction following the first dose of 2 mg of ziprasidone i.m., there was little further change in that group. Significantly more patients were BARS responders 2 hours after the first dose in the 10-mg group (36/63; 57.1%) compared with the 2-mg group (16/54; 29.6%) ($p \leq .001$).

In the 2-mg and 10-mg treatment groups, there were similar reductions from baseline in the mean PANSS total score (15% and 14%, respectively) and in the mean PANSS agitation items score (29% and 30%, respectively) at 4 hours. The mean reduction in the CGI-S score at 4 hours was 0.74 in the 2-mg group and 0.76 in the 10-mg group. The mean CGI-I score at 4 hours was 3.02 in the 2-mg group and 2.78 in the 10-mg group.

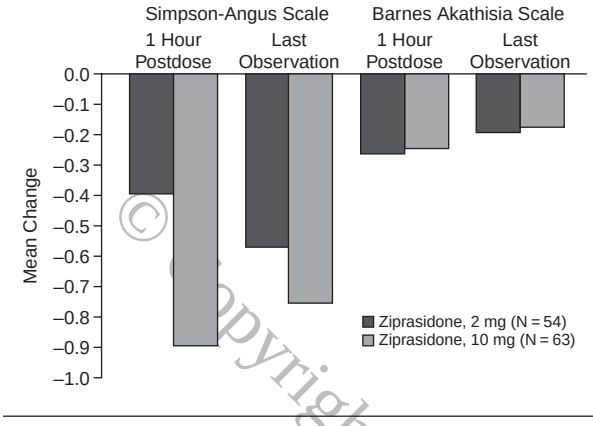
Dose Response: A Comparison of Treatment Effects With Another Study

In this study, the mean AUC of the BARS in the 2-mg and 10-mg groups, respectively, was 8.30 and 7.57 up to 2 hours and 15.88 and 13.47 up to 4 hours after the first dose (both $p < .001$). In an identically designed study,[19] comparing 2 mg with 20 mg of ziprasidone i.m., the mean AUC of the BARS in the 2-mg and 20-mg groups, respectively, was 8.48 and 6.95 at 2 hours and 15.73 and 12.23 at 4 hours after the first dose (both $p < .001$) (K.R.R., data on file, Pfizer Inc, Oct. 1997). The comparison of treatment effects for the BARS AUC, determined from these data, demonstrated that both the 10- and 20-mg i.m. doses had a statistically significant treatment effect and that this effect was dose related (all $p < .001$; Figure 2).

Tolerability

Treatment-emergent adverse events were reported in 35.2% (N = 19) of patients in the 2-mg group and 42.9% (N = 27) in the 10-mg group. The only adverse events that were reported in more than 10% of patients in either the 2-mg or 10-mg group were headache, reported in 5.6% (N = 3) and 12.7% (N = 8), respectively, and injection-site pain. This was anecdotally described as a transient stinging or burning sensation, reported in 13% and 7.9%, respectively. Both adverse events were of mild or moderate severity, and neither resulted in discontinuation from the study.

Figure 3. Mean Change From Baseline at the Last Observation in Simpson-Angus Scale and Barnes Akathisia Scale Scores (all patients)



One patient in the 10-mg group experienced moderate akathisia, and 1 in the 2-mg group experienced mild EPS. No patient was reported to experience dystonia, akinesia, oculogyric crisis, dyskinesia, tremor, twitching, hypokinesia, or cogwheel rigidity. In addition, there were mean reductions in Simpson-Angus Scale and Barnes Akathisia Scale scores from baseline both 1 hour after the first injection and at endpoint in both groups (Figure 3).

Agitation was reported as an adverse event in 2 patients in the 2-mg group and 1 in the 10-mg group. Mild or moderate dizziness occurred in 2 patients in each group. Mild or moderate nausea and somnolence were both more frequent with 10 mg of ziprasidone (both 7.9%; N = 5) than with 2 mg of ziprasidone i.m. (1.9% [N = 1] and 3.7% [N = 2] , respectively). No tachycardia, postural hypotension, ataxia, or confusion or any adverse event that may have been related to behavioral disinhibition or respiratory depression was reported.

Clinically significant changes in blood pressure and pulse rate were rare (< 5%), and no pattern was apparent. Median blood pressures and pulse rates did not change in the 10-mg group, and there were very small median changes in the 2-mg group. There was no evidence of clinically significant changes in ECG variables. The mean change in corrected QT interval was –3.7 msec in the group receiving 2 mg of ziprasidone i.m. and –1.8 msec in the 10-mg group.

DISCUSSION

The study reported here is 1 of 2 identically designed and conducted 24-hour studies to evaluate ziprasidone i.m. in the acute control and short-term management of agitated psychotic patients. This study compared 2 mg and 10 mg of ziprasidone; the other study[19] compared 2 mg with 20 mg of ziprasidone i.m. Both 10-mg and 20-mg doses had demonstrated efficacy in a pilot study[12] of patients with acute psychosis, and in the same pilot study, doses of 2.5 mg showed some evidence of effect. Therefore, the 2-mg dose was included as the comparator to establish if lower doses were likely to be clinically useful in the treatment of acute agitation.

Patients in this study had moderate levels of activity and agitation associated with their underlying psychotic disorder (mainly schizophrenia or schizoaffective disorder), as indicated by mean baseline BARS, PANSS, and CGI-S scores, and required and consented to receive i.m. ziprasidone treatment. The mean BARS score over the 4 hours after the first 10-mg dose of ziprasidone indicated that patients were rapidly calmed but not excessively sedated, an effect that contrasted with the 2-mg dose with which only a slight reduction in the BARS was initially observed, with negligible improvement in symptoms occurring thereafter. The separation between the 10-mg and 2-mg doses was apparent 15 minutes after the first dose, at which time the mean BARS scores were significantly different, demonstrating the fast onset of action of the 10-mg dose. Two hours after the first dose, over half the patients treated with 10 mg of ziprasidone i.m. were classified as responders, a significantly higher proportion than in the 2-mg group in which fewer than one third of patients had responded at this timepoint. All analyses of the BARS demonstrated that the 10-mg dose of ziprasidone i.m., but not the 2-mg dose, was associated with a meaningful reduction in symptoms.

The apparent lack of difference between treatment groups in the improvements observed on conventional efficacy scales, the PANSS and the CGI, probably reflects the fact that these scales, particularly the PANSS, were not designed to assess changes in behavioral activity in agitated patients over a very short period. These scales do not appear to discriminate, over a few hours, between the calming effect of the 10-mg dose of ziprasidone i.m. and the very slight and insignificant effect of the 2-mg dose that was observed on the BARS in this study. In the validation of the BARS, even though convergent validity between the BARS and the PANSS agitation items was demonstrated, the BARS was more responsive to treatment differences than the PANSS agitation items, supporting the findings reported here.[15]

In the comparison of the significant treatment effect of the 10-mg dose in this study with that of the 20-mg dose of ziprasidone i.m. in the identically designed study,[19] dose-related efficacy was demonstrated at both 2 hours and 4 hours postdose. Since the mean BARS scores after the first dose in the 2-mg arms during each of the 2 studies were almost identical, the treatment effects could be compared, and the dose-related efficacy of 10 mg and 20 mg was demonstrated. The actual magnitude of the responses observed with 10 mg of ziprasidone i.m. in this study indicates that it is a therapeutic dose, albeit probably at the

lower end of the therapeutic dose range for the treatment of acute agitation associated with psychosis. For patients with more severe symptoms than the patients in this sample, higher doses up to 20 mg may be required. This finding is also supported by the comparison of BARS responder rates across the 2 studies. Two hours after the first dose, 57% of patients had responded to ziprasidone 10 mg i.m. compared with 90% who received 20 mg of ziprasidone i.m. It should be noted that the effects of ziprasidone i.m. cannot be generalized to patients with organic psychoses or substance-induced psychosis.

The responses to 10 mg of ziprasidone i.m. on the BARS, while indicating effectiveness, cannot be readily compared with responses in studies of i.m. benzodiazepines or conventional antipsychotics because of lack of consistency among studies in design, patient selection, rating scales, and duration of treatment.[20–24]

Since fewer than 10% of patients in the 10-mg group were given lorazepam during the 24-hour study period, usage similar to that in the 2-mg group, concomitant benzodiazepine use was unlikely to have obscured the assessments of either efficacy or tolerability. The finding that 10 mg of ziprasidone i.m. was effective without causing profound sedation was evident by the absence of adverse events such as confusion and ataxia. There were no signs of behavioral disinhibition or respiratory depression with either dose.

While less marked sedation is also associated with high-potency i.m. neuroleptics, such as haloperidol, and is thought to offer advantages over low-potency agents, such as chlorpromazine,[25] the higher incidence of movement disorders associated with i.m. haloperidol, particularly acute dystonic reactions, akathisia, and akinesia, can be problematic and can make it difficult to distinguish underlying symptoms of the illness such as agitation.[26–28] In this study, the absence of dystonia and the improvements in assessments of parkinsonism and akathisia are consistent with observations from other studies of ziprasidone i.m.[12,19,29,30] A feature that distinguished effective doses of ziprasidone i.m. from haloperidol i.m. is that ziprasidone i.m. was only rarely associated with extrapyramidal side effects.[29,30] This finding is very likely related to the high serotonin-2A/dopamine-2 (D_2) affinity ratio of ziprasidone,[3] an attribute that is thought to confer protection against extrapyramidal side effects associated with D_2 antagonism.[31] While protection against extrapyramidal side effects is a major advance in the management of the manifestations of psychotic disorders with the oral formulations of novel agents, it is also likely to be a very important feature of ziprasidone i.m., since extrapyramidal side effects experienced in the acute emergency setting may have an adverse effect on subsequent treatment compliance and cooperation by the patient even in the long term. This benefit of ziprasidone is particularly important, as noncompliance is thought to be responsible for approximately 40% of hospital readmissions 2 years after discharge.[32]

The low requirement for concomitant benztropine with ziprasidone i.m. means that patients will likely be spared anticholinergic side effects such as constipation and dry mouth, since ziprasidone itself does not possess intrinsic anticholinergic activity, unlike olanzapine and clozapine.[3,4] The cardiovascular safety of ziprasidone i.m., as evidenced by the lack of postural hypotension and tachycardia, is a feature that distinguishes ziprasidone from conventional low-potency antipsychotics such as chlorpromazine and is consistent with the effects of oral ziprasidone, which can be initiated at an effective dose in acutely ill patients without dose titration.[5,8] No clinically relevant changes in ECG variables were detected.

Assessments of tolerability and safety indicate that 10 mg of ziprasidone i.m. was well tolerated and, in this respect, not clinically significantly different from the ineffective 2-mg dose. In addition, the effective 10-mg dose of ziprasidone i.m. does not appear to be associated with many of the adverse effects often associated with i.m. benzodiazepines and i.m. antipsychotics. The 10-mg dose of ziprasidone i.m. rapidly reduces the symptoms of acute agitation associated with psychosis, calming patients for at least 2 hours and a substantial proportion of patients for at least 4 hours. The dose-related efficacy of 2 mg and 10 mg of ziprasidone i.m. indicates that both doses will be clinically effective. Doses up to 20 mg will most likely benefit patients with more severe agitation in whom the 10-mg dose may not be sufficiently calming. An effective, rapid-acting i.m. formulation of ziprasidone can offer physicians and patients an alternative to existing conventional i.m. treatments and also the opportunity to treat all phases of psychotic illness such as schizophrenia with the same novel agent.

Drug names: benztropine (Cogentin and others), chlorpromazine (Thorazine and others), clozapine (Clozaril and others), haloperidol (Haldol and others), lorazepam (Ativan and others), olanzapine (Zyprexa), propranolol (Inderal and others), temazepam (Restoril and others).

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