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Clinical predictors of response to treatment in catatonia☆,☆☆

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Abstract

Objective: This study aims at identifying predictors of treatment response to lorazepam in catatonia.
Methods: The clinical charts of 107 inpatients, admitted over duration of 2 years, with a primary diagnosis of catatonia were examined for response to lorazepam trial. Trial was considered as having received 3–6 mg per day of lorazepam for at least 3 days.
Results: Out of these 107 patients, 99 received lorazepam and 8 received electroconvulsive therapy as the first line of management. There were 32 responders and 67 nonresponders to lorazepam. The nonresponders were characterized by rural background (85.1% vs. 62.5%, *P*=.01), longer duration of catatonic symptoms (108.88 vs. 25.12 days, *P*=.018), mutism (63.6% vs. 31.3%, *P*=.02) and presence of first-rank symptoms like third-person auditory discussing-type hallucinations (16.4% vs. 12.0%, *P*=.03) and made phenomena (7.5% vs. 0%, *P*=.04). The presence of waxy flexibility (12.5% vs. 4.5%, *P*=.03) predicted good response.
Conclusions: This study identifies that longer duration of illness, presence of catatonic sign of mutism and certain specific phenomena like third-person auditory hallucinations and made phenomena predicted poor response to lorazepam in catatonia. This could provide insight into the prediction and planning of the appropriate treatment strategies in this psychiatric emergency.

Keywords: Lorazepam; Catatonia

1. Introduction

Catatonia can be characterized by concurrent motor, emotional, vegetative and behavioral symptoms [1]. There are more than 40 motor signs of catatonia, but the presence of two prominent features for 24 h or longer is sufficient to identify the syndrome [2]. Benzodiazepines and electroconvulsive therapy (ECT) have been found to be effective in the treatment of catatonia [3]. The literature mandates the treatment of underlying cause wherever identifiable and recommends the use of lorazepam as a first-line treatment [4]. The treatment response of catatonia to lorazepam has been recorded in the literature [1,5–8]. Benzodiazepines have been reported to be effective in 70% of the cases, with lorazepam demonstrating the highest frequency of use and up to 80% complete response rate [4,7,9,10]. Diazepam has also been found to be effective in catatonia [10]. Recent treatment guidelines list this as effective in both acute and chronic catatonia [11]. In cases where benzodiazepines are not effective, ECT has been found to be very effective [12].

In a developing country like India with limited resources in any psychiatric setting, where catatonia continues to be an important treatment challenge, the use of such cost-effective and rapidly effective treatment strategies like benzodiazepines needs to be considered at the primary care level itself. Early use of benzodiazepines can greatly decrease the duration of untreated illness and can limit disease progression and severity. However, little is known about what factors predict response to lorazepam. Thus, it is important to examine the clinical predictors of response to benzodiazepines in catatonia. Nonresponders can thus be referred to higher centers at the earliest time for resource-intensive treatments like ECT. In this study, we aimed to examine the clinical predictors of response to treatment with lorazepam in a large sample of patients with catatonia.

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2. Methodology

We evaluated the clinical charts of patients with a primary diagnosis of catatonia who were admitted to the psychiatric services of the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, from January 2004 to December 2005 (2 years). Out of 7474 patients admitted during this period, 123 had a diagnosis of catatonia. Patients with catatonia are admitted as a hospital practice in the intensive care unit. NIMHANS is a premier psychiatric research institute in India with a postgraduate residency program. It has a 650-bed hospital with both outpatient and inpatient services. There are detailed clinical charts of all admitted patients. Detailed evaluation of all admitted patients is initially done by a postgraduate student. During this time, a complete history, physical and neurological examinations, mental status examination and the basic laboratory examinations are carried out. Then all the cases are discussed with the senior residents. Finally, all the cases are again reviewed and discussed in the rounds by a senior consultant psychiatrist on the teaching faculty of the institute. The following procedures are usually adopted in the hospital to treat the catatonic signs. Injection of lorazepam 2 mg intravenously, in repeated dosages, 6 to 8 hourly for 3 days is given routinely. ECT is given either subsequent to poor response to lorazepam or as first choice depending on the severity of symptoms like extreme withdrawal of feeds.

The diagnosis of catatonia was made according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV). According to the DSM-IV criteria, at least two of the five criteria are required: (1) motor immobility or stupor, (2) extreme negativism or mutism, (3) excessive motor activity, (4) echolalia or echopraxia and (5) peculiarities of voluntary movement. Catatonic features were assessed as a routine clinical practice to ascertain the baseline severity and treatment response using the Bush–Francis Catatonia Rating Scale (BFCRS). The charts of all such patients were considered for evaluation. The clinical characteristics, method of administration of lorazepam and response rate of this sample to lorazepam have been reported earlier [13]. Response was defined as being able to move, speak and communicate with doctors, and that the patient no longer satisfied the diagnostic criteria for catatonia as per DSM-IV. Those patients who required ECTs after adequate trial of lorazepam were considered as nonresponders to lorazepam. Adequate trial of lorazepam was defined as having received 3–6 mg per day of lorazepam for at least 3 days [13]. After obtaining all the information from the chart, two senior registrars and a senior consultant reviewed all the data, and final consensus opinions were made regarding the treatment response and nonresponse. Continuous variables were analyzed using independent-samples *t* test, and categorical variables were analyzed using χ^2 test. The variables which became significant in the univariate analysis along with the variable of current age were included in the logistic regression analysis to examine the factors that predict response to lorazepam.

3. Results

In the study period, there were 123 patients admitted with catatonic symptoms in the hospital. Only 107 patients met the study criteria. Out of these 107 patients, 99 received lorazepam and 8 received ECTs as the first line of management since they were at severe risk to themselves due to the extreme degree of withdrawal to feeds and fluids. The age of subjects ranged from 16 to 67 years with a mean age of 26.1±9.1 years, and the sample comprised predominantly of males (*n*=70, 65.4%). The mean age of onset of illness was 25.3±8.81 years. Majority of the subjects hailed from a rural background (*n*=85, 79.4%). The mean number of days of catatonia at presentation was 83.8±22.1. The diagnostic composition of these cases was as follows: schizophrenia (*n*=26, 24.3%), depressive disorder (*n*=32,29.9%), acute psychosis (*n*=15, 14.0%), psychosis unspecified (*n*=12 (11.2%), bipolar affective disorder (*n*=15, 14.0%) and idiopathic catatonia (cause unknown) (*n*=7, 6.5%).

In the sample, the response rate to lorazepam was 32 (32.3%) (response defined as having no evidence of catatonia). The patients showed some improvement in 2.7±0.3 days (mean±S.D.), and for complete recovery, it required a mean of 6.1±0.6 days on lorazepam treatment. There were 32 responders (32.3%) and 67 nonresponders (67.7%) among the subjects. The differences between responders and nonresponders are shown in Table 1. The diagnoses when grouped as affective illnesses (comprising of major depression and bipolar affective disorder), nonaffective psychoses (comprising of schizophrenia, acute psychosis and unspecified psychosis) and idiopathic catatonia did not reveal any differences between responders and nonresponders. A *P* value of less than .05 was considered to be statistically significant. Among the demographic characteristics, the groups differed significantly with respect to urban and rural background, with a higher frequency of urban status among responders (37.5% vs. 14.9%, *P*=.01). A greater number of days in catatonia before treatment initiation predicted poorer response to lorazepam trial (25.12±44.94 vs. 108.88±276.14, *P*=.018), as shown in Table 1.

The clinical features significantly different between the groups were third-person auditory hallucinations (16.4% vs. 12.0%, *P*=.03) and made phenomena (0% vs. 7.5%, *P*=.04), which were significantly higher in the nonresponder group. Made phenomena refers to the passivity phenomena including the made acts and impulses [14]. Among the catatonic signs, mutism was significantly higher in the nonresponder group (31.3% vs. 63.6%, *P*=.02), whereas waxy flexibility (12.5% vs. 4.5%, *P*=.03) predicted response. On logistic regression analysis, the presence of third-person auditory hallucination (β=0.24, *P*=.02) and rural background (β=1.41,