Therapeutic Efficacy of N-Methyl D-Aspartate Antagonist Amantadine in Febrile Catatonia

We present two cases of akinetofebrile catatonic patients with nonresponse to lorazepam and/or amobarbital in previous catatonic episodes for which both were treated successfully with the NMDA antagonist amantadine—finding not previously reported.

Case 1

A 60-year-old married white housewife suffered from bipolar disorder (DSM-IV: 296.54) for 25 years with 12 hospitalizations resulting from recurrent depressive (response to trimipramine and/or fluvoxamine) and some manic (response to haloperidol) phases. She had four acute catatonic episodes previously which were treated successfully only with ECT and not with lorazepam and amobarbital. This time, because of noncompliance (as several times before), she completely discontinued her medication (lithium and fluvoxamine) 6 weeks before, became increasingly depressive and withdrawn, and was finally admitted in an acute akinetofebrile (40.2°C) catatonic state with motor rigidity, akinesia, stereotypes, posturing, paratonia ("gegenhalten"), behavioral (mutism, staring, negativism, autism, accompany "mitgehen"), echopraxia, and vegetative (hyperpyrexia, tachycardia, high blood pressure) abnormalities (Bush-Francis Catatonia Rating Scale 6 [BFCRS score = 35]). Initially she was treated with amantadine 200 mg intravenously. After 2 to 3 hours, vegetative measures (blood pressure, temperature, pulse rate) returned to normal values, whereas her motor and behavioral abnormalities persisted (BFCRS score = 25). Seven hours after the first application, we therefore treated her with a second infusion of 200 mg of amantadine. Motor and behavioral symptoms gradually diminished within the following 4 hours (BFCRS score = 17). Seven hours after the second application, she received a third infusion of 200 mg of amantadine, which led to the complete resolution of catatonic symptoms within 3 hours. In the following days, she was maintained on amantadine 3 × 100 mg orally, and because of her now apparent depressive symptoms (anxiety, loss of appetite, depressed mood, anhedonia, insomnia, irritability, poor concentration), she was also given fluvoxamine (2 × 150 mg), on which she was discharged 4 weeks later.

Case 2

A 52-year-old married white woman suffered from schizoaffective psychosis (DSM-IV: 295.70) for 13 years (11 hospitalizations) with 5 catatonic (all nonresponse to lorazepam but responsive to ECT) and recurrent depressive (responsive to trimipramine) patient. She has been successfully treated with ECT and has had no further episodes since then. She was admitted to our hospital with a severe catatonic episode that was associated with exacerbation of her affective symptoms. She was treated with amantadine during the acute episode and was discharged 4 weeks later without any catatonic symptoms.

Discussion

This is the first report of successful therapeutic reversal of acute akinetofebrile catatonia with amantadine, an NMDA antagonist and dopamine agonist, in patients with febrile catatonia. Depending on further studies, amantadine may concurrently be considered as a therapeutic alternative to lorazepam and amobarbital in akinetofebrile catatonia. In addition, catatonic patients with fever and nonresponse to lorazepam/amobarbital should be given a therapeutic trial with amantadine before undergoing ECT.
Application of amantadine may therefore be considered as a therapeutic alternative to immediate treatment with ECT in febrile catatonia and in catatonic nonresponders to lorazepam/amobarbital.

Furthermore, therapeutic efficacy of amantadine raises some interesting questions about regional alterations of NMDA-receptor function in catatonia. Cortical regions such as the prefrontal cortex \(^1\) and the anterior cingulate \(^2\), \(^3\) show glutamatergic hypofunction in schizophrenic and/or affective psychoses, so that one would expect no therapeutic efficacy of NMDA antagonists in these patients. However, amantadine given to both catatonic patients with underlying affective/schizoaffective psychoses showed good therapeutic efficacy with regard to catatonic symptoms. Catatonia may consecutively be characterized not only by prefrontal/cingulate glutamatergic hypofunction (due to underlying psychosis) but by concomitant glutamatergic hyperfunction (due to therapeutic efficacy of an NMDA antagonist) in another cortical region as well. Glutamatergic hyperfunction in the prefrontal cortex and the anterior cingulate may lead to decreased excitation of inhibitory (i.e., GABAergic) projections from prefrontal cortex/anterior cingulate to premotor (i.e., supplementary motor area) and motor (i.e., motor cortex) cortical areas, resulting in a net effect of frontostriatal glutamatergic hyperfunction. Amantadine may antagonize this frontostriatal glutamatergic hyperfunction and may consecutively lead to successful reversal of akinesia in catatonia, which is similar to results seen in Parkinson's disease. \(^4\), \(^5\) In addition, such glutamatergic corticosubcortical interactions may modulate nigrostriatal and tuberoinfundibular dopaminergic systems, thereby resolving akinesia and hyperpyrexia.

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