How Relevant is Seizure Duration in Assessing the Effectiveness of Electroconvulsive Therapy?

Dear Editor: Electroconvulsive therapy (ECT) is a highly effective treatment for major depression and other psychiatric disorders. The question of how to define a therapeutically adequate ECT treatment has been discussed from the early days of ECT (1) to the present (2). Although convention has required a minimum individual seizure duration of 15 to 25 seconds (3,4) or a total seizure duration of more than 200 seconds (5), the complex electrophysiological events involved in developing a generalized seizure make it problematic to link the therapeutic efficacy of ECT to seizure duration only. We describe the case of a patient with severe depression who completely recovered despite receiving ECT that generated only brief motor seizures.

Case Report
A woman aged 73 years presented with a sudden onset of depressed mood, insomnia, loss of appetite and interest, poor concentration, and low energy. She had stopped eating, remained in bed, and became unable to attend to her personal care. She also demonstrated severe mood-congruent paranoid delusions.

Before starting the study, one subject smoked a single joint daily at bedtime; the rest smoked 4 to 15 joints daily. During the study, they were allowed to smoke marijuana on days 1 to 4 and encouraged not to smoke on days 5 to 10. Lithium was prescribed at 600 mg on day 4, 900 mg on days 5 to 8, and 600 mg on day 9. It was discontinued on day 10. Data were obtained from the Marijuana Craving Questionnaire. We used the Withdrawal Behavior Checklist to obtain ratings of 27 symptoms on a 4-point scale (6–8).

The sample was small, the response was variable, and 3 participants (one among the improved) admitted that they smoked occasional marijuana between days 5 and 10. Therefore, quantitative results are not meaningful. Two participants reported that lithium greatly improved their withdrawal symptoms, and 2 more reported that lithium helped, particularly with mood symptoms. Five subjects did not feel that lithium helped their withdrawal symptoms.

Lithium was well tolerated; however, the serum levels on day 9 (mean 0.45 mmol/L, SD 0.12) were below therapeutic levels, and the duration of use was only 6 days. It is possible that lithium might be more effective if used longer at the usual therapeutic levels. As noted, the study was small; further, there was no control group. Future studies should include interviews or questionnaires to elicit subthreshold mood symptoms and use an inpatient setting to prevent unauthorized marijuana use (7). To conclude, of 9 regular marijuana users, 4 felt that lithium improved withdrawal symptoms.

References

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Risperidone Treatment of Periodic Catatonia

Dear Editor: Periodic catatonia is an enigmatic and underrecognized clinical entity that has mostly been described in European literature (1). Benzodiazepines remain the first-line treatment for catatonia because of their favourable efficacy and side effect profile. Patients failing to respond to benzodiazepines have been shown to respond to electroconvulsive therapy (ECT, 2). The use of atypical antipsychotics to treat catatonia remains anecdotal, owing to concerns that they may worsen catatonic symptoms (3). We report the use of risperidone in a patient with periodic catatonia whose symptoms did not improve with a benzodiazepine trial; we also discuss the role of atypical antipsychotics in treating catatonia.

Case Report

The morning before he presented, Mr A, aged 28 years, was found by his mother to be acting “strange.” He was mute, did not respond to any commands, kept staring into empty space, and sat curled up on the floor for hours without changing his posture. He refused to eat or drink anything and was brought to the medical emergency department (ED). He had a normal head CT, EEG, and blood work-up (including electrolytes, liver and renal function tests, and blood counts). His urine drug screen was negative. He was subsequently transferred to the psychiatric ED with a diagnosis of conversion disorder.

On examination, Mr A was alert, awake, and fully oriented. He exhibited psychomotor retardation and rigidity. In addition, he exhibited catatonic signs, including mutism, negativism, staring, posturing, waxy flexibility, and incontinence. Interspersed with these symptoms were stereotypic movements and facial grimacing. He scored 38 (out of a maximum of 69) on the Bush-Francis Catatonia Rating Scale (BFCRS, 2). There were no focal neurological deficits, and vital signs revealed tachycardia and tachypnea. Interestingly, Mr A had experienced 4 prior episodes of catatonia over the past 5 years. These episodes lasted from a few hours to 1 week. His first catatonic episode was successfully treated with risperidone, but neither he nor his family remembered the dosage of the medication or the duration of treatment. During his last catatonic episode 1 month earlier, which lasted a few hours, Mr A had become extremely agitated while in the medical ED and was given 5 mg of parenteral haloperidol. This single dose resulted in a dramatic resolution of his symptoms. The patient was subsequently discharged without any psychiatric referral. There was no history of treatment with ECT, and he had a normal head CT and EEG during these episodes. The family history was unremarkable.

During the index episode, Mr A had received 2 mg of lorazepam in the medical ED, with minimal response. After admission to psychiatry, he was continued on lorazepam, up to 4 mg daily; however, he showed no change in his symptoms over the next 2 days, and lorazepam was then tapered in another couple of days. ECT was considered as an option, but given the past response of his catatonia to antipsychotics (specifically, risperidone and haloperidol), we decided to treat him again with risperidone. Mr A was started on risperidone at 1 mg daily 3 days after admission, and 3 days after commencing risperidone, the catatonia began to improve. The patient began to communicate more and reported feeling “snapped from stress” after a recent break-up with his girlfriend. He provided a history of past depressive symptoms but denied having depressive symptoms just preceding the catatonia. He endorsed auditory hallucinations of a male voice but was not sure about the content. There was no evidence of delusions and he denied any recent drug or alcohol use. Risperidone was increased to 3 mg on the sixth day of admission, with improvement in the remaining catatonic signs. Mr A was no longer incontinent and disorganized and was eating properly and maintaining his hygiene. He was discharged on risperidone (3 mg daily) on the 11th day. He scored 0 on the BFCRS at the time of discharge. The diagnosis at discharge was brief psychotic disorder.

Discussion

Substance-induced catatonia is a differential that cannot be entirely excluded in this presentation, as the patient’s drug screen might not have detected all substances. Another differential is nonconvulsive status epilepticus, but the EEG did not support this diagnosis. This patient experienced previous episodes of catatonia alternating with clearing of catatonic symptoms, which clinically defines periodic catatonia (1). Periodic catatonia therefore seems the likely diagnosis for this patient. Further, coexistence of both akinetic and hyperkinetic symptoms, with one pole predominating, is typical of periodic catatonia as manifested by this patient (4). The DSM-IV does not recognize the diagnosis of periodic catatonia, and most cases are diagnosed as catatonic schizophrenia. The periodic nature of this illness, coupled with the prompt resolution of symptoms and a negative organic work-up, might have led the internists in the medical ED to misdiagnose him as suffering from conversion disorder. This case calls for greater awareness among medical ED staff of catatonia generally and, specifically, of its periodic nature in some patients.

Psychotic symptoms (classified by Leonard under “unsystematic schizophrenia”) have been described in patients with periodic catatonia, which may partly explain risperidone’s effectiveness in treating this patient’s catatonia (1). Antipsychotic medications may alter the illness course in periodic catatonia and may have the potential to limit catatonic phases (1). A recent report describes the successful treatment of periodic catatonia with ziprasidone (5). Other reports describe the use of atypical antipsychotics such as risperidone and olanzapine for treating catatonia in...
general (3). However, the use of antipsychotics in catatonia treatment is a contentious issue, given reports that high potency antipsychotics precipitated or exacerbated catatonia or neuroleptic malignant syndrome (NMS), a variant of malignant catatonia (3). In this regard, some authors suggest adjunctive use of a benzodiazepine while the antipsychotic drugs are being introduced, in the hope that a benzodiazepine may reduce the risk of NMS (6). We cannot ascertain whether this patient would have responded to higher dosages of lorazepam. However, the dosage this patient received is in the range used by other investigators to treat catatonia (2). While benzodiazepines, ECT, or atypical antipsychotics have been used to treat the acute phase of periodic catatonia, more research is needed on the duration of treating the acute phase with these modalities, as well as on the treatment of interepisode residual symptoms.

References


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Lamotrigine-Induced Neutropenia

Dear Editor: Lamotrigine’s popularity as a psychotrope continues to rise because of growing evidence for its efficacy and a favourable side effect profile. Although rare, hematological side effects, including neutropenia, have been reported (1).

Case Report

AP is a woman aged 23 years who was hospitalized for treatment of bipolar II disorder, depressed phase. Comorbid diagnoses included polysubstance abuse and eating disorder not otherwise specified. Treatment with topiramate had been initiated 2 months prior to admission, to which AP had partially adhered.

Topiramate 50 mg at bedtime was initiated on admission (day 1). This was increased to 100 mg at bedtime on day 10. It was decreased to 75 mg on day 15 and further decreased to 50 mg on day 26. Lamotrigine 12.5 mg at bedtime was added on day 15. It was increased to 25 mg on day 19 and further increased to 50 mg on day 26.

A complete blood count (CBC) on day 2 was normal. Neutropenia (1.0 × 10⁹/L) was noted in a random CBC on day 29. Topiramate 50 mg at bedtime and lamotrigine 50 mg were discontinued. The patient’s neutrophil count increased over a 2-week period to 2.0 × 10⁹/L on day 43 and 2.4 × 10⁹/L on day 44.

Rechallenge with lamotrigine 5 mg at bedtime was initiated on day 46. Neutrophils dropped to 1.8 × 10⁹/L on day 48, so lamotrigine was discontinued. Neutrophils rose to 2.2 × 10⁹/L on day 49 and to 2.4 × 10⁹/L on day 50.

Discussion

There appears to be an association between lamotrigine and the development of neutropenia in this patient. Neutropenia appeared first on a random CBC 14 days after the addition of lamotrigine. The neutrophil count normalized 14 days after medication was stopped but dropped following lamotrigine rechallenge. A longer rechallenge period with monitoring might have been warranted. However, there was concern about exposing the patient to possible risk. The patient did not experience any clinical sequelae as a result of this adverse reaction.

Other potential causes were investigated. The Topamax® product monograph reports an incidence of leukopenia of 2.7% with 200 to 400 mg daily and 1.2% with 600 to 1000 mg daily in adults (2). When neutropenia first occurred, this patient was taking topiramate and lamotrigine concurrently. She had been taking low-dosage topiramate for about 2 months prior to admission, without significant hematological events. She was not on topiramate during lamotrigine rechallenge. During her hospitalization, AP lost 7 kg. There was concern that her poor nutritional status might have contributed to neutropenia.

Eating disorders have been associated with hematological complications: anorexia nervosa has been linked to bone marrow hypoplasia and resultant hematological side effects, including neutropenia (3). During lamotrigine rechallenge, AP’s nutritional status was reasonable.

The exact pathophysiology of lamotrigine-induced neutropenia is unknown (4). A literature review produced several reports of lamotrigine-induced neutropenia that reversed upon drug discontinuation (5–7). There is limited information on rechallenge (8). In this patient, rechallenge with a minimal dosage again lowered neutrophil counts. This case further documents lamotrigine-induced neutropenia in a patient with slow up-titration, as well as the outcome of rechallenge. It highlights the need for careful monitoring of blood work.

References


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Galactorrhea With Aripiprazole

Dear Editor: Aripiprazole is a new-generation atypical antipsychotic agent. It is a partial agonist at the dopamine D2 and serotonin 5-HT1A (5-HT2) receptor sites; it is an antagonist at the 5-HT2 receptor site (1). Data from the serum prolactin and galactorrhea in association with aripiprazole may reduce serum prolactin levels (2). However, we have observed a case of raised serum prolactin and galactorrhea in association with aripiprazole. To the best of our knowledge, this is the first case of aripiprazole-induced galactorrhea in world literature.

Case Report

Mrs S, aged 36 years, presented with a 2-month history of suspiciousness, withdrawal, and neglect of personal care. She fulfilled DSM-IV criteria for schizoaffective disorder. She was drug-naive for the episode, and was prescribed aripiprazole in a dosage that was titrated from 10 mg daily to 15 mg daily over a period of 2 weeks. At week 3 of aripiprazole therapy, she developed tremor, rigidity, salivation, and bradykinesia, along with simultaneous breast tenderness and a milky discharge from the nipples. Her serum prolactin was found to be elevated to 27 ng/mL (normal range, 1.5 to 19.0 ng/mL). All other investigations, including thyroid profile and brain CT scan, were normal.

The extrapyramidal symptoms resolved with the addition of trihexyphenidyl (4 mg daily). At week 5 of aripiprazole therapy the hyperprolactinemia (23.5 ng/mL) and galactorrhea persisted despite a lowered dosage of aripiprazole to 5 mg daily. Aripiprazole was subsequently replaced with quetiapine in a dosage that was raised from 100 mg daily to 300 mg daily over a period of 5 weeks. By week 6 of quetiapine therapy, the patient’s serum prolactin had dropped to 6.0 ng/mL, and the breast tenderness and galactorrhea had resolved completely.

Three years previously, Mrs S had a similar episode of psychosis. For 6 months, she received trifluoperazine (15 mg daily) and trihexyphenidyl (2 mg daily) without developing endocrine problems.

The association between aripiprazole and breast tenderness and galactorrhea is irrefutable in our patient; the complaints developed shortly after the introduction of aripiprazole monotherapy, were associated with hyperprolactinemia, and resolved after the replacement of aripiprazole with quetiapine. The patient had received no other medication that might have explained the adverse effects.

How and why did these adverse effects arise? The partial D2 agonistic action of aripiprazole implies that the drug will augment dopamine hypoaactivity, as is likely in the prefrontal areas, and block dopamine hyperactivity, as is likely in the mesolimbic areas. In patients with schizophrenia, dopamine neurotransmission is probably normal in the nigrostriatal and tuberoinfundibular systems. One might therefore expect aripiprazole to interfere with normal functioning in these pathways, resulting in extrapyramidal symptoms and the consequences of raised serum prolactin. Aripiprazole does indeed cause extrapyramidal symptoms, possibly to the same extent as the typical antipsychotics (2). Hyperprolactinemia, however, may be either an idiosyncratic response or a dosage-dependent adverse effect in sensitive individuals. Future studies should address the epidemiology of endocrinal disturbances with aripiprazole.

References


Effects of Rivastigmine in a Case of Residual Schizophrenia

Dear Editor: Among cholinesterase inhibitors, rivastigmine is an acetylcholinesterase and butyrylcholinesterase inhibitor that is widely used in treating Alzheimer’s and subcortical vascular dementias, owing to its beneficial pharmacodynamic property.

Combined with antipsychotics, rivastigmine has been found effective in improving negative schizophrenia symptoms (1,9). We report a case of residual schizophrenia with predominant negative symptoms that responded to rivastigmine and risperidone.

Case Report

Mrs J is an Indian woman, aged 45 years, with residual schizophrenia (according to ICD-10 criteria) of 6 years’ duration. She was treated with risperidone and maintained on 6 mg daily. She presented with marked psychomotor retardation, passivity, lack of initiative, poverty of speech, and poor facial expression. With strong family support, she had maintained good drug compliance and responded to risperidone, which completely controlled her positive symptoms. She developed the presenting complaints during the prior 18 months, despite regularly taking an antipsychotic. Using the clinical interview, patient observation, and additional informant information, we evaluated her baseline negative symptom complex according to the Scale for the Assessment of Negative Symptoms (SANS, 2). We also evaluated her performance in Instrumental Activities of Daily Living (IADL, 3) and on the Satisfaction with Life Scale (SWLS, 4). Further, we administered neuropsychological tests: the Halstead-Reitan Battery (5) for psychomotor speed, attention, and scanning; the Rey Auditory Verbal Learning Test (6); and the Wechsler Memory Scale-Third Edition (7) for learning and memory.

We started the patient on rivastigmine tartrate 1.5 mg twice daily, titrated at monthly intervals to reach a maximum of 6 mg daily in 2 months’ time and maintained along with risperidone 6 mg daily. A second SANS evaluation, done after 4 weeks of drug therapy, showed 10% improvement in negative symptoms. The combined treatment of antipsychotic and rivastigmine continued for 6 months, at which time the patient was reassessed. We found a notable drop of 41% from her baseline SANS score. Similarly, her baseline IADL and SWLS scores improved by 36% and 28%, respectively. Neuropsychological tests measured after 6 months showed appreciably better cognitive functions, which were directly related to the improvement in her quality of life.

Discussion

The neurotransmitters implicated in the pathogenesis of schizophrenia are dopamine, serotonin, glutamate, and acetylcholine. Cognitive impairment in schizophrenia is partly due to diminished acetylcholine activity in the brain cortex. Patients with schizophrenia and comorbid cognitive dysfunction appeared to show an improvement in their...
Aripiprazole, a new atypical antipsychotic, has partial dopamine agonist and antagonist effects (2). Since dopamine stimulation in the nucleus accumbens has been suggested to cause addictive behaviour, aripiprazole’s partial dopamine agonist effects in this area of the brain may reduce this behaviour (3). We present a case wherein aripiprazole reduced alcohol craving and use.

**Case Report**

Mr S is white, aged 39 years, and diagnosed with schizophrenia, paranoid type, according to DSM-IV criteria. He received outpatient psychiatric treatment with psychotherapy and pharmacotherapy (olanzapine 20 mg daily). He continued to experience delusions of reference and periodic auditory hallucinations. His Brief Psychiatric Rating Scale (BPRS) score was 31.

Mr S also met the DSM-IV diagnostic criteria for alcohol dependence, which started at age 18 years with an occasional beer and progressed to his drinking a 12-pack daily. He denied any medical problems, but admitted to problems with employment and relationships caused by his alcohol use. Despite several attempts to quit, including treatment in 2 substance use treatment programs, he relapsed repeatedly. His current use amounted to 6 cans of beer daily. He refused to attend any addiction program, including Alcoholics Anonymous.

He also suffered from glaucoma. During treatment, he discovered through the Internet that olanzapine might exacerbate glaucoma, which led him to stop olanzapine on his own. At his next meeting, his psychiatrist discussed several options, including the newer atypical antipsychotic, aripiprazole. Mr S finally agreed to try this medication, which may reduce craving for and use of alcohol. More research is needed to establish the benefits of aripiprazole in regard to alcohol and other substance use disorders. Until then, some dual diagnosis patients may benefit from aripiprazole, which may reduce craving for and use of alcohol.

### References


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### Aripiprazole Reduces Alcohol Use

Dear Editor: Few pharmacotherapy options exist for the treatment of alcohol dependence. Recent reports suggest that newer atypical antipsychotic medications may reduce alcohol craving and use when prescribed to patients with alcohol abuse or dependence (1).

\[ \text{References} \]


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