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Dextromethorphan for Tardive Dyskinesia

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Authors' contributions

This work was carried out in collaboration between all authors. Authors JK, JD and TLS collected the data, analyzed the results and wrote the manuscript. All authors read and approved the final manuscript.

Case Study

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ABSTRACT

Aims: To report three cases of successful treatment of tardive dyskinesia (TD) with dextromethorphan.
Study Design: Retrospective chart review.
Place and Duration of Study: Private outpatient practice in Syracuse, NY.
Methodology: A retrospective chart review of patients with TD who were treated with dextromethorphan between 2003 and 2013 was conducted.
Results: Three consecutive patients experienced marked improvement of TD with dextromethorphan.
Conclusion: Dextromethorphan may be a useful drug for treating TD. Further prospective studies are needed.

Keywords: Tardive dyskinesia; dextromethorphan; dextromethorphan-quinidine.

1. INTRODUCTION

Tardive dyskinesia (TD) is a disfiguring side effect associated with antipsychotic medications that is potentially irreversible in up to 50% of affected patients [1]. Several pharmacologic agents have been tried for TD with marginal results and thus discontinuation of antipsychotic agents remains the cornerstone of TD management.

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Dextromethorphan (DM) is an over-the-counter cough-suppressant that is also available as a prescription in combination with quinidine for the treatment of pseudobulbar affect [2]. Interestingly, DM has been associated with suppression of abnormal involuntary movements in certain neurodegenerative disorders, such as Parkinson's Disease [3,4] but has not been utilized for patients with TD. The authors report three cases of successful suppression of TD using dextromethorphan.

2. PRESENTATION OF CASES

Case 1:

A 69-year-old woman with a 30-year history of recurrent, agitated and psychotic depression was treated for 11 years with perphenazine up to 24 mg per day. She presented with choreic hand movements and oro-facial TD. DM syrup, 21 mg twice daily, was initiated while she was switched to risperidone (4 mg per day) for her ongoing psychosis. Her AIMS score improved from 22 to 2 in the next two months. Given non-compliance with the syrup and re-emergence of TD, DM delivery was changed to the newly available DM/quinidine combination (20/10 mg per day). AIMS score lowered again to 2 and remained suppressed for the next 15 months.

Case 2:

A 68-year-old female with a long history of depressive disorder and OCD had been augmented for ten years with haloperidol (1 mg per day). This was followed by three years of intermittent augmentation with olanzapine (2.5 mg per day) and risperidone (2 mg per day) respectively. She ultimately presented with choreic hand movements, vertical and lateral jaw movements and perioral TD. She was given DM syrup (21 mg per day) while augmentation with risperidone alone continued. Over the next three months, there was a moderate reduction of TD but her buccal dyskinesias continued to be remarkable. DM was increased to 21 mg twice daily and her AIMS score decreased from 22 to 5. Her dyskinesias remained suppressed for the next two years.

Case 3:

A 68-year-old female with bipolar I disorder presented upon referral with active TD symptoms (lip smacking, tongue protrusions). She had an extensive history of first-generation antipsychotic use prior to her initial presentation. Attempts to use atypical antipsychotics minimally lowered her chronic TD. DM was started 21 mg twice daily while olanzapine therapy (20 mg per day) continued. Her AIMS score decreased from 29 to 9 over the next three months. Her TD continued to be in a moderately reduced state for the next four years.

3. DISCUSSION

The above cases suggest that DM may be a useful drug for treating TD. All three cases demonstrated marked suppression of TD with DM treatment. In the first case, TD returned when the patient was not compliant with DM treatment, but was resolved with DM reintroduction in the DM/quinidine combination form. Quinidine inhibits breakdown of DM and increases DM plasma concentration, essentially creating more gradual and sustained plasma concentrations of DM. The second case demonstrated dose-dependent

effectiveness of DM's antidyskinetic effects while the last case showed that this effect remained sustained for a lengthy duration.

DM is an over-the-counter antitussive agent that (1) blocks glutamate NMDA receptors [3,5], (2) promotes serotonin release [6] that indirectly stimulates 5HT-1A receptors [7] and (3) protects dopaminergic neurons against possible inflammation-mediated endotoxicity [8]. DM's glutamate receptor antagonism activity and anti-inflammatory neuroprotection theoretically may have allowed for the observed anti-dyskinetic effects because the evidence to date suggests that glutamate-induced, NMDA receptor-mediated excitotoxicity [9,10] and free radical-induced oxidative stress [11,12] may be the actual basis of TD pathology. Theoretically, using a glutamate activity dampener like DM may directly address the pathological etiology of TD. In addition, DM's indirect 5HT-1A receptor agonism has been shown to be responsible for suppression of involuntary movements in rat models [13]. 5HT-1a receptor agonism tends to allow better functioning of dopamine pathways and might possibly restore functioning in the nigrastriatal system, thus lowering TD movements. Together, these properties may explain our patients' improvement in TD.

Although DM is a drug with relatively few side effects [14]. DM at high dose (above 10 mg/kg) antagonizes NMDA receptors [15] and may cause effects similar to classic hallucinogens [16]. Patients in our study took at most 42 mg per day (less than 1 mg/kg), which is a low systemic dose and none reported dextromethorphan-associated hallucinations. Another potential problem of using DM for long-term treatment of TD is abuse. DM preparations have been noted to be misused by adolescents given its ease of over-the-counter access [17]. Both DM and DM/quinidine, however, were taken by our patients at the described doses for years without any evidence of clinically significant addiction, misuse, overuse, or adverse effects.

Despite these drawbacks, the above cases clearly demonstrate DM's marked anti-dyskinetic effects. We believe that these observations make a strong case for using DM in the treatment of TD. Further, more stringent studies involving DM for the treatment of TD are needed.

4. CONCLUSION

DM preparations have a viable mechanism of action and clinical application that may be used to lower TD in patients treated with antipsychotics.

CONSENT

This is a retrospective case series and no patient care was manipulated as this was not a prospective study. No informed consent document was required.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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