Efficacy of Nuedexta on TBI-related Behaviors and Role for Future Research

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Background

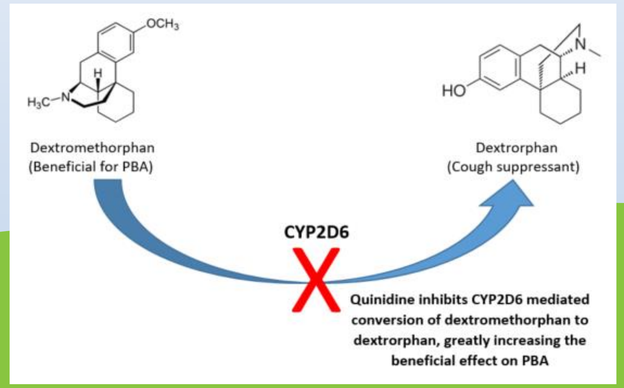
Dextromethorphan/quinidine (DM/Q; brand name Nuedexta) is currently an FDA approved treatment for pseudobulbar affect (PBA), a condition characterized by emotional lability. DM/Q was initially approved to treat PBA symptoms in MS and ALS patients. In a subsequent 12-week open label study, DM/Q showed evidence to be effective in reducing PBA episodes in patients with other neurological conditions, including non-penetrating TBI (Hammond, 2018). We present two cases in which DM/Q was used to treat TBI-related agitation and additional neuropsychiatric symptoms throughout their medical hospitalizations, as prescribed by the psychiatry consult-liaison team.

Case 1:

A 34-year-old male with a history of depression, anxiety, opioid use and alcohol use disorder presented in the setting of numerous injuries sustained in a MVC rollover, including cervical fracture, left frontal subdural hematoma, scattered subarachnoid hemorrhage, and diffuse axonal injury. Psychiatry was consulted on hospital day 21 to manage persistent agitation. Prior to consultation, multiple psychotropic medications were trialed, which included; quetiapine, divalproex sodium, sertraline, buspirone, gabapentin, and propranolol. Agitation did not significantly decrease despite titration of preexisting medications and additional trials of olanzapine, chlorpromazine, lorazepam, and clonidine. Dextromethorphan 20mg/quinidine 10mg (daily for one week, then twice daily) was started on hospital day 45. Episodes of severe agitation decreased as did impulsivity. On hospital day 80, cross taper from chlorpromazine to paliperidone was initiated. DM/Q was discontinued on hospital day 88. The patient subsequently became increasingly restless, anxious, and experienced tremors, tachycardia, and EPS-like symptoms, causing concern for withdrawal. DM/Q was restarted on hospital day 94. The patient improved significantly and was discharged to a facility providing cognitive rehabilitation.

Case 2:

A 34-year-old male with a history of opioid use disorder, in remission, bipolar disorder, and attention-deficit hyperactivity disorder presented after being thrown from an ATV. He was found to have bilateral subdural hematoma with right shift, bilateral uncal herniation, skull fracture, among other injuries, and underwent bilateral decompressive craniectomies. PM&R and psychiatry were consulted to manage persistent agitation, which remained a problem despite treatment with quetiapine, carbamazepine, valproic acid, risperidone, olanzapine, chlorpromazine, propranolol, and gabapentin. DM/Q was started on hospital day 150. The patient remained intermittently agitated and aggressive, particularly after chlorpromazine was decreased before transition to olanzapine. Patient remained on a medication regimen including DM/Q.



Discussion

Dextromethorphan is a low affinity NMDA receptor antagonist and high-affinity sigma-1 antagonist. By reducing glutamate toxicity, it is thought to be neuroprotective. It is also a nicotinic alpha-3-beta-4 receptor antagonist and inhibits serotonin and norepinephrine reuptake. Quinidine is a CYP450 2D6 inhibitor that serves to increase bioavailability of dextromethorphan (Taylor, 2016). Originally studied in patients with PBA in MS or ALS, DM/Q has since been shown to be an effective treatment of PBA secondary to other neurological conditions, including TBI (Hammond, 2018). Furthermore, there have been case reports to suggest DM/Q may decrease agitation and other neuropsychiatric symptoms of TBI (Alexandroni, 2013; Garcia-Baran, 2016). As seen in the aforementioned cases, the effectiveness of DM/Q in TBI-related agitation is variable. Research on the use of DM/Q for behavioral treatment of TBI-related disinhibition and aggression secondary to other neurological conditions is ongoing.

Conclusion

Dextromethorphan/quinidine may be an effective treatment for TBI-related behaviors and agitation. Further research is warranted.

References

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