Comment

Dopamine agonist withdrawal syndrome

Managing dopamine agonist withdrawal syndrome in Parkinson’s disease

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Dopamine agonist withdrawal syndrome (DAWS) has recently been named in the Archives of Neurology. It describes a cluster of symptoms occurring in Parkinson’s disease patients with impulse control disorders on tapering down or withdrawal of their dopamine agonist. Drs Lindahl and MacMahon discuss the risk factors for the development of DAWS and some approaches to its management.

Dopamine agonists have become widely used in the management of Parkinson’s disease (PD) with considerable benefits for many patients. However, as their use has extended, hitherto unrecognised problems have emerged – most recently impulse control disorders (ICDs) and, as a consequence of the need to down-titrate or withdraw the agonist, the recently named dopamine agonist withdrawal syndrome (DAWS).

Anecdotal experiences of the adverse effects of sudden withdrawal of dopaminergic therapies have been recognised for many years – especially the physical manifestations of the neuroleptic malignant syndrome – and yet one still hears horrific stories of well-intentioned, yet potentially disastrous, effects of agonist withdrawal. The case report described by Cunnington et al. in this issue (see p. 24) is included to stimulate discussion, particularly among non-specialists in movement disorders who may not be familiar with these syndromes. A recent posting on the National Parkinson Foundation website shows this still to be a very real and live issue, and Parkinson’s UK has recently established a Steering Group to address the issue. The prominence of ICDs has led to increased recognition of the prevalence of DAWS, and an urgent need for it to be managed better.

While dopaminergic medication, particularly dopamine agonists, may induce ICDs in a minority of patients, the majority are somehow protected from this adverse effect. Antonini’s group reported a prevalence of ICDs of 28 per cent in an Italian cohort (and 20 per cent in controls). Curiously, they also found in another study that 17.5 per cent of drug-naïve PD patients screened positive for at least one ICD, although none had a disorder based on DSM-IV criteria, and so were presumed to have less severe illness. These frequencies were similar to healthy controls.

Nevertheless, male patients with early-onset PD appear to be more susceptible to ICDs, and other predisposing factors – including personality traits, prior dependency on drugs or alcohol and any family history of alcohol or drug abuse – are contentious, but should suggest caution. The possible identification of genetic predisposition requires a genome-wide search, with interesting analogies to dopaminergic receptor genotypes predisposing to gambling tendencies. Functional imaging may also provide an important tool to study this phenomenon in vivo.

Management approaches

In terms of management, most authors favour a gradual (rather than sudden) withdrawal of dopamine agonist, as tolerated, with additional therapies to address the dopaminergic deficit. Other approaches have included the off-licence use of apomorphine and several case reports have been published suggesting a possible role for subthalamic stimulation (although this has also been reported as a cause of ICDs and DAWS); enteral carbidopa/levodopa infusions; carbamazepine; amantadine (although this drug has also been incriminated in the genesis of the syndrome); zonisamide; or clozapine. We have anecdotal experience (unpublished) of the use of rotigotine patches, although these too have also been rarely cited as yet another cause of ICDs.

The case of DAWS described in this issue demonstrates the need for careful monitoring of patients, and the importance of patient and carer/mentor education. It is important to warn (and carefully annotate for medicolegal reasons) patients and their close family before starting these drugs, and at regular intervals thereafter, of the importance of seeking help should ICDs become apparent, and also advocate caution during any drug titration or surgery.

Potentially, the QUIP questionnaire (or a shorter simplified version thereof) may be helpful in
clinical practice. Non-specialists need to be aware of the consequences of ill-advised dosage adjustment, and especially to exercise caution in the management of nil by mouth situations when transdermal or enteral medication should be carefully considered.

Perhaps one could suggest that this is a suitable topic to be aired at journal clubs, grand rounds and other postgraduate events in order to increase awareness among colleagues and improve patient care from both hospitals’ and patients’ perspectives. There is a wealth of up to date information and resources on ICDS for healthcare professionals and patients on the Parkinson’s UK website www.parkinsons.org.uk or by calling its helpline on 0808 800 0303.

Declaration of interests
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References

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