

Nabilone® shows potential for symptomatic relief of Huntington's disease

Huntington's disease (HD) is a progressive neurodegenerative condition in which CAG repeats at the huntingtin gene (IT15) locus on chromosome 4 (4p16.3) lead to the accumulation of Huntingtin protein and a neuropathology involving the basal ganglia and neocortex.^{1,2} Symptoms, most commonly developing during the middle years of life, comprise uncontrollable motor movements affecting coordination, speech and swallowing; cognitive impairment affecting concentration, perception, awareness, thinking, judgement and short-term memory; and psychiatric disturbances including depression, obsessive compulsive disorder, mania, Schizophrenia and mood changes, such as aggressive and antisocial behaviour.^{1,2}

No specific pharmacologic therapy for Huntington's disease exists.² Treatments are limited to managing symptoms with usual pharmaceuticals and providing support for the patient. Depression is therefore treated with tricyclic antidepressants and selective serotonin reuptake inhibitors.¹ Motor symptoms are treated with tetrabenazine, haloperidol, fluphenazine and other treatments used in parkinsonism and dystonias.¹ Behavioural and psychotic symptoms are treated as appropriate with agents such as chlorpromazine, sulpiride, clozapine, quetiapine, risperidone.^{1,2} The condition cannot be reversed or slowed by current therapeutic measures. Researchers at the University of Birmingham reported previously a case of a female patient with Huntington's disease in whom irritability improved after the introduction of cannabis and was maintained by treatment with Nabilone®.³ This observation and suggestions from others that cannabinoids might offer neuroprotective benefits⁴ led these researchers to undertake a randomised, double-blind, placebo-controlled, cross-over pilot study to evaluate Nabilone® for symptomatic relief in 44 patients with Huntington's disease.⁵ Of the 44 patients recruited, 37 completed the trial — four were withdrawn before treatment began, one patient withdrew because of severe sedation when taking Nabilone®, one withdrew because of asthma and palpitations when taking placebo, and one patient was unable to manage the trial procedures and did not begin taking medication.

Patients were randomised to two treatment groups: (a) Nabilone® followed by placebo and (b) placebo followed by Nabilone®. The two 5-week treatment periods were separated by a 5-week washout period and the second treatment period was followed by a 12-day dose reduction period. In both groups Nabilone® was up-titrated in 250 microgram doses at four-day intervals to either 1mg/day or 2mg/day, which was maintained for 10 days. After four days of treatment the daily dose was split between the morning and evening. At the end of each treatment block the number of capsules taken was halved every four days until the medication ceased. Testing for outcome measures of total motor score, chorea, cognitive score and behaviour score using the unified Huntington's disease rating scale; the neuropsychiatric inventory (NPI) score and adverse effects was undertaken at baseline and at the end of each treatment block.

The authors reported that Nabilone® was generally well-tolerated and safe and there were no psychiatric episodes. Although in this small pilot study there was no significant difference in total motor scores, behaviour scores or cognitive scores when patients received Nabilone® for 5 weeks compared with placebo, there was a significant improvement in chorea and encouraging suggestions of improvement in NPI score, which did not reach significance because the study was underpowered.

The study investigators concluded that a longer (3–6 months) and larger (375 patients) multicentre study should now be undertaken comparing placebo, Nabilone® 1mg and Nabilone® 2mg with NPI scores as the primary outcome measure. Dr Hugh Rickards, the study coordinator, said: 'The findings of the study are very encouraging and the results demonstrate that Nabilone® has the potential to ease both the motor and psychiatric symptoms of Huntington's disease. This potential to treat multiple symptoms could allow Nabilone® to make a real difference to patients in a therapy area where the current treatment options are limited. In order to confirm our findings I am keen for additional multi-centre research to be undertaken into Nabilone®.'

The study, carried out under the auspices of the Trent Multi-Centre Research Ethics Committee (MREC), by the research team from the University of Birmingham and the Birmingham and Solihull Mental Health Trust was presented at the 12th International Conference of the Movement Disorder Society on 25 June 2008.⁵

References

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