New drug seems well-tolerated and merits further investigation in patients with Huntington's disease

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A novel drug (pridopidine) that stabilises dopamine signalling in areas of the brain that control movement and coordination, appears well tolerated and warrants further study in patients with Huntington's disease (HD), a condition characterised by an imbalance in the signalling chemical dopamine. The findings of the phase 3 MermaiHD trial are published Online First in The *Lancet Neurology*.

Until now, no drug has been shown to improve the loss of the ability to move muscles voluntarily. The only drug currently approved for HD, tetrabenazine, treats only chorea (involuntary movements) and is associated with serious side-effects.

Pridopidine belongs to a new class of drugs known as dopidines, which act as dopaminergic stabilisers and are designed to restore the brain's dopamine levels to normal. Findings from a phase 2 study suggested that pridopidine improved voluntary motor function without worsening chorea.

A team led by Justo Garcia de Yebenes from the Hospital Ramón y Cajal in Madrid, Spain, conducted a phase 3 trial to further assess the potential efficacy and safety of pridopidine as a treatment of HD motor symptoms. 437 patients with HD from eight EU countries were randomly assigned to take pridopidine (45 mg once daily or 45 mg twice daily) or placebo for 26 weeks.

In the primary analysis, the effects of pridopidine were assessed using a modified motor score (mMS) designed to measure 10 items relating to voluntary movements from the unified Huntington's disease rating scale (UHDRS) total motor score (TMS). UHDRS-TMS, cognitive function, behaviour, and depression and anxiety were also evaluated.

After 6 months of treatment, the difference in average mMS score between the groups was not significant. However, in a tertiary analysis, pridopidine treatment resulted in improvement in total motor function (specifically in eye movements, hand movements, dystonia, and gait and balance) as measured by UHDRS-TMS in patients taking the higher dose of pridopidine compared with those given placebo.

Further analyses that included only patients who completed all study visits and had drug compliance greater than 70% also showed a significant benefit for the higher dose of pridopidine. Pridopidine was well tolerated and had a similar side-effect profile to placebo.

The authors conclude: "Pridopidine has the potential to complement available treatments by improving a different range of motor deficits. Its lack of severe side-effects... suggests that pridopidine might be useful even for those patients who are treated at sites that are not centres of excellence for Huntington's disease."

In an accompanying Comment, Andrew Feigin from The Feinstein Institute for Medical Research, New York, USA explains: "A well tolerated drug that produces even small benefits for patients with Huntington's disease would be a very welcome addition to the currently available treatments for this debilitating disorder… Analysis of individual items within the UHDRS-TMS in the MermaiHD study also suggests that pridopidine might benefit features of HD for which there are currently no treatments (eye movements, hand coordination, dystonia, and gait or balance problems)."

More information: www.thelancet.com/journals/lan … (11)70233-2/abstract

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