Psychosis in Parkinson's dementia—new treatment provides hope

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Around 80 per cent of people with Parkinson's disease develop dementia. Credit: University of Exeter

New research involving King's College London and the University of Exeter has highlighted the benefits of a promising new treatment which could relieve psychosis in thousands of people with dementia related to Parkinson's disease.

Around 80 per cent of people with Parkinson's disease develop dementia , totalling around 100,000 people in the UK. ,The majority of these individuals will experience psychotic symptoms such as delusions and hallucinations, often particularly intense in Parkinson's disease.

These symptoms can be terrifying and have a devastating effect on individuals and their families, yet commonly-prescribed sedative antipsychotic medications only have a marginal benefit in reducing

psychotic symptoms. Currently, clinicians are advised only to prescribe antipsychotics as a last resort, because of their terrible impacts on health, quadrupling the risk of stroke and death, as well as worsening symptoms of Parkinson's diseases.

The paper, in *Nature Reviews Neurology*, presents key new information regarding the benefits of pimavanserin, - a novel antipsychotic treatment that follows a completely different mechanism of action than widely-used drugs, and improves psychosis effectively without the damaging impact of other drugs.

A previous paper in *The Lancet* in 2014 reported a rigorous six week, randomised, double-blind placebo-controlled trial, in which 199 people were allocated to groups to receive pimavanserin or a placebo. The study demonstrated benefits in treating psychosis in people with Parkinson's disease, leading to the licensing of pimavanserin for this purpose in the USA.

The newly published results from the same trial, presented in the current paper, indicate that pimavanserin is even more effective in improving psychotic symptoms in people with Parkinson's disease dementia. The treatment is well tolerated, causes less negative impact than other antipsychotics in a particularly vulnerable group for whom psychotic symptoms are a major challenge.

Professor Clive Ballard, of the University of Exeter Medical School, said: "Quite rightly, campaign groups have urged clinicians to reserve antipsychotics as a last resort because of the damaging side-effects, however the new results from our clinical trial of pimavanserin show that it effectively improves psychosis in people with Parkinson's disease dementia without this terrible impact. This is a crucial step towards changing an unacceptable situation for millions of people living with Parkinson's disease and Parkinson's disease dementia worldwide.."

Parkinson's Disease and the related disease dementia with Lewy bodies affect up to 15 per cent of all people with dementia – around six million people worldwide. People with these dementias are far more likely to experience highly visual and distressing psychotic episodes.

All other antipsychotics target a receptor for a chemical messenger on neurones called dopamine. This has proved effective in treating psychosis in Schizoprenia, but in Parkinson's Disease and dementia with Lewy bodies, where these receptors are already being lost as a result of the disease, this blocking can significantly worsen motor symptoms of Parkinson's disease causing tremor, slow movements and resulting in problems with walking and falls..

Pimavanserin works differently. It targets the brain's 5HT2A receptors, restricting the activity of another chemical messenger, serotonin.

According to Professor Dag Aarsland at King's College London, "Psychosis in Parkinson's disease is often extremely distressing to patients and their carers, and until now there have been few treatment options available. These findings are extremely encouraging, and we hope that our continuing work in this area eventually leads to better treatment options for the thousands of people in the UK and worldwide affected by this condition."

Claire Bale, Head of Research Communications and Engagement at Parkinson's UK, said: "This new analysis suggests that pimavanserin is even more effective for treating psychotic symptoms – like hallucinations and delusions – in people with Parkinson's dementia than in those with Parkinson's without dementia.

"This is extremely promising because psychotic symptoms are a very common and distressing feature of Parkinson's dementia and current treatment options are extremely limited.

"Pimavanserin has been approved for use by the Food and Drug Administration (FDA) in the US but has not yet been submitted for approval to the European equivalent, the European Medicines Agency.

"It is now imperative that pimavanserin goes through the European approval process to be made available to people who would benefit hugely from the drug. People with Parkinson's can't wait any longer for better treatments."

More information: Jeffrey Cummings et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial, *The Lancet* (2013). DOI: 10.1016/S0140-6736(13)62106-6

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