'Adults with Parkinson's disease and hallucinations or delusions can have treatment with clozapine if they need to'. Commentary on Setting up a clozapine service for Parkinson's psychosis

Eileen Joyce, UCL Queen Square Institute of Neurology, London WC1N 3BG

Abstract:
Neurologists and geriatricians are commissioned to manage the motor symptoms of people with PD but there is no care pathway mandating access to mental health services when psychiatric disorders arise such as Parkinson's disease psychosis (PDP). Clozapine is the only antipsychotic medication licensed for treatment of PDP but is infrequently used because of obstacles to the integration of hospital-based neurological/geriatric services with clozapine clinics run by community mental health teams. The article by Taylor et al describes 3 innovative models for providing clozapine treatment for PDP which can be universally adopted. The forthcoming integrated care systems should be able to overcome obstacles so that clozapine treatment becomes a right for PDP patients and their families.

Parkinson's disease (PD) is classified as a neurological disorder (ICD 11, A80) but in practice can be viewed as a neuropsychiatric illness. This is because the movement abnormalities are frequently accompanied by psychiatric symptoms reflecting either the underlying neuropathology of PD or the action of medication prescribed for motor control. From the onset and throughout the course of PD, mental disorders commonly arise including depression, anxiety, impulse control disorder, psychosis, and dementia.

Neurologists or geriatricians are commissioned to manage the motor symptoms of people with PD but there is no care pathway mandating access to psychiatric and psychological services and there are too few neuropsychiatrists and neuropsychologists to make such specialist care feasible. In 2019, The National Neuroscience Advisory Group reported that 40% of patients with a neurological condition felt that their mental health needs are not being met. Nowhere is there a starker example of the inequity of access to mental health services than that of the provision of clozapine for patients with Parkinson's disease psychosis (PDP). As pointed out in the article by Taylor et al in this journal, PDP is common, developing in about 60% of patients at some point during their illness. Not all will require intervention with antipsychotic medication, but this is often the last recourse because of the failure of other approaches, the distress of the patient, the strain on the family and the attendant risks. Randomised controlled trials (RCT) of antipsychotic medication for PDP have demonstrated unequivocally that low dose clozapine significantly alleviates psychosis without worsening motor symptoms (Kyle and Bronstein, 2020). As a consequence, clozapine treatment allows antiparkinsonian medication to be increased as motor symptoms worsen with disease progression and it can even alleviate parkinsonian tremor and levodopa induced dyskinesia (Yaw et al, 2015). RCTs of other antipsychotics showed little or no antipsychotic potency at the doses prescribed and/or worsened motor function (Kyle and Bronstein, 2020). NICE guidelines (NG71, 2017) recommend that the unlicensed use of quetiapine should be considered as 'standard' treatment despite all but one placebo-controlled trials being negative (Shotbolt et al 2010). This decision was based on low quality evidence of efficacy and the observation that it does not worsen motor

symptoms. Clozapine is the only antipsychotic licensed for PDP in the UK and NICE recommends that this is offered if quetiapine is ineffective.
Another NICE consideration was that clozapine is impractical as a first-line antipsychotic. Clozapine has potentially life-threatening adverse effects, mainly agranulocytosis and myocarditis, and because of these the NHS has a well-established, effective and safe system for administering and monitoring clozapine for patients with a primary psychosis. So why is there a problem with access to this service for PDP? The answer is that initiating clozapine and sustaining safe monitoring requires the will and determination to embark on a process that requires integration across medical disciplines and services, is effortful and resource demanding. Initiating treatment requires patients to be admitted to hospital or intensely monitored in the community. This is particularly important for PDP patients who tend to be older and frailer than patients with primary psychosis. Mental health beds for this group are difficult to come-by and, as mentioned by Taylor et al, admission to a psychiatric bed usually only occurs when a crisis develops. Community initiation of clozapine is more common these days but is resource demanding and mental health teams may not be confident working with people with PD. Another difficulty is the lack of crosstalk between hospital neurological/geriatric medical services and community mental health services which have different budgets and commissioning processes.

NICE Quality Standards (QS164 2018), in recognition of this, begins with a very important principle: 'Adults with Parkinson's disease and hallucinations or delusions can have treatment with clozapine if they need to'. It exhorts commissioners to 'encourage joint working between services to ensure that the specific needs of adults with Parkinson's disease are understood and met… this may mean joint arrangements with mental health services are needed'. Unfortunately, this guidance has got off to a slow start. In 2019 PD UK (Carney, S personal communication) undertook a survey of neurology and geriatric services and found that 71% do not prescribe clozapine for PDP yet over 90% of respondents said they would like their patients to have access to this medication. The main reason stated for lack of progress in this initiative was they had no safe system for initiation, monitoring and dispensing clozapine. Taylor at al have shown in their article that this obstacle can be overcome with innovative approaches. One important component of all three services described is that the consultant neurologist or geriatrician has overcome the usual stipulation that only consultant psychiatrists can prescribe clozapine by becoming prescribers themselves. This enables them to manage both the psychotic and physical symptoms of their own patients. A second important element is the ability to initiate clozapine, monitor symptoms and look out for potential adverse effects in a community setting. A third is 'buy-in' from mental health services (clozapine clinics for blood tests and CPN-led health monitoring) and/or primary care (district nurses for blood tests and health monitoring). The input of a specialist pharmacist to track blood results and prescriptions is also invaluable. These three services are successful but each one is different because they have adapted to their local context and circumstances. Therefore, it is highly likely that around the UK clozapine services will adopt different models of care that work in their catchment areas.

Management of PDP requires the input of neurological, psychological and psychiatric services to optimise motor and mental function which can be a fine balancing act. The time is now ripe for the commissioning of clozapine care systems for PDP that work flexibly

within the local landscape of community mental health and hospital physical health services. In England, clinical commissioning groups (CCGs) are being subsumed into single regional integrated care systems (ICSs) that will come into action very soon. A main aim is 'to deliver joined-up support for growing numbers of older people and people living with long-term conditions' (The Kings Fund, 2020). In practice this will bring together CCGs, GPs, hospital and mental health services, hopefully breaking down the purchase-provider split to provide integrated care. There should be no barrier now, funding or otherwise, to the provision of a clozapine service that will keep families together and improve the quality of life and wellbeing of people with Parkinson's disease.

Declarations of interest: none.

References

Internal Classification of Diseases 11. https://icd.who.int/en. Last accessed 07.05.2021.
Kyle K, Bronstein JM. Treatment of psychosis in Parkinson's disease and dementia with Lewy Bodies: A review. Parkinsonism Relat Disord. 2020; 75:55-62.
National Institute of Health and Care Excellence. Parkinson's Disease in Adults. Nice guideline 71. 2017. https://www.nice.org.uk/guidance/ng71. Last accessed 03.09.2021.
National Institute of Health and Care Excellence. Parkinson's Disease. Quality standard 164. https://www.nice.org.uk/guidance/qs164. Last accessed 03.09.2021.
The National Neuroscience Advisory Group. Mental Health and Neurosciences Away Day. https://www.nnag.org.uk/publications. Last accessed 07.05.2021.
The Kings Fund. Integrated care systems explained; making sense of systems, places and neighbourhoods. https://www.kingsfund.org.uk/publications/integrated-care-systemsexplained.
Last accessed 08.05.2021.
Shotbolt P, Samuel M, David. Quetiapine in the treatment of psychosis in Parkinson's disease. A.Ther Adv Neurol Disord. 2010 Nov;3(6):339-50
Taylor C, Marsh-Davies A, Skelly R, Archibald N, Jackson S. Setting up a clozapine service for Parkinson's psychosis. BJPsychAdv-20-0113.R1
Yaw TK, Fox SH, Lang AE. Clozapine in Parkinsonian Rest Tremor: A Review of Outcomes, Adverse Reactions, and Possible Mechanisms of Action. Mov Disord Clin Pract. 2015 Dec 30;3(2):116-124