Clozapine for Psychosis in Parkinson's' Disease

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Introduction:

Parkinson's Disease (PD) will affect approximately 0.2% of the population, with 25% suffering from psychosis at some point in the course of the illness, most commonly visual hallucinations.

NICE advises monitoring for psychotic symptoms, notably visual hallucinations or delusions, which may be either iatrogenic or organic (NICE, 2017). Typical antipsychotics are not recommended due to the risk of neuroleptic malignant syndrome (NMS), the risk of which is higher in patients with Parkinson's disease (Kirrane et al, 2018). It is advised to offer clozapine if standard treatment is not effective (quetiapine is recommended first line), alongside regular monitoring (NICE, 2017). It should be noted that psychosis does not always require treatment however if the symptoms are infrequent and not troubling to the patient.

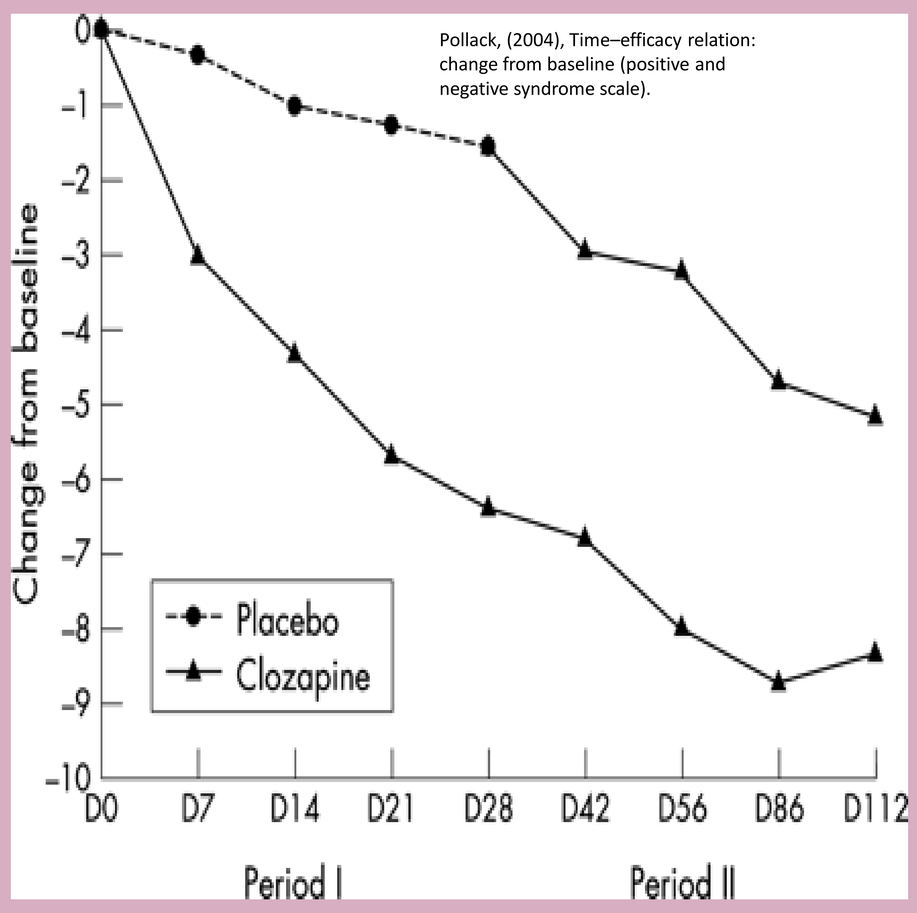
Clozapine is thought to be more effective in comparison to typical antipsychotics due to its affinity for D4 receptors, as opposed to D2, which is the main target of action for typical antipsychotics.

	Treatment-resistant schizophrenia	Parkinson's disease
Starting therapy	6.25–12.5 mg/day Dose should be increased by no more than 6.25–12.5 mg once or twice a week	6.25 mg/day
Therapeutic dose range	50–100 mg/day	25–37.5 mg/day
Maximum dose	100 mg/day	50 mg/day
Ending therapy	Gradual reduction over 1–2 weeks (in non-emergencies)	Gradual reduction by steps of 12.5 mg for a period of at least 1 week (preferably 2 weeks)

Clozapine doses in treatment resistant schizophrenia vs PD, (Kirrane et al, 2018).

Benefits

A randomised double-blind study in 2004 looked at the efficacy and safety of prescribing clozapine in PD in comparison to placebo. This study found that clozapine improved drug induced psychosis without significant impact on motor function, as demonstrated with improvement in patients' Clinical Global Impressions (CGI) scales and Positive and Negative Syndrome Scale (PANSS). They also noted that the effect of clozapine wore off once it had been stopped. They mentioned an increased rate of somnolence with clozapine in comparison to placebo (Pollack, 2004)



Pollack, (2004), Time–efficacy relation: change from baseline (positive and negative syndrome scale).

Limitations:

One reason for its decreased use is thought to be consultants within old age psychiatry expressing concerns regarding the lack of published data regarding the safety as well as the practical challenges in monitoring patients on clozapine via repeated blood test monitoring for agranulocytosis (Paranthamam and Baldwin, 2006), ECGs to assess for prolongation of the QTc and clozapine serum levels in some trusts (Kirrane et al, 2018).

Case studies:

An audit of Hertfordshire clozapine prescriptions in the over 65s identified two patients who were on clozapine for psychosis secondary to Parkinson's Disease.

Case 1: The first patient had been trialled on quetiapine, which had worsened his PD symptoms and a reduction in his pramiprexole, which was of limited benefit. His hallucinations were predominantly visual, musical, and tactile in nature, with persecutory delusional thinking regarding spousal infidelity. He was prescribed clozapine, which led to a resolution in his hallucinations and delusions, with no obvious adverse effects.

Case 2: The second patient had trialled quetiapine, initially with good effect, but over time it contributed to a deterioration in motor symptoms, leading to a recommendation from his neuropsychiatrist to wean off it. His psychotic symptoms returned after an orthopaedic operation, with visual hallucinations and persecutory thoughts regarding the police and staff in the hospital where was admitted. Quetiapine was restarted and increased, with only partial resolution of the delusions. Clozapine was started, with good effect; however, he went on to experience significant weight gain.

Bibliography

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