Asian Journal of Psychiatry 43 (2019) 55–56

Contents lists available at ScienceDirect

Asian Journal of Psychiatry

journal homepage: www.elsevier.com/locate/ajp

Short Communication

An octogenarian with Parkinson's disease psychosis that has responded favourably to low-dose sulpiride with facilitated motoric agility

Ahmed Naguy[a,*], Abdulmohsen AlHumoud[b]

[a] Kuwait Centre for Mental Health, Jamal Abdul-Nassir St., 21315, Shuwaikh, Kuwait
[b] Consultant Forensic and General Adult Psychiatrist, Head of Forensic Psychiatry Department, KCMH, Kuwait, and vice President of Kuwait Psychiatric Association

1. Case report

An 82-year-old, empty-nester, Egyptian male patient with a long-standing diagnosis of idiopathic Parkinson's disease (PD), at age of 69, has been referred to our outpatient clinic for the evaluation of a three-month history of conjugal paranoid delusions that he began to act upon and physically assaulted his wife. He has reported tactile hallucinations described as formication. No affective component could be elicited on mental status examination (MSE). He was totally insightless. His current antiparkinsonian regimen has been stable for a quite long time, that is, Stalevo® 100/25/200 tab tds started at Hoehn Yahr Stage-3, almost 2 years from disease onset. Response was well-sustained on this formulation, apart from occasional 'wearing-off'. He was vitally stable with intact sensorium and fully orientated. He is non-smoker. Apart from Stalevo® and baby aspirin 81 mg/d, no other meds are currently being taken. Baseline laboratory investigations, including toxic screen had a negative yield. Urgent CT head and EEG were entirely unrevealing. MMSE (mini-mental state examination) score read 26. A diagnosis Parkinson's disease-associated psychosis (PDP) was entertained. Reducing Stalevo® was not an option after liaison with neurologists. Quetiapine 12.5 mg was prescribed. The patient had severe orthostasis and oversedation that quetiapine trial was prematurely aborted. Clozapine was suggested but baseline CBC read 2500/mm^3 and was detracting. Pimavanserin is unfortunately not yet available in this country. We embarked on trial of risperidone 0.25 mg that was pushed up to 0.5 mg after a week. There was a tangible improvement regarding the psychotic phenomena, but sorely with progressive rigidity and freezing of gait. We suggested a trial of low-dose sulpiride instead. At a twice-divided dose of 150 mg/d of sulpiride before meals, over 4 weeks, the patient was in full symptomatic remission, and, to our surprise, with better motoric agility. Sulpiride was well-tolerated and the clinical response was well-sustained 16 weeks at time of writing this report. Periodic monitoring of CBC and S. PRL remained within normal lab reference range all through.

2. Discussion

Parkinson's disease-associated psychosis (PDP) is a recognized symptom cluster that tends to arise late in the course of disease. It is commonplace and may be as high as 60%. PDP has been tied to poor prognosis as these patients are at a higher risk of weight loss, caregiver burden, placement in a nursing home and institutionalization, poor quality of life, disability and mortality (Diederich et al., 2009; Goetz and Stebbins, 1993)

It can be diagnosed formally if recurrent /continuous hallucinations (commonly visual but also other modalities e.g. auditory/tactile), delusions, visual illusions, or false sense of a presence occurs for at least one month after the onset of PD (Riedel et al., 2010). These should not be better explained by delirium, a primary psychiatric disorder, or dementia of Lewy bodies (DLB). It might be associated with retained insight, dementia, and antiparkinsonian treatment (Ravina et al., 2007).

Diagnosis of PDP is largely clinical and is corroborated by collateral history from caregivers. Importantly, baseline memory, orientation, and cognition are usually unimpaired in PDP, this in stark contradistinction to delirium, which is also common in patients with PD due to medical comorbidities and co-pharmacy. Constellation of fluctuating cognition, REM (rapid eye movement) sleep behaviour disorder, parkinsonism, prominent visual hallucinations, dysautonomia, and, supersensitivity to antipsychotics should raise the possibility of DLB. Parkinsonism and psychosis may be part of Alzheimer's disease. Affective psychosis or (very) late-onset schizophrenia remain a possible differential, albeit rare.

Multiple rating scales have been used to screen for psychotic symptoms including, but not limited to Parkinson's Psychosis Rating Scale (PPRS), and Unified Parkinson Disease Rating Scale Thought Disorder (UPDRS-TD) (Eng and Welty, 2010)

Common comorbidities are depression, sleep disturbance, and cognitive decline.

It was once thought an exclusively medication-induced phenomenon. However, disease-related factors are clearly contributory. These mechanisms are given in Table 1 (Llebaria et al., 2010; Thota et al.,

* Corresponding author.
E-mail address: ahmednagy@hotmail.co.uk (A. Naguy).

https://doi.org/10.1016/j.ajp.2019.05.001
Received 14 February 2019; Received in revised form 23 April 2019; Accepted 2 May 2019

Table 1
Possible Mechanisms of Parkinsonian Psychosis Inherent to the Disease Itself.

Dysfunction of visual pathways- Parkinsonian retinopathy and functional alterations of extrastriate visual pathways
REM sleep disturbance
Central DA hyperactivity
Cholinergic neurotransmission imbalance
Lewy bodies deposition in ventral/medial temporal regions
Co-occurrence of visual association cortex and frontal executive dysfunction

Table 2
Risk factors for PDP.

1	Genetics (e.g. CCK polymorphism)
2	Advancing Age (< 65 ys)
3	Exposure to Dopaminomimetics
4	Executive Dysfunction
5	Dementia
6	Severity and long duration of PD
7	Psychiatric comorbidities- Depression/Anxiety
8	Daytime fatigue
9	Sleep disorders
10	Visual impairment
11	Polypharmacy

2017). Other risk factors for PDP are depicted in Table 2 (Fenelon et al., 2006)

Early intervention is recommended to halt or slow the progression of debilitating psychosis (Weintraub and Hurting, 2007**)**. It may be responsive to reduction of dopaminergic agents to the lowest effective doses and simplifying the treatment regimen and polypharmacy (especially anticholinergic drugs, amantadine, MAO-BIs). If this fails, introduction of acetylcholine esterase inhibitors (ACE-is) and atypical antipsychotics are next on list. Clozapine has demonstrated more robust evidence over quetiapine (Zahodne and Fernandez, 2010) An RCT by Pollak et al. (2004) has attested to its efficacy without motor worsening. Work-up and monitoring of clozapine therapy in these patients is quite onerous (Mukku et al., 2018). Quetiapine has been used alternatively based on open-label trials and case reports (Lenka et al., 2018) An RCT by Shotbolt et al. (2009) was negative, though. Other atypical antipsychotics have been tried, but with limited efficacy and at the expense of motor worsening, and better to be avoided altogether. Needless to say, high-potent conventional antipsychotics (e.g. haloperidol) are contra-indicated. Acetylcholine-esterase inhibitors (ACE-is), especially, rivastigmine, can be used and is currently FDA approved for mild-to-moderate dementia of AD as well as PD dementia. Antidepressants might help the affective component, if any. Bupropion which is NDRI is mechanistically appealing to boost DA tone. TCAs might be advantageous helping the motoric syndrome too. SSRIs (selective serotonin reuptake inhibitors) are typically first-line, though (Rocha et al., 2013) Improving nocturnal sleep with e.g. trazodone is often very helpful. Last but not least, ECT (electro-convulsive therapy) has been used successfully to target PDP with concomitant improvement in the Hoehn and Yahr staging (Ueda et al., 2010**)** and meanwhile can help with 'on-off' phenomenon. Recently, pimavanserin, 5-HT2A inverse agonist has been granted FDA approval for PDD (Hunter et al., 2015) It sounds an attractive agent since it is the only currently available antipsychotic that is largely devoid of D2 blockade properties that can induce motoric worsening. It is dosed at 34 mg OD. It is metabolic friendly (cf. atypical antipsychotics), non-sedating, and, above all, does not require dose reduction of antiparkinsonian dopaminergic therapy given concomitantly.

In our case, use of low-dose of sulpiride was advantageous. Sulpiride is a substituted benzamide antipsychotic. It might be considered 'atypical of the typical' (conventional) antipsychotics. At lose-dose, it blocks the presynaptic D2 autoreceptors, thus enhance DA neurotransmission with motoric facilitation and this might explain the outcome in this report. At higher doses (typically above 600 mg/d), it blocks postsynaptic D2/D3 receptors with opposite pharmacodynamic actions (O'Connor and Brown, 1982; Velasco and Luchsinger, 1998) Another possible contributory mechanism might be related to actions at GHB (gamma-hydroxy butyrate) receptors; inhibitory receptors in cortex and hippocampus that possess hyperpolarizing properties through Ca2+ and K + channels. Activation of these latter receptors has been shown to stimulate DA release (Castelli, 2004) To our knowledge, this report is one of the earliest to report on sulpiride superiority in PDP whilst improving motoric agility. This might open new venues of treatment for such complicated clinical scenarios.

Financial disclosure

Authors declare no financial affiliations or sponsorship.

Acknowledgements

Authors extend their deepest gratitude to Dr Naif El-Harby, Director General of KCMH for his unfaltering support.

References

Castelli, M., 2004. A review of pharmacology of NCS-382, a putative antagonist of γ-hydroxybutyric acid (GHB) receptor. CNS Drug Rev. 10, 243–260.
Diederich, N.J., Fénelon, G., Stebbins, G., et al., 2009. Hallucinations in Parkinson disease. Nat. Rev. Neurol. 5 (6), 331–342.
Eng, M.L., Welty, T.E., 2010. Management of hallucinations and psychosis in Parkinson's disease. Am. J. Geriatr. Pharmacother. 8, 316–330.
Fenelon, G., Goetz, C.G., Karenberg, A., 2006. Hallucinations in the Parkinson disease in the prelevodopa era. Neurology 66, 93–98.
Goetz, C.G., Stebbins, G.T., 1993. Risk factors for nursing home placement in advanced Parkinson's disease. Neurology 43, 2227–2229.
Hunter, N.S., Anderson, K.C., Cox, A., 2015. Pimvanserin. Drugs Today (Barc.) 51 (11), 645–652.
Lenka, A., Reddy, Y.C., Pal, P.K., 2018. Isolated tactile hallucination in a patient with Parkinson's disease: quetiapine conquers the snakes and stones. Asain J. Psychiatry 35, 34–35.
Llebaria, G., Pagonabarraga, J., Martínez-Corral, M., et al., 2010. Neuropsychological correlates of mild to severe hallucinations in Parkinson's disease. Mov. Disord. 25 (December (16)), 2785–2791.
Mukku, S.S., Sivakumar, P.T., Varghese, M., 2018. Clozapine use in geriatric patients-challenges. Asian J. Psychiatry 33, 63–67.
O'Connor, S.E., Brown, R.A., 1982. The pharmacology of sulpiride- a dopamine receptor antagonist. Gen. Pharmacol. 13 (3), 185–193.
Pollak, P., Tison, F., Rascol, O., et al., 2004. Clozapine in drug-induced psychosis in Parkinson's disease: a randomized, placebo controlled study with open follow up. J. Neurol. Neurosurg. Psychiatry 75, 689–695.
Ravina, B., Marder, K., Fernandez, H., et al., 2007. Diagnostic criteria for psychosis in Parkinson's disease: report of an NINDS, NIMH work group. Mov. Disord. 22, 1061–1068.
Riedel, O., Klotsche, J., Spottke, A., et al., 2010. Frequency of dementia, depression, and other neuropsychiatric symptoms in 1,449 outpatients with Parkinson's disease. J. Neurol. 257 (7), 1073–1082.
Rocha, F.L., Murad, M.G., Stumpf, B.P., et al., 2013. Antidepressants for depression in Parkinson's disease: systematic review and meta-analysis. J. Psychopharmacol. 27 (5), 417–423.
Shotbolt, P., Samuel, M., Fox, C., et al., 2009. A randomized controlled trial of quetiapine for psychosis in Parkinson's disease. Neuropsychiatr. Dis. Treat. 5, 327–332.
Thota, N., Lenka, A., George, L., et al., 2017. Impaired frontal lobe functions in patients with Parkinson's disease and psychosis. Asian J. Psychiatry 30, 192–195.
Ueda, S., Koyama, K., Okubo, Y., 2010. Marked improvement of psychotic symptoms after electroconvulsive therapy in Parkinson disease. J. ECT 26, 111–115.
Velasco, M., Luchsinger, A., 1998. Dopamine: pharmacologic and therapeutic aspects. Am. J. Ther. 5 (1), 37–44.
Weintraub, D., Hurting, H.I., 2007. Presentation and management of psychosis in Parkinson's disease and dementia with Lewy bodies. Am. J. Psychiatry 164, 1491–1498.
Zahodne, L.B., Fernandez, H.H., 2010. Parkinson's psychosis. Curr. Treat. Opt. Neurol. 12, 200–211.