Case study

Parkinson's symptoms worsening with antidiabetic medications: a case study

UNDER PEER REVIEW

Abstract

Introduction: Parkinson's disease (PD) is one of the most prevalent neurologic disorders, leading to progressive disability; it is characterized by tremors, slow movements, stiffness in arms and legs, and balance impairment; PD symptoms can be slowed but not stopped by treatment such as a combination of Carbidopa/Levodopa. Although it's widely used for PD, it risks dyskinesia, orthostatic hypotension, and dizziness. The prevalence of PD in Saudi Arabia has been estimated to be 27 per 100,000 populations, and the occurrence of PD in the U.S. is approximately 20 cases per 100,000 people per year.

Case presentation: A 61 years old male presented with worsening PD symptoms, especially dysarthria symptom; he had a history of diabetes with A1C of 8.5%, on metformin, insulin glargine, liraglutide, and linagliptin, with good adherence, and he had a history of Parkinson on levodopa/carbidopa. Even there are no known drug-drug interactions between antidiabetic medication and levodopa/carbidopa, he reported that coadministration of antidiabetic medications with levodopa/carbidopa cause PD symptoms worsening, especially dysarthria worsening. This drug-drug interaction was noticed when the patient tried to stop all of his antidiabetic medication except insulin mixtard, when he noticed dysarthria symptoms improved. He is currently on insulin mixtard for diabetes with an A1C of 6.7%.

Conclusion: Unintentional drug-drug interaction poses a challenge to the healthcare provider, so this report highlights the importance of adverse drug-drug interaction of antidiabetic with Sinemet, its presentation, and management.

Aim:
To highlighted the importance of unintentional drug-drug interaction, which may pose a challenge to a healthcare provider, and the importance of adverse drug-drug interaction of antidiabetic with levodopa/carbidopa, its presentation, and management.

Introduction
Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease characterized by motor and nonmotorfeatures. The infection clinically influences patients, families, and caregivers through its dynamic degenerative ramifications for adaptability and muscle control. The motor appearances of PD are credited to the insufficiency of striatal dopaminergic neurons, but the presence of non motor signs maintains neuronal disaster in no dopaminergic districts too. The term parkinsonism is an appearance perplexing used to portray the motor components of PD, which join tremer, bradykinesia, and solid resoluteness. Notwithstanding the way that it is fundamentally a sickness of the more established, individuals have made PD in their 30s and 40s, sex contrasts in the recurrence of PD are reflected in a 3:2 extent of folks to females, with conceded starting in females attributed to the neuroprotective effects of estrogen on the nigrostriatal dopaminergic system [1].
Wearing-off is a complication that can occur after a few years of using levodopa to treat Parkinson's. During wearing-off, symptoms of Parkinson's start to return or deteriorate before the following portion of levodopa is expected and further develop when the following portion is taken [2].
Motor fluctuations ordinarily happen when levodopa is wearing off, however they can occur at different occasions as well. This is called 'end of portion wearing off' or just 'wearing off.' Sometimes the impacts of wearing off happen rapidly. These are called "switching off" or "on/out [2].
The study found young age of Parkinson's onset, longer duration of disease, longer time on levodopa treatment, a higher dose of levodopa, and dopamine agonist were associated with WO phenomena. A few examinations have revealed younger onset PD as a danger factor for fostering the WO peculiarity regardless of the study of disease transmission. Our study found that WO frequently occurred at the early and middle stage of PD as clinicians identified WO in 12.9% of patients within one year of disease duration.WO is considered a levodopa-related complication that usually occurs in the late stage of PD. WO was seldom screened in patients treated without levodopa [3].

UNDER PEER REVIEW

There is developing proof recommending that patients with Type 2 diabetes have an expanded danger of fostering Parkinson's infection and offer comparative dysregulated pathways common underlying pathological mechanisms. Although the details of the pathogenesis of PD remain to be further defined, a growing body of evidence links insulin resistance to PD, and while the underlying mechanisms remain unclear, there is accumulating evidence suggesting that alpha-synuclein can interfere with normal insulin signaling via its action on inflammation and the AKT pathway [4].

Case presentation

A 61 years old male with a known case of Parkinson's disease presented to his scheduled appointment in a diabetic clinic complained of dysarthria worsening. He had a history of Parkinson's disease since five years ago on Sinemet(carbidopa25 mg/levodopa 25 mg), diabetes since ten years ago with A1C of 8.5%, was on insulin glargine ten u daily, and metformin 750 mg 2 tabs once daily, linagliptin 5 mg daily, and liraglutide 1.6 mg. He mentioned that anti-diabetic medication affects levodopa/carbidopa and causes PD symptoms to worsen.
His past medical history was notable for hypertension was on lisinopril 2.5 mg currently stopped due to hypotension, dyslipidemia with LDL of 3.97 mmol /L, HDL 1.10 mmol/L, and cholesterol 5.96 mmol/L on atorvastatin 20 mg daily, PBH on solifenacin 5mg daily, IHD s/p CABG on clopidogrel 75 mg daily, prostate cancer s/p prostatectomy, colon resection, and GERD on pantoprazole 40 mg.

When his diabetes was controlled with HA1C of 6% and fasting blood glucose of 100 mg/dL, he switched to metformin only with a dose of 750 mg daily, that he experienced it's the effect on Sinemet(carbidopa 25 mg/levodopa 25 mg) response when he decided to stop taking it. His glucose worsened again with an A1C of 8.5%, so he started on liraglutide 0.6 mg with metformin 850 mg after that. His A1C improved to 6.7%, but he can't tolerate dysarthria worsening, so he switched to insulin mixtard20 u morning and ten u pm only for his diabetes with no PD symptoms worsening.

UNDER PEER REVIEW

Discussion

Parkinson's disease (P.D.) is viewed as quite possibly the most widely recognized neurodegenerative disease [5], and Diabetes mellitus (D.M.) is the most common chronic metabolic disease[6].
There are numerous likenesses among D.M and P.D. Clinical highlights of the two illnesses result from the obliteration of specific cells, in particular pigmented dopamine cells in P.D. and pancreatic beta cells in D.M. The deficiency of these cells brings about diminished insulin in D.M.and dopamine in P.D.[7][8].Both disorders are ongoing sicknesses. The two illnesses result from a decline in a particular substance: dopamine in P.D. and insulin in D.M. In addition, the two infections emerge because of the annihilation of specific cells, dopaminergic cells in P.D., and pancreatic beta-cell in D.M. As of late, numerous epidemiological and trial studies showed an association among D.M. and P.D. There are normal basic systems in the pathophysiology of the two sicknesses. These hidden systems incorporate mitochondrial brokenness, oxidative pressure, hyperglycemia, and irritation. Insulin resistance is the hallmark of D.M., primarily type 2 diabetes mellitus (T2DM)[8]. The association between T2DM and P.D. has been previously reported since patients with T2DM appear to have an increased risk of developing P.D. In a large cohort of 8 million people, Pablo Fernandez et al. showed a higher rate of post-PD after T2DM. However, some studies have shown the opposite or the absence of a relationship between these diseases[9].

Parkinson's disease (P.D.) is one of the most well-known neurodegenerative issues and a main source of death and inability. P.D. is perhaps the most widely recognized neurodegenerative disorder. The Parkinson's Disease Foundation reports that around 1 million Americans at present have the infection. The rate of P.D. in the U.S. is around 20 cases for every 100,000 individuals each year (60,000 every year), with the mean period of beginning near 60 years[1]. P.D. affects ~2% of the population over 65 years of age, and its prevalence increases as the population ages(Brakedal et al., 2017). The etiology of Parkinson's relies upon a blend of genetic factors(10% of cases) and conceivably natural variables. Besides, most instances of Parkinson's are idiopathic, and the specific etiology stays unclear.[10][11].
Motor features includes in P.D. patients incorporate tremer, inflexibility, and bradykinesia. The motor features of P.D. might correspond with the patient's age at beginning explicitly; tremertoward the start is twice as normal in patients more established than 64 years contrasted and those more youthful than 45 years old. What's more, difficulties identified with the term of treatment, for instance, the relationship of dystonias and dyskinesias with the length of levodopa treatment, are more normal in patients analyzed at more youthful ages (45 to 55 years old)[1].
Epidemiological investigations have recommended that T2DM expands the danger of Parkinson's infection. What's more, clinical investigations portrayed that side effects of Parkinson's sickness were essentially more awful after the beginning of

UNDER PEER REVIEW

T2DM.Concerning treatment, the action of antidiabetic drugs, especially incretin-mimicking agents, appears to confer a certain degree of neuroprotection in P.D. patients[9].
Antidiabetic drugs are emerging as promising therapeutic agents for Parkinson's disease. One potential therapeutic strategy is to treat Parkinson's disease patients with a class for T2DM medicines that target glucagon-like peptide-1 (GLP-1) receptor activity. For instance, exenatide, a GLP-1 agonist that reestablishes glucose homeostasis in T2DM patients, has evoked neuroprotective impacts in a clinical preliminary for P.D. Exenatide treatment was very much endured and worked on engine and intellectual activities in P.D. patients. Albeit the component by which exenatide upgrades neuroprotection is indistinct, proof from P.D. creature models shows that exenatiderepresses microglia enactment and matrix metalloproteinase-3(MMP3) articulation.Thus, inhibition of inflammatory pathways is suggested to stimulate insulin signaling downstream and ultimately lead to neuroprotection in P.D. [12]. The elevated risk of Parkinson's disease in people with diabetes may be reduced depending on the type of diabetes medication prescribed[13].
A long-term retrospective cohort study was performed to investigate the association between P.D. use and GTZ. The results showed that GTZ use was associated with a 28% lower risk of diabetes compared to metformin use in the nationwide population using these drugs for diabetes[14].
A systematic review was recently published on the diabetes risk associated with diabetes. It concluded that diabetes was a risk factor for Parkinson's disease according to several data from 4cohort studies[15].
We reported a case of unintentional drug-drug interaction between antidiabetic medication and levodopa/carbidopa, leading to P.D. symptoms worsening, especially dysarthria declining in 61 years old males with known cases of diabetes since ten years ago and Parkinson's disease since five years ago. He can't tolerate antidiabetic medication except for insulin mixtard.

Conclusion

This case highlighted the importance of unintentional drug-drug interaction, which may pose a challenge to a healthcare provider, and the importance of adverse drug-drug interaction of antidiabetic with levodopa/carbidopa, its presentation, and A few epidemiological and exploratory investigations have uncovered .management the relationship between diabetes (DM) and Parkinson's illness (PD), as these studies have shown an expanded danger of creating diabetes in diabetic patients. It additionally showed that different components of insulin affect Parkinson's illness. All things neuroprotectively drugs antidiabetic and considered, more broad clinical preliminaries are expected to inspect the adequacy of

UNDER PEER REVIEW

insulin and other antidiabetic drugs in the event and movement of Parkinson's infection. Later on, more investigations could prompt the disclosure of a single .medication that can be utilized in the treatment of both DM and PD

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

UNDER PEER REVIEW

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UNDER PEER REVIEW