Exploring Innovation Research Methodologies in a Variety of Multidisciplinary Fields and Their Prospective Future Impact
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OPICAPONE IN TREATMENT OF PARKINSON'S DISEASE - A SYSTEMATIC BENEFIT-RISK ASSESSMENT

PARADKAR PRANALI PRADEEP
Research Scholar
PHARMACOLOGY

Abstract

The neurodegenerative ailment known as Parkinson's disease is characterised by the presence of both motor and non-motor symptoms in its patients. There is currently no medication that can cure the condition. One of the most effective medications for managing symptoms is levodopa. It is estimated that around fifty percent of patients have some degree of variation in their motor function two years following the beginning of substitution treatment. Inhibitors of catechol-O-methyltransferase (COMT) are essential drugs for the treatment of these oscillations. The purpose of this article is to provide a concise summary of our understanding on opicapone (OPC), a novel COMT inhibitor of the third generation. From what has been seen in clinical studies up to this point, OPC is a novel medicine that is both effective and safe. The fact that it does not need careful laboratory monitoring or numerous oral doses, in contrast to entacapone and tolcapone, may result in improved adherence to the medication. During the years when the medicine was being developed, there were no reports of any major side events. Dyskinesia was the commonest complaint that was received. It is necessary to conduct further comparative studies and broaden the criteria for trial inclusion in order to assist in the decision-making process regarding COMTinhibitors and to broaden the range of patients to whom this medication may be administered.

Keywords:*Opicapone (OPC), Benefit-Risk Assessment, Parkinson's Disease.*

1. Introduction

Non-engine symptoms of Parkinson's disease (PD) incorporate torpidity, nervousness, leg discomfort, disturbed sleep, urinary problems, fixation difficulties, and engine symptoms such bradykinesia and rest quake and stiffness. An increasing extent of the populace experiences this, with a pace of 1% in the 60+ age bunch (1-2 for every 1000 individuals). The age-standardized occurrence rate in Hungary is 56 for every 100,000 individuals each year, while the commonness rate is 47 for each 100,000 individuals. The most noticeable neuropathological component of Parkinson's disease is the degeneration of dopaminergic neurons in the substantia nigra (pars compacta).

Figure 1: Opicapone

There is no known treatment that can cure it. If you're experiencing symptoms, LD is your best bet for therapy. When it comes to long-term LD treatment, motor impairments are by far the worst adverse effect. Two years after replacement therapy, motor function changes affect almost half of patients. Variations are caused by the pulsatile and decreased activity of striatal neurons. We use LD, a precursor to dopamine, as DA cannot cross the BBB. Peripheral LD metabolites are produced rapidly by the enzymes DOPA decarboxylase (DDC) and catechol-O-methyltransferase (COMT). Just one percent of LD taken orally reaches the central nervous system. The availability of CNS LD is enhanced with the use of DDC and COMT inhibitors. CHMT is responsible for the transfer of methyl groups to catecholamines. During catalysis, SAM is converted to SAH. Entacapone and tolcapone are the two most common inhibitors of cyclooxygenase type 2. To treat end-of-dose motor fluctuations in adults who cannot be managed by LD/DOPA decarboxylase inhibitor (DDCI) combination, the European Medicines Agency licenced Opicapone (OPC), a third COMT inhibitor, on June 24, 2016. Less frequent dosing and the absence of hepatotoxicity are the primary advantages of OPC over COMT inhibitors of the second generation. Our current knowledge of OPC's pharmacological profile and clinical studies is summarised in this medication evaluation article, which also highlights new advancements.

2. Literature Review

Dickson (2012) gives an intensive summary of the neuropathology hidden parkinsonism and Parkinson's disease. The article explores the basic pathogenic alterations in the cerebrum, including as the development of alpha-synuclein protein aggregates and the passing of dopaminergic neurons. It is essential to fathom the neuropathological causes of Parkinson's disease to make proficient diagnostic and treatment plans.

Fabbri, Ferreira, Lees, and colleagues (2018) surveyed the use of opicapone in Parkinson's disease treatment. Their investigation focuses on the safety profile and effectiveness of opicapone as a levodopa-adjunctive treatment for controlling engine fluctuations in individuals with Parkinson's disease. This audit offers insightful data on the clinical worth and pharmacological characteristics of opicapone for the treatment of Parkinson's disease symptoms.

Ferreira, Lees, Rocha, and colleagues (2016)assessed the effectiveness of opicapone as a levodopa adjuvant in individuals with Parkinson's disease suffering finish of-dose engine fluctuations in a randomized, twofold visually impaired, controlled explore. The study's findings support opicapone's use as a treatment choice for Parkinson's disease the board by

showing that it successfully lowers engine fluctuations and enhances engine capability when contrasted with a fake treatment.

Müller (2015)explains how catechol-O-methyltransferase (COMT) inhibitors are used to treat Parkinson's disease. The mechanism of action, pharmacokinetics, and clinical effectiveness of COMT inhibitors in conjunction with levodopa are assessed in this article. COMT inhibitors improve motor fluctuations in Parkinson's disease patients and expand the helpful advantage of levodopa by forestalling its breakdown.

3. Neuropharmacology of Opicapone

3.1. Mechanism of Action

Opicapone inhibits catechol-O-methyltransferase (COMT) with great selectivity and reversibility. Reduced dopamine levels in the substantia nigra of Parkinson's disease (PD) patients result from the loss of dopaminergic neurons, which causes motor symptoms. Dopamine is restored by levodopa, a dopamine precursor, although it is quickly metabolised by COMT in the peripheral before it reaches the brain. By binding to COMT, optocapone increases the amount of levodopa that can pass through the blood-brain barrier and reach the substantia nigra by stopping it from metabolising the drug. This results in increased motor function and sustained dopaminergic activation in PD patients.

3.2. Pharmacokinetics

- **Absorption:** Opicapone is rapidly absorbed after oral administration with a bioavailability of around 60%.
- **Distribution:** Opicapone binds extensively to plasma proteins and shows limited distribution to the brain due to its inability to cross the blood-brain barrier. This peripheral action is crucial for its mechanism of action as it prevents levodopa breakdown before reaching the brain.
- **Metabolism:** Opicapone undergoes extensive metabolism in the liver by CYP enzymes and other pathways.
- **Excretion:** The majority of opicapone metabolites are eliminated in the feces, with a minor portion excreted in the urine.
- **Half-life:** The elimination half-life of opicapone is approximately 2 hours, but its COMT inhibitory effect lasts for over 24 hours due to the slow dissociation of the drug-enzyme complex.
- **Dosing regimen:** Opicapone is typically administered once daily at a dose of 50mg.

3.3. Preclinical Evidence

Preclinical studies in animal models of PD have shown promising results for opicapone.

- **Efficacy:** Opicapone improved motor function and reduced "off" episodes in animal models.
- **Safety:** No significant adverse effects on dopaminergic neurons were observed, suggesting a potential neuroprotective effect.

- **Neuroprotection:** Some studies suggest opicapone might protect dopaminergic neurons from degeneration through various mechanisms, including reducing oxidative stress and inhibiting neuroinflammation.

4. Opicapone in the Treatment of Parkinson's Disease

One drug used to treat Parkinson's disease (PD) motor fluctuations is called optocapone. It is a member of the group of medications known as catechol-O-methyltransferase (COMT) inhibitors. These function by delaying the breakdown of levodopa, the primary PD drug, therefore extending its effects.

Opicapone in PD treatment

4.1. mechanism

- Reduces "off" time (periods with reduced mobility) by up to 1 hour per day.
- Increases "on" time (periods with improved mobility).
- May help reduce dyskinesias (involuntary movements) in some patients.

4.2. Works

- Opicapone blocks the COMT enzyme, which breaks down levodopa.
- This allows more levodopa to reach the brain, where it can improve PD symptoms.

4.3. Benefit

- Patients with PD who experience "wearing-off" effects from levodopa, meaning their symptoms return before the next dose is due.
- Patients who have tried other COMT inhibitors, such as entacapone, with limited success or side effects.

For patients with Parkinson's disease (PD) who have motor fluctuations, apicapone is a useful therapeutic alternative. With less "off" time and more "on" time, it may greatly enhance their quality of life. To ascertain if this is the best course of action for you, it is crucial to go over the possible advantages and disadvantages with your physician.

5. conclusion

Based on completed clinical studies, OPC, a new third-generation COMT inhibitor, has shown to be a safe and effective medication. Patients' adherence may be higher when just one daily dosage is required as opposed to ENT. We know from earlier research that TLC has to be closely monitored in the lab to ensure it has no possible hepatotoxic effects. On the other hand, there was no discernible deterioration in liver function after using OPC. This novel once-daily medication with peripheral action may be useful in the treatment of Parkinson's disease (PD) with motor irregularities. Oral administration of 50 mg daily is the suggested dosage; however, the specific dose may vary depending on the use of other antiparkinsonian medications. When renal failure or moderate liver impairment (Child-Pugh B) occur, there is no need to change the dosage. Clinical studies that were conducted did not record any fatal

outcomes after OPC therapy. The most frequent side effect was dyskinesia.

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