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Research Article

Ophthalmic Features of Parkinson's Disease - Underreported and Unacknowledged: An Observational Study

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Abstract

Parkinson's disease is a common neurological disease common in middle aged and elderly men. Parkinson's disease involves the degeneration of the extrapyramidal motor system resulting in movement related symptoms such as tremor, rigidity, postural instability, ataxia etc. [1]. Some patients may also develop and experience sensory changes involving olfactory disturbances and auditory and visual disturbances. This paper will explore the ophthalmologic and overall visual problems experienced by Parkinson's Disease patients in a study conducted at the Berat and Pogradec Ambulatory Clinics in Albania.

Keywords: Parkinson's Disease; Albania; Apraxia of Eyelid Opening (AEO)

Introduction

Visual disorders such as visual acuity defects, dry eyes and visual hallucination are often under accounted for within Parkinson's Disease (PD). It is believed to be underreported by patients and also not acknowledged by their treating physicians. This study aims to identify the prevalence and the clinical effects of ophthalmic symptoms in patients with PD using a basic neuro-ophthalmic screening tool.

In a non-PD patient, decisions about movements take place in the motor cortex within the cerebellum via intra-cranial neurons. The action potential for the movement to take place travels to the basal ganglia. At the basal ganglia, the caudate and putamen receive the action potential for the movements required. The substantia nigra and subthalamic nucleus stimulate dopaminergic neurons to cause the binding of dopamine to the GABA receptors at the globus pallidus. The lack of inhibition now from the globus pallidus allows the firing of the thalamus to take place and so allows the generation of action potentials. These action potentials will travel along efferent neurons through the extrapyramidal pathway in order to generate movement [2].

In PD patients there is a neurodegenerative disorder of the substantia nigra causing a depletion of dopamine binding to GABA receptors. This means that the globus pallidus cannot be inhibited sufficiently, leading to the continued stimulation of the thalamus and therefore unwanted movements take place. This leads to the symptoms seen in Parkinson's disease such as tremor, rigidity, ataxia and postural instability.

The lack of dopamine also leads to a lack of stimulation of the innervation of the visual cortex as well as retinal dopamine depletion [3].

To further consider this, dopamine also plays an important role in vision through oculomotor control, adaptation to light, visuo-spatial construction, colour vision and spatial working memory [4]. Therefore, the lack of dopamine can lead to various PD-related ophthalmic symptoms. Some of the ophthalmic signs and symptoms reported in PD patients in this study include reduction in visual acuity, apraxia of eyelid opening, dry eyes, corneal erosion and visual hallucinations.

For a patient, this can lead to additional complications including health related complications, reduction ADL's and alterations to their quality of life, such as increased falls, loss of ability to drive, loss of ability to read, loss of confidence and therefore social isolation amongst many other complications. This draws the idea, the importance of this study for PD patients and associated required interventions will have a huge beneficial impact on their quality of life.

The aim of this study is to investigate the prevalence and clinical effect of ophthalmic symptoms for PD patients. This was completed using a basic ophthalmic-neuro screening tool. This study further aims to increase awareness of ophthalmic symptoms in PD to ensure appropriate interventions can be put in place [2].

Visual disorders in PD

Parkinson's Disease patients often report a range of ophthalmic symptoms and visual disturbances. These range from a reduction in visual acuity, apraxia of eyelid opening and ocular surface changes [5].

Reduction in visual acuity

Patients diagnosed with Parkinson's Disease often complain of poor eyesight resulting from a reduction in visual acuity. Several factors may contribute to the reduction in visual acuity in PD patients including a lack of dopamine in the retina [6].

Furthermore, reduced visual acuity may contribute to an increased risk of developing visual hallucinations in PD patients [5].

For patients, this means the resolution and accuracy of their vision may be decreased. Leading to symptoms described such as visuo-spatial complications. This may lead to increased falls if they cannot accurately see their step, leading to a fall and further health complications.

Apraxia of eyelid opening

Apraxia of eyelid opening (AEO) is a neurological abnormal feature characterized by difficulty eyelid elevation [7]. AEO has been strongly associated with diseases affecting the extrapyramidal system [7]. Parkinson's disease is one of the main causative factors of apraxia of eyelid opening [8]. In PD patients, apraxia may present with focal, segmental or generalized dystonia including blepharospasm. AEO has been strongly associated with the use of levodopa in the treatment of PD and in PD patients, AEO is known to occur under wearing-off states of levodopa [8].

Ocular surface changes

Ocular surface changes depict a common finding in Parkinson's disease patients. Some of the surface changes involve corneal changes in different corneal layers and dry eyes. These conditions often occur simultaneously [9]. These changes may alter the protective layer to the eye and could possibly lead to increased infections, artifacts in vision etc. Dry eyes are also uncomfortable for the patient and can be easy to manage, therefore it is important to recognise and manage these symptoms for PD patients [6].

Corneal features

Changes to corneal layers in PD patients are attributed not only to the disease process but also to the drug treatments of the disease. Certain medications have been shown to cause endothelial cell changes to the cornea in PD patients. In this study reduced corneal thickness was observed in 35% of the patients. Patients also complained of ocular surface irritation which was found to be due to slight corneal erosions most likely linked to reduced blinking and an alteration in tear composition in PD patients. Again, this can lead to complications such as ophthalmic irritation for the patient and a reduction in the protective layer to the eye leaving the patient vulnerable to further complications such as infections [6].

Dry eyes

Some of the features of PD involve changes in meibum lipid composition, deficiency in the tear film mucin layer and changes in the tear composition as proven by previous studies.

Blepharitis, which is a common occurrence in PD patients, can also exacerbate dry eye syndrome in PD. This can irritate the ophthalmic region for patients and also reduce their quality of life if they find this a limiting factor to their ADL's [4].

Visual hallucinations

Visual hallucinations are a complex chronic consequence of Parkinson's Disease (cite). Patients treated with L-dopa and dopamine agonists are at an increased risk of developing visual hallucinations. Patients may experience hallucinations with flickering lights and may often see colorful images as a result. Poor primary vision and reduced visual acuity are two of the main risk factors for developing visual hallucinations in PD patients [4].

In terms of suggestive management for post-study intervention, it is important to consider the causative agent, whether these medications are the causative agent or whether it's the disease process.

Methods

51 patients diagnosed with PD were included in this study, conducted as an observational study.

In this observational study, 51 patients diagnosed with PD and followed up in ambulatory Clinics in Pogradec and Berat Hospitals in Albania have been screened for visual disorders.

The neuro-ophthalmologic tests used were visual acuity tests using snellen chart, visual field tests, optical coherence tomography (OCT), colour vision tests using Ishihara's charts, examination of the eye.

It is a retrospective study extended in two years between March 2019 and January 2021. The mean age of patients involved was 55.6 years old. Data processing involved the use of type cards for all patients, Crosstab, Chi Square test, T-Test, Fisher's Exact Test.

Results

From the 51 patients investigated in this retro-spective, observational study, one or more ophthalmic symptoms were reported by patients. Within this proportion of the patients, the percentage of reporting of the ophthalmic symptoms are listed below:

- 72% reduction in visual acuity
- 68% apraxia of eyelid opening
- 35% dry eyes and corneal features
- 18% visual hallucinations

This graph below illustrates the proportions of ophthalmic disorders described by those who stated they had ophthalmic symptoms.

Figure 1: Representation of proportions of symptoms.

To further investigate the clinical effects on the patients, they were asked to state if they felt this interfered with their daily activities. 56% of patients reported ophthalmic symptoms experienced have a daily impact for them. However, the evidence of ophthalmic features of Parkinson's is disproportionate ($p < 0.005$). Therefore, showing its under-recognized within this patient group. Assumably, this also means there is a lack of management of ophthalmic features within PD.

Study evaluation

This observational study has a moderate sample size which increases its generalizability. However, the sample size is strictly within two ambulatory clinics in two community-based hospitals. The study would need to be replicated at a larger scale involving large regional hospitals in Albania in order to consider the results' generalizability at a national or international level. The small scale of this study, therefore limits the application of the suggested prevalence and management plan for ophthalmic symptoms in other countries.

As well as considering the reported symptoms, it's also important to consider medications that the patient is taking. As these medications may be a contributing factor to the ophthalmic symptoms experienced. Therefore, the study could extend further completing ophthalmic screening in PD patients who are taking different medications. You may notice that one medication could be the causative agent.

There are also several confounding factors that should be taken into account, such as can the ophthalmic symptoms be simply explained by increasing age rather than Parkinson's disease. This may have accounted for some of the ophthalmic symptoms reported, meaning the study may lack internal validity and generalization to all PD patients.

It would also be best practice to use electrical retinopathy, optic retino-physiology test and multifocal EGR's. These would increase the reliability of the examination and give more in depth findings about the pathophysiology and about what the specific patient experience is.

There were also several different clinicians examining which also may be suggestive there may be presence of inter-observer bias. This means that the result of each examination per individual patient may be interpreted slightly differently and therefore results may be slightly skewed. However, in this study this is reduced, as all the clinicians have had similar training resulting in techniques and examination interpretation to be similar.

Discussion and Conclusions

Patients with Parkinson's disease are at risk of developing a range of ophthalmic disturbances during the course of their disease. The ophthalmic changes in PD can result in a reduction in visual acuity, dry eyes, apraxia of eyelid opening, corneal erosion and visual hallucinations [10].

Due to the ophthalmic changes, patients with PD may have problems with visuo-spatial awareness and such can interfere with their daily activities, as over half of the sampled patients reported. Some activities that may be impaired include reading, cooking, picking up and moving objects and limb placement [10].

Addressing and correctly identifying visual changes can have a significant impact on the quality of life in patients diagnosed with PD. It can be speculated that in PD falls may be due to extrapyramidal symptoms and not visual changes, thus possibly leading to the underreporting of ophthalmic symptoms in PD patients.

There is a general need for clinicians to perform further tests to rule out ocular manifestations. It is also important to distinguish between visual symptoms that may be caused by drug treatment from those used to treat Parkinson's disease. Structural imaging of the retina would help to provide more objective parameters and could be more reliable in the evaluation of the disease**.** If ophthalmic side effects are identified, it is essential for patients to be referred to neurology for further clinical evaluations. These patients could also benefit from immediate (at the time of diagnosis) and regular follow-up ophthalmic examinations including ocular surface tests in order to investigate ophthalmic changes which may be taking place in order to manage these appropriately for patients. These examinations may include TBUT, Schirmer's test, fluorescein staining and OSDI. This would identify the ophthalmic symptoms that patients are experiencing and therefore would help patients to manage their symptoms in order to improve their quality of life.

Ophthalmologists and neurologists should form multi-disciplinary relationships in order to investigate PD patient prescriptions, as some medications may be the causative factor for the visual symptoms. Amantadine has been shown to cause toxicity to the cornea leading to corneal erosions and therefore may reflect the symptoms reported by the patient [8].

Further long-term studies in larger patient groups for general data retrieval are needed in order to determine the cause and effective prevention/management for the patients affected.

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