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IP International Journal of Ocular Oncology and Oculoplasty

Journal homepage: https://ijooo.org/

Original Research Article

Ocular morbidity in patients on long-term selective serotonin reuptake inhibitors (SSRIs)

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ARTICLE INFO

Article history:
Received 09-09-2021
Accepted 22-10-2021
Available online 07-02-2022

Keywords:
SSRI
Dry eye
Cataract
Glaucoma

ABSTRACT

Purpose: To assess ocular morbidity in patients on long time anti-psychotic medication- SSRI.
Materials and Methods: Cross- sectional observational study was conducted on 96 patients on anti-psychotic medication (SSRI) who attended the OPD in Department of Ophthalmology and Psychiatry, from July 2019 to July 2021.
Results: Of 96 patients, 71(73.9%) patients had ocular morbidity. Most common ocular morbidities were dry eye 62 (87.3%) followed by, reduced corneal sensitivity 3(4.2%), cataract 3 (4.2%), glaucoma 2(2.8%), ischemic optic neuropathy 1 (1.4%).
Conclusion: Dry eye was the most common ocular morbidity seen. SSRIs on long term usage have significant ocular side effects, which should be kept in mind by both Ophthalmologists and Psychiatrics in their clinical practise.

1. Introduction

Major depressive disorder (MDD), among the psychiatric conditions, is one of the leading causes of global disability-adjusted life years (DALYs).[1] In the recent statistics of 2019, its been ranked 11^{th} globally as leading cause of DALYs which had significantly increased from the 15th rank in 1990.[2] Anti- depressant medications include Selective serotonin reuptake inhibitors (SSRIs), selective Norepinephrine Reuptake Inhibitors (SNRIs) and Tri Cyclic Antidepressants (TCA). Among them, SSRIs are the most commonly prescribed drugs for MDD.[3]

Serotonin (5-hydroxytryptamine, 5-HT), a biogenic monoamine, has various actions on the both central and the peripheral nervous systems.[4] Serotonin and its receptors are found in different ocular structures such as cornea, iris, ciliary muscle, iris sphincter muscle, lens and retina.

Serotonin has varied actions in numerous ocular tissues like- 5-HT1A receptors found in the iris and ciliary body reduce the production of aqueous humour, thus decreasing the intraocular pressure; In contrast, aqueous humour synthesis is increased via 5-HT7 receptors and they also induce mydriasis by relaxing the pupillary sphincter. The 5-HT2A/2C receptor play a significant role in the corneal homeostasis.[4]

Selective serotonin reuptake inhibitors (SSRIs) increase availability of serotonin by inhibiting pre-synaptic serotonin transport. This effect has been used in the treatment of depression, anxiety and other mood disorders such as eating disorders.[5] SSRIs group consists of citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline. Along with these advantages, this group has disabling systemic side effects such as weight gain, insomnia, increased appetite, vertigo, nausea, sexual problems, itching. Various previous studies have

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https://doi.org/10.18231/j.ijooo.2021.076

documented SSRIs ocular side effects such as cataracts,[6,7] central retinal vein occlusion[8], acute angle-closure glaucoma,[9] optic neuropathy[10] and diplopia.[11] However, these studies are not well researched in humans.[12,13]

SSRIs are among the first-line medication for MDD and since cataracts, glaucoma are the leading cause of blindness, it has become more pertinent to assess the ocular side effects of SSRIs for follow up monitoring and providing advice to patients.

2. Materials and Methods

A Cross sectional observational study of 96 patients diagnosed with depression based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, and a history of SSRIs usage at least for 6 weeks in psychiatry and ophthalmology outpatient clinics between the time period of July 2019 to July 2021, were included.

The study was conducted after approval from the ethics committee. Patients were explained about the study in their own understandable language and individual written informed consent was taken. All subjects were questioned about age, sex, gender, demographic details, history of any other systemic diseases, medications. Patients taking SSRI for more than 6 months were included in the study. Patient underwent routine ophthalmic examination which included best corrected visual acuity, retinoscopy, corneal sensation, Schirmer's test, slit lamp examination for thorough anterior segment evaluation TBUT, cataract if present was graded using LOCS III classification. Intraocular pressure examination by rebound tonometer, gonioscopy using Zeiss four mirror gonioscope and fundus examination using both direct and indirect ophthalmoscope using 20D lenses, 90D lens.

We adjusted for potential confounding variables, including age, gender, income, urbanization, hypertension, diabetes and hypercholesterolemia, prescriptions with antipsychotics, anticholinergics, topiramate, steroids, hormone replacement treatment, and other antidepressants: tricyclic antidepressants, as possible confounding factors.

3. Results

Out of 96 patients, 32 were men and 64 were women. Age of patients in our study was on an average 46.64 years. The mean duration of SSRI usage was 24±3 months. In our study, 81 (81.4%) patients were diagnosed with depression, 5 (5.2%) patients diagnosed with depression with anxiety disorder and 10 (10.4%) patients were diagnosed with generalised anxiety disorder. Fluoxetine was the most commonly prescribed SSRI (37.5%) and out of 96 patients, 71 (73.9%) patients had ocular morbidity. Dry eye was most commonly seen comprising of 62 (87.3%) of cases. Reduced corneal sensitivity 3 (4.2%) patients, cataract 3 (4.2%) patients, glaucoma in 2(2.8%) patients and ischemic optic neuropathy in 1 (1.4%) patient.

Table 1: Sociodemographic variables of patient on SSRI.

Variables	Numbers
Age (years)	46.64 ± 12 years
Gender (M: F)	1:2 (M - 32, F – 64)
Duration of SSRI usage, months	24± 3 months

Table 2: Diagnosis of psychiatric condition.

Type of psychiatric disease	Number (%)
Depression	81 (81.4%)
Depression with anxiety disorder	5 (5.2%)
Generalized anxiety disorder	10 (10.4%)

Table 3: SSRI used in the study.

SSRI	Number (%)
Sertraline	28 (29.1%)
Fluoxetine	46 (37.5%)
Paroxetine	10 (10.4%)
Escitalopram	5 (5.2%)

Table 4: Associated ocular morbidity.

Ocular morbidity	Number (%)
Dry eye	62 (87.3%)
Reduced corneal sensitivity	3 (4.2%)
Glaucoma	2 (2 .8%)
Cataract	3 (4.2%)
Ischemic optic neuropathy	1 (1.4%)

4. Discussion

Dry eye (DE) is a frequently under-recognized clinical condition characterised by ocular discomfort due to tear deficiency or excessive evaporation.[14–17] Previously numerous studies, including population based epidemiological studies, have shown a strong link between the use of antidepressant medications and increased risk of dry eye,[18,19] The proposed mechanism for altered tear film production is its inhibition of muscarinic receptors.[20] Various types of serotonin receptors have been identified in the conjunctival and corneal epithelium. SSRIs by altering the level of serotonin can affect the sensitivity thresholds of corneal nerves.[21] Escitalopram, among the SSRI, seems to cause this side effect significantly.[22] In our study we found that 87.3 % patients suffered from dry eye and 4.2% patients had reduced corneal sensitivity. This in concordance with other studies like Kocer E et al, in which dry eye was seen in 35% of patients.[22] Wen W et al study which included 472 patients, concluded that long term SSRIs usage had an increased risk of dry eye.

Even though the role of serotonin in lens metabolism remains unidentified, in the animal models- large number of serotonin receptors have been found in the crystalline lens[23] and also altered serotonin levels cause lens opacities in rats.[24] In our study 4.2% patients had developed cataract. This is in-line with other population-based study like the study of Erie et al,[25] which showed that in patients over 50 years using SSRI for 1 year or more, had significantly increased risk of cataract surgery. Among the SSRIs, citalopram had the highest association.[26] The association of SSRI usage and increased incidence of cataract has been proven by various meta-analysis- like the 2018 Fu Y et al study from China, where they found this significant with fluoxetine and fluvoxamine administration. Other SSRIs were not associated with the risk of cataract development.[27]

SSRIs alter the intraocular pressure via serotonergic effects on ciliary body and pupil dilation. 5-HT1A receptors of iris and ciliary body reduce the intra-ocular pressure by decreasing aqueous humour production. Long term use of SSRIs may lead to altered sensitivity of these receptors resulting in increased intra ocular pressure. 5-HT7 receptors present in the pupil sphincter, causes mydriasis by relaxation of the sphincter muscle. In patients with narrow iridocorneal angle, this effect can precipitate a glaucomatous attack. In our study, we found 2.8 % patients to have angle closure glaucoma. In a recent study Chen et al, there was a 5.8-fold elevated risk for acute angle closure glaucoma within 7 days initiation of SSRIs usage.[13] But this association was not significant on a longer usage, like Chen et al study, where they reported that long-term use (>1 year) of SSRIs was not associated with increased risk of both primary open-angle or angle-closure glaucoma (POAG/PACG) in patients with depression. However, this study included only population of Major Depressive Disorder (MDD).[28] Several animal and human studies have reported that fluoxetine is associated with significant elevation in intraocular pressure (IOP).[29]

In our study, we had 1 case of ischemic optic neuropathy. Costagliola postulated that increased plasma serotonin level may be responsible for vasospasm leading to decreased optic nerve perfusion. Patients with atherosclerosis have higher risk of serotonin enhanced platelet aggregation in atheroma of ocular arteries. Thus, both multiple transient vasospasm and increased platelet aggregation cause optic neuropathy.[30,31] Rarely this non-vasculitis ischaemic optic neuropathy has vision recovery. These patients are on long term SSRIs, mean of 7 years (range 1–14 years) and thus this side effects may be cumulative result of prolonged treatment.[32]

This vision threatening vascular side effects should be kept in mind. Precaution must be taken while prescribing SSRIs in conjunction with known systemic vascular risk factors or pre-existing vascular eye disease until the origin of this neuropathy becomes clearer.

5. Conclusion

In our study, dry eye was most common ocular morbidity among the patients on SSRI. The vast majority of drug-induced ocular disorders could easily be prevented and monitored, provided that clinicians and patients become aware of and watchful for ocular signs and symptoms.

6. Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

7. Source of Funding

None.

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Cite this article: Pooja H V, Gowda HTV, Prasad RV. Ocular morbidity in patients on long-term selective serotonin reuptake inhibitors (SSRIs). *IP Int J Ocul Oncol Oculoplasty* 2021;7(4):364-367.