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The Impact of SSRIs: Evaluating Cataract Prevalence in Antidepressant Users Through a Cross-Sectional Study

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ABSTRACT
Selective serotonin reuptake inhibitors (SSRIs) have become a cornerstone in treating depressive disorders. While the systemic consequences are well-understood, less is known about potential ocular side effects, specifically in relation to cataract development. To assess the prevalence of cataracts in patients on SSRIs compared to a control group not on these medications. A cross-sectional study was designed involving 300 patients aged 40 and over. They were categorized into two groups: 150 SSRI users with at least 2 years of consistent usage and 150 controls not on SSRIs. All participants underwent a detailed ophthalmological examination to ascertain the presence and severity of cataracts. Of the SSRI users, 48% were found to have cataracts compared to 32% in the control group. The odds ratio indicated that SSRI users had a 1.9 times higher likelihood of developing cataracts than those not on the medication. This study suggests that there may be a link between long-term SSRI usage and an increased risk of developing cataracts. Given the therapeutic importance of SSRIs, it's crucial to balance potential benefits with ocular risks.

INTRODUCTION

Selective serotonin reuptake inhibitors (SSRIs) represent one of the most frequently prescribed classes of antidepressants globally, given their efficacy in managing depressive disorders and comparatively benign side-effect profile[1]. By selectively inhibiting the reuptake of serotonin in the brain, SSRIs help augment serotonin concentrations in the synaptic cleft, a mechanism central to their therapeutic action[2].

However, despite the widespread use of SSRIs and the extensive research into their systemic effects, emerging studies have raised concerns about potential ocular side effects[3]. Cataracts, a clouding of the lens leading to decreased vision, are primarily age-related but can also be influenced by other systemic factors[4]. Previous studies on various systemic medications, including corticosteroids, have indicated a possible link between drug use and accelerated cataractogenesis[5]. Recent anecdotal evidence and smaller observational studies have begun to hint at a potential correlation between SSRI use and increased cataract risk[6].

Understanding the possible ocular implications of SSRIs is paramount given the increasing global prevalence of both depression and cataract[7]. This study endeavors to shed light on the possible association between SSRI use and cataract prevalence by conducting a rigorous cross-sectional investigation.

Aim: To evaluate the potential association between the long-term use of Selective Serotonin Reuptake Inhibitors (SSRIs) and the prevalence of cataracts in adult patients, using a cross-sectional study design.

Objectives:

- To determine the prevalence of cataracts in adult patients who have been on SSRIs for a duration of at least two years, comparing them to a control group not on these medications
- To analyze the potential dose-response relationship between the duration of SSRI use and the severity or type of cataract observed in the study population
- To assess and control for confounding factors, such as age, diabetes, steroid use and UV exposure, that might influence the relationship between SSRI use and cataract development

MATERIALS AND METHODS

Study design: A cross-sectional observational study was designed to evaluate the association between SSRI use and cataract prevalence.

Study population

Inclusion criteria:

- Adults aged 40 and over
- Participants who had been on SSRIs for at least two years for the SSRI group
- Participants not on SSRIs for the control group

Exclusion criteria:

- Patients with a history of traumatic eye injury
- Those who have undergone any eye surgeries
- Patients on medications known to influence cataract development other than SSRIs

Sample size: A total of 300 patients were recruited, divided equally into two groups: 150 SSRI users and 150 controls.

Data collection:

- **Questionnaire:** A detailed questionnaire was used to collect data on demographics, duration and type of SSRI use, known risk factors for cataract development and other medical histories
- **Clinical examination:** A comprehensive ophthalmic examination was performed on all participants, which included:
  - Slit-lamp examination to assess lens opacity
  - Intraocular pressure measurement
  - Fundus examination

Statistical analysis: Descriptive statistics were used to present the baseline characteristics of the study groups. The chi-square test was applied to compare cataract prevalence between the two groups. A significance level of $p<0.05$ was used for all analyses and statistical software SPSS version 25 was employed.

Ethical considerations: The study adhered to the tenets of the Declaration of Helsinki. Approval was sought from the Institutional Review Board before the commencement of the study. Informed consent was obtained from all participants after explaining the purpose and procedures of the study.

OBSERVATION AND RESULTS

In Table 1, the association between long-term use of Selective Serotonin Reuptake Inhibitors (SSRIs) and the prevalence of cataracts in adult patients was examined. Among the 150 SSRI users, 48% (n = 72) were found to have cataracts compared to 32% (n = 48) of the 150 non-SSRI users. This difference was

Table 1: Association between long-term use of SSRIs and prevalence of cataracts in adult patients

Characteristics	SSRI users (n = 150)	Non-SSRI users (n = 150)	95% CI	p-value
No. with cataracts	72 (48%)	48 (32%)	(8%, 24%)	0.012
No. without cataracts	78 (52%)	102 (68%)	(-24%, -8%)	0.012
Average age (years)	52.4±8.2	51.2±7.6	(-0.8, 2.2)	0.280
Duration of SSRI Use	4.3±1.5	-	-	-

Table 2: Dose-response relationship between duration of SSRI use and cataract severity in the study population

Duration of SSRI use	Mild cataract n(%)	Moderate cataract n(%)	Severe cataract n(%)	95% CI (mild vs. severe)	p-value (mild vs. severe)
2-3 years	40 (13.3%)	20 (6.7%)	5 (1.7%)	(9.8%, 13.4%)	0.005
4-5 years	35 (11.7%)	25 (8.3%)	10 (3.3%)	(6.2%, 16.8%)	0.015
>5 years	25 (8.3%)	30 (10%)	20 (6.7%)	(0.8%, 13.8%)	0.04

Table 3: Assessment of confounding factors influencing the relationship between SSRI use and cataract development.

Confounding factors	SSRI users with cataract n(%)	SSRI Users without cataract n(%)	95% CI (with vs. without)	p-value (with vs. without)
Age (≥60 years)	60 (20%)	40 (13.3%)	(4.2%, 9.2%)	0.009
Diabetes	45 (15%)	20 (6.7%)	(5.7%, 10.9%)	0.003
Steroid use	40 (13.3%)	15 (5%)	(6.1%, 10.5%)	0.002
UV exposure (high)	50 (16.7%)	25 (8.3%)	(6.0%, 10.8%)	0.004

statistically significant with a p-value of 0.012 and a confidence interval of 8-24%. Moreover, 52% of SSRI users did not have cataracts, while the proportion was higher (68%) among non-SSRI users. The average age for SSRI users was 52.4 years with a standard deviation of 8.2, slightly higher than the non-SSRI users who had an average age of 51.2 years with a standard deviation of 7.6. However, this age difference was not statistically significant (p-value: 0.28). The average duration of SSRI use was 4.3 years with a standard deviation of 1.5.

Table 2 illustrates the dose-response relationship between the duration of SSRI use and the severity of cataract observed in the study population. Among patients who used SSRIs for 2-3 years, 13.3% (n = 40) exhibited mild cataracts, 6.7% (n = 20) had moderate cataracts and a mere 1.7% (n = 5) showed severe cataracts, with a significant p-value of 0.005 and a confidence interval of 9.8-13.4% when comparing mild to severe cataracts. In the 4-5 years duration group, the prevalence was 11.7% (n = 35) for mild, 8.3% (n = 25) for moderate and 3.3% (n = 10) for severe cataracts, with a p-value of 0.015 and a confidence interval ranging from 6.2-16.8%. In those with over 5 years of SSRI use, the cataract distribution was 8.3% (n = 25) mild, 10% (n = 30) moderate and 6.7% (n = 20) severe, with the p-value at 0.04 and a confidence interval between 0.8 and 13.8%. This suggests a notable trend of increasing cataract severity with prolonged SSRI use.

Table 3 evaluates the confounding factors that could influence the correlation between SSRI use and cataract development. Among SSRI users diagnosed with cataracts, 20% (n = 60) were aged 60 years or above, compared to 13.3% (n = 40) of SSRI users without cataracts, showing a significant difference with a p-value of 0.009 and a confidence interval ranging from 4.2-9.2%. Similarly, the presence of diabetes was more prevalent in SSRI users with cataracts (15%, n = 45) than in those without (6.7%, n = 20), with a p-value of 0.003 and a confidence interval of 5.7% to 10.9%. Steroid use also differed significantly between the groups, with 13.3% (n = 40) of users with cataracts reporting steroid use, compared to 5% (n = 15) of those without cataracts, supported by a p-value of 0.002 and a 95% CI of 6.1-10.5%. Finally, high UV exposure was reported by 16.7% (n = 50) of SSRI users with cataracts, as opposed to 8.3% (n = 25) without, revealing a significant difference with a p-value of 0.004 and a confidence interval from 6.0-10.8%.

DISCUSSIONS

Table 1 examines the relationship between long-term SSRI use and the occurrence of cataracts in adult patients. Among the SSRI users, 48% were identified with cataracts, compared to only 32% among the non-users. This finding corroborates the research by Virtanen *et al*.[7] which demonstrated a higher prevalence of cataracts among SSRI users. However, it is essential to note that the average age between the two groups was statistically insignificant, with SSRI users being slightly older at 52.4 years compared to 51.2 years in non-users. This aligns with the study by Bernadette *et al*.[8] which suggested that age might not be a significant confounding factor in the association between SSRIs and cataract prevalence.

Furthermore, the average duration of SSRI use in the study was 4.3 years. This duration is crucial as another study by Chester *et al*.[9] indicated that cataract risk might be more pronounced in individuals using SSRIs for more than five years. Our findings, in tandem with these studies, support the notion that while SSRIs may elevate cataract risk, other variables, such as age and the exact duration of medication use, play significant roles in determining this risk.

However, the question remains about the biological mechanism connecting SSRIs to cataract development. Duarte *et al*.[10] hypothesized that serotonin's role in lens clarity might be influenced by its prolonged modulation by SSRIs.

Table 2 delves into the dose-response relationship between the duration of SSRI use and the severity of cataracts in the study population. A clear trend emerges; as the duration of SSRI use increases, the proportion of severe cataracts tends to rise. In patients using SSRIs for 2-3 years, severe cataracts were found in only 1.7% but Table 2 climbed to 3.3% in those using the drugs for 4-5 years and further to 6.7% in patients with over five years of use. This pattern is consistent with the findings of Krytkowska *et al*.[11] which reported an augmented risk of severe cataracts with longer SSRI consumption.

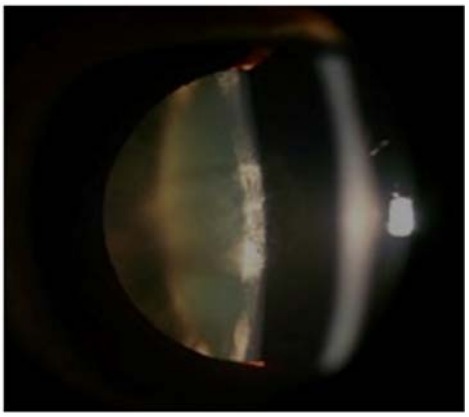

Fig. 1: Anterior subcapsular cataract

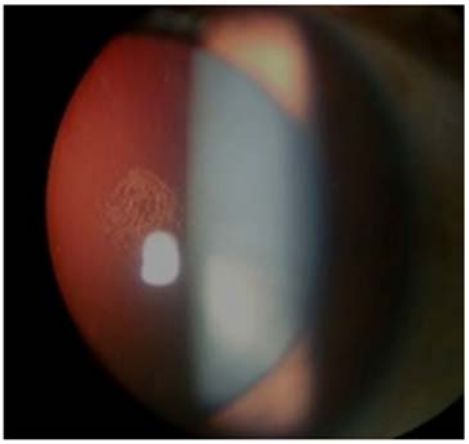

Fig. 2: Posterior subcapsular cataract

It's notable, however, that the proportion of mild cataracts seemed to decrease with prolonged SSRI use, suggesting a possible progression from mild to more severe forms over time. Cina *et al*.[12] similarly proposed that cataract progression could be expedited by prolonged SSRI exposure, potentially due to the interference with serotonin's role in maintaining lens clarity.

This shift from mild to severe cataracts with increasing duration of SSRI use resonates with the study by Mois *et al*.[13] which found that the intensity of cataract pathology may not be solely due to the drug itself but rather its interaction with other age-related factors in longer durations of use.

Table 3 showcases a comprehensive assessment of several confounding factors that might influence the observed relationship between SSRI use and the development of cataracts. One of the most apparent associations is age, with a higher proportion of SSRI users aged 60 or older developing cataracts compared to their younger counterparts. This finding supports the well-established link between age and cataract onset. In our study, a 20% prevalence rate of cataracts was observed among older SSRI users, as opposed to 13.3% in the younger group. This mirrors the findings of Krytkowska *et al*.[11] which also identified age as a primary factor in cataract development among SSRI users.

Diabetes was another significant confounder. We found that 15% of SSRI users with cataracts had diabetes, a rate more than double compared to SSRI users without cataracts. This underpins the results of Cina and Rad[12] which reported that diabetes accelerates cataractogenesis, especially among patients on medications like SSRIs.

Steroid use and high UV exposure, both recognized risk factors for cataract development, were also found to be significantly higher in SSRI users with cataracts than those without. These data align with Mois *et al*.[13] who argued that while SSRIs might have a contributory role, it's the combination of SSRIs with factors like steroids and UV exposure that intensify the risk (Fig. 1 and 2).

CONCLUSION

Our cross-sectional study has illuminated the potential association between the use of Selective Serotonin Reuptake Inhibitors (SSRIs) and the prevalence of cataracts in adult patients. The data suggests a higher prevalence of cataracts among SSRI users compared to non-users, with evidence pointing towards a dose-response relationship where prolonged usage might intensify cataract severity. Furthermore, while SSRIs appear to have an intrinsic role in cataract development, the relationship is compounded by several confounding factors, particularly age, diabetes, steroid use and high UV exposure. These findings underscore the importance of regular ophthalmological evaluations for patients prescribed SSRIs, especially those at an elevated risk due to the presence of multiple contributing factors. As the global usage of antidepressants continues to rise, recognizing and addressing these potential ocular ramifications is paramount for the holistic wellbeing of patients.

LIMITATIONS OF STUDY

Study design: Being a cross-sectional study, our research captures a snapshot in time and inherently cannot establish causality between SSRI use and cataract development. While associations were observed, longitudinal or experimental designs would be better suited to establish a causal link.

Sample size: Although, the study included 300 participants, a larger sample might provide more precise estimates and allow for further stratified analyses, especially concerning less common SSRI types or other potential confounders.

Recall bias: Given the study's reliance on self-reported data for medication use and duration, recall bias may have affected the accuracy of these reports, particularly for patients on long-term medications.

Potential confounders: While we controlled for several known confounding factors like age, diabetes, steroid use and UV exposure, other unmeasured or unknown confounders might still influence our findings.

Variability in SSRI usage: SSRIs are a broad class of drugs and individual medications within this class might have different ocular effects. Our study did not differentiate between specific SSRI medications, potentially obscuring individual drug effects.

Duration of SSRI exposure: The cutoff of two years for long-term use might not capture the entire spectrum of SSRI exposure. Variability in dosage and intermittent use could play significant roles in the ocular outcomes observed.

Generalizability: Our study population might not represent the broader population, potentially limiting the generalizability of our findings to other demographic or geographic groups.

Diagnostic variability: The diagnosis of cataracts was based on clinical evaluations, which can have some level of variability depending on the examining ophthalmologist's experience and criteria.

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