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Original Research Article

Pattern of Ocular Toxicity in Patients on Long-term Antipsychotic Drug

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Abstract

Background: The eye is supported to be the second organ to manifest drug toxicity following liver. Systemic drugs are frequently administered in persons of all age group ranging from children to the elderly for various disorders. There has been increased reporting of ocular side effects of various antipsychotic drugs in the past two decades. Psychiatrists, ophthalmologists and patients need to be aware of and prepared for any medication-induced toxic effect. Early prevention and intervention can avoid most of the serious and potentially irreversible ocular toxicities. ***Objective:*** The aims of the present study were to evaluate the occurrence of toxic ocular effects of antipsychotic drugs, evaluate intraocular pressure of chronic psychotic patients treated with psychiatric medications, correlate toxic ocular effects in patients treated with a variety of antipsychotics to duration of treatment. ***Methods:*** The present study was conducted on 100 chronic psychotic patients attending the Dr. Sirajul Islam Medical College and Hospital Ltd, Dhaka, Bangladesh who on treatment of antipsychotic drugs for a period more than six months period with age group between20 - 60 years. Data was entered in MS Excel and Statistical analysis was done using SPSS trial version 22. ***Results:*** 14% of those patients were on typical therapy alone, 16% on atypical antipsychotic alone while 70% were on combined therapy. As regard lens opacity, 7% was suffered from lens opacity, six cases due to typical therapy while one cases due to atypical therapy. Intraocular pressure was manifested in 11% of all cases. Optic disc examination revealed two cases had increased cup disc ratio who on typical therapy alone. ***Conclusion*:** It can be concluded that many systematic drugs can produce ocular and visual side effect which range from mild to severe and can be even vision threatening.

Keywords: Pattern of Ocular; Toxicity in Patients; Antipsychotic.

INTRODUCTION

Many common systemic medications can affect ocular tissues and visual function to varying degrees. When a systemic medication is taken to treat another part of the body, the eyes frequently are affected. Systemic medications can have adverse effects on the eyes that range from dry eye syndrome, keratitis and cataract to blinding complications of toxic retinopathy and optic neuropathy [1]. Antipsychotic drug treatment is a key component of schizophrenia treatment [2]. The main effect of treatment with antipsychotics is to reduce positive symptoms, including delusions and hallucinations. There is mixed evidence to support a significant impact of antipsychotic use on negative symptoms or on the cognitive symptoms of schizophrenia [3, 4]. First-generation antipsychotics, known as typical antipsychotics, neuroleptics or major tranquilizers, were discovered in the 1950s. Most second-generation drugs, known as atypical antipsychotics, have been developed more recently, although the first atypical antipsychotic, clozapine, was discovered in the 1960s and introduced clinically in the 1970s. Both generations of medication tend to block receptors in the brain's dopamine pathways, but atypical tend to act on serotonin receptors as well [5].When patients with ocular symptoms that have no apparent cause, it is important to consider whether the condition could be caused by a systemic medication they are taking. Patients often neglect to mention the maintenance drugs that they take every day, so ophthalmologists may need to ask specifically

about these types of medication. One of the most important aspects is obtaining a thorough medical history which includes specific medication dosage and duration of treatment [6]. Patient safety is essential during treatment for a particular disorder.

OBJECTIVE

The aims of the present study were to evaluate the occurrence of toxic ocular effects of antipsychotic drugs, evaluate intraocular pressure of chronic psychotic patients treated with psychiatric medications, correlate toxic ocular effects in patients treated with a variety of antipsychotics to duration of treatment.

METHODS

The study design used for this study is observational study and the study period is from May 2019 to April 2020. The study was done Dr. Sirajul Islam Medical College and Hospital Ltd, Dhaka, Bangladesh and done by the Department of Ophthalmology. The sampling technique used is systematic random sampling. However, those patients who had examination followed up ocular comorbidity such as glaucoma, age-related macular degeneration, corneal opacity, intra- or postoperative complications, previous history of ocular trauma, and systemic health problems as in diabetes mellitus and hypertension were excluded from the study.Ophthalmological examination was uncorrected and best corrected visual activity measurement. Distant BCVA for each eye was measured by using log mar chart; anterior segment examination by slit lamp; Measurement of intraocular pressure (IOP) by Goldman applanation tonometer; Dilated fundus examination using slit lamp bio microscopy and a non-contact fundus lens. Follow up was done every 4 months. Data was entered in MS Excel and Statistical analysis was done using SPSS trial version 22. Institutional Ethical committee clearance obtained.

RESULTS

In the present study, the demographic data showed that Majority of cases who Ocular Toxicity in Patients on Long-term Antipsychotic Drugwere 31-40 years (44%) of age. The total study population was 100 Patients aged 20 years to ≥60 years, 26.0% were 20 years to 30 years, 44.0% were 31 years to 40 years, 22.0% were 41 years to 50 years and 8.0% ware≥60years.Majority of cases who atypical antipsychotic medicationswere Typical alone years (14%) of study population. The total study population was 100 Patients according to typical and atypical antipsychotic medications14% population were Typical alone, 16% population was Atypical alone and 70% population was both. There was non-significant relation between visual acuity and the type of antipsychotic drug used for both eyes (p = 0.841 and 0.617 for right and left eyes respectively). Table 3 showing that intraocular pressure in studied cases ranged from 8.0 - 24 with a mean of 13.84 ± 3.89 in the right eye while intraocular pressure in left one ranged from 8.0 - 24 with a mean of 13.85 ± 4.04. Eleven cases (11%) show increased intraocular pressure (more than 21 mmHg) seven cases of them treated with combination therapy and four cases of them on typical only but no cases of elevated intraocular pressure among cases treated with atypical antipsychotics alone.

Table-I: Distribution of study patients by age (n=100)

Age	n=100	%
20 years to 30 years	26	26.0
31 years to 40 years	44	44.0
41 years to 50 years	22	22.0
≥60 years	8	8.0
Total	100	100.0

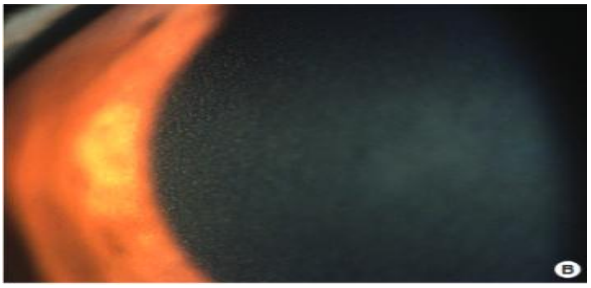

Photo I (Corneal opacity)

Photo II (Lens opacity)

Photo III (Increased cup to disc ratio)

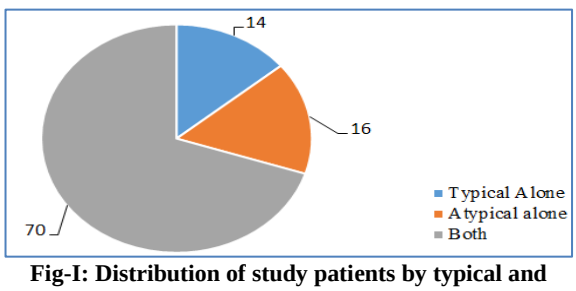

Fig-I: Distribution of study patients by typical and atypical antipsychotic medications (n=100)

Table-II: Relation between the type of the used antipsychotic drug and I.O.P.

I.O. P	Drugs			H	P
	Typical	Atypical	Both		
Right					
Min. – Max.	12.0 – 24.0	10.0 – 16.0	8.0 – 24.0	8.353*	0.015*
Mean ± SD.	16.14 ± 5.27 1	12.0 ± 1.26	13.80 ± 3.77		
Median	13.0	12.0	12.0		
Left					
Min. – Max.	12.0 – 24.0	8.0 – 14.0	8.0 – 24.0	6.803*	0.033*
Mean ± SD.	16.14 ± 5.27 1	11.88 ± 1.36	13.84 ± 3.97		
Median	13.0	12.0	12.0		

Table-III: Correlation between duration and I.O.P (n= 100).

I.O. P	Duration	
	r_s	P
Right	0.454*	<0.001*
Left	0.379*	<0.001*
Correlation between duration and I.O.P(typical alone)		
Right	0.698*	0.005*
Left	0.779*	0.001*
Correlation between duration and I.O.P (Atypical alone)		
Right	0.007	0.987
Left	-0.248	0.353
Correlation between duration and I.O.P (both)		
Right	0.482*	0.001*
Left	0.419*	0.001*

Table-IV: Relation between duration of treatment with I.O.P

I.O.P	Duration of the treatment (years)						P
	<5 (n=17)	5 - <10 (n=28)	10 - <15 (n=7)	15 - <20 (n=8)	20 - <25 (n=3)	25+ (n=3)	
Right							
Min. – Max.	8.0 – 16.0	10.0 – 15.0	12.0 – 18.0	10.0 – 20.0	12.0 – 14.0	22.0 – 24.0	<0.001
Mean ± SD. * 1	12.0 ± 1.58						
Median	12.0						
Left							
Min. – Max. 1	10.0 – 14.0 8	8.0 – 18.0 1	12.0 – 22.0	10.0 – 22.0	10.0 – 15.0	22.0 – 24.0	<0.001*
Mean ± SD.	12.06 ± 1.03	12.43 ± 1.83	14.14 ± 3.67	14.75 ± 4.68	12.33 ± 2.52	23.14 ± 0.69	
Median	12.0	12.0	12.0	12.50	12.0	23.0	

DISCUSSION

Eleven patients (39%) were on phenothiazines, visual acuity was normal in 82% of cases. A slight reduction of visual acuity was found in 16% of them, and only 2% had moderate reduction of its visual acuity. For the cornea, in the present study, all of them were on typical antipsychotics. There was non-significant relation between corneal opacity and duration of treatment with antipsychotics and also there was non-significant relation between corneal opacity and duration of treatment with typical antipsychotics alone. Obviously there were no cases with corneal opacity among patients treated with atypical antipsychotics alone or combination therapy. Those results were in accordance to some study [15, 16] who recorded in their previous reports ocular adverse effects like a cataract of the lens and corneal endothelial deposits with prolonged use of chlorpromazine. Also, they reported three patients who developed corneal deposits and cataracts in both eyes secondary to prolonged chlorpromazine use resulting in visual impairment. For typical antipsychotics, different studies revealed that the use of high doses typical antipsychotics for long periods is very much associated with eye opacities. Patients exposed to 800 mg/ day for 2 years exhibited such findings which consist of swirling lines or fine streaks in the corneal epithelium [7, 17]. That is not a serious condition because it does not cause visual impairment and tends to disappear, or at least diminish, after cessation of the drug [17]. In another study, reported that 33% of patients using long term chlorpromazine have shown deposits in the cornea that was in near agreements with the present study as it was 28% on typical alone. On the other hand, no changes were found in the cornea in all cases treated with antipsychotics in a study done by Souza, et al. [14]. Regarding the lens in the present patients, only 7% of studied cases suffered from cataract. There was a significant relation between lens opacity and duration of

treatment with typical antipsychotics alone. That was in accordance to some study [18], who mentioned that Cataractous changes can result from antipsychotics, mainly high dosages typical antipsychotics for prolonged periods, they frequently cause lenticular opacifications [19], reported that typical antipsychotics, particularly the phenothiazines and with the exception of haloperidol, increase risk of cataract. This unwanted effect is related to the drug used and the dose. For typical antipsychotics [7], reported that the use of high doses for long periods was very much associated with eye opacities. They explained that as the atypical antipsychotics were used his dataset 1.5 to 2.5 times more in than typical antipsychotics, a trend reflecting current practice methods for psychosis and other antipsychotic indications. Furthermore, the most prevalent typical antipsychotic in current use, haloperidol, has not been shown to increase cataract risk. As regards to atypical antipsychotics there was much debate as to whether the atypical antipsychotics can cause cataract or not. Studies on dogs received four times the recommended human dose of atypical antipsychotics revealed cataract occurrence [20]. That may be explained by diabetogenic changes that sometimes occur with certain antipsychotics (e.g. olanzapine and clozapine) and an increased risk for cataractous changes (probably due to the effect of hyperglycaemia on the eye) [7]. In contrast, some study indicated in their studies that are no risk of cataract in their patients, and they explained that by presence of serotonin receptors in the intraocular lens which play an important role in lens transparency [14, 19]. And serotonin itself was found to be cataractogenic in animal models [23] Serotonin levels are increased with the use of serotonin reuptake inhibitors and have been associated with an increased risk of cataract. A serotonin receptor blocker may provide a potential protective role. Atypical antipsychotics also demonstrate variable abilities to block muscarinic and histamine receptors. Topical miotics and anticholinesterases have a history of cataractogenesis [24], also certain atopic conditions associated with cataracts have elevated histamine levels in ocular tissues [25]. Therefore, the inhibition of these receptors provides further possibilities for the potential protective effect of atypical antipsychotics. Some study reported trials in monkeys (at 5.5 times the recommended human dose) that did not increase cataract formation [7].

Ocular changes during quetiapine therapy were observed in humans and a periodic ophthalmic evaluation is formally recommended for patients taking this drug. In our study, just one patient had taken quetiapine at 50 mg/day for 1 year. This 35-year-old male patient had cortical cataract, with no clouding of anterior capsule, and he had taken phenothiazines, levomeprazine and fluphenazine for 23 years. In addition, he was used to smoking 20 cigarettes a day, so being exposed to several risk factors for this lenticular pathology. Some study reported lenticular opacities in 15 patients who had taken quetiapine, at a rate of 0.005%, which is much lower than in the general population. Some study reported a case of a patient who had no lenticular opacities on the examination of the lens right before the onset of treatment with quetiapine and 15 months after the use of this drug cataract has been formed. Thus, patients from group 1 who had a rate of use of benzodiazepines higher than that form group 2 could have been exposed to one additional contributing factor. Schizophrenia itself does not appear to be associated with an increased risk and studies have shown that the use of a general antipsychotic drug is not associated with the occurrence of cataract but long-term chlorpromazine and other phenothiazines use is related to cataract formation.

CONCLUSION

It was concluded that ocular toxicity was manifested mainly with phenothiazine therapy that affected by duration of treatment. The incidence of toxicity decreased with combination of typical and atypical. It is recommended that psychiatrists, ophthalmologists and patients need to be aware of and prepared for any medication-induced ocular toxic effect.

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