



# Psychotropic Drugs and Ocular Side Effects

## Psikotropik İlaçlar ve Oküler Yan Etkileri

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### Summary

Nowadays the number of patients using the types of drugs in question here has significantly increased. A study carried out in relation with the long term use of psychotropic drugs shows that the consumption of this group of drugs has substantially increased in terms of variety and quantity. This compilation is arranged in accordance with the ocular complications of psychotropic drugs in long term treatment profile of numerous patients to the results of related literature review. If the doctor and the patients are informed about the eye problems related to the use of psychotropic drugs, potential ocular complications can be easily prevented, supervised and controlled and can even be reversed. (Turk J Ophthalmol 2013; 43: 270-7)

**Key Words:** Psychotropic drugs, ocular, side effects, adverse effects

### Özet

Günümüzde kronik ilaç kullanan hasta sayısı önemli derecede artmıştır. Uzun süreli psikotrop ilaç kullanımı açısından yapılan bir çalışma, hem çeşitlilik hem de miktar açısından bu grup ilaç tüketiminin önemli derecede arttığını göstermektedir. Bu derleme günümüzde çok sayıda hastanın uzun süreli tedavi profilinde yer alan psikotrop ilaçların oküler komplikasyonlarına ilişkin literatür taraması sonucu hazırlanmıştır. Hekim ve hastalar psikotrop ilaç kullanımına bağlı göz problemleri açısından bilgilendirildiklerinde potansiyel oküler komplikasyonlar kolayca önlenir, gözlem ve kontrol altına alınabilir ve hatta geriye döndürülebilirler. (Turk J Ophthalmol 2013; 43: 270-7)

**Anahtar Kelimeler:** Psikotropik ilaç, oküler, yan etki, ters etki

### Introduction

Psychotropic drugs can potentially lead to many ocular adverse effects depending upon the idiosyncrasies, dosages and the interactions with specific mechanisms of the body organs. After liver, the eye is supposed to be the second most frequent organ to manifest drug toxicity. The visual system consists of numerous tissues derived from different origins and the eye has an extensive, rich blood supply although having a relatively small mass. Besides, neural tissues within the eye exhibit a very high metabolic rates. All these factors are important for the

human eye becoming sensitive to psychotropic treatments.

In this review, we report the ocular adverse effects of common psychotropic agents and conclude that the majority of the psychotropic drug induced eye disorders can easily be prevented, supervised and even be reversed, if both the clinicians and the patients become aware of ocular sign and symptoms.

### Antipsychotics

In typical antipsychotics, phenothiazine family forms the most examined group in psychotropic agents. The group of phenothiazines has the potential of creating ocular and

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dermatological side effects. Chlorpromazine, especially when used high dose, causes abnormal pigmentation in eyelids, interpalpebral conjunctiva, cornea and lens.<sup>1</sup> Moreover, epithelial keratopathy related to chlorpromazine is discussed by many writers in literature. Abnormal pigment accumulations related to chlorpromazine, especially dose of drugs used more than 2 grams daily develops secondarily.<sup>2-4</sup>

Typical antipsychotics also have effects on uveal tissues. Antipsychotics which have strong anticholinergic and/or antiadrenergic effects (such as chlorpromazine and fluphenazine) cause mydriasis and cycloplegia.<sup>4</sup> Due to this effect profile, the feature of weakening accommodation by phenothiazines is identified.<sup>5</sup>

Theoretically, anticholinergics and antiadrenergics which have high dose antipsychotics (such as phenothiazine) should be foreseen that they might form a risk factor in terms of angle closure glaucoma (ACG) Actually, when antipsychotics are compared with the tricyclic antidepressants (TCAs), they relatively have less effects on ocular smooth muscles and risk of producing ACG is far less in proportion to TCA.<sup>6</sup> A report on ACG induced with antipsychotics has not been encountered in literature.

Almost all drugs in the group of antipsychotics can form eye opacity. Chlorpromazine and thioridazine are the mostly examined two drugs in this group<sup>1,5,7,8</sup> This unwanted side effect is related to drug being used and the dose. Eye opacities emerge after using high dose. In 35 of 61 patients who have used 800 mg of chlorpromazine for two years have faced the development of pigment accumulation.<sup>9</sup> In another study, 33% of 384 patients using long term chlorpromazine have shown deposits in the lens and cornea.<sup>10</sup> However, there is not a finding of risk of high opacity creation subject to phenothiazines in relation with exact dose/period relation yet.<sup>11</sup>

Butyrophenones such as haloperidol do not show cataractous effect in long term use.

In treatments by typical antipsychotics, oculogyric crisis is not a side effect seen rarely. It can be quickly seen after the haloperidol injection form treatment in 12-24 hours.<sup>12</sup>

Antipsychotic drugs also show effects on retina which is ontogenetically a part of the brain. Most frequently retinal lesion occurring as a result of using phenothiazine is retinitis pigmentosa. Phototoxic period plays an important role both in retinitis pigmentosa and retinal degeneration Pigment accumulation progresses from periphery retina through centre area. By this way, periphery vision loss, night blindness, centre scotoma and as a result total lost of sight is developed.<sup>13-15</sup> Knowing this retinal diseases' early symptoms is highly important in terms of controlling it before disease progression. Before the occurrence of retinitis pigmentosa these patients state either that they have visual haze or loss in the scotopic vision sharpness. If these initial

symptoms are early diagnosed and the use of drugs are stopped, disease progression can be prevented. In this case, even if the pigmentation is permanent, an increase in vision function can be provided.<sup>15</sup> A study done on dogs has shown that histological lesions are clear and retinitis pigmentosa has an aptness to be irreversible.<sup>16</sup>

In most cases where the retinal complications are stated, thioridazine is shown as the responsible drug. Less frequently, cases related to chlorpromazine and rarely to other phenothiazines are stated.<sup>4,13,15</sup> Retinopathy can be seen on people who have used high dose phenothiazine in long term. The dangerous quantities for thioridazine regarding retina are 800 mg, and especially doses over 1000 mg daily.

For chlorpromazine, this side effect is related to the dose and period. Unwanted effects related to thioridazine rises earlier when compared to the other phenothiazines. In high dosed treatments, toxic cases can be seen in weeks. After retinopathy being induced with phenothiazine, retina undergoes pigment epithelium and there develops a heavy vision loss.<sup>1,4,13,14,15</sup>

Discussion on potential of atypical antipsychotics forming cataract is still present. Especially the studies in relation to quetiapine and the relation of this drug to cataract are worth referring.<sup>17</sup> When the recommended dose of quetiapine for people is given four times to the dogs, cataract is seen but although this drug is used on monekys 5 times the dose given to people, it has not increased the risk of cataract formation.<sup>17</sup> In the survey of PubMed, the case of cataract induced with quetiapine on humans is not described. However, the producing company mentions about the cases which may cause changes in the lens and the relation of these changes with quetiapine is not defined literally.<sup>17</sup> Cataract can be formed due to numerous different reasons as well as the age and even it is related to a drug, causal relation cannot be explained literally. Nevertheless the producing company offers routine eye examination to the users of this drug.<sup>11,18</sup>

The effects of clozapine and risperidone, which especially provide an effective treatment for resistant schizophrenia, on formation of cataract is not known. Developing lens changes are rarely mentioned on the prospectus of ziprasidone and olanzapine.<sup>11</sup> Despite this, in study done on all users of atypical antipsychotic agents, potential of forming of cataract is found less than in it is in population.<sup>11</sup> In a 55 year old patient being treated with long term clozapine, the development of pigmentary changes and stellate cataract affecting cornea and retina have been notified. This is the only case notifying the pigmentation development in association with the use of clozapine.<sup>19</sup> Diabetogenic effect, formed by certain antipsychotics such as olanzapine ve clozapine, might cause an increase on risk of cataractous change on lens. There is not a known relation between aripiprazole and secondary cataract. It is indicated

that amisulpride might cause secondary pseudomyopia and supplementation of anticholinergic agent might be effective on this side effect.<sup>20</sup> In a study done with schizophrenic patients using antipsychotics, abnormalities have been determined on the users of ziprasidone on intraocular pressure and optical disc cavitation ratios.<sup>21</sup> In literature, there is a case of transient myopia induced with aripiprazole.<sup>22</sup>

When the atypical antipsychotics are compared to typical ones, dystonic reactions and therefore cause of oculogyric crisis are not expected. In literature, there are stated oculogyric crisis cases concerning clozapine, aripiprazole, amisulpride, ziprasidone and sertindole. Here, the responsible mechanism can be striatum sensitisation due to the use of typical antipsychotics and underlying genetic predisposition in some patients.<sup>23-27</sup>

Not only with unaccepted new antipsychotics in the treatment process, but also in the early periods of the treatment and semiannual periods in long term periods, an eye examination is recommended.

## Antidepressants

### Tricyclic Antidepressant Agents (TCAs)

TCAs can cause serious ocular side effects in the early periods of the treatment.<sup>28,29</sup> The most two common side effects are mydriasis and cycloplegia. When mydriasis occur on a person that TCAs has no tolerance on ocular smooth muscles, visual haze and/or myopia arise. Cycloplegia is related to the paralytic effect on ciliary muscle. Mydriasis and cycloplegia rise in result of TCAs' anticholinergic effect. Moreover, noradrenaline uptake blockage and alpha-adrenergic receptor blockages should also be considered in effective mechanisms.<sup>29</sup> Visual haze in patients having TCA treatment is seen in the early periods of the disease and in one third of the patients roughly. Patients generally develop tolerance to this side effect and vision function returns to normal in the forthcoming days of the treatment instinctively. If the visual haze and wish for remaining the TCA treatment continue, topical cholinergic agonist (pilocarpine) can be used additionally.<sup>6</sup> The weaker the TCAs in terms of anticholinergic, the lesser the frequency and intensity of visual symptoms.

TCAs can trigger glaucoma attacks in people inclined to angle closure due to anterior chamber anatomy. This case is fundamentally related to these drugs' anticholinergic effect (mydriasis and cycloplegia).<sup>28,30,31</sup> In 1994, Ritch et al.<sup>30</sup> have stated that in 4 narrow- angled patients, who were given oral imipramine in routine dose, acute angle closure triggered glaucoma attack. For this reason, TCAs should be carefully prescribed in narrow-angled patients and these patients should be kept under supervision by their ophthalmologist during the treatment.

The decrease of lacrimation of TCAs due to anticholinergic effect does not cause a substantial problem clinically.<sup>32</sup>

Amitriptyline has caused visual haze and ocular irritation on a patient and when the use of drugs were stopped the symptoms disappeared.<sup>33</sup> In practice, artificial tears are very useful in overcoming this side effect.

Amitriptyline, which is a TCA, has caused the increase of palpebral aperture. This case has formed an appearance similar to exophthalmos. Mechanism and the importance of clinical situation is not known yet.<sup>34</sup>

Mianserin can be confidently used in patients with glaucoma.<sup>35</sup>

Development of bilateral ACG is stated in a 71 year old patient using maprotiline and alprazolam.<sup>36</sup>

Planopsia is seen in three patients using trazodone. Its mechanism is not known and the effect has a relation with the dose. Decreasing the dose or stopping the use of antidepressants has removed planopsia.<sup>37</sup>

### Selective Serotonin Reuptake Inhibitors (SSRI's)

The drugs in this group are the drugs mostly used as antidepressants and anxiolytic. Since their use in 1980, they have been used by millions of people in the world.<sup>38</sup> Fluoxetine, fluvoxamine, citalopram, escitalopram, paroxetine and sertraline are all SSRIs. They all increase serotonergic conduction in SSRI; this effect develops secondarily on the reuptake inhibition of serotonin synapse level. These drugs generally have the perfect profiles of security and tolerance. Possible ocular side effects related to SSRI are mydriasis, increase in intraocular pressure (IOP), glaucoma and oculogyric crisis.<sup>38-40</sup> In the studies done with the patients being treated by SSRI, the most common reason of patients leaving the study was the rise of visual impairment.<sup>41-43</sup>

It is propounded that mydriasis related to SSRI, increased IOP and development of glaucoma have a relation between themselves.<sup>38,44-50</sup>

There are seven different serotonin receptor families (5HT1-5HT7). Serotonin receptors functioning in eye are; 5-HT1A, 5-HT2A, 5-HT2C ve 5-HT7.<sup>38,40,51-55</sup> All these receptors have a role in IOP dynamics and effect can be seen on IOP increase and development of glaucoma. With the effect of serotonin on pupil sphincter localized 5-HT7 receptor and as a result of activation of adenylate cyclase it causes an increase in c-AMP and muscle relaxation and rise passive mydriasis.<sup>38-53</sup>

It is shown that SSRIs such as sertraline, paroxetine, fluoxetine and citalopram specifically cause pupil dilation.<sup>38,56,57</sup>

As long as the mydriatic effect of SSRIs does not cause a dramatical increase in IOP and the development of glaucoma, it does not cause a major visual impairment or problem. If the mydriatic effect related to SSRI are complicated with ACG, the side effect disappears by stopping the use of drug. Patients who will start using SSRI are recommended ophthalmologic examination and the investigation of the risk of angle closure

presence.

Paroxetine, which has the strongest potential in terms of NA reuptake inhibition, is the most blamed agent in SSRI in terms of ACG.<sup>38</sup> Like in paroxetine, SSRI's and SNRI's like venlafaxine noradrenergic effects with sympathomimetic effects might cause active mydriasis. With passive mydriasis related to serotonergic activity, conglomeration and crowding occur in active mydriasis at an important ratio. Therefore, aqueous outflow is prevented and glaucoma attack develops with IOP increase.<sup>38,51</sup> Indeed, more and more evidence has risen for the fact that IOP is increased by SSRIs day by day. With this, most of these cases are not reported, stays asymptomatic or turns into an ACG.<sup>38,51</sup> In the PubMed survey, 11 articles are stated reporting the glaucoma in relation with SSRI. While 6 of these are related with paroxetine, 2 are citalopram, one is escitalopram, one is Fluoxetine, one is Fluvoxamine, there is not case notified on sertraline.<sup>38,44,50,58,59,60</sup> For this reason, paroxetine is responsible for most of the glaucoma cases.<sup>38</sup> In three of the six cases paroxetine is identified in geriatric patients (aged between 70-91), 2 of the cases are used in young patients who are hypermetropic and plateau iris configuration is identified in one patient.<sup>25,61</sup>

Two glaucoma attacks related with the use of citalopram are described. One of the cases is an alcoholic woman used overdose of citalopram and the other is described as a patient using citalopram regularly.<sup>58,59</sup>

In literature, ACG related with escitalopram is described in one case. The use of escitalopram in a 41 year old woman caused rotation in anterior chamber angle as a result of uveal effusion and development of acute bilateral ACG. The use of escitalopram is stopped steroid treatment is started and the patient has shown complete recovery.<sup>60</sup>

Fluoxetine is the first SSRI correlated with ACG. ACG has developed in a young man patient after using oral fluoxetine for 5 weeks.<sup>44</sup> The patient's tendency to angle closure anatomically is not known. Apart from this, the symptomatic glaucoma case related with his drug is not reported but the experimental studies have shown that fluoxetine might cause a significant IOP increase both on animals and human beings.<sup>51,62</sup>

In conclusion, a 66 year old male patient was started using fluvoxamine for headache and ACG has developed. When the use of drug was stopped, the symptoms of high IOP disappeared.<sup>50</sup>

In addition to these articles, in the report of "Australian Adverse Drug Reaction Bulletin of February 2001" 11 glaucoma attacks related to SSRI are stated. Three of the cases were associated with fluoxetine and paroxetine, 4 with sertraline and 1 with citalopram. The age of the patients varied between 32-70, most of them were asymptomatic and the GIB increase was determined at the routine examination.<sup>63</sup>

In this case, the need of taking precaution before prescribing

SSRI for patients who have the potential of IOP increase arises. Ophthalmologic consultation should be done periodically before starting antidepressant treatment and during the usage period especially on people with glaucoma predispose. If there is a case of glaucoma, the use of drug should be stopped immediately and medical surgery should be started by the ophthalmologists.<sup>64</sup>

One case of decreased visual acuity as a result of maculopathy related with sertraline is described.<sup>65</sup> In this patient, maculopathy was solved after stopping the use of antidepressant drug but in the following 20 months the visual acuity remained the same on suboptimal level. In this study, there is not an explanation on causality. Retinal vein occlusion is stated in relation to citalopram and fluoxetine.<sup>66,67</sup>

The use of SSRI may cause extrapyramidal symptoms. In compilation of the articles, akathisia is reported as the most extrapyramidal side effect in relation with SSRI after dystonia.<sup>68,69</sup> Gerber et al.<sup>69</sup> have identified 127 extrapyramidal symptoms induced with SSRI. 19 of these symptoms are described as dystonia. Dystonia generally affects the muscles which are not related with eye but it rarely holds the eye muscles and visual symptoms arise.

In a case where escitalopram is being used, dose related ocular dystonia and anaphylactic symptoms are stated.<sup>39</sup> While "ocular dystonia and SSRI" is the only arisen case in PubMed, this patient was thought to have developed panic attack but dystonic symptoms disappeared after IM adrenalin injection.

## Benzodiazepines

These are the drugs mostly used in anxiety, insomnia, agitation and many other psychiatric situations. Development of allergic conjunctivitis related to the use of diazepam is previously reported.<sup>70</sup> This situation is only notified for diazepam and no relation is identified on ocular allergy development in relation to other benzodiazepines (e.g.: clonazepam, lorazepam).<sup>32</sup> In this case, if ocular allergy develops as a result of the use of diazepam, use of another benzodiazepine is recommended.

Only one case and diazepam is presented as it might cause ACG.<sup>71</sup> For this reason, it can be said that benzodiazepines out of diazepam are secure in terms of glaucoma.

Clonazepam is stated to cure acquired nystagmus.<sup>72-74</sup> In the year of 2001, Young et. al.<sup>75</sup> have shown that clonazepam is 100% effective in treatment of 5 patients with idiopathic downbeat nystagmus.

In another article published in 2006, Giersch et.al.<sup>76</sup> have made literature review on visual acuity of benzodiazepines on acute or chronic basis and the effect on contrast sensitivity. In addition, 15 patients who had a long term treatment of lorazepam were compared to healthy control group. As a result, the use of benzodiazepine was determined to have a global loss on contrast sensitivity.<sup>76,77</sup> Furthermore, the rise of development of contrast

sensitivity and exophoria in patients using long term lorazepam is found to be free of sedative efficiency of benzodiazepines. Visual acuity has remained normal on these patients. Due to this reason, it is propounded that testing visual acuity singly will not be determinant in terms of all visual dysfunctions .

### Antiepileptics

Carbamazepine is not only in the group of antiepileptic drugs but also used in treatment of some psychiatric illnesses such as affective disorders.<sup>78</sup>

In a 22 year old asymptomatic case in 2007, the use of carbamazepine was blamed for the development of conjunctival squamous metaplasia.<sup>79</sup> In this case, cause and effect relation is not proven and carbamazepine is still thought to be a secure drug for conjunctiva.

In a prospective study on 45 patients of epilepsy who were long term treated with carbamazepine and valproic acid, a change related to retinal nerve fiber layer and macula thickness is not determined.<sup>80</sup> Nowadays, valproic acid, which is used as a mood stabilizer and an antiepileptic drug, is not determined as a cause for important or irreversible visual impairment.<sup>80,81</sup>

In relation with the use of carbamazepine , it is stated that two epileptic middle-aged female patients using this drug for more than 7 years have developed retinopathy.<sup>82</sup> However, the causal relation between carbamazepine and retinopathy could not be established in these cases. Despite this, when the use of carbamazepine was stopped, both the symptoms and objective retinal findings receded.<sup>82</sup>

Ocular dystonia related to carbamazepine is reported several times.<sup>83,84</sup> When the other antiepileptics are used as polytherapy, carbamazepine might cause various eye movement disorders including muscle palsy. This antiepileptic drug may cause dystonia both on ordinary and toxic dose.<sup>84-86</sup> At the same time it may rarely cause a idiosyncratic type of dystonia.<sup>83</sup>

Carbamazepine may induce a slight but specific colour vision disability. In patients of one year carbamazepine treatment, central and paracentral colour vision function decrease transparently.<sup>87</sup> However, as this case was not identified in some human studies, this effect is not accepted by everyone.<sup>72</sup> In a cross-sectional study done on 18 patients being treated by valproate monotherapy for two-twenty years, colour vision defect was only seen on 2 patients at minor level.<sup>88</sup> Cones sensitive to short wavelength are thought to be effected by antiepileptic drugs. This rarely seen side effect mostly stays at subclinical level and does not require monitoring. Visual acuity is protected permanently.<sup>88</sup>

### Lamotrigine

This drug is used in the treatment of bipolar disorders.

In some neuropathic pains it has a therapeutic efficiency.<sup>89</sup> Lamotrigine rarely causes nystagmus.<sup>90,91</sup> In 2005, Alkawi et.al.<sup>91</sup> have presented two down-beat nystagmus cases related to lamotrigine toxicity. These kind of cases are seen in low-ordinary doses. Authors warn that lamotrigine might form this kind of unwanted ocular effects on high doses. When used with valproat, lamotrigine prolongs the half life and risk increases. Disorders in diplopia and eye movements are especially stated in low-high dose lamotrigine monotherapy.<sup>72,91</sup> When lamotrigine is used in high dose or combined with carbamazepine, eye movement anomalies should be expected.<sup>92,93</sup>

### Lithium

It is the oldest and very important mood stabilizer and can be effective apart from bipolar disorders. Mechanism of action is not entirely known and it changes sodium transport during nerve and muscle cell membranes, shows effect on intracellular signals and causes nerve cell membrane stabilization.<sup>89</sup> A side effect in relation with lithium is the case irritation in eye which is generally observed at the first week of the treatment.<sup>94</sup> The reason of this side effect is explained with the increase in lacrimal fluid sodium content. Lauf et.al.<sup>95</sup> have shown the presence of sodium-chlorine co-transport in lens epithelium cells. Irritation is thought to be developed due this effect. The complaint of the patients is for a short time. It is possible to keep it under control with the use of artificial tears.

Lithium can form various ocular effect including therapeutic doses. The adversity in all these is down-beat nystagmus.<sup>96-99</sup> By reducing the dose of lithium or stopping the use of drug makes the side effect disappear. Nystagmus may rarely remain despite stopping the use of drug.<sup>98</sup> In these cases, disorders in slow-observer eye movement at subclinical level may arise.<sup>96</sup>

Until today only 5 cases have notified optical disc edema in the ones using lithium at therapeutic dose. Blurred vision and papilledema end by stopping the use of the drug. Papilledema and related symptoms appear in patients who continue using the drug.<sup>100</sup>

### Conclusion

Long term use of psychotropic drugs is gradually becoming widespread and occurrence incidence of ocular side effects belonging to these drugs is increasing concordantly. Knowing the side effects of psychotropic agents potentially is extremely important. Rare ocular problems rising in relation to use of these drugs have important effect on psychiatric patients' physical and psychical situations who have a tendency to be crumpled. When an anxious, psychotic, depressed or agitated patient meets an ocular disorder which will cause trouble in his/her daily life, he/she will feel himself/herself worse.

Typical antipsychotics, TCAs, lithium, benzodiazepins, carbamazepin and topiramate are drugs known for causing ocular problems.

Thioridazine, which is a phenothiazine, may cause retinitis pigmentosa in high doses and visual impairment related to this.

Chlorpromazine, which is another phenothiazine antipsychotic, not only causes rare pigmentary or granular retinosis but also mostly causes benign natured pigmentary segregation on these tissues on lens or cornea with photosensitization mechanism. Corneal edema is the rarely occurring most serious visual disorder related to chlorpromazine.

Butyrophenones create serious risk of oculogyric crisis and although these dystonic reactions are reversible, they irritate the patient substantially.

TCAs mostly cause accommodation disorder. When compared with the side effect of serious angle closure glaucoma which mostly develops in narrow-angled eyes, accommodation disorder can be qualified as a slight and temporal side effect.

SSRIs form mydriatic effect. They may cause glaucoma attacks in patients at the risk of angle closure.

Benzodiazepines have the potential to form various eye movements related to dose. For this reason, it should not be used while consuming alcohol and driving.

Antiepileptic type of mood stabilizers also cause eye movement disorder. Carbamazepine provokes nystagmus and sometimes causes oculogyric crisis.

Lamotrigine, especially when combined with valproate, causes clear eye movement disorders. Valproate rarely causes subclinical colour perception disorders.

Topiramate causes myopic situation as well as nystagmus and other eye movement disorders. On sensitive individuals as a result of idiosyncratic reaction induced with topiramate, all lens and ciliary body complex faces transformation (if the use of drug is stopped, it is reversible). This situation causes refraction defects, obstruction in angle and decrease in vision.

Lithium, especially at high doses, causes down-beat nystagmus.

If psychiatrists, ophthalmologists and patients are informed on side effects of the drugs and precautions are taken in the early period, most of serious and potential irreversible ocular damage can be prevented.

## References

- Li J, Tripathi RC, Tripathi BJ. Drug-induced ocular disorders. *Drug Saf.* 2008;31:127-41.
- Bond WS, Yee GC. Ocular and cutaneous effects of chronic phenothiazine therapy. *Am J Hosp Pharm.* 1980;37:74-8.
- Johnson AW, Buffalo WJ. Chlorpromazine epithelial keratopathy. *Arch Ophthalmol.* 1966;76:664-7.
- Edler K, Gottfries CG, Haslund J, Ravn J. Eye changes in connection with neuroleptic treatment especially concerning phenothiazines and thioxanthenes. *Acta Psychiatr Scand.* 1971;47:377-84.
- Hansen TE, Casey DE, Hoffman WF. Neuroleptic intolerance. *Schizophr Bull.* 1997;23:567-82.
- Oshika T. Ocular adverse effects of neuropsychiatric agents: incidence and management. *Drug Saf.* 1995;12:256-63.
- Feldman PE, Frierson BD. Dermatological and ophthalmological changes associated with prolonged chlorpromazine therapy. *Am J Psychiatry.* 1964;121:187-8.
- Greiner AC, Berry K. Skin pigmentation and corneal and lens opacities with prolonged chlorpromazine therapy. *CMAJ.* 1964;90:663-5.
- Satanove A. Pigmentation due to phenothiazines in high and prolonged dosage. *JAMA.* 1965;191:263-8.
- Siddall JR. Ocular complications related to phenothiazines. *Dis Nerv Syst.* 1968;29(Suppl):10-3.
- Shahzad S, Suleman MI, Shahab H, et al. Cataract occurrence with antipsychotic drugs. *Psychosomatics.* 2002;43:354-9.
- Jhee SS, Zarotsky V, Mohaupt SM, Yones CL, Sims SJ. Delayed onset of oculogyric crisis and torticollis with intramuscular haloperidol. *Ann Pharmacother.* 2003;37:1434-7.
- Siddall JR. Ocular toxic changes associated with chlorpromazine and thioridazine. *Can J Ophthalmol.* 1966;1:190-8.
- Hagopian Y, Stratton DB. Five cases of pigmentary retinopathy associated with thioridazine administration. *Am J Psychiatry.* 1966;123:97-100.
- Meredith TA, Aaberg TM, Willerson WD. Progressive chorioretinopathy after receiving thioridazine. *Arch Ophthalmol.* 1978;96:1172-6.
- Legros J, Rosner I, Berger C. Ocular effects of chlorpromazine and oxypertine on beagle dogs. *Br J Ophthalmol.* 1971;55:407-15.
- Seroquel\_ (quetiapine) [package insert]. Wilmington (DE); Zeneca Pharmaceuticals, 2001.
- Stip E, Boisjoly H. Quetiapine: are we overreacting in our concern about cataracts (the beagle effect) [abstract]? *Can J Psychiatry.* 1999;44:503.
- Borovik AM, Bosch MM, Watson SL. Ocular Pigmentation Associated With Clozapine. *Med J Aust.* 2009;190:210-1.
- Stratos AA, Peponis VG, Portaliou DM, Stroubini TE, Skouriotis S, Kymionis GD. Secondary Pseudomyopia Induced By Amisulpride. *Optom Vis Sci.* 2011;88:1380-2.
- Souza VB, Moura Filho FJ, Souza FG et al. Intraocular Pressure In Schizophrenic Patients Treated With Psychiatric Medications. *Arg Bras Oftalmol.* 2008;71:660-4.
- Nair AG, George RJ, Gandhi RA. Aripiprazole Induced Transient Myopia: A Case Report And Review Of Literature. *Cutan Ocul Toxicol.* 2012;31:74-6.
- Viana Bde M, Prais HA, Camargos ST et al. Ziprasidone-related Oculogyric Crisis In An Adult. *Clin Neurol Neurosurg.* 2009;111:883-5.
- Tutuncu R, Gunay H. Oculogyric Crisis With Sertindole Monotherapy. *Pharmacopsychiatry.* 2010;43:119-20.
- Mendhekar DN, Lohia D, Kataria P. Tardive Oculogyric Crisis Associated With Amisulpride Monotherapy. *J Postgrad Med.* 2010;56:305-6.
- Uzun O, Doruk A. Tardive Oculogyric Crisis During Treatment With Clozapine: Report Of Three Cases. *Clin Drug Investig.* 2007;27:861-4.
- Bhachech JT. Aripiprazole-induced Oculogyric Crisis. *J Pharmacother.* 2012;3:279-81.
- Lieberman E, Stoudemire A. Use of tricyclic antidepressants in patients with glaucoma: assessment and appropriate precautions. *Psychosomatics.* 1987;28:145-8.
- Shur E, Checkley S. Pupil studies in depressed patients: an investigation of the mechanism of action of desipramine. *Br J Psychiatry.* 1982;140:181-4.
- Ritch R, Krupin T, Henry C, Kurata F. Oral imipramine and acute angle closure glaucoma. *Arch Ophthalmol.* 1994;112:67-8.
- Lowe RF. Amitriptyline and glaucoma. *Med J Aust.* 1966;2:509-10.
- Malone Jr DA, Camara EG, Krug Jr JH. Ophthalmologic effects of psychotropic medications. *Psychosomatics.* 1992;33:271-7.
- Litovitz GL. Amitriptyline and contact lenses [letter]. *J Clin Psychiatry.* 1984;45:188.
- Goode DJ. Increased palpebral aperture in a patient receiving amitriptyline. *Am J Psychiatry.* 1977;134:1043-4.

35. Calanca MA. Indications For Mianserin In Relation To Its Absence Of Side Effects. *Acta Psychiatr Belg.* 1978;78:781-6.
36. Kadoi C, Hayasaka S, Tsukamoto E, Matsumoto M, Hayasaka Y, Nagaki Y. Bilateral Angle Closure Glaucoma and Visual Loss Precipitated by Antidepressant and Antianxiety Agents In a Patient With Depression. *Ophthalmologica.* 2000;214:360-1.
37. Hughes MS, Lessell S. Trazodone-induced palinopsia. *Arch Ophthalmol.* 1990;108:399-400.
38. Costagliola C, Parmeggiani F, Sebastiani A. SSRIs and intraocular pressure modifications: evidence, therapeutic implications and possible mechanisms. *CNS Drugs.* 2004;18:475-84.
39. Patel OP, Simon MR. Oculogyric dystonic reaction to escitalopram with features of anaphylaxis including response to epinephrine. *Int Arch Allergy Immunol.* 2006;140:27-9.
40. Schmitt JA, Riedel WJ, Vuurman EF, Kruizinga M, Ramaekers JG. Modulation of the critical flicker fusion effects of serotonin reuptake inhibitors by concomitant pupillary changes. *Psychopharmacology (Berl).* 2002;160:381-6.
41. Preskorn SH. Comparison of the tolerability of bupropion, fluoxetine, imipramine, nefazodone, paroxetine, sertraline and venlafaxine. *J Clin Psychiatry.* 1995;56(Suppl 6):12-21.
42. Trindade E, Menon D, Topfer LA, Coloma C. Adverse effects associated with selective serotonin reuptake inhibitors and tricyclic antidepressants: a meta-analysis. *CMAJ.* 1998;159:1245-52.
43. Beasley CM Jr, Koke SC, Nilsson ME, Gonzales JS. Adverse events and treatment discontinuations in clinical trials of fluoxetine in major depressive disorder: an updated metaanalysis. *Clin Ther.* 2000;22:1319-30.
44. Ahmad S. Fluoxetine and glaucoma [letter]. *DICP.* 1991;25:436 .
45. Kirwan JF, Subak-Sharpe I, Teimory M. Bilateral acute angle closure glaucoma after administration of paroxetine [letter]. *Br J Ophthalmol.* 1997;81:252.
46. Lewis CF, DeQuardo JR, DuBose C, Tandon R. Acute angleclosure glaucoma and paroxetine. *J Clin Psychiatry.* 1997;58:123-4.
47. Eke T, Bates AK. Acute angle closure glaucoma associated with paroxetine [letter]. *BMJ.* 1997;314:1387.
48. Bennett HG, Wyllie AM. Paroxetine and acute angle closure glaucoma. *Eye.* 1999;13:6912.
49. Browning AC, Reck AC, Chisholm IH, et al. Acute angle closure glaucoma presenting in a young patient after Administration of paroxetine. *Eye.* 2000;14:406-8.
50. Jimenez-Jimenez FJ, Orti-Pareja M, Zurdo JM. Aggravation of glaucoma with fluvoxamine. *Ann Pharmacother.* 2001;35:1565-6.
51. Costagliola C, Mastropasqua L, Capone D, Verolino M, Ciancaglini M, Pisanti N. Effect of fluoxetine on intraocular pressure in the rabbit. *Exp Eye Res.* 2000;70:551-5.
52. Tobin AB, Unger W, Osborne NN. Evidence for the presence of serotonergic neurons and receptors in the irisciliary body complex of the rabbit. *J Neurosci.* 1988;8:3713-21.
53. Chidlow G, Le Corre S, Osborne SS. Localization of 5-hydroxytryptamine1A and 5-hydroxytryptamine7 receptors in rabbit ocular and brain tissues. *Neuroscience.* 1998;87:675-89.
54. Osborne NN, Chidlow G. Do beta-adrenoceptors and serotonin 5-HT1A receptors have similar functions in the control of intraocular pressure in the rabbit? *Ophthalmologica.* 1996;210:308-14.
55. Tobin AB, Osborne NN. Evidence for the presence of serotonin receptors negatively coupled to adenylate cyclase in the rabbit iris-ciliary body. *J Neurochem.* 1989;53:686-91.
56. Deijen JB, Loriaux SM, Orlebeke JF, et al. Effects of paroxetine and maprotiline on mood, perceptual-motor skills and eye movements in healthy volunteers. *J Psychopharmacol.* 1989;3:148-55.
57. Ramaekers JG, Muntjewerff ND, O'Hanlon JF. A comparative study of acute and subchronic effects of dothiepin, fluoxetine and placebo on psychomotor and actual driving performance. *Br J Clin Pharmacol.* 1995;39:397-404.
58. Croos R, Thirumalai S, Hassan S, Davis Jda R. Citalopram associated with acute angle-closure glaucoma: case report [letter]. *BMC Ophthalmol.* 2005;5:23.
59. Massaoutis P, Goh D, Foster PJ. Bilateral symptomatic angle closure associated with a regular dose of citalopram, an SSRI antidepressant. *Br J Ophthalmol.* 2007;91:1086-7.
60. Zelefsky JR, Fine HF, Rubinstein VJ, Hsu IS, Finger PT. Escitalopram-induced effusions and bilateral angle closure glaucoma. *Am J Ophthalmol.* 2006;141:1144-7.
61. Levy J, Tessler Z, Klemperer I, Shneck M, Lifshitz T. Late bilateral acute angle-closure glaucoma after administration of paroxetine in a patient with plateau iris configuration. *Can J Ophthalmol.* 2004;39:780-1.
62. Costagliola C, Mastropasqua L, Steardo L, Testa N. Fluoxetine oral administration increases intraocular pressure [letter]. *Br J Ophthalmol.* 1996;80:678.
63. Adverse Drug Reactions Advisory Committee (ADRAC). SSRIs and increased intraocular pressure [abstract]. *Aust Adv Drugs Reac Bull.* 2001;20:3.
64. Tripathi RC, Tripathi BJ, Haggerty C. Drug-induced glaucomas: mechanism and management. *Drug Saf.* 2003;26:749-67.
65. Sener EC, Kiratli H. Presumed sertraline maculopathy. *Acta Ophthalmol Scand.* 2001;79:428-30.
66. Hardisty AD, Hemmerdinger CM, Quah SA. Citalopram Associated Central Retinal Vein Occlusion. *Int Ophthalmol.* 2009;29:303-4.
67. Knox Cartwright NE, Smith P, Tole DM. Branch Retinal Vein Occlusion And Fluoxetine. *Ann Ophthalmol.* 2007;39:253-4.
68. Leo RJ. Movement disorders associated with the serotonin selective reuptake inhibitors. *J Clin Psychiatry.* 1996;57:449-54.
69. Gerber PE, Lynd LD. Selective serotonin-reuptake inhibitor induced movement disorders. *Ann Pharmacother.* 1998;32:692-8.
70. Lutz M. Allergic conjunctivitis due to diazepam [abstract]. *Am J Psychiatry* 1975;132:548.
71. Hyams SW, Keroub C. Glaucoma due to diazepam. *Am J Psychiatry* 1997;134:447-8.
72. Hilton EJ, Hosking SL, Betts T. The effect of antiepileptic drugs on visual performance. *Seizure.* 2004;13:113-28.
73. Khouzam HR, Highet VS. A review of clonazepam use in neurology. *Neurobiologist.* 1997;3:120-7.
74. Rucker JC. Current treatment of nystagmus. *Curr Treat Options Neurol.* 2005;7:69-77.
75. Young YH, Huang TW. Role of clonazepam in the treatment of idiopathic downbeat nystagmus. *Laryngoscope.* 2001;111:1490-3.
76. Giersch A, Speeg-Schatz C, Tondre M, Gottenkiene S. Impairment of contrast sensitivity in long-term lorazepam users. *Psychopharmacology (Berl).* 2006;186:594-600.
77. Klein BE, Klein R, Knudtson MD, Lee KE, Danforth LG, Reinke JO, Adler AM. Associations of selected medications and visual function: the Beaver Dam Eye Study. *Br J Ophthalmol.* 2003;87:403-8.
78. Yu Y, Koss MC. Alpha(1A)-adrenoreceptors mediate sympathetically evoked pupillary dilation in rats. *J Pharmacol Exp Ther.* 2002;300:521-5.
79. Doughty MJ, McIntosh M, McFadden S, Button NF. Impression cytology of a case of conjunctival metaplasia associated with oral carbamazepine use? *Cont Lens Anterior Eye.* 2007;30:254-7.
80. Lobefalo L, Rapinese M, Altobelli E, et al. Retinal nerve fiber layer and macular thickness in adolescents with epilepsy treated with valproate and carbamazepine. *Epilepsia.* 2006;47:717-9.
81. Hansen TE, Casey DE, Hoffman WF. Neuroleptic intolerance. *Schizophr Bull.* 1997;23:567-82.
82. Nielsen NV, Syversen K. Possible retinotoxic effect of carbamazepine. *Acta Ophthalmol (Copenh).* 1986;64:287-90.
83. Berchou RC, Rodin EA. Carbamazepine-induced oculogyric crisis. *Arch Neurol.* 1979;36:522-3.
84. Henry EV. Oculogyric crisis and carbamazepine [letter].
85. Arnstein E. Oculogyric crisis: a distinct toxic effect of carbamazepine. *J Child Neurol.* 1986;1:289-90.
86. Gorman M, Barkley GL. Oculogyric crisis induced by carbamazepine. *Epilepsia.* 1995;36:1158-60.
87. Verrotti A, Lobefalo L, Priolo T, Rapinese M, Trotta D, Morgese G. Colour vision in epileptic adolescents treated with valproate and carbamazepine. *Seizure.* 2004;13:411-7.

88. Sorri I, Rissanen E, Mäntyjärvi M, Kälviäinen R. Visual function in epilepsy patients treated with initial valproate monotherapy. *Seizure*. 2005;14:367-70.
89. Stahl SM. *Essential psychopharmacology: the prescriber's guide*. Cambridge: Cambridge University Press, 2005.
90. Hadjikutis S, Morgan JE, Wild JM, Smith PE. Ocular complications of neurological therapy. *Eur J Neurol*. 2005;12:499-507.
91. Alkawi A, Kattah JC, Wyman K. Downbeat nystagmus as a result of lamotrigine toxicity. *Epilepsy Res*. 2005;63:85-8.
92. Besag FM, Berry DJ, Pool F, Newbery JE, Subel B. Carbamazepine toxicity with lamotrigine: pharmacokinetic or pharmacodynamic interactions? *Epilepsia*. 1998;39:183-7.
93. Loiseau P. Tolerability of newer and older anticonvulsants: a comparative review. *CNS Drugs*. 1996;6:148-66.
94. Pakes GE. Eye irritation and lithium carbonate [letter]. *Arch Ophthalmol* 1980;98:930.
95. Lauf PK, Chimote AA, Adragna NC. Lithium fluxes indicate presence of Na-Cl cotransport (NCC) in human lens epithelial cells. 2008;21:335-46.
96. Coppeto JR, Monteiro ML, Lessell S, Bear L, Martinez-Maldonado M. Downbeat nystagmus: long-term therapy with moderate-dose lithium carbonate. *Arch Neurol*. 1983;40:754-5.
97. Williams DP, Troost BT, Rogers J. Lithium-induced downbeat nystagmus. *Arch Neurol*. 1988;45:1022-3.
98. Rosenberg ML. Permanent lithium-induced down-beating nystagmus [letter]. *Arch Neurol*. 1989;46:839.
99. Halmagyi GM, Lessell I, Curthoys IS, Lessell S, Hoyt WF. Lithium induced downbeat nystagmus. *Am J Ophthalmol*. 1989;107:664-74.
100. Lobo A, Pilek E, Stokes PE. Papilledema following therapeutic dosages of lithium carbonate. *J Nerv Ment Dis*. 1978;166:526-9.