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OLGU SUNUMU / CASE REPORT

Acute angle closure glaucoma induced by selective serotonin reuptake inhibitor, and reversed by agomelatine

Selektif serotonin geri alım inhibitörünün neden olduğu ve agomelatin ile düzelen akut açı kapanması glokomu

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Abstract
Agomelatine, a MT1 (Melatonin) and MT2 receptor agonist and 5-HT2C (5-Hidroksitriptamin) antagonist, is an antidepressant agent used in the treatment of major depressive disorders. Intraocular pressure lowering effect of melatonin and its analogues have been demonstrated in a few experimental studies. In the present case report, we have documented the reversal of angle closure glaucoma by oral agomelatine in a patient with major depressive disorder under selective serotonine reuptake inhibitor treatment. The patient, who had previously been diagnosed with glaucoma, was also receiving antiglaucomatous treatment.
Keywords: Agomelatine, Angle closure glaucoma, Selective serotonin reuptake inhibitor

Öz
Bir MT1 ve MT2 reseptör agonisti ve 5-HT2C antagonisti olan agomelatin, majör depresif bozukluk tedavisinde kullanılan bir antidepresandır. Melatoninin ve analoglarının göz içi basıncı düşürücü etkisi birkaç deneysel çalışmada gösterilmiştir. Bu olgu sunumunda, oral agomelatin tedavisi ile düzelen açı kapanması glokomu aynı anda selektif serotonin geri alım inhibitörü alan majör depresif bozukluk tanılı bir hastada anlatılmaktadır. Daha önce glokom teşhisi konan hastaya ayrıca antiglokomatöz tedavi uygulanmıştır.

Anahtar kelimeler: Agomelatin, Açı kapanması glokomu, Seçici serotonin geri alım inhibitörü

INTRODUCTION

Patients who develop acute angle closure glaucoma (AACG) have usually small axial lengths and shallow anterior chambers. Family predisposition, female gender, Asian ethnicity and advanced age are among the other risk factors[1] AACG occurs when sudden blockage of the drainage angle by the iris. As a results of angle closure, intraocular pressure increases rapidly.

Systemic or local drugs can cause AACG. Selective serotonin reuptake inhibitors (SSRIs) are used in the treatment of psychiatric conditions such as depressive disorders, panic disorders, obsessive compulsive disorder, and eating disorders. Nowadays, SSRIs are very frequently preferred agents in the first-line treatment of depressive disorders. SSRIs exert their effects via blocking neuronal reuptake of neurotransmitter serotonin in the synaptic gap. Angle closure glaucoma secondary to SSRI use have been reported in the literature[2]. The basic mechanism for the development of angle closure is thought to be supraciliary effusion induced by serotonin stimulation[3].

Melatonin receptors have been found in almost all ocular tissues including retina, cornea, ciliary body, lens, choroid and sclera[4]. Agomelatine is a melatonin agonist used in the treatment of major depressive

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disorders. Its intraocular pressure (IOP) decreasing effect has been shown in experimental animals[5].

In this case report, we presented a patient who developed acute angle closure glaucoma following sertraline treatment for major depressive disorder. Addition of agomelatine to the treatment relieved the symptoms of angle closure glaucoma.

CASE

A 48-years-old female who had glaucoma and under antiglaucomatous treatment complaining periorbital pain, redness and decreased visual acuity for 2 days consulted to ophthalmology clinics of our hospital. Ophthalmologic examination revealed conjunctival hyperemia, shallow anterior chamber and closure of iridocorneal angle. Intraocular pressures were 30 mmHg, and 28 mmHg in the right, and left eyes, respectively. Ocular ultrasonography showed the presence of choroidal effusion. Ultrasonographic biomicroscopy examination demonstrated the closure of iridocorneal angle secondary to anterior displacement of lens-iris diaphragm, shallow anterior chamber, supraciliary choroidal effusion, and condensation of ciliary body. She was previously consulted to neurology clinic, and her cranial magnetic resonance (MR) imaging was unremarkable. Her medical history revealed that she was using hypotonizing drugs for glaucoma, and also she recently started to use sertraline for major depressive disorder. It was determined from the history that used antiglaucomatous medication regularly, that no source of infection could be detected and that did not use any medication in the etiology of glaucoma non-antidepressant . The development of acute myopia and angle closure glaucoma is presumed to be secondary to choroidal effusion induced by SSRI use. Therefore, she was consulted to psychiatry clinic.

Psychiatric interview with the patient revealed that she had been diagnosed as major depressive disorder, and use of sertraline at a dose of 150 mg daily, gradually increasing the dose for the previous three months. Previous complaints of suicidal thoughts, unhappiness, and feelings of despair resolved markedly with this treatment, but she was experiencing difficulties in falling asleep. Modification of her treatment was planned for the patient who had used various antidepressants for her major depressive disorder with no avail. There fore the patient refused any change in her drug treatment. But recommended to reduce the dose of the drug to the patient

Oral agomelatine (25 mg daily) was started without cessation of sertraline therapy. Then she was referred to ophthalmology clinic and a control visit at a psychiatry outpatient clinic 2 weeks later was recommended. When she returned for a control visit, it was noticed that she hadn't attended to control visit at outpatient clinics of eye diseases, and continued her antiglaucomatous drugs. Again, she was consulted to the ophthalmology clinic. On ophthalmic examination, intraocular pressure was 25 mmHg in the right eye and 24 mmHg in the left eye. Fundus examination was in normal limits in both eyes. Her psychiatric examination revealed that her sleep problems resolved after agomelatine treatment. During agomelatine treatment, activities of liver enzymes were monitored. Their levels remained within normal limits.

DISCUSSION

Local and systemic agents are responsible for the development of AACG in nearly 30% of the cases.[6] Ciliary body, and cornea of the human eye contain serotonin receptors.[7] Stimulation of 5-HT7 serotonin receptors in iris leads to relaxation of pupillary sphincter, and midriasis.[8] Although pathophysiology of angle closure glaucoma developed secondary to SSRI use has not been elucidated fully, the most probable underlying causes of AACG presumably include pupillary dilation due to weak anticholinergic, and adrenergic effect associated with increased amounts of serotonin or supraciliary effusion.[9] In animal experiments, local serotonin administration led to increase in intraocular pressure.[8] Many AACG cases associated with SSRI use have been reported in the literature.

Croos et al.10 presented a case with angle closure developed after high doses of citalopram. They speculated the potential mechanism for the development of angle closure as mydriasis induced by anticholinergic effect, and supraciliary effusion caused by serotonergic effect of the drug. Similar cases with AACG as a result of SSRI use have been reported in the literature[2].

One experimental animals study demonstrated that melatonin and its analogues decrease intraocular pressure when given as a monotherapy or in combination with antiglaucoma drugs[5]. Another

study evaluated the effects of topical melatonin agonist on experimentally induced unilateral glaucoma in monkeys[11]. Twice daily administration of melatonin agonist reduced the intraocular pressure from 1 hour to 5 hours after the first dose. Three hours after each morning dose, the maximum decrease in intraocular pressure was observed. Ismail et al.[12] reported oral melatonin (10 mg) administration 90 minutes as a premedication before routine cataract surgery significantly decreased the intraocular pressure and anxiety scores. Although agomelatine has been developed as a nonselective MT1/MT2 agonist, and 5 HT $_{2C}$ antagonist, it exerts its hypotonizing effect on intraocular pressure through its ability to activate both MT2, and MT3 receptors[13]. Antagonists specific to these receptors, such as prazosin, could alleviate the effects of agomelatine on intraocular pressure in rabbits[14]. Since noradrenergic, and cholinergic antagonists decrease hypotensive effects of melatonin, the underlying mechanism of this effect appears to be related to the sympathetic component of the MT3 receptor which controls synthesis, and drainage of intraocular fluid[15].

In the present case, AACG thought to have developed after sertraline use in a patient under antiglaucomatous treatment. Our case differs from other cases with AACG, in that increased intraocular pressure of our patient related to SSRI use was treated with intraocular pressure decreasing drugs combined with a melatonin agonist agomelatine without discontinuing SSRI treatment of the patient.

In conclusion, we have demonstrated that oral administration of a melatonin agonist, agomelatine, can decrease SSRI related intraocular pressure increase and AACG without discontinuation of SSRI treatment. These data demonstrate agomelatine as a potentially valid treatment alternative in patients with AACG, and emphasize the need of performing more comprehensive investigations on this issue.

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