Does Topica Moxiflxacin Have Uveitis Like Ocular Side Effect?

Topikal Moksifloksasinin Üveit Benzeri Oküler Yan Etkisi Var mıdır?*

Sina EVSEN[1], Şeyhmus ARI[2], Zeynep ÖZKURT[3]

ABSTRACT

The aim of this case study is to report a possible side effect associated with topical moxifloxacin in a patient who had a flu like infection before.A twenty-seven years old female admitted to our clinic having signs of bacterial conjunctivitis was instructed to use topical moxifloxacin. At the control visit she was experiencing blurred vision because of bilateral pigmented cells at anterior chamber. Also she had diffuse punctuate transillumination of irises bilaterally. She was prescribed prednisolone and tropicamide containing eye drops. At the tenth day of this treatment she had irregular middilated pupils, intraocular pressure increase in the left eye and heavily pigmented iridocorneal angles. Tropicamide was discontinued and antiglaucomatous treatment was started. One week later introcular pressure was normal, pupils are atonic bilaterally. She had a slight posterior subcapsular cataract and iridocorneal angle pigmentation was remained.

Key Words: Moxifloxacin, atonic pupils, bilateral acute iris transillumination.

ÖZ

Bu olgu sunumunun amacı öncesinde gribal enfeksiyon geçirmiş bir hastada topikal moksifloksasin ile muhtemel ilişkili olabileceğini düşündüğümüz bir yan etkiyi bildirmektir. Yirmi yaşında bakteriyel konjonktivit bulgusuyla kliniğimize başvuran kadın hastaya topikal moksifloksasin kullanması önerildi. Hasta kontrolde görüldüğünde bilateral ön kamaradaki pigmente hücreler nedeniyle bulanık görmesi mevcuttu. Ayrıca bilateral iriste diffüz punktat transilüminasyonu vardı. Prednizolon ve tropikamid içeren göz damlaları reçete edildi. Bu tedavinin onuncu gününde hastanın düzensiz middilate pupilleri, artmış göziçi basıncı ve yoğun pigmente iridokorneal açıları vardı. Tropikamid kesilip antiglokomatöz tedavi başlandı. Bir hafta sonra göziçi basıncı normal iken bilateral pupiller atonikti. Hafif arka subkapsüler kataraktı vardı ve iridokorneal açı pigmentasyonu mevcuttu.

Anahtar Kelimeler: Moksifloksasin, atonik pupiller, bilateral akut iris transiluminasyonu.

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CASE REPORT

A twenty-seven years old female was admitted to our clinic with the complaint of injected conjunctiva, pain and purulent discharge from both eyes. Signs indicative of bacterial conjunctivitis were identified on ocular examination, and she was instructed to use topical moxifloxacin four times daily. One week after the treatment she reported that her ocular symptoms were decreased; however, she was experiencing blurred vision. Upon performing another ocular examination it was determined that her corrected vision was 0.9 OD and 0.8 OS. Biomicroscopic examination revealed + cells in the right eye and ++++ cells in the left eye and there was no apparent flare. On examining the cells closer it was determined that they were not inflammatory in origin but they were pigmented instead. A diffuse punctuate transillumination was observed in both irises (Figure 1). Fundoscopic examination was unremarkable and intraocular pressures were 14 mmHg OD and 16 mmHg OS. Corneal sensitivities were intact bilaterally. The patient reported no previous episodes of uveitis, although she recalled having a slight flu-like illness about twenty days ago. She was prescribed prednisolone and tropicamide containig eye drops at eight times daily and once a day doses, respectively.

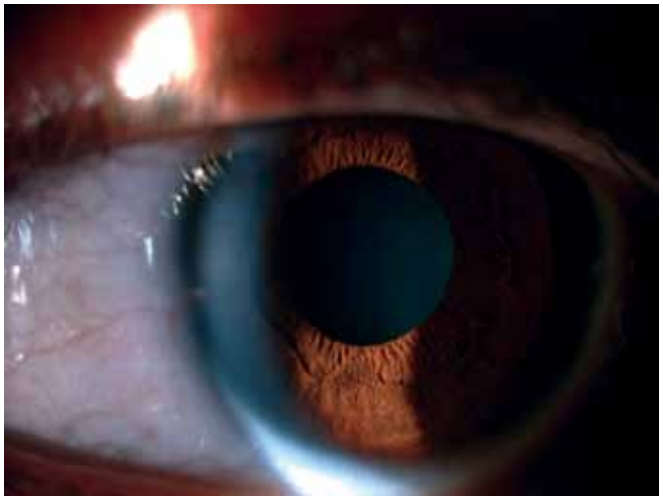

Figure 1: *Pigmented cells in the anterior chamber and iris transillumination.*

After ten days she returned to the clinic. At that time her previous complaints had largely subsided, although she acquired new photosensitivity and ocular pain that was worse in the left eye. Ocular examination revealed that vision did not change in either eye, but there were ++ cells in the left eye. Bilaterally pupils were middilated and the pupillary borders were slightly irregular (Figure 2). Intraocular pressures were 15 mmHg OD and 32 mmHg OS. Gonioscopic examination demonstrated that the iridocorneal angles were open, and the left iridocorneal angle had considerably heavier pigmentation than the right one (Figure 3). Due to the patient's photosensitivity tropicamide was discontinued and she was prescribed twice daily dorsolamide timolol and brimonidine containing eye drops for the left eye.

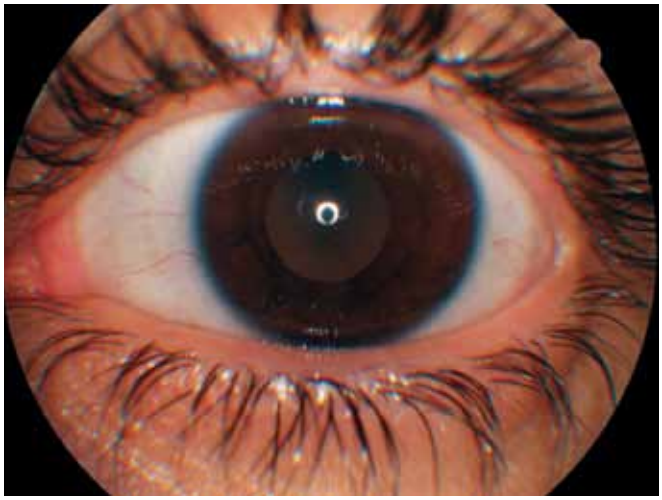

Figure 2: *Middilated pupil with irregular borders.*

Figure 3: *Heavy pigmentation of iridocorneal angle.*

One week later her intraocular pressures were normal bilaterally (14 mmHg OD and 13 mmHg OS). However, her pupillary light reponse was quite diminished. No pigmented cells were identified in the anterior chamber and so the steroid eye drops were tapered and completely stopped after two weeks. A slight posterior subcapsular cataract was determined in both eyes and her pupils were atonic bilaterally. Moreover, her blurred vision and photosensitivity worsened, and her iridocorneal angle pigmentation still remained. The patient's corrected vision was determined to be 0.7 bilaterally. She was advised to use sunglasses when outside and topical antiglocomatous drops were continued.

Laboratory Studies: The patient's complete blood count, blood chemistries, anti-streptolysin O titer, rheumatic factor, and C-reactive protein were all within normal limits. Her chest x-ray was unremarkable. Serum titers of herpes simplex virus and cytalomegalovirus IgG and IgM did not suggest current or previous infection. An aqueous humor tap could not be obtained as the patient elected to decline the procedure.

DISCUSSION

The differential diagnosis for this case report includes herpetic iridocyclitis, Fuchs' heterochromic iridocyclitis, pigment dispersion syndrome, pseudoexfoliation syndrome, bilateral acute iris transillumination (BAIT) and bilateral acute depigmentation of the iris (BADI). There is no obvious sex differences in these aforementioned conditions, but BAIT is mostly observed in females. Herpetic uveitis is typically unilateral with inflammatory keratic precipitates on the endothelium. However, this case demonstrated pigmented cells in the anterior chamber. In herpetic uveitis iris transillumination is patchy but this patient had diffuse and punctuate iris transillumination. Pupillary irregularities are also seen in herpetic uveitis, but the pupils are not atonic and unreactive to the light as observed in bilateral acute iris transillumination (BAIT) patients.[1]

Fuchs' heterochromic iridocyclitis is generally asymptomatic and is typically unilateral. Keratic precipitates are inflammatory and diffuse and no pigment is observed in the anterior chamber. Rarely there may be peripupillary transillumination. Diffuse iris stromal atrophy causes heterochromia and pupillary change is not commonly seen. An increase in intraocular pressure is a common complication, but it develops over along period of time along with widening of the iridocorneal angle due to angle neovascularization . Pseudoexfoliation syndrome is also frequently observed among female patients. It does not have an acute onset and usually has an asymptomatic clinical course. This condition is usually bilateral but the degree of severity can differ between each eye. Generally the pupil and iris are unaffected, but intraocular pressure elevation occurs often and develops over years. Exfoliation material can be observed in the iridocorneal angle.[1]

Pigment dispersion syndrome occurs more frequently in males. Patients mostly do not manifest ocular symptoms, but they may suffer from headaches, blurred vision and seeing halos around lights. This condition usually affects both eyes equally, and keratic precipitates are pigmented and Krukenberg spindle is common. Iris transillumination is localized in the mid-periphery and demonstrates a moth-eaten pattern. There may be anisocoria but light and near reflexes are not impaired. Intraocular presssure elevation occurs often but it slowly progresses. Pigment accumulation is also observed in the iridocorneal angle.[1]

Moxifloxacin (8-methoxy flouroquinolone) is a synthetic broad spectrum antibiotic. It has been administered both in systemic way and topically for almost four to five years in Turkey. In studies performed with radiolabeled moxifloxacin, it was found that it accumulates at high concentrations in melanin containing tissues such as the eyes, meninges and pigmented hair follicles.[2]

Moxifloxacin containig eye drops are formulated as an isotonic solution at 290 mOsm/kg. Plasma moxifloxacin concentrations were measured in healthy adult males and females after a three times daily dosage in both eyes. It was then determined that the steady state mean, maximum serum concentration of moxifloxacin was 2.7 ng/ml and the estimated dailly exposure was 45 ng/ml. These values are 1600 and 1000 times lower respectively, than those values determined with a 400 mg oral dose of moxifloxacin. Nevertheless Knape et al. reported that after topical administration, there is a greater than ten-fold higher concentration of moxifloxacin in aqueous than vitreous, whereas oral administration producessimiliar aqueous and vitreous concentrations. The steady serum and vitreous reservoirs of moxifloxacin during oral administration may maintain drug levels in the tissue at risk better than intermittent topical therapy.[3] For that reason this findings also may support the possibility that uveitis like syndrome after topical moxifloxacin administration may be milder and milder.

Wefer et al.,[4] reported similar ocular reactions as observed in this case study in five patients after prescribing oral moxifloxacin. In their study, iris transillumination and sphincter paralysis was observed 3 to 4 weeks following oral moxifloxacin usage; however, the patients' transilluminations were more intense. It is possible that this case's relatively mild ocular reaction is due to the lower moxifloxacin exposure from eye drops.

Tugal Tutkun et al.,[1] reported 26 cases of bilateral acute iris transillumination (BAIT). Of note, 20 of the patients were females. It was found that the severity of BAIT can be different for each eye. In this case study the patient was female and her left eye was more severely affected. Moreover, they reported bilateral cataract formation in seven cases, and this case developed a posterior subcapsular cataract during the follow up period. In fact 73% of these cases reported experiencing a flu-like illnesses before demonstrating BAIT and 35% of patients were prescribed moxifloxacin. This patient expressed that she had a flu-like illness about twenty days ago. However her ocular symptoms, bilateral pigment dispersion, and iris transillumination were all observed after she started to use topical moxifloxacin. It has been suggested that the patient's viral load and immunity status also influences whether ocular symptoms develop. Also, it was posited that flouroquinolone exposure may potentiate virus-related iris ischemia leading to iris transillumination and pigment dispersion.[5]

Hinkle et. al.,[6] reported in a case series of 40 patients that other fluoroquinolones in addition to moxifloxacin may cause acute uveitis. They observed iris transillumination, atonic pupils and pigment dispersion in 21 patients.

Another similar ocular reaction is bilateral acute depigmentation of the iris (BADI).[7-9] BADI is characterized by a stromal bilateral pigment dispersion with no observed transillumination. A granular appearance of the iris may be observed in addition to geographic or diffuse iris depigmentation. There are no pupillary changes in BADI cases, but for BAIT cases the pupils are bilaterally dilated and atonic and so respond to light weakly.1 Nevertheless, both BADI and BAIT are often observed in females and affect both eyes.

Dunconbe et al.,[10] reported a similiar case that developed 11 days after oral moxifloxacin usage. The authers emphasized that a relationship between this type of uveitis-like reaction and systemic quinolone treatment is possible according to World Health Organisation's criteria. In a retrospective analysis of patients prescribed moxifloxacin an uveitis-like reaction was suspected in 25 of 40 case. From this evidence it is possible that moxifloxacin eye drops may cause an uveitis-like reaction such as BAIT. Furthermore, Bringo Calvo et al., [8] observed a similiar ocular reaction in a 77 years old female patient after pneumonia treatment with moxifloxacin. Morshedi et al.,[5] reported two cases that experienced uveitis-like reactions following systemic moxifloxacin use.

CONCLUSION

Previous investigators have suggested that BAIT may be related to administration of systemic moxifloxacin. However, this patient demonstrated ocular signs and symptoms after using topical moxifloxacin. We posit that this patient's ocular reaction may be possibly related to the usage of moxifloxacin containing eye drops and her remote viral illness. She likely experienced a milder reaction than the cases prescribed with oral moxifloxacin as exposured drug levels are much lower with topical forms than the systemic forms. In addition more case reports are needed to support the possible relation of topical moxifloxacin and BAIT as a toxic reaction.

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