

High dose sildenafil citrate induced persistent binocular anomalous: A case report

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Case Report

Keywords: Sildenafil citrate, high dose, anomalous, persistent, outer layer of retina

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Abstract

Background: When taking the recommended dose of sildenafil citrate for male erectile dysfunction (ED) and pulmonary hypertension (PAH), the incidence of ocular side effects, including a sense of blue-tinted vision and changes in brightness perception in the form of increased sensitivity to light, was 0.1–11%, and the visual symptoms were almost transient. Only a few cases reported the large dose of sildenafil citrate. The visual symptoms of these cases were all reversible. Up to now, no case was reported that the visual symptoms was irreversible, except this one.

Case Presentation: A 39-year-old man was sent to emergency department for taking over dosage of 800mg sildenafil citrate (trade name Viagra) to commit suicide. Visual symptoms appeared 4 hours later, including photophobia, blue halo in center field and gray stripes over red background. Sildenafil citrate toxicity caused the damage to outer layer of retina, including of myoid zone, ellipsoidal zone and interdigitation zone on OCT. Pattern visual evoked potential (P-VEP) demonstrated that the amplitudes of bilateral 1 degree spatial frequency P100 was declined mildly, and full-field electroretinogram (ERG) showed slightly-reduced amplitudes of dark-adapted ERG b-wave in both eyes. The patient was diagnosed as bilateral drug toxic retinopathy and ametropia. He was treated with compound anisodine hydrobromide. At 3-week follow-up, myoid zone, ellipsoidal zone and interdigitation zone of macular was improved on OCT, the amplitude of bilateral 1 degree spatial frequency P100 and dark-adapted ERG b-wave was improved slightly, but still remained abnormal. However, the visual symptoms did not improve any more over more than 1 year.

Conclusions: High dose of sildenafil may lead to irreversible death of the photoreceptor cells and permanent visual impairment. The ocular side effects of recommended dose and potential visual risks of drug overdose should be paid more attention.

Keywords: Sildenafil citrate, high dose, anomalopia, persistent, outer layer of retina.

Background

Sildenafil citrate acts as a phosphodiesterase (PDE) inhibitor. PDE-5 has been demonstrated to be present in bipolar cells, ganglion cells and the endothelial and smooth muscle cells of the vascular wall in retinal and choroidal vessels[1]. PDE-6 is a key isoenzyme located in the outer segments of rods and cones for the conversion of light stimulation to electrical signals[2]. The relative selectivity of sildenafil for PDE-5 was 10 times of PDE-6[3].

When taking the recommended dose of sildenafil citrate for male erectile dysfunction (ED) and pulmonary hypertension (PAH), the incidence of ocular side effects, including a sense of blue-tinted vision and changes in brightness perception in the form of increased sensitivity to light, was 0.1–11% [4-7], and the visual symptoms were almost transient.

Only a few cases reported the large dose of sildenafil citrate. The visual symptoms of these cases were all reversible.

Case Presentation

A 39-year-old male patient presented to our eye hospital with complaint of binocular anomalous vision over 1 week. He took 800mg (50mg×16 tablets) sildenafil citrate (trade name Viagra) which was bought on the internet, attempting to commit suicide for pressure 1 week ago. Visual symptoms appeared 4 hours later, including photophobia, blue halo in center field, gray stripes over red background, accompanied with dizziness and nausea, without vomiting and vision loss. The patient was physically healthy with no noteworthy medical history. Six hours after taking the medicine, the patient was sent to the emergency department of the second affiliated hospital of Wenzhou Medical University. After blood tests (i.e. blood count, liver and kidney function, and coagulation) and Magnetic Resonance Imaging (MRI), he was diagnosed as drug poisoning and treated with liver protection. The attending doctor then referred the patient to our hospital for his visual complaints.

Ophthalmic examination revealed his best corrected vision acuity(BCVA) was 1.0 in both eyes. Color vision examination showed anerythrochloropsia. There were no afferent pupillary defects and no apparent pathological changes in the anterior segment of either eye. Intraocular pressure was 9.9mmHg in the right eye and 11.8mmHg in the left eye. Fundus photography showed that there was a round yellow-white macular lesion with the size of approximately 2/3 papillary diameter (PD) in the right eye (figure 1-A1), and the left eye was normal (figure 1-A2). Optical coherence tomography (OCT) showed there were a focal choroidal excavation in the fovea of right eye (figure 2-A1) and disrupted myoid zone, ellipsoidal zone and interdigitation zone in the macular region of both eyes (figure 2-A1,A2). Fundus fluorescein angiography (FFA) revealed high fluorescence in the macular of right eye (Figure 1-B1,B2), whereas the left eye was normal (Figure 1-B3). Visual field (VF) revealed a general decline of binocular sensitivity. Pattern visual evoked potential (P-VEP) demonstrated that the amplitudes of bilateral 1 degree spatial frequency P100 was declined mildly (figure 3A). Full-field electroretinogram (ERG) showed slightly-reduced amplitudes of dark-adapted ERG b-wave in both eyes (figure 4A). The patient was diagnosed as bilateral drug toxic retinopathy and ametropia. He was treated with compound anisodine hydrobromide (2ml subcutaneous injection around the superficial temporal artery) once a day for 1 week. OCT showed improved myoid zone, ellipsoidal zone and interdigitation zone of macular (figure 2-B1,B2), and the amplitude of bilateral 1 degree spatial frequency P100 and dark-adapted ERG b-wave was improved slightly, but still remained abnormal at 3-week follow-up (figure 3C, figure 4B). However, the symptom of binocular anomalous vision persists over the following 1 year.

Discussion And Conclusions

When taking the recommended dose ranging of 25 to 100mg/day for male ED and 20 mg three times a day for PAH [8], the incidence of ocular side effects, including a sense of blue-tinted vision and changes in brightness perception in the form of increased sensitivity to light, was 0.1–11% [4-7]. There was a

reduction in a-wave, b-wave amplitude and sensitivity of S-cone [9,10], and a prolongation of the photopic a-wave and scotopic b-wave[11].The visual symptoms and ERG changes were almost transient [3,12], which were at peak periods in 1~2 hours and disappeared in 3~24 hours after taking sildenafil[9,13].

According to the literature, there were a few vision-threatening complications when taking recommended dose of sildenafil, including nonarteritic anterior ischemic optic neuropathy(NAION)[14-16], central retinal artery occlusion(CRAO)[17], acute angle closure glaucoma[18], pupil-sparing third nerve palsy [19], and central serous chorioretinopathy (CSC)[20]. They were more likely to be caused by the systemic or ocular hemodynamic changes following vasodilatation of retina and choroid by PED-5 inhibition .

Concerning the large dose of the drug usage, there were less reported studies and cases.Vision symptoms occurs in 40~50% individuals when taking over a dose of 100 mg sildenafil, 50% individuals using 200mg, and 100% individuals using 600–800mg [21]. Kimet et al reported a case that a patient took 750 mg sildenafil presented blurred vision, OCT demonstrated irregularities in the photoreceptor line, his full-field and multifocal ERG were reduced in amplitudes.The toxicity of sildenafil persisted over several months in the ERG and OCT, these changes returned to normal 1 year later[22]. Izadi et al reported a patient took 1500mg dosage of sildenafil persisted the symptoms of central visual blurring and chromatopsia for 5 months, then returned to normal[23].

In our case, the patient who took 800mg sildenafil was under medical attention immediately, but his visual symptoms still existed 4 hours later.The symptoms of anomalopia and photosthesia, and the changes of macular outer layer in OCT, were consistent with previous studies.However, the visual symptoms did not improve any more at more than 1 year. It was speculated that a higher dose of sildenafil may lead to irreversible death of the photoreceptor cells and permanent visual impairment, which differs from the previous cases of reversible vision change.

With the increasing number of sildenafil users in China, the ocular side effects of recommended dose and potential visual risks of drug overdose should be paid more attention.

Abbreviations

Abbreviations:

PDE: phosphodiesterase

ED: erectile dysfunction

PAH: pulmonary hypertension

MRI: Magnetic Resonance Imaging

BCVA: best corrected vision acuity

PD: papillary diameter

OCT: Optical coherence tomography

FFA: Fundus fluorescein angiography

VF: Visual field

P-VEP: Pattern visual evoked potential

ERG: electroretinogram

NAION: nonarteritic anterior ischemic optic neuropathy

CRAO: central retinal artery occlusion

CSC: central serous chorioretinopathy

Declarations

Declarations

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

The patient has read and signed the statement of the informed consent. We have obtained consent to publish from the patient to report his data including detailed medical history and clinical examination images. A copy of the written consent is available for review by the Editor of BMC Ophthalmology.

Availability of data and material:

All data generated or analyzed during this study are included in this published article.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions

Ying Huang has made the conception of the manuscript, has contributed to analysis and interpretation of data and has been involved in drafting, writing and revising the manuscript. Changbiao Xu has contributed to analysis and interpretation of data and has been involved in drafting the manuscript.

Qianqian Zhu performed the OCT, FFA, ERG, VEP examination of the patient. Yikui Zhang has been involved in revising the manuscript. Bing Lin was the attending physician and responsible for the treatment and follow-up of the patient, has made the conception of the manuscript, has been involved in drafting and revising the manuscript and given the final approval of the version to be published. All authors read and approved the final manuscript.

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Figures

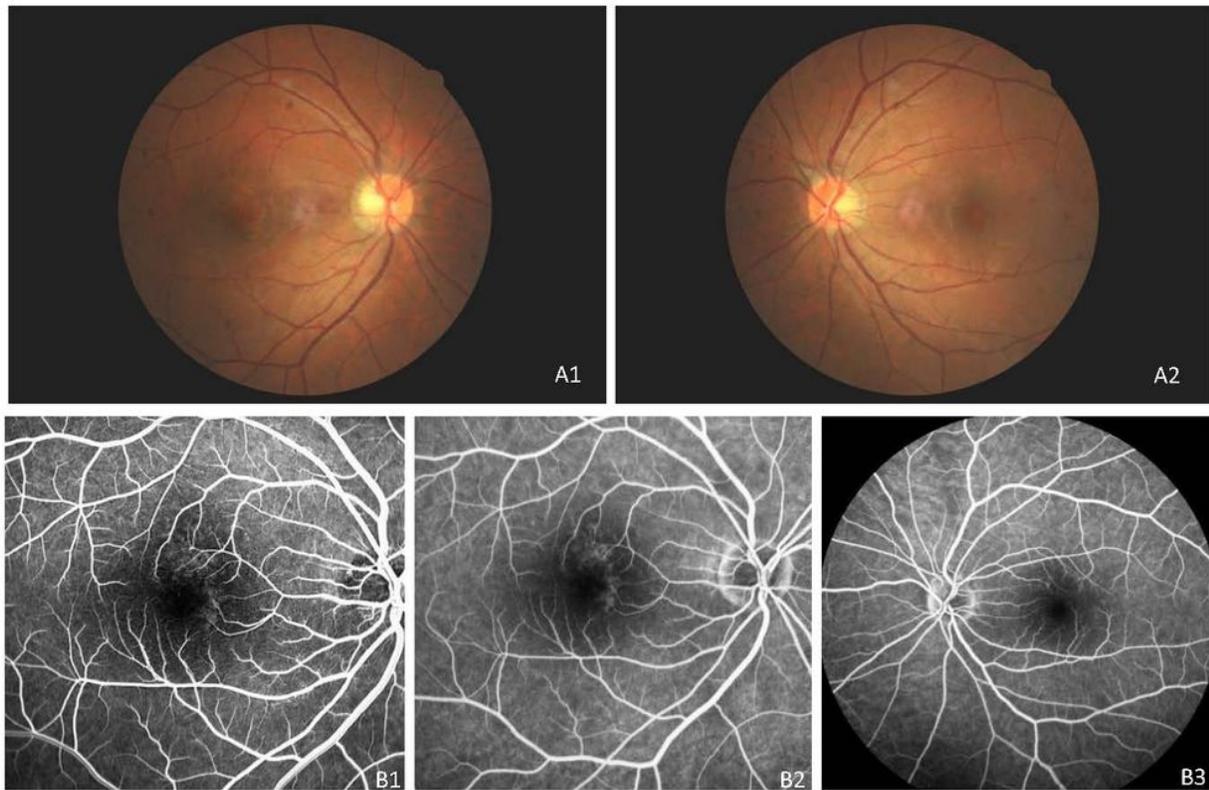


Figure 1 FP and FFA

A1, A2: FP, 2/3PD round and yellow-white lesion in macular of right eye(A1), whereas the left eye was normal(A2). B1, B2, B3: FFA, high fluorescence in macular of right eye(B1: early stage, B2: late stage), whereas the left eye was normal(B3).

Figure 1

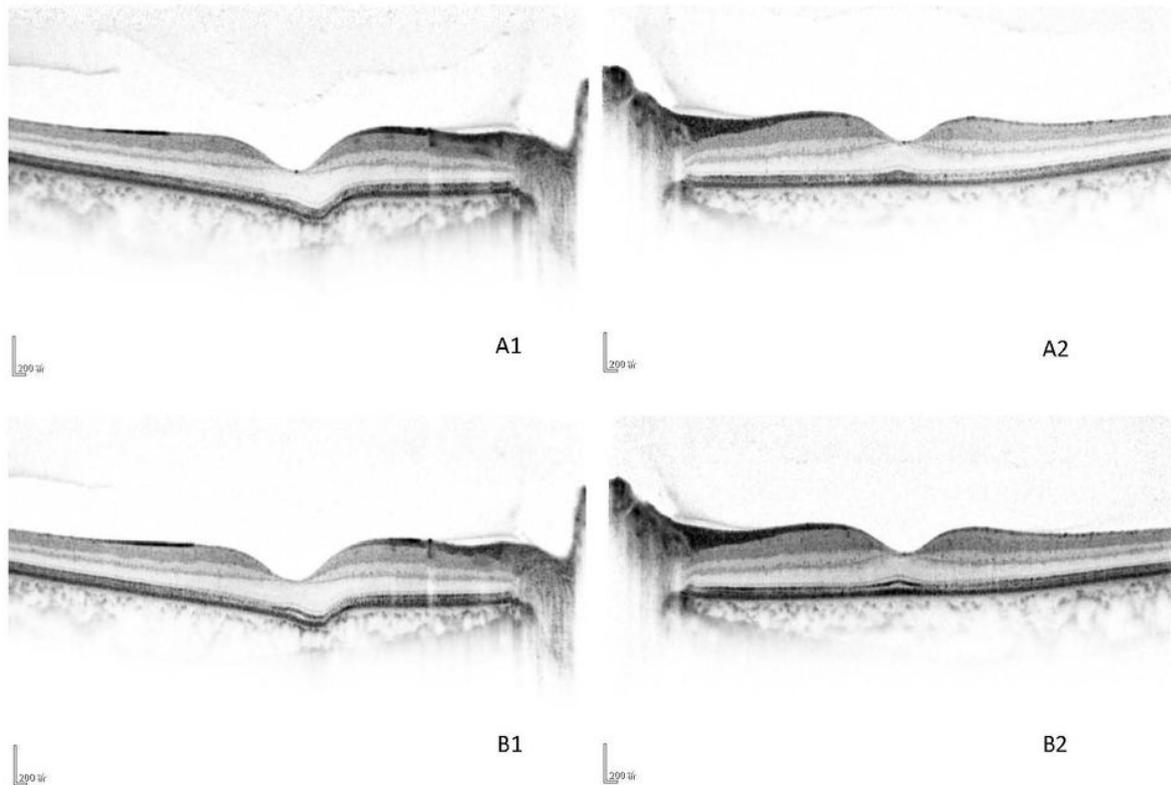
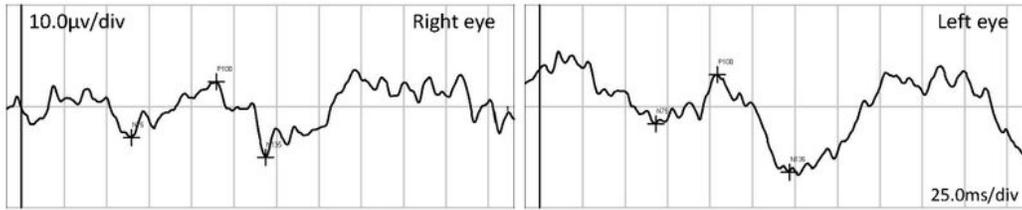


Figure 2 OCT

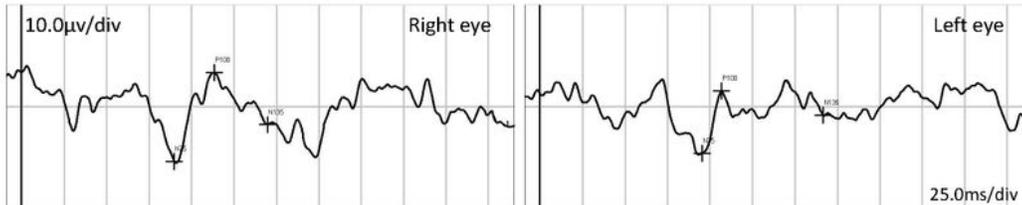
A1: right eye at the first visit, a focal choroidal excavation in fovea , myoid zone, ellipsoidal zone and interdigitation zone of macular disrupted.
 A2: left eye at the first visit, myoid zone, ellipsoidal zone and interdigitation zone of macular disrupted.B1: right eye at 3-week follow-up, myoid zone, ellipsoidal zone and interdigitation zone of macular improved, but still remained abnormal.B2: left eye at 3-week follow-up, myoid zone, ellipsoidal zone and interdigitation zone of macular improved, but still remained abnormal.

Figure 2

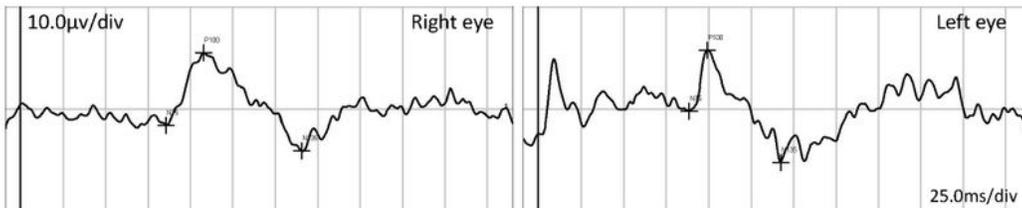
A: 1.0 degree Pattern-VEP at 1st visit



B: 15 min Pattern-VEP at 1st visit



C: 1.0 degree Pattern-VEP at 3 weeks follow-up



D: 15 min Pattern-VEP at 3 weeks follow-up

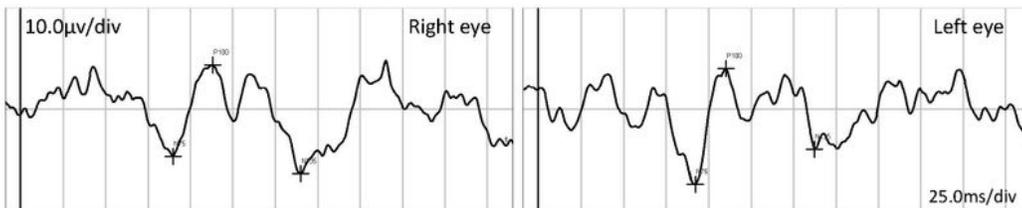


Figure 3 P-VEP

A: 1 degree spatial frequency P-VEP at the first visit, the amplitude of P100 was mild to moderate declined of both eyes (N75-P100 was 5.49µV of right eye and 4.84 µV of left eye, normal N75-P100 was 7.70-16.7µV). B: 15 minutes spatial frequency P-VEP at the first visit. C: 1 degree spatial frequency P-VEP at 3-weeks follow-up, the amplitude of P100 improved slightly, but still remained abnormal(N75-P100 was 7.16µ V of right eye and 6.00µV of left eye, normal N75-P100 was 7.70-16.7µV). D: 15 minutes spatial frequency P-VEP at 3-weeks follow-up.

Figure 3



Figure 4 ERG

A: the amplitude of binocular dark-adapted ERG decreased slightly (The amplitude of scotopic 0.01 ERG b-wave was $198\mu\text{V}$ of right eye and $225\mu\text{V}$ of left eye, the amplitude of scotopic 3.0 ERG b-wave was $425\mu\text{V}$ of right eye and $474\mu\text{V}$ of left eye. Normal amplitude of scotopic 0.01 ERG b-wave was $289\text{--}437\mu\text{V}$, normal amplitude of scotopic 3.0 ERG b-wave was $515\text{--}694\mu\text{V}$). B: The amplitude dark-adapted ERG b-wave improved a little, but still abnormal at 3-week follow-up (The amplitude of scotopic 0.01 ERG b-wave was 232 of right eye and 241 of left eye, the amplitude of scotopic 3.0 ERG b-wave was $460\mu\text{V}$ of right eye and $476\mu\text{V}$ of left eye. Normal amplitude of scotopic 0.01 ERG b-wave was $289\text{--}437\mu\text{V}$, normal amplitude of scotopic 0.01 ERG b-wave was $515\text{--}694\mu\text{V}$).

Figure 4

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