

Bilateral Simultaneous Nonarteritic Anterior Ischemic Optic Neuropathy Associated with The Use of Sildenafil: A Case Report

Saeed Karimi,¹ Hamed Esfandiari,¹ Homayoun Nikkhah,¹ Mohammad Gozin,¹ and Seyed Aliasghar

Mosavi^{1*}

¹Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences, Torfeh Eye Hospital, Tehran, Iran

*Corresponding author: Seyed Aliasghar Mosavi, Ophthalmology Department, Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. E-mail: a.a.mosavi@gmail.com

Received 2016 February 03; Accepted 2016 October 08.

Abstract

Introduction: Nonarteritic anterior ischemic optic neuropathy (NAION) is a rare condition but one of the most important ocular side effects of sildenafil.

Case Presentation: We presented a 65-year-old man with the history of sudden painless loss of vision in both eyes following taking sildenafil.

Conclusions: Fundus examination revealed blurred margin and elevated disc in both eyes. Visual field defects were bilateral inferior altitudinal defects, and optical coherence tomography (OCT) displayed a prominent nerve fiber layer edema in both eyes. We asserted that use of sildenafil may lead to reduce blood pressure and interfere with microcirculation in the optic nerve head. So, the potential risks of unregulated over-the-counter sexual enhancement supplements such as sildenafil must be educated to the patients using these supplements.

Keywords: Nonarteritic Anterior Ischemic Optic Neuropathy, Visual Acuity, Visual Fields, Sildenafil

1. Introduction

Phosphodiesterase-5 (PDE) inhibitors are normally prescribed for erectile dysfunction (1-4). Sildenafil citrate (Viagra, Pfizer Pharmaceuticals, and New York, NY) as a Phosphodiesterase-5 (PDE) inhibitor selectively prevents cyclic guanosine monophosphate (cGMP)- specific phosphodiesterase type 5 (PDE 5). Its mechanism of action includes improving cGMP and nitric oxide pathway outcome, smoothing muscle relaxation in the corpus cavernous and letting blood inflow into the sex organ during sexual stimulation. It has been reported that Phosphodiesterase type 5 inhibitors cause temporary changes in color perception or lightness perception (typically an increased sensitivity), blurred vision as well as transient ERG changes (5).

In fact, the most severe potential ocular side effect of using sildenafil is nonarteritic anterior ischemic optic neuropathy (NAION) (6). Here we describe a case of bilateral simultaneous NAION following taking sildenafil citrate to treat erectile dysfunction.

2. Case Presentation

We presented a 65-year-old non-diabetic man who was complaining of bilateral painless loss of visual acuity dur-

ing the past 7 days. His medical and surgical history was unremarkable, except he had started to take sildenafil to treat his sexual dysfunction since 20 days ago.

Upon examination, BCVA was reported 6 / 10 in the right eye and 2 / 10 in the left eye, and RAPD was negative. On slit lamp examination, mild lens opacity was observed in both eyes. Intraocular pressure was 15 mmHg in the right eye and 13 mmHg in the left eye. The fundus exam disclosed blurred margin and elevated disc in both eyes (Figure 1). Central 24-2 threshold visual field test was compatible with altitudinal visual field defect in both eyes (Figure 2). Optical coherence tomography revealed a prominent nerve fiber layer edema in both eye (Figure 3).

Laboratory analysis revealed normal blood count. Moreover, C-reactive protein (CRP) test and erythrocyte sedimentation rate were reported normal. Magnetic resonance image (MRI) scan of orbit and brain with gadolinium contrast injection was normal. Meanwhile, systemic evaluation showed no evidence of cardiovascular disease, hypertension, diabetes, or hyperlipidemia.

The patient was advised to discontinue using sildenafil due to bilateral simultaneous NAION assessment and regularly monitoring of blood pressure. Three months later, fundoscopy showed a slightly pale disc in both eyes.

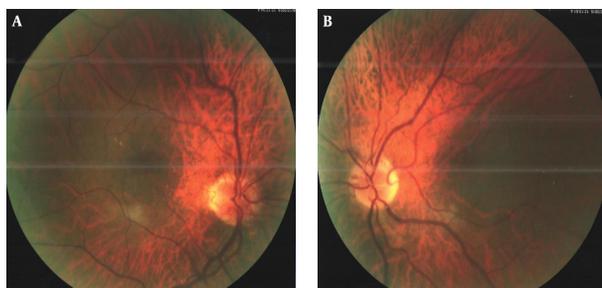


Figure 1. A Dilated Fundus Examination of the Right Eye Revealed Blurred Margin and Elevated Disc in Both Eyes A, Fundus Photograph of the Right Eye Shows a Cup-to-Disc Ratio of 0.2; B, Fundus Photograph of the Left Eye Shows Cup-to-Disc Ratio of 0.25

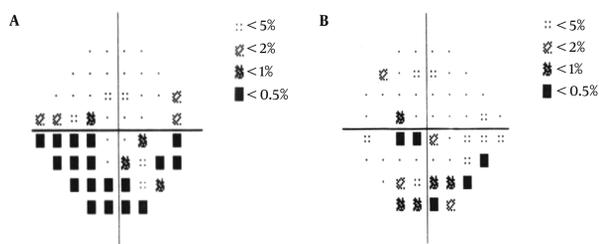


Figure 2. 24-2 SITA-Standard Field Test of the Right (A) and Left Eyes (B) at the Initial Examination Revealed an Altitudinal Visual Field Defect in the Both Eyes

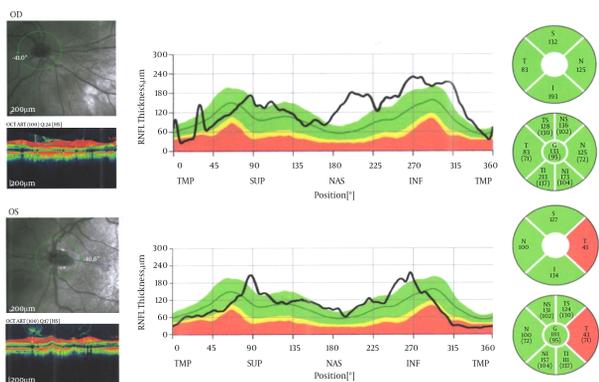


Figure 3. Ocular Coherence Tomography Shows Nerve Fiber Loss of the Left Eye. TMP = Temporal; SUP = Superior; NAS = Nasal; INF = Inferior; OD = Right Eye; OS = Left Eye

3. Discussion

Nonarteritic Anterior Ischemic Optic Neuropathy (NAION) is known to be the most common cause of acute and sub-acute optic neuropathy in people over 50 years old with incidence varying from 10.5% to 73%. This wide-ranging disparity is due to several factors such as retrospective recovery of data in almost all studies besides

the quality and length of follow up (7).

The typical clinical characteristics of NAION include sudden painless visual acuity reduction, frequently labelled as visual field cloudiness in the affected region, most often inferiorly. Patients' visual acuity may range from 20/20 to no light perception. Visual loss upon awakening was reported by many patients (8). VA usually remains constant, with some improvement occurring in about 23.8% of the cases (9-11).

The NAION appearance was described by numerous case series following the consumption of PDE-5 inhibitors in healthy individuals (12-16). Shibayama et al. (17) reported a case of bilateral NAION in a sixty one-year-old man. The patient had a small disc with a small physiologic cup that was poorly controlled for diabetes. Moschos et al. (18) also reported a bilateral simultaneous NAION 4-5 times a month in a 55-year-old man after Sildenafil ingestion.

Karli et al. (19) reported right-sided headache and vision loss in a 42-year-old man who had developed anterior ischemic optic neuropathy resulting from use of phosphodiesterase-5 (PDE) inhibitor.

Pomeranz et al. (4) reported five cases of NAION which had occurred as a result of sildenafil taking. They recommended the patients need to consult with the physician before using sildenafil.

Based on these studies, some investigators suggest restriction on use of erectile dysfunction drugs in patients with cardiovascular risk factors, diabetes mellitus, hypertension, and those with a history of previous NAION (16).

Furthermore, sexual stimulation activates the release of nitric oxide (NO) from non-cholinergic, non-adrenergic nerve endings as well as corpus cavernous sinusoids and arterial endothelial cells. Sildenafil consumption results in changes in NO balance altering the normal vascular auto regulation that may not be able to compensate for a drop in systemic blood pressure. Moreover, the indirect involvement of sildenafil in NO system may affect microcirculation in the optic nerve head, causing breakdown of the blood-ocular barrier which leads to NAION damages (20). According to this study, it is supposed that hypotension and small cup-to-disc ratio are probably the most common risk factors (4). Although our patient did not have systemic risk factors, the optic discs seemed small.

In summary, we assert that use of sildenafil may lead to reduce blood pressure and interfere with microcirculation in the optic nerve head. So, the potential risks of unregulated over-the-counter sexual enhancement supplements such as sildenafil must be educated to patients using these supplements.

Footnotes

Consent: Written informed consent was obtained from the patient in order to publish this case report and accompanying images.

Conflict of Interests: none of the authors has a conflict of interests with the submission.

References

- Gorkin L, Hvidsten K, Sobel RE, Siegel R. Sildenafil citrate use and the incidence of nonarteritic anterior ischemic optic neuropathy. *Int J Clin Pract.* 2006;**60**(4):500-3. doi: [10.1111/j.1368-5031.2006.00904.x](https://doi.org/10.1111/j.1368-5031.2006.00904.x). [PubMed: [16620369](https://pubmed.ncbi.nlm.nih.gov/16620369/)].
- Hayreh SS. Non-arteritic anterior ischaemic optic neuropathy and phosphodiesterase-5 inhibitors. *Br J Ophthalmol.* 2008;**92**(12):1577-80. doi: [10.1136/bjo.2008.149013](https://doi.org/10.1136/bjo.2008.149013). [PubMed: [19029161](https://pubmed.ncbi.nlm.nih.gov/19029161/)].
- Laties AM. Vision disorders and phosphodiesterase type 5 inhibitors: a review of the evidence to date. *Drug Saf.* 2009;**32**(1):1-18. doi: [10.2165/00002018-200932010-00001](https://doi.org/10.2165/00002018-200932010-00001). [PubMed: [19132801](https://pubmed.ncbi.nlm.nih.gov/19132801/)].
- Pomeranz HD, Smith KH, Hart WM Jr, Egan RA. Sildenafil-associated nonarteritic anterior ischemic optic neuropathy. *Ophthalmology.* 2002;**109**(3):584-7. doi: [10.1016/S0161-6420\(01\)00976-9](https://doi.org/10.1016/S0161-6420(01)00976-9). [PubMed: [11874765](https://pubmed.ncbi.nlm.nih.gov/11874765/)].
- Fraunfelder FW. Visual side effects associated with erectile dysfunction agents. *Am J Ophthalmol.* 2005;**140**(4):723-4. doi: [10.1016/j.ajo.2005.02.049](https://doi.org/10.1016/j.ajo.2005.02.049). [PubMed: [16226525](https://pubmed.ncbi.nlm.nih.gov/16226525/)].
- Egan RA, Fraunfelder FW. Viagra and anterior ischemic optic neuropathy. *Arch Ophthalmol.* 2005;**123**(5):709-10. doi: [10.1001/archophth.123.5.709-b](https://doi.org/10.1001/archophth.123.5.709-b). [PubMed: [15883302](https://pubmed.ncbi.nlm.nih.gov/15883302/)].
- Beri M, Klugman MR, Kohler JA, Hayreh SS. Anterior ischemic optic neuropathy. VII. Incidence of bilaterality and various influencing factors. *Ophthalmology.* 1987;**94**(8):1020-8. doi: [10.1016/S0161-6420\(87\)33350-0](https://doi.org/10.1016/S0161-6420(87)33350-0). [PubMed: [3658362](https://pubmed.ncbi.nlm.nih.gov/3658362/)].
- Hayreh SS, Podhajsky PA, Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: time of onset of visual loss. *Am J Ophthalmol.* 1997;**124**(5):641-7. doi: [10.1016/S0002-9394\(14\)70902-X](https://doi.org/10.1016/S0002-9394(14)70902-X). [PubMed: [9372718](https://pubmed.ncbi.nlm.nih.gov/9372718/)].
- Arnold AC, Hepler RS. Natural history of nonarteritic anterior ischemic optic neuropathy. *J Neuroophthalmol.* 1994;**14**(2):66-9. doi: [10.1097/00041327-199406000-00002](https://doi.org/10.1097/00041327-199406000-00002). [PubMed: [7951929](https://pubmed.ncbi.nlm.nih.gov/7951929/)].
- Mathews MK. Nonarteritic anterior ischemic optic neuropathy. *Curr Opin Ophthalmol.* 2005;**16**(6):341-5. doi: [10.1097/01.icu.0000188361.52166.93](https://doi.org/10.1097/01.icu.0000188361.52166.93). [PubMed: [16264343](https://pubmed.ncbi.nlm.nih.gov/16264343/)].
- Boghen DR, Glaser JS. Ischaemic optic neuropathy. The clinical profile and history. *Brain.* 1975;**98**(4):689-708. doi: [10.1093/brain/98.4.689](https://doi.org/10.1093/brain/98.4.689). [PubMed: [1218373](https://pubmed.ncbi.nlm.nih.gov/1218373/)].
- Escaravage GK Jr, Wright JD Jr, Givre SJ. Tadalafil associated with anterior ischemic optic neuropathy. *Arch Ophthalmol.* 2005;**123**(3):399-400. doi: [10.1001/archophth.123.3.399](https://doi.org/10.1001/archophth.123.3.399). [PubMed: [15767487](https://pubmed.ncbi.nlm.nih.gov/15767487/)].
- Pomeranz HD, Bhavsar AR. Nonarteritic ischemic optic neuropathy developing soon after use of sildenafil (Viagra): a report of seven new cases. *J Neuroophthalmol.* 2005;**25**(1):9-13.
- Fraunfelder FW, Pomeranz HD, Egan RA. Nonarteritic anterior ischemic optic neuropathy and sildenafil. *Arch Ophthalmol.* 2006;**124**(5):733-4. doi: [10.1001/archophth.124.5.733](https://doi.org/10.1001/archophth.124.5.733). [PubMed: [16682597](https://pubmed.ncbi.nlm.nih.gov/16682597/)].
- Margo CE, French DD. Ischemic optic neuropathy in male veterans prescribed phosphodiesterase-5 inhibitors. *Am J Ophthalmol.* 2007;**143**(3):538-9. doi: [10.1016/j.ajo.2006.10.006](https://doi.org/10.1016/j.ajo.2006.10.006). [PubMed: [17317413](https://pubmed.ncbi.nlm.nih.gov/17317413/)].
- Hayreh SS. Erectile dysfunction drugs and non-arteritic anterior ischemic optic neuropathy: is there a cause and effect relationship?. *J Neuroophthalmol.* 2005;**25**(4):295-8. [PubMed: [16340497](https://pubmed.ncbi.nlm.nih.gov/16340497/)].
- Shibayama J, Oku H, Imamura Y, Kajiura S, Sugasawa J, Ikeda T. Bilateral, nearly simultaneous anterior ischemic optic neuropathy complicated by diabetes and bilateral, small, crowded optic discs. *Jpn J Ophthalmol.* 2005;**49**(3):235-8. doi: [10.1007/s10384-004-0179-3](https://doi.org/10.1007/s10384-004-0179-3). [PubMed: [15944831](https://pubmed.ncbi.nlm.nih.gov/15944831/)].
- Moschos MM, Margetis I. Bilateral simultaneous anterior ischemic optic neuropathy associated with sildenafil. *Case Rep Ophthalmol.* 2011;**2**(2):262-5. doi: [10.1159/000331111](https://doi.org/10.1159/000331111). [PubMed: [21941503](https://pubmed.ncbi.nlm.nih.gov/21941503/)].
- Karli SZ, Liao SD, Carey AR, Lam BL, Wester ST. Optic neuropathy associated with the use of over-the-counter sexual enhancement supplements. *Clin Ophthalmol.* 2014;**8**:2171-5. doi: [10.2147/OPH.S73059](https://doi.org/10.2147/OPH.S73059). [PubMed: [25378904](https://pubmed.ncbi.nlm.nih.gov/25378904/)].
- Taner P, Ergin A, Basar MM, Batislam E, Bilgili YK. Sildenafil does not alter retrobulbar hemodynamics in postural variations. *J Neuroophthalmol.* 2009;**29**(2):59-64. doi: [10.1080/01658100590933433](https://doi.org/10.1080/01658100590933433).