Erectile Dysfunction Agents and Nonarteritic Anterior Ischemic Optic Neuropathy

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KEYWORDS

• Erectile dysfunction drug • Non-arteritic anterior ischemic optic neuropathy
• Phosphodiesterase 5 inhibitor • Pfizer • Sildenafil • Tadalafil • Vardenafil

KEY POINTS

- Phosphodiesterase-5 inhibitors (PDE5I) are used for treatment of erectile dysfunction and pulmonary arterial hypertension.
- PDE5Is have been implicated in being a causative factor for development of nonarteritic anterior ischemic optic neuropathy (NAION).
- The relationship between PDE5I and NAION has been based on the publication of case reports that have documented loss of vision due to NAION after ingestion of sildenafil or tadalafil.
- A case-crossover study has shown a twofold risk of developing NAION within 1 day after use of PDE5I.
- Neuro-ophthalmologists have accepted that there is a potential relationship and inquire about PDE5I use when evaluating a patient with a new diagnosis of NAION.

INTRODUCTION

Phosphodiesterase-5 inhibitors (PDE5I), which are used for treatment of erectile dysfunction (ED) and pulmonary arterial hypertension, have been implicated in being a causative factor for development of nonarteritic anterior ischemic optic neuropathy (NAION). The relationship between PDE5I and NAION has been based on the publication of case reports that have documented loss of vision due to NAION after ingestion of sildenafil or tadalafil starting in 2000, but more recently has been supported by a case-crossover retrospective study. There still remains controversy regarding a cause-and-effect relationship between PDE5I and NAION. The mechanism by which

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NAION occurs is still not well understood. This raises doubts about its potential relationship with PDE5I because one must explain how this class of medications has its effect on circulation to the optic nerve in a situation in which the pathophysiology of NAION itself is not known. Nonetheless, neuro-ophthalmologists have accepted that there is a potential relationship and inquire about PDE5I use when evaluating a patient with a new diagnosis of NAION.

History of Erectile Dysfunction Drug Development and Mechanism of Action

The PDE5Is that are approved by the Food and Drug Administration (FDA) include the following:

- Sildenafil
- Vardenafil
- Tadalafil
- Avanafil

Sildenafil was first synthesized by pharmaceutical chemists working at Pfizer and was initially studied for use in treatment of hypertension and angina. Phase I clinical trials suggested that the drug had little effect on angina but could induce penile erection.

The FDA approved these medications for treatment of ED as follows:

- Sildenafil (Viagra) in March 1998
- Vardenafil (Levitra) in August 2003
- Tadalafil (Cialis) in November 2003
- Avanafil (Stendra) in April 2012

Udenafil (Zydena) is not FDA approved for sale in the United States, but is available in other countries.

Cialis is available in the following size tablets:
- 2.5 mg
- 5 mg
- 10 mg
- 20 mg

Viagra is available in the following size tablets:
- 25 mg
- 50 mg
- 100 mg

Levitra is available in the following size tablets:
- 2.5 mg
- 5 mg
- 10 mg
- 20 mg

Stendra is available in the following size tablets:
- 50 mg
- 100 mg
- 200 mg

The PDE5Is act by selectively preventing cyclic guanosine monophosphate (GMP) breakdown in the corpora cavernosa and the pulmonary arterial vasculature, which potentiates the downstream effects of nitric oxide. Nitric oxide induces