Nasal Obstruction as a Common Side-Effect of Sildenafil Citrate

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KIROGLU, A.F., BAYRAKLI, H., YUCA, K., CANKAYA, H. and KIRIS, M. *Nasal Obstruction as a Common Side-Effect of Sildenafil Citrate.* Tohoku J. Exp. Med., 2006, **208** (3), 251-254 — Sildenafil citrate is an effective oral drug for erectile dysfunction. The main action of sildenafil is the enhancement of the effect of nitric oxide (NO) by inhibiting the cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase-5 (PDE-5), an enzyme responsible for degradation of cGMP. NO is also present in the nasal mucosa and is responsible for vasodilation causing congestion and nasal obstruction. The aim of this study was to detect the effect of sildenafil on nasal mucosa in terms of nasal obstruction. A total of 16 patients presented to urology clinic suffering from impotence and medicated with sildenafil were included in the study. Before and after oral administration of 50 mg sildenafil, in all of the patients the nasal patency was examined by active anterior rhinomanometry (a method of assessing nasal resistance) using air pressure of 150 Pascal. In addition, all patients were asked about their sensation of nasal patency to detect the symptomatic nasal obstruction. There was a significant decrease in nasal air flow values (cm³/s) ($p < 0.05$). Except for three cases, all patients indicated that they had the sensation of nasal obstruction after the use of sildenafil ($p < 0.05$). Nasal obstruction is a common complaint for the patients using Sildenafil. ——— Sildenafil; nasal patency; obstruction; rhinomanometry

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Sildenafil citrate (Viagra[®], Pfizer Inc., New York, NY, USA) is the first oral agent to be introduced for the management of erectile dysfunction. During sexual stimulation nitric oxide (NO) is released in the corpus cavernosum. NO activates the guanylate cyclase and results in increased levels of cyclic guanosine monophosphate (cGMP)

from guanosine monophosphate (GMP). cGMP is broken down by phosphodiesterase-5 (PDE-5). Sildenafil, as a potent and selective inhibitor of the cGMP-specific PDE-5 enzyme, relaxes the smooth muscle in the corpus cavernosum, and allows greater inflow of blood, thereby causing erection (Boolell et al. 1996). Sildenafil is rapidly

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absorbed with maximal plasma concentrations within 1 hour after oral intake and has a mean terminal half-life of 3 to 5 hours (Goldstein et al. 1988). NO regulates a variety of cellular and tissue functions, and is present in orally exhaled air (Gustafsson et al. 1991) but higher levels are found in the human nasal airways (Alving et al. 1993), especially in the paranasal sinuses (Lundberg et al. 1995). As a biologic mediator serving many functions, NO is present in nasal cavities and paranasal sinuses (Lundberg 1996). In addition to human corpus cavernosum smooth muscle, PDE-5 is also found in other tissues including vascular, visceral smooth muscle, and skeletal muscle (Moreira et al. 2000). In keeping with the known functions of NO as a vasodilator in the pulmonary and systemic vascular beds (Wallis et al. 1999), NO could potentially cause vasodilation in nasal cavity.

Rhinomanometry is a method of assessing nasal resistance, which represents the obstruction to airflow through the nasal passages. Nasal resistance is calculated by measuring the flow through the nose and also the pressure of force required to cause the airflow. Rhinomanometry measures the air pressure and the rate of airflow in the nasal airway during respiration. We determined changes in nasal patency in patients taking Sildenafil by anterior active rhinomanometry.

MATERIALS AND METHODS

After ethical approval was obtained from Yuzuncu Yil University Faculty of Medicine ethical committee, patients presented to urology clinic suffering from impotence and medicated with sildenafil were included in the study. The written permission was taken from all patients. A total of 16 patients with no history of previous nasal surgery, any nasal medication, clinical evidence of present rhinitis, gross septal deviation were included in the study. The median age was 58 years (range 50 to 65 years). Before the administration of sildenafil all subjects were evaluated by anterior active rhinomanometry (Hortmann®, Rhinomodule 180, Neckartenzlingen, Germany) at 150 Pascal (Pa). After one hour of administration of 50 mg sildenafil, rhinomanometric measurement was repeated. In addition, all patients were asked about their sensation of nasal patency to detect the symptomatic nasal obstruction. Statistically the results were

evaluated using paired *t*-test and chi-square test.

RESULTS

Following the administration of sildenafil, there was a significant decrease in nasal air flow values (cm^3/s) at 150 Pa ($p < 0.001$). The mean air flow value was 115.25 ± 96.14 (Table 1). Except for three cases, all patients indicated that they had the sensation of nasal obstruction after the use of sildenafil ($p < 0.05$) (Table 1).

DISCUSSION

Sildenafil is a specific PDE-5 inhibitor that facilitates erection by the inhibition of cGMP breakdown in the corpus cavernosum (Boolell et al. 1996). NO is normally found in nasal cavity in very high concentrations (Lundberg et al. 1995), and NO has been proposed as a marker in inflammatory diseases of the upper airways (Lundberg 1996). Immunohistochemical techniques have shown strong staining for inducible NO synthase in the epithelial cells of turbinates (Rosbe et al. 1996). Some authors suggest that NO synthase is located within the granules of human nasal mucosal mast cells (Baccì et al. 1994).

NO is a potent biological mediator and it was initially described as an endothelium derived relaxing factor due to its action as a vasodilator. Also NO regulates the mucociliary function in the nasal airway. Therefore, children with cystic fibrosis and Kartagener's syndrome were found to have very low or absent levels of NO (Lundberg et al. 1994; Dotsch et al. 1996).

There have been several studies identifying the presence of three isoforms of NO synthase, but the reports show different results according to the subjects and analytic methods (Oh et al. 2003). Ferguson and Eccles reported that nasal concentration of NO is not related to the total nasal airway resistance as they measured by posterior rhinomanometry (Ferguson and Eccles 1997).

Motamed et al. (2003) first assessed the effect of sildenafil on nasal patency on five patients. They have used a Youlten flowmeter for their measurements and have found reduced nasal

TABLE 1. *Patients' nasal airflow values and presence of sensation of nasal obstruction*

Patient no.	Nasal air flow (cm ³ /s) at 150 Pa (A)		Sensation of nasal obstruction (B)
	Before	After	
1	95	90	—
2	196	181	—
3	59	28	+
4	227	35	+
5	226	167	+
6	59	16	+
7	59	57	—
8	280	35	+
9	388	274	+
10	290	162	+
11	394	225	+
12	154	92	+
13	481	149	+
14	594	388	+
15	450	373	+
16	288	129	+

(A): ($p < 0.01$) *t*-test.(B): ($p < 0.05$) chi-square test.

patency after the administration of sildenafil. The present study is the second report on the effect of sildenafil on nasal patency, but we used a different method of anterior active rhinomanometry. We thus confirmed the findings reported by Motamed et al. (2003).

In our study three cases had mild decrease in nasal air flow values compared with the other patients and these three patients felt no change in the sensation of nasal obstruction after the use of sildenafil. We do not know the reason exactly, but nasal obstruction is not seen in all patients using Sildenafil (Moreira et al. 2000).

In conclusion, the present study suggests that patients using sildenafil may complain of nasal obstruction.

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