

·Original Article·

Characteristics of sildenafil erections in healthy young men

Onder Yaman¹, Zafer Tokatli¹, Murat Akand¹, Atilla H. Elhan², Kadri Anafarta¹

¹Department of Urology, ²Department of Biostatistics, University of Ankara, School of Medicine, Ankara 06100, Turkey

Abstract

Aim: To determine the effect of sildenafil citrate on the nocturnal penile erections (i.e. time to onset, the duration of erection, and the interval between first and second erections) of healthy young men. **Methods:** Twenty-two potent men, 23–29 years old, were recruited for the study. All subjects completed three sessions over consecutive nights using the RigiScan monitoring device (Dacomed, Minneapolis, USA). After a first night of adaptation, night 2 records were their baseline values, and on night 3 they received 100 mg of sildenafil citrate. Statistical comparisons were done between the second and third night data. **Results:** The mean time to onset of the first erection with sildenafil citrate was (34 ± 18) min, whereas it was (74 ± 24) min ($P < 0.001$) without sildenafil citrate. The number of erections observed during the first 5 h after sildenafil citrate medication was 3.6 ± 0.5 in contrast to 2.4 ± 0.5 with no medication ($P = 0.001$). The interval between first and second erections was shorter with sildenafil citrate: (52 ± 26) min vs. (85 ± 34) min ($P = 0.01$). The duration of the last erection was statistically significantly longer with the sildenafil citrate: (64 ± 33) min vs. (42 ± 28) min ($P < 0.01$). **Conclusion:** Healthy young men achieved erection within 34 min after sildenafil citrate administration, which is shorter than the 1 h interval proposed by the manufacturer. The interval between the first and second erections was shorter and the duration of the last nocturnal erection was longer. (*Asian J Androl 2005 Dec; 7: 395–398*)

Keywords: sildenafil citrate; nocturnal erection; nocturnal penile tumescence; rigidity testing; erectile dysfunction

1 Introduction

The introduction of sildenafil citrate, the first effective oral agent for erectile dysfunction (ED), has led to major changes in ED management and widespread use of this medication worldwide [1–4]. More than 20 million patients have been treated with sildenafil citrate for ED [5, 6]. Therefore, sildenafil is one of the most widely studied drugs effective in ED [7–9].

Although pharmacokinetic parameters of sildenafil were well established in previous studies, the aim of our study was to observe the effect of the drug on nocturnal penile tumescence and rigidity (NPTR) (time to onset, duration of erection and the interval between the first and second erections) in healthy young male volunteers.

2 Materials and methods

2.1 Patients

Twenty-two medical students ($n = 8$) and urology residents ($n = 14$), 23–29 years old at University of Ankara, Turkey, were recruited for the study. A disorder-free medical and sexual history and normal erectile

Correspondence to: Dr Onder Yaman, Sehit Ersan Cad., Pembe Köşk Sitesi, B-1 Blok, No 15, 06680, Çankaya, Ankara, Turkey.
Tel: +90-312-427-69-71 Fax: +90-312-311-21-67
E-mail: yaman@medicine.ankara.edu.tr
Received 2004-09-27 Accepted 2005-05-08

function were recorded.

2.2 Study protocol

According to the study protocol, changes in NPTR of the subjects' penises were determined at home for the 3 consecutive nights using the RigiScan monitoring device (Dacomed, Minneapolis, USA).

During the first night which was considered as adaptation night (night 1), the RigiScan monitoring device was applied to the penis and turned off; participants were then studied for further 2 nights, which involved the record of penile erectile activity. The night 2 records were treated as baseline values, while on night 3, they received 100 mg of sildenafil (Pfizer, New York, NJ, USA). Participants were invited to go to bed at their usual time, at least 2 h after the end of a meal without the intake of any alcohol- or caffeine-containing beverages as well as any kind of medication.

2.3 Data analysis

After each monitoring period, all data were transferred to a personal computer. At the end of the study, data were analyzed with RigiScan Plus software version 4.0. The software recognized erectile activity as a 20 % increase in the base loop circumference that persisted for at least 3 min. It also calculated units of tumescence and rigidity each night separately. Sessions lasting for less than 5 h were excluded from further analysis. The correlation between duration and erectile activity during sleep was measured by determining the following parameters: number of erection during the first 5 h (with tip rigidity greater than 60 % and duration greater than 10 min), time to onset of first erection, interval between the first and second erections and duration of last erection.

2.4 Statistical analysis

Data were expressed in mean \pm SD if applicable. Paired *t*-test and Wilcoxon signed ranks test were used

as appropriate. $P < 0.05$ was considered significant.

3 Results

All 22 subjects completed the study protocol and no session was less than 6 h in duration. The average duration of sleep was 7 h. We only observed transient headache in one subject as a side-effect of sildenafil.

The mean time for onset of erection with sildenafil citrate was (34 \pm 18) min but (74 \pm 24) min without sildenafil citrate ($P < 0.001$). The number of erections observed during the first 5 h after the administration of sildenafil citrate medication was 3.6 \pm 0.5 in contrast to 2.4 \pm 0.5 with no medication ($P = 0.001$). The interval between the first and second erections was shorter when sildenafil citrate was administered: (85 \pm 34) min *vs.* (52 \pm 26) min ($P = 0.01$). The duration of the last erection was significantly longer with sildenafil citrate: (64 \pm 33) min *vs.* (42 \pm 28) min ($P < 0.01$) (Table 1).

4 Discussion

Previous studies have shown that following oral administration, sildenafil absorption occurred rapidly, with maximum plasma concentrations (C_{max}) occurring within 1 h (30 min–120 min in fasted state) [10–12]. The ingestion of high-fat meals delays the absorption by 40 min–65 min probably because of delayed gastric emptying [13]. Hence most studies evaluated the efficacy of sildenafil directed patients to take sildenafil approximately 1 h before sexual activity, and it was commonly thought by the patients that sildenafil takes at least 1 h to work [14]. However, Padma-Nathan *et al.* [15] showed that the time to onset of erection induced by sildenafil was as brief as 14 min after dosing, and most of the men with ED who took sildenafil were able to achieve at least one erection that resulted in successful intercourse within 20 min (51 %) or 30 min (68 %). Overall, the median time to

Table 1. Results of NPTR data.

	Night without sildenafil	Night with sildenafil	<i>P</i> value
Time to onset of first erection (min)	74 \pm 24	34 \pm 18	< 0.001
Number of erections during first 5 h	2.4 \pm 0.5	3.6 \pm 0.5	= 0.001
Interval between first and second erections (min)	85 \pm 34	52 \pm 26	= 0.01
Duration of latest erection (min)	42 \pm 28	64 \pm 33	< 0.01

onset of an erection after taking sildenafil that resulted in successful intercourse was 36 min.

Although there was a wealth of conventional information on pharmacokinetics and pharmacodynamics of sildenafil on patients with ED, there has not been much published in the area of young healthy volunteers using occasional sildenafil. In our study when we analyzed our NPTR data, we calculated that the mean time to onset of erection with sildenafil was 34 min; however, it was 74 min on night 2 (without sildenafil). Our result of 34 min was slightly longer than Eardly's findings (27 min) [11].

However, Eardly's study [11] was different from ours as results were determined by the RigiScan monitoring device following visual sexual stimulation after different dosages (50 mg vs. 100 mg) of sildenafil citrate were administered.

It has been suggested that erections occurring during rapid eye movement (REM) sleep were initiated by the release of nitric oxide from nonadrenergic-noncholinergic nerves that then activated the hemodynamic cascade of events leading to rigidity [16]. As a contrast to the classical knowledge about sildenafil that it worked at patients with ED, we observed significant improvement in the nocturnal erections of healthy young men without ED and without sexual stimulation after sildenafil administration [17]. Since sildenafil used the same cascade of erection physiology, this could explain the night time effect of sildenafil. In fact there was no sexual stimulation during nocturnal penile erections, but the other steps to erection were same.

In our study we also observed that the number of erections observed during the first 5 h after sildenafil medication was significantly more than without medication ($n = 3.6$ vs. $n = 2.4$, $P = 0.001$). And also the interval between the first and second erections was shorter on the nights when sildenafil was administered (85 min vs. 52 min, $P = 0.01$). This observation was supported by Mondaini *et al.* [18], who stated that sildenafil reduced the postorgasmic refractory time (although the postorgasmic refractory period was linked to hormonal, and neurohormonal factors related to orgasm and not just to the occurrence of an erection). However, in contrast to our previous study [17], Mondaini *et al.* [18] also stated that sildenafil did not improve erections in healthy young men. We knew that our study was preliminary and a more rigorous, double-blinded, placebo-controlled, randomized trial was required, perhaps even one in a sleep

laboratory setting where sleep architecture can be examined.

In conclusion, our NPTR data showed that healthy young men achieve erection within 34 min of taking sildenafil, which is shorter than the generally accepted 1 h interval. Secondly, sildenafil might reduce the length of time between the first and second nocturnal erections, which implies that it is a potential therapeutic for different sexual disorders.

References

- 1 Sadowsky R, Miller T, Moskowitz M, Hackett G. Three-year update of sildenafil citrate efficacy and safety. *Int J Clin Pract* 2001; 55: 115–28.
- 2 McCullough AR. Four-year review of sildenafil citrate. *Rev Urol* 2002 Suppl; 4: S26.
- 3 Rosenstock HA, Axelrad SD. Erectile dysfunction: on the efficacy of a phosphodiesterase inhibitor in patients with multiple risk factors. *Asian J Androl* 1999; 1: 211–4.
- 4 Rosenstock HA, Axelrad SD. Erectile dysfunction: on the efficacy of a phosphodiesterase inhibitor in patients with concurrent sex therapy. *Asian J Androl* 1999; 1: 207–10.
- 5 Padma-nathan H, Eardley I, Kloner RA, Laties AM, Montorsi F. A 4-year update on the safety of sildenafil citrate (Viagra). *Urology* 2002; 60: 67–90.
- 6 Son H, Park K, Kim SW, Paick JS. Reasons for discontinuation of sildenafil citrate after successful restoration of erectile dysfunction. *Asian J Androl* 2004; 6: 117–20.
- 7 Huang XB, Xiong CL, Yu CG, Zhou JL, Shen JY. Effect of sildenafil citrate on penile erection of rhesus macaques. *Asian J Androl* 2004; 6: 233–5.
- 8 Low WY, Ng CJ, Tan NC, Choo WY, Tan HM. Management of erectile dysfunction: barriers faced by general practitioners. *Asian J Androl* 2004; 6: 99–104.
- 9 Kilinc K, Gunduz MI, Gumus BH, Vatansever S, Kaymaz F. Ultrastructural effect of sildenafil citrate on corpus cavernosum and other genital organs in female rats. *Asian J Androl* 2003; 5: 37–41.
- 10 Nichols DJ, Muirhead GJ, Harness JA. Pharmacokinetics of sildenafil citrate after single oral doses in healthy male subjects: absolute bioavailability, food effects and dose proportionality. *Br J Clin Pharmacol* 2002; 53: 5S–12S.
- 11 Eardley I, Ellis P, Boolell M, Wulff M. Onset and duration of action of sildenafil citrate for the treatment of erectile dysfunction. *Br J Clin Pharmacol* 2002; 53: 61S–65S.
- 12 Boolell M, Allen MJ, Ballard SA, Gepi-Attee S, Muirhead GJ, Naylor AM, *et al.* Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction. *Int J Impot Res* 1996; 8: 47–52.
- 13 Sjöqvist F, Borga D, Dahl ML, Orme ML. Fundamentals of clinical pharmacology. In: Speight TM, Holford NHG, editors. *Avery's Drug Treatment*, 4th ed. Auckland: Adis International;

Characterics of sildenafil erections

1997. p1–73.
- 14 Goldstein I, Lue TF, Padma-Nathan H, Rosen RC, Steers WD, Wicker PA, Sildenafil Study Group. Oral sildenafil in the treatment of erectile dysfunction. *N Engl J Med* 1998; 338: 1397–1404.
- 15 Padma-Nathan H, Stecher VC, Sweeney M, Orazem J, Tseng LJ, Deriesthal H. Minimal time to successful intercourse after sildenafil citrate: results of a randomized, double-blind, placebo-controlled trial. *Urology* 2003; 62: 400–3.
- 16 Montorsi F, Maga T, Strambi LF, Salonia A, Barbieri L, Scattoni V, *et al.* Sildenafil taken at bedtime significantly increases nocturnal erection: results of a placebo-controlled study. *Urology* 2000; 56: 906–11.
- 17 Yaman O, Tokatli Z, Inal T, Anafarta K. Effect of sildenafil on nocturnal erections of potent men. *Int J Impot Res* 2003; 15: 117–21.
- 18 Mondaini N, Ponchietti R, Muir GH, Montorsi F, Di Loro F, Lombardi G, *et al.* Sildenafil does not improve sexual function in men without erectile dysfunction but does reduce the postorgasmic refractory time. *Int J Impot Res* 2003; 15: 225–8.