



EFFECT OF SILDENAFIL CITRATE ON SEMEN PARAMETERS IN HEALTHY INDIAN INDIVIDUALS

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**ABSTRACT**

**AIM:** This study was conducted to evaluate the acute effects of oral sildenafil 100mg single dose on sperm count, density, motility, morphology, and ejaculate volume in healthy male volunteers

**METHODS:** A total of 50 healthy male volunteers aged between 19 to 36years were randomized to take a single dose of 100mg sildenafil citrate and a single dose of placebo. The doses were given on two separate occasions with a gap of 7 days. Sperm and ejaculate properties were evaluated from samples taken at screening and 1.5 hours after the dose

**RESULTS:** Sildenafil administration showed a significant increase in sperm motility but did not show any statistically significant change in count, density, or morphology of sperms. It also did not affect the ejaculate volume

**CONCLUSIONS:** Sildenafil citrate administration could modestly increase sperm motility.

**KEYWORDS :**

**INTRODUCTION**

Erectile dysfunction(ED) is a widespread condition that can have a negative impact on quality of life<sup>1</sup> affecting both young and old men. Sildenafil is the first oral agent introduced for the management of ED. When administered before sexual activity it produces reliable efficacy, good tolerability, and the prompt onset of action has a plasma half-life that produces appropriate duration of action while avoiding accumulation on repeated once daily use<sup>2</sup>.

In clinical trials sildenafil has been shown to increase duration and rigidity of penile erection and also enhances the ability to achieve erections, leading to successful completion of intercourse.

A large number of drugs can be transported into the seminal plasma, where they have a direct effect on sperm motility in particular<sup>3</sup>. These include phosphodiesterase inhibitors that have the potential to increase motility. One such drug is pentoxifylline which is a cAMP PDE inhibitor that has shown to improve sperm motility both in vitro and in vivo<sup>4</sup>.

Sildenafil is a potent and selective inhibitor of the cyclic guanosine monophosphate (cGMP)-specific PDE type 5 enzyme<sup>5</sup>. It enhances the activity of the nitric oxide-cGMP pathway that promotes penile erection. The drug is relatively lipophilic and would therefore be expected to distribute into the seminal fluid.

A clinical study was conducted to investigate the effect of a single oral dose of sildenafil on several semen parameters, sperm motility and morphology parameters.

**MATERIALS & METHODS**

Healthy male volunteers were eligible for entry into this study if they were between the ages of 18 and 45 years, and had a body mass index of 18–25 kg m<sup>-2</sup>. Exclusion criteria were as follows: azoospermia or extreme oligospermia, as the nospermia, or teratospermia or any combination of these at baseline; clinically significant disease; abnormality in prestudy laboratory data and physical examination, any comorbidity including diabetes and hypertension, alcohol consumption; drug abuse; and cigarette smoking. Written and informed consent was obtained from each subject before study entry.

This study compared 100-mg doses of sildenafil with placebo. All doses were administered as single oral doses for two times separated by 7 days.

Subjects who met the inclusion criteria underwent a physical examination, measurement of supine blood pressure and pulse rate, a 12-lead electrocardiogram, laboratory safety tests (blood and urine). A semen sample was also collected to exclude subjects who were azoospermic.

Abstinence for a minimum of 3 days before each dose of the study drug. Caffeine or alcohol consumption was stopped before the study.

**Assessments**

Semen samples were obtained at screening and 1.5 after dose.

**The following parameters were determined:**

- Sperm count
- Sperm morphology
- Percentage of sperm exhibiting any movement (% motile)
- Percentage of static sperm (% static)
- Percentage of motile sperm that swam rapidly (% rapid)
- Percentage of motile sperm that swam progressively (% progressive)
- The subjects were divided into two groups with group A labeled as Sildenafil group and group B as Placebo group. The mean values of semen parameters studied were taken to compare the two groups.

**RESULTS**

**Table 1**

Parameters	Normal value	Group A Sildenafil	Group B Placebo	Sildenafil-placebo (95% confidence intervals)
Sperm count	100-500 (x10 <sup>6</sup> )	389	370	22.3 (-44.7, 88.7)
Sperm density	50-100(x10 <sup>6</sup> )	117	110	10.5 (-8.5, 29.4)
Abnormal forms	<85%	82	80	1.16 (-0.01, 2.32)
Ejaculate volume	2.5-6ml	3.66	3.63	0.027 (-0.299, 0.352)

Sildenafil did not have any significant effect vs placebo on parameters of sperm count, sperm density, morphology, and ejaculate volume.

**Table 2**

Parameters	Normal value	Group A	Group B	Sildenafil-placebo (95% confidence intervals)
Motile	>50	70.3	60.1	7.05; 95%CI: 2.59-11.51
Static	<50	30.7	39.8	3; 95%CI: 0.23, 5.2
Rapid	>25	45.2	37.1	3.11; 95%CI: 0.23-5.99
Progressive	>15	34.2	27.4	6.23; 95%CI: 2.43-10.04

The percentage of motile spermatozoa (MD=7.05; 95%CI: 2.59-11.51), the percentage of total progressive motility (Md=6.23; 95%CI: 2.43-10.04), and rapid progressive motility (MD=3.11; 95%CI: 0.23-5.99) were increased after oral Sildenafil.

## DISCUSSION

A total of 50 healthy male volunteers aged between 19 to 36 years were randomized to take a single dose of 100mg sildenafil citrate and a single dose of placebo. The doses were given on two separate occasions with a gap of 7 days. Sperm and ejaculate properties were evaluated at screening and after 1.5 hours after the dose

Sildenafil administration showed a significant increase in sperm motility but did not show any statistically significant change in count, density, or morphology of sperms. It also did not affect the ejaculate volume.

In previous studies, the semen and plasma concentrations of sildenafil suggest that the drug rapidly equilibrates between the blood and the accessory genital glands that produce the constituents of the ejaculate. Total semen concentrations of sildenafil compared well with total and free plasma concentrations. The concentration of the drug in semen appeared to be greater than its free plasma concentration, indicating a disequilibrium. This may be caused by ion trapping of sildenafil in prostatic secretions (pH 6.5). However, previous studies have demonstrated that ion trapping can result in seminal fluid to plasma concentration ratios of 5–10<sup>6</sup>, which emphasizes that several factors are involved in determining the distribution of drugs into the seminal fluid. These factors include the dissociation constant, lipid solubility, equilibration time, and plasma protein binding.

Cuadra et al.<sup>7</sup> and Glenn et al.<sup>8</sup> observed increased sperm motility, as well the proportion of acrosome-reacted sperm, suggesting that sildenafil may affect male fertility.

Similarly, Mostafa et al. found a concentration-dependent stimulatory effect of sildenafil<sup>9</sup> and tadalafil<sup>10</sup> on sperm motility in asthenozoospermic patients.

In a recent meta analysis, it was observed that a significant increase in the percentage of motile spermatozoa, the percentage of rapidly progressive spermatozoa, and the percentage of total progressive spermatozoa and sperm morphology after PDE5 inhibitors administration in infertile patients with or without oligoasthenospermia, but not in fertile men.<sup>11</sup>

## CONCLUSION

A comparison of sildenafil vs placebo on the semen parameters in this study showed no effect on sperm count, density, morphology and no change in ejaculate volume or viscosity. However, a significant effect was seen on motility, percentage of progressive motility, and percentage of rapid progressive motility.

With Oral Sildenafil treatment, there is a modest increase the sperm motility and morphology in infertile men.

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