



## PRIAPISM INDUCED WITH SINGLE ORAL DOSE OF SILDENAFIL: A RARE CASE REPORT

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### ABSTRACT

Phosphodiesterase enzyme inhibitors like Sildenafil citrate and tadalafil has revolutionised the treatment of erectile dysfunction. Priapism as a side effect of Sildenafil has been reported very rarely. We report a case of priapism caused by usual dose of Sildenafil.

### CASE REPORT

A 25 years old married healthy male presented in emergency department with history of priapism of 72 hours duration after consuming a non-prescribed single tablet of sildenafil (50 mg) purchased over the counter along with 250ml of alcohol. He developed painful priapism 30 minutes after drug intake, when he was viewing pornographic material for sexual stimulation. There was no history of intake of any priapism inducing drugs like antihypertensive or antipsychotics or any other drugs that affect the metabolism of Sildenafil. There was no history suggestive of sickle cell trait, leukemia or multiple myeloma.

Haemogram, coagulation parameters and serum chemistry were all within normal limits. Work up for sickle cell trait was negative.

On examination, the corpus spongiosum and glans was soft and the corpus cavernosa was rigid. Patient was reluctant for any kind of surgical intervention and insisted for oral medication. On repeated perusation, aspiration and corporal wash followed by a winter procedure were done but with no relief. Fifteen milliliters of dark blood was aspirated with 16 G needle. Consent was taken after explaining the negligible chance of regaining potency for proximal caverno-spongiosal shunting but patient refused for any surgical intervention and left the hospital against medical advice. Further follow up could not be done.

### DISCUSSION

Priapism is defined as a genuine erectile disorder, in which erection persists uncontrollably without sexual purpose. The significance of priapism is further emphasized by the fact that this disorder commonly causes erectile tissue damage and leads to the loss of functional erections. Hematologic dyscrasias like sickle cell disease, thrombophilia and thalassemia have been associated with priapism. Hematologic malignancies including leukemia and multiple myeloma have also been identified for their risk associations with this disorder.<sup>1</sup>

The identification of the cyclic GMP/NO pathway as the final neurotransmitter messengers responsible for penile erection and the subsequent development of highly specific phosphodiesterase enzyme inhibitors like sildenafil has revolutionised the treatment of erectile dysfunction. Sildenafil citrate and tadalafil citrate are effective, well tolerated and safe treatments for erectile dysfunction caused by a broad range of aetiologies.<sup>2-3</sup> Sildenafil though has no direct relaxant effect on isolated human corpus cavernosum, but it enhances the effect of nitric oxide (NO) by inhibiting phosphodiesterase type 5 (PDE5), which is responsible for degradation of cGMP in the corpus cavernosum. When sexual stimulation causes local release of NO, inhibition of PDE5 by sildenafil causes increased levels of cGMP in the corpus cavernosum, resulting in smooth muscle relaxation and inflow of blood to the corpus cavernosum.<sup>4-5</sup> Sildenafil at recommended doses has no effect in the absence of sexual stimulation. Sildenafil has been reported to restore sexual activity in low-flow priapism, recurrent priapism, corporal fibrosis associated with recalcitrant priapism and as a preventative strategy for priapism. Sildenafil has also been used to relieve priapism in patients with sickle cell disease.<sup>6-9</sup>

Sildenafil, a selective inhibitor of cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type 5 (PDE5), is a white to off-white crystalline powder with a solubility of 3.5 mg/mL in water and a molecular weight of 666.7. In addition to the active ingredient, each tablet contains the inactive ingredients like: microcrystalline cellulose, anhydrous dibasic calcium phosphate, croscarmellose sodium, magnesium stearate, hypromellose, titanium dioxide, lactose, triacetin, and FD & C Blue #2 aluminum lake. There may be a hypersensitivity to any component of the tablet. For most patients, the recommended dose is 50 mg taken, as needed, approximately 1 hour before sexual activity. Based on effectiveness and toleration, the dose may be increased to a maximum recommended dose of 100 mg or decreased to 25 mg. The onset of activity of sildenafil is 14 min. The peak plasma levels are attained within 30 to 120 min (median 60 min) of oral dosing in the fasted state. It is rapidly absorbed after oral administration, with a mean absolute bioavailability of 41%. It is eliminated predominantly by hepatic metabolism (mainly cytochrome P450 3A4) and is converted to an active metabolite with properties similar to the parent, sildenafil. Both sildenafil and the metabolite have terminal half lives of about 4 h. sildenafil clearance is reduced in severe renal impairment or hepatic cirrhosis. The concomitant use of potent cytochrome P450 3A4 inhibitors (e.g., erythromycin, ketoconazole, itraconazole) as well as the nonspecific CYP inhibitor, cimetidine, is associated with increased plasma levels of sildenafil. Side effects like back pain, flu syndrome, arthralgia, hyperglycemia, paresthesia, tremor, dyspepsia, photosensitivity reaction, abdominal pain, syncope, tachycardia, palpitation, anemia and leukopenia are observed. Non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, has been reported rarely.<sup>10</sup>

An extensive review of the published medical literature and the manufacturer's clinical trial and post marketing database identified six reports of priapism following the use of sildenafil in an estimated 1.2 billion users.<sup>11-14</sup> The earlier reports of priapism following the use of sildenafil have been with self-administration of very large doses or in conditions predisposing to priapism or had used drug for prolonged period. The first case report of priapism induced by oral sildenafil was due to a high dose (200mg)<sup>15</sup>. Priapism may also follow simultaneous oral dose and intracavernous injection. of alprostadil or trimix.<sup>11</sup> Recently, an accidental consumption of six 50 mg tablets (up to 30 mg/kg) in a 19-month-old child resulting in facial flushing and priapism has been reported.<sup>15</sup> Priapism following the use of sildenafil in safe oral doses for a healthy individual has been reported earlier but very rarely; 17-19

Our patient had priapism following a single dose of the usually prescribed dosage of 50 mg and had no predisposing condition. Although he has consumed tablet with alcohol, however extensive review of literature does not show any interaction between alcohol and sildenafil. Sildenafil (50 mg) did not potentiate the hypotensive effect of alcohol in healthy volunteers with mean maximum blood alcohol levels of 0.08%. On the contrary in a recent study it is reported that sildenafil dramatically reduces alcohol-induced gastric damage in rats. The authors provide convincing evidence that such protection not only occurs via the nitric oxide (NO)/cGMP pathway, but also involves regulation of ATP-sensitive potassium channels.<sup>20</sup>

An escalating dose starting at 12.5 mg and then increasing to 25 mg and followed by the usual prescribed dose of 50 mg may help to avoid the side effects of priapism. [4] This case highlights the existence of unfortunate myths surrounding the omnipotence of Sildenafil, in all sorts of sex related problems. It points toward an urgent need for steps to prevent unauthorized prescription and misuse of this drug. It should only be used under professional guidance as abuse of such drug may lead to severe morbidity. It is difficult to predict which individuals are more prone to develop priapism, though a genetic basis with cross-reactivity of PDE-3 in addition to PDE-5 resulting in a cumulative erection effect may be possible elucidation. In the eventuality of only few case reports, highlighting this side effect of sildenafil, it is difficult to draw concrete conclusion. Therefore more research directed towards the etiopathogenesis of this side effect of sildenafil is needed.

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