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#### **CASE REPORT**

# Fatal Haemorrhagic Stroke Due to Concomitant Abuse of Sildenafil and Alcohol: A Case Report

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#### **Abstract**

Sildenafil is increasingly being abused recreationally for improving sexual endurance. The combined use of sildenafil with alcohol increases the risk of cerebrovascular accidents. We present the case of a 39-year-old male with no significant medical history who suffered a fatal stroke after consuming high doses of sildenafil while intoxicated with alcohol. Notable findings at autopsy include left ventricular hypertrophy, left capsuloganglioninc bleed and atherosclerotic changes in the coronary arteries. This case report highlights the risks of recreational sildenafil use, especially when combined with alcohol, and underscores the need for pharmacovigilance and public awareness.

**Keywords:** Sildenafil, Erectile Dysfunction, Recreational Abuse, Stroke, Dangerous Sexual Practices, Death

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#### Introduction

Sex is a fundamental aspect of human existence not just intended for reproduction but a way of self-expression and intimacy. Like many aspects of human behaviour, it has evolved over time, shaped by biology, culture, social norms, and more recently, technology. What someone may find as a weird sexual fantasy could often be normal for others in the vast diverse spectrum of human sexuality. Nowadays, many aspects of sexual adventures are shaped by exposure to explicit content and curiosity to personalise those experiences. The global porn industry, with its exploration of various fantasies, mirrors the growing human desire to experiment with different forms and expressions of sex [1].

Deaths occurring during or shortly after sexual activity have been documented in literature. For instance, in a 12-year multi-centric study although the overall incidence of deaths was low, middle-aged men during heterosexual intercourse are the largely affected group. Most of the fatalities are cardiac in origin, classically linked to undiagnosed ischemic heart disease. The abuse of cocaine and erectile dysfunction medications like sildenafil are common contributory factors in them, along with a higher prevalence of obesity engagement in unusual sexual practices [2].

Sildenafil is the first globally approved drug for erectile dysfunction. It was initially developed as a treatment for pulmonary hypertension and angina pectoris. However, during the clinical trials researchers unexpectedly observed marked penile erections among the volunteers, prompting the pharma company to repurpose this drug for erectile dysfunction. As a phosphodiesterase type 5 (PDE5) inhibitor, sildenafil works by selectively inhibiting PDE5, which increases the levels

of cyclic guanosine monophosphate (cGMP) in the corpus cavernosum, leading to smooth muscle relaxation and vasodilation, thereby improving erectile function [3].

Currently, sildenafil is primarily indicated for the treatment of erectile dysfunction pulmonary and arterial hypertension. However, it is contraindicated in individuals with hypersensitivity sildenafil, those to undergoing concurrent nitrate therapy, and those with severe cardiovascular disease. Common adverse effects include headache, flushing, dyspepsia, nasal congestion, impaired vision, and indigestion.

Sildenafil is often recreationally abused worldwide, driven by myths of enhanced duration of intercourse and the pursuit of greater sexual satisfaction. combining sildenafil However, alcohol, cocaine, or other drugs of abuse to enhance sexual endurance can pose serious health risks. While sildenafil is an effective treatment for erectile dysfunction when used as prescribed, misuse can cause serious complications including death. This combination can disrupt blood pressure regulation and cardiovascular function, increasing the risk of stroke and other severe effects [4,5].

## **Case presentation**

A 39-year-old male, who was on vacation with his friend without any significant history of medication or recreational drug abuse, developed acute right-sided hemiparesis the next morning after consuming 3-4 tablets of 50 mg sildenafil in an intoxicated state with alcohol. On examination in the emergency department, the patient was diagnosed with left capsulo-ganglionic hemorrhage. The etiology of the hemorrhage was suspected

to be induced by the synergistic effects of sildenafil and alcohol. The patient was initially stabilized and managed in the hospital for five days, after which he was transferred to a tertiary care facility in another city for ongoing management. On day 10, following stabilization, the patient was discharged with a recommendation for physiotherapy to aid in neurological rehabilitation. However, the day after discharge, while undergoing physiotherapy, the patient suffered a seizure, followed by loss of resuscitation Despite consciousness. efforts, he was subsequently pronounced dead at another hospital. Since the patient was brought dead and the case fell under the category of suspicious deaths, it was subjected to a medico-legal autopsy.

At autopsy, the deceased was found to be obese, and the heart had left ventricular hypertrophy (20-25 mm) (Figure 1), and the brain revealed a left capsulo-ganglionic hemorrhage with intraventricular extension, showing both a dark brownish red color old clot and a bright red fresh hemorrhage (Figure 2). Chemical analysis of stomach contents and viscera detected no poisonous substances or sildenafil. Histopathological examination showed hemorrhage within the left lateral

ventricle and white matter of the brain, accompanied by reactive gliosis, extravasated red blood cells, hemosiderinand macrophages, edematous changes. The heart revealed left ventricular wall thickening, and the left coronary artery exhibited irregular thickening with a lipid core and scattered foamy histiocytes in the tunica media. The liver displayed fat accumulation and congestion, while the demonstrated kidneys glomerular congestion, acute tubular necrosis, luminal hemorrhage in the collecting ducts, and interstitial hemorrhage with edema in the medulla (Figure 3).

The initial cause of death was opined as a cerebrovascular accident due to unknown substance poisoning. However, upon reviewing the scene of the offence report, inquest findings, autopsy report, chemical analysis of viscera, histopathology, the cause of death was determined to be a cerebrovascular accident temporally associated with the abuse of sildenafil and alcohol. Negative findings included the absence of signs of trauma, infection, or other systemic abnormalities. These autopsy findings are consistent with the complications of sildenafil (drug) and alcohol abuse.

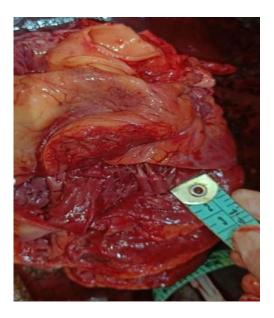


Figure 1. Left ventricle transverse cut section: hypertrophy of heart.

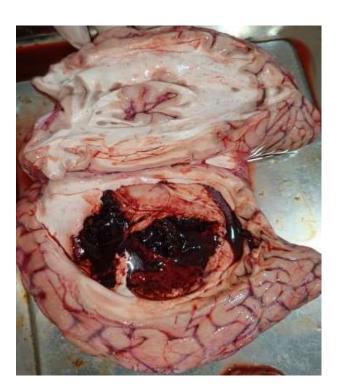


Figure 2. Resolving and fresh left capsulo-ganglionic bleed with ventricular extension on sagittal section.

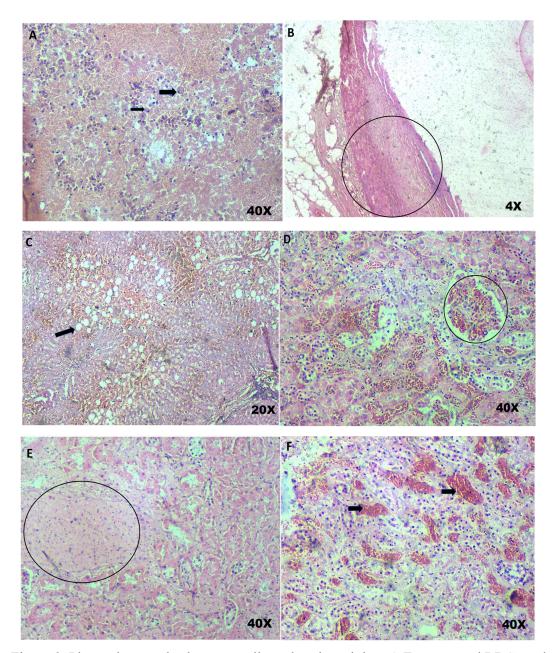


Figure 3. Photomicrographs, haematoxylin and eosin staining. **A** Extravasated RBCs and haemosiderin laden macrophages in brain (arrow) associated with reactive gliosis; **B** Irregular thickening of left coronary artery in heart (circled); **C** Fat cells and congestion in liver (arrow); **D** Glomerular congestion in kidney (circled); **E** Tubular Necrosis (circled); **F** Interstitial haemorrhage (arrow)

#### Discussion

The recommended of dose sildenafil is 50 mg, and the maximum dose is 100 mg within 24 hours [6]. Though be sildenafil could not detected qualitatively or quantitatively from the chemical analysis of viscera due to a lapse approximately 10 days of since consumption, it was inferred from the discovery of an empty blister pack at the scene and subsequent investigation that the deceased had consumed at least 200 mg of sildenafil which is an abnormally high dose.

The concomitant use of sildenafil alcohol can induce substantial and vasomotor effects, leading to blood pressure fluctuations that may directly or indirectly trigger cerebrovascular accidents, as reported in the literature [3,6]. The exact pathophysiology of stroke in such scenarios remains unclear. Sildenafil influences cerebral circulation through the nitric oxide (NO)-cGMP pathway, leading to vasodilation and increased cerebral blood flow. This heightened blood flow can raise the risk of intracranial haemorrhage, particularly in individuals with underlying conditions such as latent atherosclerosis or undiagnosed hypertension, as seen in this case. Additionally, sildenafil's effects on enzymes like PDE-1 and PDE-2 in the brain may further alter cerebral hemodynamics, exacerbating the risk of vascular complications.

The misuse of sildenafil, markedly among young populations without underlying erectile dysfunction, has grown, often as a countermeasure to the erectile dysfunction caused by other recreational drugs. High-dose sildenafil is sometimes combined with substances like MDMA (ecstasy), stimulants, or opiates in dangerous mixes referred to as "sextasy" or "trail mix." The concurrent use of sildenafil

with amyl nitrite or alcohol is potentially fatal and can cause haemorrhagic stroke.

The risk of rebleeding is a critical consideration in this case, as the patient developed a secondary haemorrhage over a resolving haemorrhagic stroke occurred 10 days prior. Rebleeding in cases of cerebrovascular accidents (CVA) of the haemorrhagic type can occur at variable intervals, ranging from days to years, depending on several factors. [7] These include the use of anticoagulants, persistent vascular injury, and uncontrolled hypertension, all of which contribute to vascular instability. However, one of the major limitations of this case report is absent data from the medical records and the previous medical history or drug history of the decedent [7].

Alcohol is known to cause cerebral vasodilation by several mechanisms including modulation of the biogenic amine and NO pathways. Alcohol potentiates the effects of sildenafil on the brain by increasing the production of nitric oxide (NO) from the endothelial cells, which promotes vasodilation and lowers vascular smooth muscle tone. This enhanced NO production can lead to further cerebral vasodilation, increasing the risk of adverse cerebrovascular events like stroke or transient ischemic attacks (TIA), particularly in individuals with pre-existing cardiovascular risk factors. It is also known that sildenafil redistribution in the arterial flow because of vasodilatory effect reduce the perfusion and cause myocardial leading circulatory insufficiency ischemia [6].

The misuse of sildenafil and similar drugs by younger individuals is increasingly associated with psychological dependence, potentially masking underlying issues related to sexual function.

Furthermore, combining these drugs with alcohol or other substances can impair cognitive function, leading to reduced inhibitions which can lead to engaging in unsafe sexual practices, thereby elevating the risk of contracting sexually transmitted infections (STIs) due to unprotected sex [5].

## Conclusion

The crux of the present discussion is to bring to limelight the adverse effects of unprescribed use of sildenafil, which has become a matter of concern. In the present case, the contributory role of key factors, such as the potentiating effect of alcohol and the presence of underlying comorbidities like hypertension and atherosclerotic heart disease precipitating a cerebrovascular accident cannot be overlooked. Sildenafil is commonly used by both younger and older adults, and its over-the-counter availability has led to misuse without prescription. Public awareness campaigns are crucial to educate high risk groups like young adults on the dangers of non-prescribed sildenafil use.

The expectations surrounding sexual performance have become distorted, often driven by unrealistic ideals and external pressures. This leads some to misuse drugs like sildenafil, not out of medical indication, but to fit an imagined standard of performance. It's important to recognize that sexual experiences vary intra-individually and inter-individually, influenced by factors such as stress, fatigue, underlying health conditions and the emotional dynamics between the partners. These variations often don't require any medical attention as generally perceived. To foster better understanding, these topics should be discussed openly, without stigma, through anonymous platforms where young

adults, and healthcare professionals, including andrologists, can engage in meaningful dialogue.

## **Statements and Declarations Conflicts of interest**

The authors declare that they do not have conflict of interest.

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