Reconsidering PDE5 Inhibitors as a Harm Reduction Strategy in Receptive Anal Intercourse: Addressing the Regulatory and Clinical Gaps in Access to Amyl Nitrite

Authors:
George Forgan-Smith[1]

[1] Collins Street Medical Centre, Melbourne, Australia

Background:
Amyl nitrite is a potent relaxant of smooth muscle and is sometimes used by gay, bisexual, and other men having sex with men (GBMSM) as a measure to lessen risk for localised trauma during receptive anal intercourse. It is activated by the release of nitric oxide ,activating guanylate cyclase results in increased intracellular cGMP promoting relaxation of the internal anal sphincter (IAS).

Despite being classified as a prescription-only medicine in Australia, no regulated product is currently available. Access remains unregulated and inconsistent. Internationally actions, including raids and manufacturing closures in the USA, have disrupted availability and raised safety concerns.

Problem Statement:
The regulatory vacuum around amyl nitrite leaves sexually active populations at risk. Without access to safe, standardised products, individuals rely on illicit supply chains or go without, potentially increasing the incidence of trauma, pain, and associated complications. This situation presents a pressing clinical and public health gap.

Evidence and Opportunities:
PDE5 inhibitors—such as sildenafil and tadalafil—act downstream in the same nitric oxide–cGMP pathway by inhibiting phosphodiesterase type 5 and sustaining smooth muscle relaxation. Small studies suggest significant reductions in IAS tone:

- 10% topical sildenafil reduced IAS pressure by 18% in patients with chronic anal fissures, with rapid onset and minimal systemic effects.

- A crossover trial with 40 mg oral tadalafil showed significant anal resting pressure reductions in healthy women.

- PDE5 inhibitors showed comparable efficacy to inhaled nitrates with fewer adverse events. Due to similar actions, it is important to not mix nitrates PDE5 inhibitors.

Conclusion:
There is now a credible pharmacological rationale, supported by early human data,

to reframe PDE5 inhibitors as potential harm reduction tools in sexual health. With a known safety profile, legal availability, and demonstrated mechanism, these medications merit clinical trials and guideline consideration as regulated alternatives to amyl nitrite for anal relaxation and trauma prevention.

Disclosures:
Dr George Forgan-Smith has no disclosures with regards to this abstract.