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Short Communication

Sildefanil and Epistaxis

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Abstract

Reports about Sildefanil (Viagra®) and Epistaxis are anecdotal. This review could identify only three reports in world literature with a total number of four patients. In a 20 year period since the Viagra® approval by the FDA in 1998, this seems to be a rather low number of cases. All persons developed Epistaxis secondary to Viagra intake, two persons had also taken Cialis®. None had Erectile Dysfunction, all had consumed the PDE-5-inhibitors to enhance their sexual performance, the undesired side-effects therefore rather affect consumers than patients. On the other hand this may be an indication that Viagra® is a very safe substance, since no reports about multimorbid patients and Viagra-related Epistaxis have been published so far.

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Keywords

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- Epistaxis
- Erectile dysfunction
- Pulmonary hypertension
- Rhinology

INTRODUCTION

Epistaxis secondary to Sildefanil intake is a possibly underreported problem, since Epistaxis patients generally are more or less reluctant to disclose the state of their sex life on admission to an ENT-doctor. We therefore decided to check the scientific literature for case reports on Sildefanil-related Epistaxis.

METHOD

Cross-referenced, extensive Data-base search on Google, Google Scholar and PubMed with the search terms: Sildefanil, Viagra, PDE-5-inhibitors, drugs, side-effects, bleeding, hemorrhage, Epistaxis, Erectile Dysfunction and Pulmonary Hypertension.

RESULT

The search revealed three publications, which actually reported about persons, who had developed Epistaxis secondary to Viagra intake. A total of 4 persons have been reported so far, three of them men in the age range late 50ies to early 70ies. One case report is about a man, 32 years of age. Two patients had a history of arterial hypertension and were on regular medication with antihypertensives. All persons had taken Viagra®, two had, in an interval, also consumed Cialis®. None of the persons suffered from Erectile Dysfunction, all had consumed the drugs to enhance their sexual performance. Epistaxis was controlled by a variable combination of the following options: cessation of PDE-5-inhibitor consumption, cautery, packing, antihypertensive treatment and admission to hospital. In one case the bleeding stopped spontaneously.

DISCUSSION

The first selective PDE-5 inhibitor, Sildefanil-Citrate, was released in 1991, for the treatment of cardiac diseases. In 1998 it was approved by the FDA for the treatment of Erectile Dysfunction and Pulmonary Hypertension. Apart from the medical indications Sildefanil is also popular as a recreational drug and as an enhancer of sexual activities [1]. This observation might explain, why all persons in this review were actually not patients, but rather consumers of Sildefanil. Sildefanil is the oldest and most popular PDE-5-inhibitor on the market. Other selective inhibitors of Phosphodiesterase V are Tadalafil (Cialis®, Adcirca®), Vardenafil (Levitra®) and Avanafil (Spedra®). Levitra® and Cialis® were launched in 2003, Spedra® in 2014. The drugs may be distinguished by their onset of effect, half-life-time, side-effect profile and mode of consumption. Cialis®, for example, is popular as a "Weekend-pill," because of its long half-life time, Levitra® is popular because of its rapid onset of effect and Spedra® because it is highly selective. All PDE-5-inhibitors have similar side-effects, like flush, dizziness and a congested nose [2-6]. Epistaxis as an undesired side-effect has so far only been described in connection with Viagra® and Cialis® [3-6]. Other side-effects of PDE-5-inhibitor consumption in the head and neck region may be Sudden Hearing Loss, Optic Nerve Atrophy and Variceal Bleeding [1,7]. So far only a small amount of cases has been reported in literature concerning PDE-5 inhibitors and side effects. However there is a potential that the actual number of PDE-5 related Epistaxis is much higher than reported so far. One reason may be that these events are under reported, another reason may be the consumption of PDE-5-inhibitors as a recreational drug, not as a therapeutic agent. PDE-5 inhibitors can be purchased in many countries without prescription, and the Internet offers an almost unlimited access to all kinds of medications. PDE-5 inhibitors are available as Sildenafil (Viagra®), Revatio®,

Generics), Tadalafil (Cialis®, Adcirca®), Vardenafil (Levitra®) and Avanafil (Spedra®). During sexual stimulation, nitric oxide is released from nerve cells and subsequently from the endothelial cells in the corpus cavernosum of the penis. Nitric oxide activates guanylate cyclase, which catalyzes the synthesis of cGMP from guanosine triphosphate (GTP). This cGMP causes the vascular smooth muscle to relax, which leads to an increased blood flow into the penis. The cGMP level is regulated by maintenance of a balance between its production and degradation. cGMP is degraded by phosphodiesterases (PDEs). The respective drugs inhibit the enzyme „cyclic Guanosine-Monophosphate-specific-Phosphodiesterase Typ 5" (PDE 5). The inhibition leads to higher levels of cGMP and therefore to a relaxation of the smooth muscle cells of the vessels, which results in an increase of blood flow, not only within the Corpora cavernosa, but also in other areas of the body like the turbinates. Aside from Epistaxis other side-effects, such as head-aches, flush and vertigo have been observed. Furthermore Epistaxis is facilitated by the inhibition of thrombocyte aggregation, which has also been reported for PDE-5 inhibitors in vitro. The first report about Sildenafil and Epistaxis was published by Hicklin and coworkers in 2002 [6], a further report followed in 2005 by Ismail and Harris and in 2006 Pomara and coworkers reported about Epistaxis secondary to Tadalafil [3,4]. Reports about Vardenafil have been published on vocal Fold (F) hemorrhages within the larynx, visual field defects and intracerebral hemorrhages [10,11]. So far no reports could be found on hemorrhages in the head and neck related to Adanafil intake. This finding could be explained by the following: Adanafil is highly selective, therefore acts only in the vessels of the Corpova cavernosa. Second, the drug has been released in 2014; i.e., it is so new that no reports have been published so far.

Epistaxis secondary to drugs should be treated by cessation of the causative agent. With regard to PDE-5-inhibitors patients and consumers could switch to Adanafil, which seems to have the least number of undesired effects. Patients should also condition their nasal mucosa with lubricants and should avoid other substances with an impact on coagulation. In the majority of all cases Epistaxis in adults is caused by a combination of medical and environmental problems: heating period, dry climate, air conditioning, arterial hypertension, anticoagulative substances, heart disease etc. [8]. In some cases it can also be caused by hereditary disorders or malignant growths. It is therefore mandatory, that Epistaxis patients should be seen by an ENT-specialist, even if a correlation to a drug is more than plausible. If the bleeding cannot be stopped by conservative means and the origin of the hemorrhage cannot be identified within the nose, the bleeding has to be stopped by packing the nose. In recent years numerous new packing materials have been developed, which have great potential to stop the bleeding, with the least possible damage to the nasal mucosa [9].

In conclusion it can be said that Sildefanil seems to be a safe drug with regard to Epistaxis. No reports on Epistaxis secondary to Sildefanil use in actual patients have been published so far. All reported cases showed that Epistaxis actually occurred in consumers, who took the drug to enhance their sexual performance. Adanafil could be used as a substitute for Sildefanil, due to its high selectivity and low side-effect profile.

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