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Postorgasmic Illness Syndrome: What do we know so far?

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ABSTRACT

Post-orgasmic illness syndrome (POIS) is rare condition that is characterized by transient flu-like symptoms and cognition disorders that occur shortly after ejaculation and last for 2-7 days. There are about 50 cases of POIS in the literature. The prevalence and incidence of POIS are still unknown due to a paucity of studies. The exact pathogenesis of POIS remains unknown; the most acceptable hypothesis is an autoimmune/allergic process. We made a literature search via PubMed for publications from 2002 to 2018 with the "post orgasmic illness syndrome" medical subject heading term to analyze current data regarding symptoms, burden, pathophysiology, and to discuss potential management options for POIS. POIS is diagnosed by five preliminary diagnostic criteria. It is categorized into two types: primary and secondary. There is the concomitance between POIS and PE. The autoimmune/allergy hypothesis is the most accepted hypothesis explaining POIS pathogenesis. A competing hypothesis involves a disorder of endogenous μ-opioid receptors. Patients with POIS have been symptomatically treated with antihistamines, selective serotonin reuptake inhibitors, and benzodiazepines. A trial of hyposensitization therapy with autologous semen was successful. A trial of nonsteroidal anti-inflammatory medication helped in a single case report but failed to successfully treat other patients with POIS.

Introduction

Post-orgasmic illness syndrome (POIS) is a rare condition that was first described by Waldinger and Schweitzer in 2002[1]. Two men in their study suffered from exhaustion, flulike symptoms (intense warmth, perspiration, headache, burning eyes, sore throat, general myalgia), erythema of the skin (itching, pimples), urinary hesitation, disordered stooling, and mental disturbances (reduced concentration and agitation). Notably, all of these symptoms occurred shortly after ejaculation and lasted to 2 - 7 days[1].

In an effort to limit the symptomatology, most patients suffering from POIS resort to reducing sexual activity or abstinence[1-8]. The physical and psychological effects of POIS significantly affect the quality of life of both patients and their partners[1-12].

Approximately, 50 cases have been recorded in the literature since 2002[4,5]. The prevalence and incidence of POIS are unknown owing to a paucity of studies[5,12]. Most of the studies are case reports. POIS is underdiagnosed and underreported, although there are an increasing number of self-reported cases of POIS in Internet forums[5,6].

Various theories have been postulated on the pathophysiology of POIS[2,4,5]. The most pervasive explanation is attributed to Waldinger and Schweitzer who hypothesized an immune-modulated mechanism as the underlying etiology[4].

This mini-review seeks to provide an update on the current literature on POIS. The authors also aim to provide updated information regarding the pathophysiology of POIS and to discuss potential management options.

Methods

We conducted a 2002 to 2018 literature search using PubMed. The following medical subject heading terms were used: "orgasm illness", "post-orgasmic", "post-orgasmic illness syndrome." Inclusion criteria for article selection were studies (of any design) on post-orgasmic illness in men, and publication in a peer-reviewed journal. The reference lists of identified publications were reviewed manually for additional relevant articles. Manuscripts written in languages other than English were accepted.

Clinical Presentation

In 2011, Waldinger et al. reported the clinical characteristics of 45 Dutch patients with POIS and were able to define five diagnostic criteria[3] (Table 1).

They proposed that the presentation of POIS was highly variable; however, the most common symptoms were: concentration difficulties, extreme fatigue/ exhaustion and fever/ body warmth/ perspiration/ shivering[3].

Furthermore, POIS symptoms started within 30 minutes of ejaculation in 87% of afflicted men in the Waldinger et al. study[3]. Notably, of the 33 men (73%) with a partner, the intercourse frequency was 1.04 ± 1.00 times per week; three men had decided to abstain completely from intercourse[3]. Eight of these 33 men reported an intercourse frequency of once in two to six months[3]. Of the males older than 30 years old without a partner, six men refrained from masturbation or intercourse as much as possible[3]. Other authors recorded similar reduced sexual activity frequency in POIS patients[2,5,7,15]. All of these represent the consequences of POIS (Figure 1).

It should be emphasized that POIS not only affected men but also their partners[13,14]. Nearly all men were concerned about the relationship with their sexual partner and expressed feelings of guilt for having the disorder[3]. In the series of 33 couples in the Waldinger et al. study, there were three divorces during follow-up; two of which were due to patients' strategy of abstinence or avoidance of sexual activity. On the other hand, two initially single males married female partners who accepted the negative sexual consequences of their disorder[3]. The majority of case reports emphasized that POIS caused a negative impact on the partners[2,6,7].

The patients with POIS should undergo a complete medical history that includes existing allergies, sexually transmitted diseases, and any history of prostatitis. In addition, a neuropsychiatric interview regarding possible neurological or psychiatric disorders, as well as a sexual function interview with special attention to ejaculatory disorders and their partner relationship should both be recorded[2,3,16,18]. Patients should be carefully examined and screened for other diseases that have similar symptoms to POIS. This should include recording the duration of symptoms, an assessment of bothersome symptoms and a detailed lower urinary tract symptoms review. A digital rectal examination (DRE) needs to be performed after

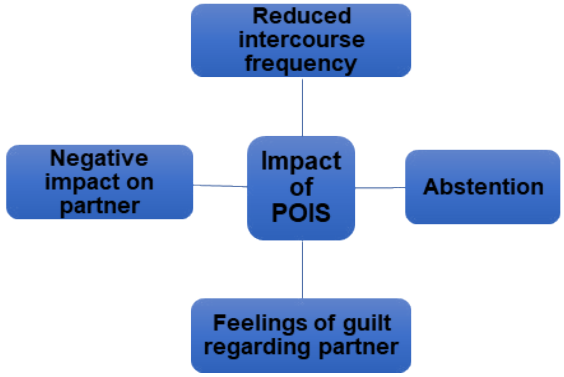

Figure 1: Impacts of POIS on afflicted patients and their partners[2,3,5-7,13]

Table 1 *Five preliminary diagnostic criteria of POIS*[3]

1. One or more of these following symptoms:
- General: Extreme fatigue, exhaustion, palpitations, anomic aphasia, incoherent speech, dysarthria, concentration difficulties, irritability, hyperacusis, photophobia, depressed mood
- Flu-like: Fever, extreme warmth, perspiration, chills, prodrome, cold intolerance
- Head: Headache, fogginess, heaviness in the head
- Eyes: Burning, conjunctival injection, blurry vision, eye pain, watery discharge, eye irritation and itchiness
- Nose: Nasal congestion, rhinorrhea, sneezing
- Throat: Dirty taste in mouth, dry mouth, sore throat, tickling cough, hoarse voice
- Muscle: Muscle tension in the back or neck, muscle weakness and pain, heaviness in the legs, muscle stiffness
2. Symptoms occur seconds to a few hours after ejaculation
3. Symptoms occur always or nearly always, i.e., in more than 90% of ejaculation events
4. Symptoms last for about 2 to 7 days
5. Symptoms then disappear spontaneously

a midstream urine sample has been collected for urine dipstick, microscopy, and culture[2,3,16,18]. The males who are clinically diagnosed as having POIS undergo routine tests, including full blood count, electrolytes, creatinine, liver function tests and hormonal laboratory (follicle stimulating hormone, luteinizing hormone, prolactin, testosterone). Magnetic resonance imaging brain scans may be needed to rule out abnormal conditions in the brain that might lead to a headache after ejaculation. Notably, no condition associated with ejaculation has been recorded in cases of POIS through pathology history, examination findings or laboratory tests[2,3,5,6,15,16,18].

A thorough history and examination are both important in making a differential diagnosis, especially prostatitis or chronic pelvic pain, which can manifest similarly as flu-like symptoms, weakness and pain of the muscle localized to the perineum or suprapubic area. Nevertheless, symptoms of prostatitis typically last longer than those of POIS (2-7 days). In addition, pain during or after ejaculation and lower urinary tract symptoms are the most prominent, and bothersome features in prostatitis patients. A DRE may reveal a nodule or tenderness and pain in the prostate [8,9,10].

Primary POIS and Secondary POIS

Based on the study of 45 males who fulfilled the aforementioned five criteria, Waldinger et al categorized two types of POIS: a primary type in which POIS becomes manifest from the first ejaculation in puberty or adolescence, and a secondary type in which POIS manifests later in life[3]. Among 45 males in their study, 49% had the primary type, whereas 51% had the secondary type[3]. According to this classification, there were 5 primary and 4 secondary POIS patients who have been described in the literature by other authors[2,4,5,7,15-18].

POIS and PE

Waldinger et al commented that one POIS patient in his study suffered from lifelong premature ejaculation (PE), and another had acquired PE[1]. Among 45 POIS cases in the Waldinger et al. study, 56% of men reported lifelong PE with an intravaginal ejaculation latency time of less than one minute[3]. The authors estimated that the relative risk of men with POIS was 22.4-fold higher to develop PE than for healthy individuals[3]. Jiang et al., Shigeta et al. and Bignami et al have also reported lifelong PE in their three POIS patients[5,7,19]. It may be speculated that PE in this group of men is induced by forced abstinence and the low frequency of sexual activity[3]. Another reason was these men also had to cope with reducing ejaculation frequency as much as possible even when the urge to have sex and intimacy is normal or even strong, as the consequences of an ejaculation would be a disturbance to their life and work[14].

Pathophysiology

Different hypotheses have been postulated on the pathophysiology of POIS, including an immunological phenomenon, an opioid-like withdrawal or a neuro-endocrine response[2-5,15] (Table 2). Nevertheless, the most predominant explanation is attributed to Waldinger et al., who hypothesized an immune modulated mechanism as the underlying etiology[3]. This theory was supported by a study of skin-prick tests (SPT). After performing this test in 33 patients with POIS using extremely diluted samples of their own semen (1:40,000), the authors reported that 88% had positive reactions[3]. Limitations of this study were the lack of performing the SPT with autologous semen in an age-matched control group of healthy men and the lack of measuring the serum specific immunoglobinE (IgE) in the POIS patients. To address this limitation of the Waldinger et al. study, Kim et al. confirmed the existence of serum semen-specific IgE in their patient with POIS[15].

In contrast to the autoimmune/allergy hypothesis, Jiang et al. proposed that an IgE-mediated semen allergy in POIS-afflicted men might not adequately account for the symptomatology[5]. They performed a SPT and other intracutaneous tests in a patient with POIS and three healthy controls[5]. The results countered the immune-mediated hypothesis; three healthy men without POIS showed positive skin test reactions to injection with autologous semen. The authors suggested that there was no evidence of semen-specific IgE antibodies in men with POIS and positive skin reactions to autologous semen[5]. Instead, they compared the symptoms of POIS to opioid withdrawal, which include similar physical and psychological manifestations[5,20].

Ashby and Goldmeier proposed an alternate hypothesis where POIS was driven by a disordered cytokine or

Table 2 *Hypothesis and management of POIS*

Year	Authors	Numbers of cases	Hypothesis	Treatment recommendation
2011	Waldinger et al [3,4]	47	Immune modulated mechanism	Subcutaneous immunotherapy with autologous semen
2018	Kim et al [15]	1		Intralymphatic immunotherapy with autologous semen
2010	Ashby et al [2]	2	Disordered cytokine or neuroendocrine response	Symptoms treatment [2,17,19]: Antihistamines, selective serotonin reuptake inhibitors, and benzodiazepines
2015	Jiang et al [5]	1	Opioid withdrawal	Diclofenac 75mg 1-2 hours prior to sexual activities with orgasm, continue twice daily 24-48 hours

neuroendocrine response[2]. This was supported by the improvement of POIS symptoms in the patient following administration of prophylactic diclofenac, a nonsteroidal anti-inflammatory drug(NSAID)[2].

Management

Currently, there is no specific treatment for POIS, in part, due to varying pathophysiological hypothesis (Table 2). Patients with POIS-like symptoms have been treated with antihistamines, prednisone, benzodiazepines, and tramadol[1,17,19]. Selective serotonin reuptake inhibitors may be considered in the concomitant treatment of POIS and PE[19].

Considering the successful outcomes of hyposensitization therapy in clinical allergic diseases, Waldinger et al. reported the improvement of POIS symptoms by the hyposensitization treatment with autologous semen in two Dutch patients[4]. The protocol of treating POIS was developed by Marcus Meinardi[3,4]. He intensified the hyposensitization by starting with extremely diluted autologous semen and gradually employing higher concentrations of autologous semen[4]. To modify this treatment, Kim et al. performed intralymphatic immunotherapy with autologous semen instead of subcutaneous delivery on a Korean male with POIS[15]. This is a novel method of allergen-specific immunotherapy being used in allergic diseases. Using ultrasound guidance and a 25-gauge needle, autologous semen was aseptically injected into an inguinal lymph node at a dilution of 1:40,000[15]. Then, the concentration was increased by 3-fold, as in a previous study by Waldinger[4,15]. After the 3rd and 4th injections, the patient complained of flu-like symptoms which persisted for 3 to 4 weeks with an intensity that remained at 50% to 60% 5 days after the 3rd injection and at 60% to 70% 5 days after 4th injection[15]. Notably, at 8 and 15 months after the first injection, all POIS- related symptoms except sore throat and urinary symptoms were alleviated and their durations were shortened[15]. The authors recommended that hyposensitization therapy could have therapeutic effects in patients with POIS in whom allergies are a dominant etiologic factor[15]. Nevertheless, limitations of hyposensitization treatment include a lack of healthy male controls for the autologous semen skin test results. Consequently, its true efficacy remains unconfirmed.

Another successful trial of therapy is a NSAID (diclofenac), which succeeded in reducing symptoms (up to 80% improvement) and allowed the patient in that case report to increase his sexual frequency from twice a month to four times a month[2,5,16]. However, NSAIDs therapy has failed in other patients, highlighting the need for further investigation into the nature and treatment of POIS. Additionally, numerous anecdotal therapies have been suggested to be efficacious in improving POIS symptoms, including niacin, olive leaf, fenugreek, saw palmetto, and wobenzym[6].

Conclusion

POIS is a rare condition and its true prevalence remains unknown. POIS can cause severe distress that can affect both the POIS-afflicted male and his partner. Patients with POIS manifest with a constellation of flu-like and allergic symptoms that commence seconds, minutes, or hours after ejaculation and last for several days. POIS characterized by five criteria and its symptoms can be described by seven clusters. Depending on the time of onset, POIS is classified into primary and secondary categories. Notably, the combination of POIS and lifelong PE is apparent and deserves further attention in future POIS treatment strategies. The exact pathogenesis of POIS remains unknown, but the most acceptable hypothesis is an autoimmune/allergic process. On the other hand, chemical imbalances in the brain similar to opioid withdrawal or dysregulation in cytokine and chemokine response are postulated. Hence, no definitive treatment for POIS has been confirmed, but hyposensitization was successful in three patients[4,15]. Further research on the reactivity of healthy men to autologous semen, the roles of neurotransmitters in POIS as well as the relationship between POIS and PE need further investigation.

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Conflicts of Interest

All authors claim no conflict of interest regarding the content of this paper.

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