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Mini Review

Postorgasmic Illness Syndrome: An Update

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Abstract

Postorgasmic illness syndrome (POIS) is a rare condition affecting men who experience a cluster of flu-like and allergic symptoms after ejaculation. POIS can occur after intercourse, masturbation, or spontaneous ejaculation, and may persist for up to 7 d. Recurrent symptoms often negatively impact quality of life and sexual activity, leaving those affected with mental sequelae, diminished concentration, and mood changes. While it has been shown that various treatment options can alleviate symptoms in the short term, acute management remains controversial. In addition, follow-up data are severely lacking, resulting in the absence of established long-term management options for men suffering from POIS. This review highlights hallmark studies and the current state and promising developments surrounding clinical approaches to POIS.

Patient summary: In this review, we discuss what is known about postorgasmic illness syndrome (POIS), a disease that causes flu-like symptoms in some men after ejaculation. Little research has been on POIS, so its causes, diagnosis, and appropriate treatments are poorly understood.

1. Introduction

In 2002, Waldinger and Schweitzer [1] first described a postejaculatory syndrome on the basis of two men presenting with flu-like symptoms, including fatigue, warmth, and myalgia following ejaculation, resulting in avoidance of sexual activity. This cluster of symptoms was named postorgasmic illness syndrome (POIS) and was subsequently validated in a cohort of 45 men [2]. POIS can cause significant impairment of the relationships, sexual encounters, and self-image of affected men. While various pathophysiological mechanisms have been proposed, including immunologic hypersensitivity and sympathetic dysregulation, the exact underlying causes remain unclear [2,3]. Workup thus far relies on unvalidated diagnostic tools, including skin prick testing (SPT) and serum total immunoglobulin E (IgE) [4]. POIS treatment has seen numerous developments in recent years that are centered around targeted immunotherapy and alleviation of the associated psychological burden [5]. Despite recent advances, POIS remains an underdiagnosed condition; better insight is needed into the epidemiology, pathophysiology, proper workup, and management of the disease.

2. Pathophysiology

Studies have offered differing hypotheses on the pathophysiology of POIS, including the involvement of an immunological response [2,5], opioid-like withdrawal [6], and neuroendocrine response [7]. Waldinger et al. [2] posited that POIS is an immunogenic hypersensitivity reaction induced by repeated close contact between seminal pep-

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tides and T lymphocytes during ejaculation, corroborated by a study using SPT [5]. In contrast to Waldinger et al. [2], Jiang et al. [6] found no evidence of IgE-mediated semen allergy. In addition, Jiang et al. reported that the physical and psychological manifestations of POIS appear to be aligned more with those seen in opioid withdrawal syndrome rather than an immune reaction. Thus, they hypothesized that endogenous μ-receptors may be implicated [6].

Other studies have highlighted testosterone deficiency as a potential factor on the basis of low testosterone intake levels and symptom improvement following hormone replacement therapy [3,8]. Ashby and Goldmeier [7] noted that the POIS clinical picture is similar to that experienced during cytokine release/sympathetic dysregulation and found an improvement for one patient with a nonsteroidal anti-inflammatory drug (NSAID). Thus, the exact pathophysiology is not well established, leaving challenges for accurate diagnosis and targeted treatment.

3. Clinical manifestations

Waldinger and Schweitzer [1] first reported two cases of men presenting with rapid onset of flu-like symptoms, followed by cognitive disturbances and mood changes. These symptoms were present after most ejaculation events (90%) and lasted for up to 7 d. In the first large observational study performed, POIS was classified according to five preliminary criteria based on similar complaints from 12 Dutch males (Table 1). These criteria were then evaluated in a group of 45 males whose complaints aligned with most of the criteria. As a result of the psychological burden imposed by POIS, most affected men reported avoiding sexual activity and felt that the syndrome negatively affected their sexual relationships.

Since the symptoms for criterion 1 may vary substantially depending on the patient's clinical presentation, Waldinger et al. [2] categorized the disease into seven clusters based on the patients' own words (Table 2).

Waldinger et al. [2] also classified POIS into primary and secondary types on the basis of reports from their 45 participants. The primary type manifests during the earliest ejaculations following initiation of sexual activity (49%). The secondary type arises later in life (51%) [2].

Table 1 – The five diagnostic criteria for postorgasmic illness syndrome proposed by Waldinger et al. [2] in 2011

Criterion 1	One or more of the following symptoms: sensation of a flu-like state, extreme fatigue or exhaustion, weakness of the musculature, feverishness or perspiration, mood disturbances and/or irritability, memory difficulties, concentration problems, incoherent speech, congestion of the nose or watery nose, itching eyes
Criterion 2	All symptoms occur immediately (eg, in seconds), soon (eg, in minutes), or within a few hours after ejaculation that is initiated by coitus and/or masturbation and/or is spontaneous (eg, during sleep)
Criterion 3	Symptoms occur always or nearly always (eg, >90% of ejaculation events)
Criterion 4	Most of these symptoms last for approximately 2–7 d
Criterion 5	The symptoms disappear spontaneously

Table 2 – The seven clusters for criterion 1 proposed by Waldinger et al. in 2011 [2]

Cluster 1 (general)	Extreme fatigue, exhausted, palpitations, problems finding words, incoherent speech, dysarthria, concentration difficulties, quickly irritated, cannot stand noise, photophobia, depressed mood
Cluster 2 (flu-like)	Feverish, extreme warmth, perspiration, shivery, ill with flu, feeling sick, feeling cold
Cluster 3 (head)	Headache, foggy feeling in the head, heavy feeling in the head
Cluster 4 (eye)	Burning, red injected eyes, blurred vision, watery, irritating, itching eyes, painful eyes
Cluster 5 (nose)	Congestion nose, watery, runny nose, sneezing
Cluster 6 (throat)	Dirty taste in mouth, dry mouth, sore throat, tickling cough, hoarse voice
Cluster 7 (muscle)	Muscle tension in back or neck, muscle weakness, pain muscles, heavy legs, stiffness in muscles

4. Diagnostic workup

Owing to the unclear pathophysiology of POIS, diagnosis is often challenging and relies on exclusion of other causes. Other diagnoses that can mimic components of various clusters described by Waldinger et al. [2] include, but are not limited to, benign orgasmic cephalgia, orgasmoplexy, and sneezing/rhinorrhea. In addition to a thorough history and physical examination, routine tests are warranted, including a complete blood count, serum electrolytes, kidney and liver function, sex hormone levels (follicle-stimulating hormone, luteinizing hormone, testosterone), and urine studies [9]. SPT is perhaps the diagnostic tool most frequently utilized, with high sensitivity and specificity found in various studies. However, many existing studies did not use age-matched controls, including men without POIS symptoms; thus, more studies are needed [4,10]. Several studies have attempted to correlate serum total IgE with POIS incidence. While semen-specific IgE antibodies were found in some studies [11,12], others found normal IgE levels [3,4,13]. Other diagnostic tools, including The International Index of Erectile Function scale, brain/vessel imaging, and cystoscopy, have been used to rule out other causes, but their clinical utility remains to be proven in the POIS setting [12–14].

5. Management

Owing to the scarcity of published studies, both short- and long-term therapeutic recommendations for POIS are lacking. Thus, management largely relies on clinicians' experience and is typically individualized according to the patient's presentation.

Waldinger and Schweitzer [1] initially approached POIS using antihistamines and prednisone taken before and after intercourse, without relief. Benzodiazepines and selective serotonin reuptake inhibitors yielded partial improvements in psychological symptoms, with no somatic changes. To target ejaculation frequency, flutamide, an androgen receptor antagonist, was given, resulting in decreases in spontaneous ejaculations and intercourse frequency with no effect on somatic and psychological symptoms.

Reisman [13] investigated the potential of a novel treatment regimen including on-demand silodosin, considered to cause anejaculation, as first-line therapy. Subsequent

treatment with ibuprofen and prednisone was then administered on the basis of clinical response. In this study, 57% of males (eight of 14) were effectively managed on silodosin, 28.5% (two of seven of patients refractory to silodosin) on ibuprofen, and 80% (four of five refractory to silodosin and ibuprofen) on prednisone.

Previous studies have examined the link between testosterone deficiency, orgasmic function, and ejaculatory dysfunction [15]. Bolanos and Morgentaler [8] managed a case of POIS associated with hypogonadism with human chorionic gonadotropin (hCG) injections three times per week. After 6 wk, most of the patient's previous symptoms were resolved and his testosterone level had recovered.

Takeshima et al. [3] successfully managed a patient with hypogonadism and POIS with a combination of testosterone enanthate and NSAIDs. The patient's Aging Male Symptom score decreased from 45 to 21, and his Sexual Health Inventory for Men score increased from 3 to 7 during follow-up.

On the basis of assumption of an immunogenic/allergic mechanism, Waldinger et al. [5] initiated a hyposensitization program, including autologous semen subcutaneous injections, in two males. The patients reported 90% and 60% reductions in POIS-associated complaints at 15 and 31 mo, respectively. Kim et al. [12] reported symptom resolution in a Korean man with POIS after an allergen-specific immunotherapy regimen consisting of three to six injections into the inguinal lymph nodes at 4-wk intervals.

Huang et al. [16] performed bilateral epididymectomy and vasoligation in a patient refractory to immunosuppressive therapy, including prednisone and mycophenolate. The patient reported symptom resolution at 2-mo follow-up.

While treatment regimens including prednisone, autologous semen injections, silodosin, and hCG (when hypogonadism is present) have shown promise in recent studies, low sample sizes, a general lack of age-matched controls, and the unclear underlying pathophysiology cloud the current management landscape. However, it is clear that the treatment approach for POIS should ideally be centered around patient presentation, diagnostic findings, and patient preferences.

6. Conclusions

POIS remains an underdiagnosed and poorly understood condition. More studies are needed to better elucidate the underlying mechanisms to establish appropriate diagnostic criteria and direct targeted therapeutic modalities.

***Conflicts of interest*:** The authors have nothing to disclose.

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