



# Clinical experience with post-orgasmic illness syndrome (POIS) patients—characteristics and possible treatment modality

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## Abstract

Post-orgasmic illness syndrome (POIS) is a rare condition that includes a cluster of post-ejaculatory symptoms with debilitating physical and psychological consequences. The prevalence and incidence of POIS remain unknown as well as the pathophysiology of the syndrome, and there are no well-studied recognized treatment modalities. The current retrospective observational study describes a series of 14 highly selected patients who were actively looking for medical help as POIS has a significant effect on patients and their partners. The aim is to increase knowledge about this syndrome and possible treatment modality. According to a standard protocol, patients have been systematically interviewed, had a physical examination, laboratory blood tests, and treatments. Mean age was  $34.07 \pm 6.65$  years. The majority of patients had only one symptom in common—extreme fatigue. The most prevalent complaints were head pressure/heaviness, nose congestion and muscle tension; all patients suffered from more than 1 symptom. POIS started on average within 30 min of ejaculation and lasted for 3.5 days. The patients reported emotional and psychosocial burden of their symptoms, which also influence their partner and relationships. Immunoglobulin-E measurements did not show elevated levels and/or significant increase within 24 h after ejaculation. Silodosin, a highly selective  $\alpha_1A$ -blocker, which actually causes anejaculation, was effective treatment in 57% of the patients.

## Introduction

In 2002, Waldinger and Schweitzer describe for the first time two patients who suffer from post-ejaculation flu-like symptoms and introduce the post-orgasmic illness syndrome (POIS) [1]. POIS is a rare sex-related condition that affects men and includes a cluster of post-ejaculatory symptoms with debilitating physical and psychological consequences [2, 3]. The presentation of POIS is highly variable in the intensity, duration, type of symptoms, and their order of appearance. All symptoms occur immediately (e.g., seconds), soon (e.g., minutes), or within a few hours after ejaculation and most of these symptoms last for 2 to 7 days [3]. A large number of the men included in the study by Waldinger et al. [4] and Jiang et al. [5] reported lifelong premature ejaculation (PE). Many of the patients avoided

sexual activity, including masturbation, dampening and avoidance of sexual or intimate relationships to avoid the symptoms. Furthermore, the symptoms that accompany ejaculation may interfere with daily activities, such as work or study, and may also have a negative impact on the partner [6].

Due to lack of awareness about the syndrome and a limited number of studies, the prevalence and incidence of POIS remain unknown. A few hypotheses about the aetiology of POIS have been proposed, among others an immunological or autoimmune mechanism (supported by skin-prick test results of autologous semen), a disorder of cytokine response, and consumption of endogenous molecules that act on the opioid receptors, but the condition is not well understood [4, 5, 7, 8]. As a consequence, there is no accepted effective treatment.

In 2011, Waldinger et al. [4] proposed preliminary diagnostic criteria, which have recently been adapted by Strashny [9]. Three of these criteria are considered minimum for diagnosis [9]. The preliminary diagnostic criteria are as follows:

1. One or more symptoms from among these seven symptom clusters:

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- General cluster: extreme fatigue/exhausted, palpitations, problems finding words/incoherent speech, dysarthria, concentration difficulties, quickly irritated, cannot stand noise, photophobia, depressed mood.
  - Flu-like cluster: feverish, extreme warmth, perspiration, shivery, ill with flu, feeling sick, feeling cold.
  - Head cluster: headache, foggy feeling in the head, heavy feeling in the head.
  - Eyes cluster: burning, red-injected eyes, blurred vision, watery, irritating, itching eyes, painful eyes.
  - Nose cluster: congested nose, watery, runny nose, sneezing.
  - Throat cluster: dirty taste in mouth, dry mouth, sore throat, tickling cough, hoarse voice.
  - Muscle cluster: muscle tension in back or neck, muscle weakness, painful muscles, heavy legs, stiffness in muscles.
2. Symptoms begin from within a few seconds to within a few hours after ejaculation that occurs during coitus, masturbation, or nocturnal emission.
  3. Symptoms occur after all or almost all ejaculations, or in at least one ejaculatory setting (sex, masturbation, or nocturnal emission).
  4. Most symptoms last for about 2–7 days.
  5. Symptoms disappear spontaneously, without treatment.

In clinical practice, patients suspected of having POIS should undergo an interview regarding their complaints and a sexual function interview, with attention paid to ejaculation disorders, a complete medical history, interview regarding possible neurological or psychiatric disorders and a discussion about the impact of the POIS on the patient and his relationship should be included. Patients should be carefully examined and screened for other diseases that have similar symptoms to POIS (e.g. post-orgasmic cataplexy, orgasm-associated headaches, post-coital asthma, and rhinitis). Males who are clinically diagnosed as having POIS should undergo routine tests including a full blood count and hormonal laboratory tests (follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone) [4, 7, 8].

There are no recognized treatment modalities. POIS patients have been treated with antihistamines, selective serotonin reuptake inhibitors, nonsteroidal anti-inflammatory medication, analgesics, benzodiazepines, and hyposensitization therapy. None of these therapies have a confirmed efficacy and have many limitations [2, 4, 8, 10, 11].

This retrospective observational analysis of selected patients from one institution describes the clinical findings and the efficacy of suggested treatment modalities.

## Methods

In this retrospective study, all patients who were referred to our institution because of complaints suggestive for POIS have been evaluated. Patients have not been actively recruited. Informed consent was given for systematically anonymously recording their data for retrospective evaluation. According to a standard protocol, patients have been interviewed and questions included were about their complaints (type, duration, intensity, and clinical course), sexual function, medical history including medication, existing allergies, possible psychological or psychiatric disorders, substance use, coping strategies with complaints, impact of the complaints on their relationship and on their quality of life. PE was defined as intravaginal ejaculation latency time (IELT) of less than 60 s and determined according to the estimated IELT. As no validated questionnaire is available, measurement of these aspects was done using a Likert rating scale from 1 to 10 aiming at qualification the impact of the complaints.

Patients were asked to fill in the International Index of Erectile Function (IIEF) [12] for screening of erectile dysfunction and sexual satisfaction and the validated Dutch version of the Symptom Checklist-90 (SCL-90) [13], which shows to what extent a person has suffered from various psychological complaints in the past period. Patients underwent a physical examination screening, which included the genitals and a digital rectal examination.

All patients received a routine laboratory test, including total serum Immunoglobulin E (IgE), LH, FSH, testosterone, prolactin, Sex Hormone Binding Globulin (SHBG), and Thyroid Stimulating Hormone (TSH). A skin-prick test of autologous semen was done according to the protocol suggested by Waldinger et al. [4]. and have been asked to perform a serum laboratory test including C-reactive protein and IgE less than 24 h after ejaculation. The 24 h after ejaculation term has been chosen, as IgE has a half-life of about 2 days in serum [14].

As symptoms related to POIS are thought to be elicited by ejaculation, we decided to try to prevent ejaculation and informed patients about the possibility of experiencing orgasm even without ejaculation. Therefore, Silodosin, a highly selective  $\alpha_1A$ -blocker, which considered to cause anejaculation [15] was chosen as the first-line therapy. Patients who fulfil the preliminary diagnostic criteria received treatment with Silodosin 8 mg 2 h before sexual activity. In the case of unresponsiveness, a sperm count in urine after ejaculation was performed to exclude retrograde ejaculation. In the case of ongoing POIS complaints or side-effects, a second-line therapy with a nonsteroidal anti-inflammatory drug (Ibuprofen 400 mg, twice a day starting 2 h before sexual activity, for 2 days) was prescribed, in accordance with previous reports [3]. An immunological or

autoimmune mechanism have been proposed as possible aetiology of POIS. Prednisone is mostly used to suppress the immune system and decrease inflammation in many conditions, and in short use with limited side effects. Therefore, third-line therapy was Prednisone 30 mg, taken 2 h before sexual activity and continued with 20 mg the day after.

Quantitative variables were described using the mean and standard deviation (SD) or the median and range. Categorical variables (symptoms, complaints, and comorbidities) were summarized with numbers and percentages.

## Results

### Cohort

In a period of 18 months, 17 patients have been referred to our institution because of complaints suspected to be due to POIS. Fifteen of them had had previous urological, psychiatric, or sexology consultations in relation to these complaints. One patient did not give consent for the protocolary recording of the medical data and two patients reported the disappearance of complaints less than 12 h after ejaculation and were excluded from the study. The remaining 14 patients fulfilled at least 4 of the 5 diagnostic criteria of POIS, defined as highly selective, and were available for analysis of the data.

### Disease presentation

The characteristics of the patients are described in Table 1. Two patients (14%) had POIS complaints from their first sexual experience. Twelve (86%) had POIS complaints in all sexual activity circumstances, while one had only experienced them after intercourse and one only after masturbation. The latter had avoided any sexual contact, despite desire, over the last 9 years.

### Symptoms and comorbidities

The prevalence of complaints, according to the different clusters, related to POIS is given in Table 2. The most prevalent complaints were extreme fatigue, pressure of a heavy head, nose congestion, and muscle tension, all experienced by more than 30% of the patients. All patients suffered from more than one symptom. Four patients had known allergy (two with hay fever, one with eczema, and one with an allergy to penicillin).

**Table 1** Characteristics of 14 POIS patients.

Item	Unit	Mean $\pm$ SD range
Age	Years	34.07 $\pm$ 6.65 (23–44)
Duration of POIS	Years	7.5 $\pm$ 3.5 (2–15)
Time to complaints after ejaculation	Minutes	32.07 $\pm$ 41.1 (1–120)
Duration of complaints	Days	3.5 $\pm$ 1.74 (2–7)
Quality of life	Likert Scale (1–10)	5.78 $\pm$ 1.42 (4–8)
		<i>N</i> (%)
Smoker		5 (35.7)
Alcohol use	None	5 (35.7)
	1–2 U/day	7 (50.0)
	>2 U/d	3 (21.4)
Drugs use	Cannabis	2 (14.3)
	Others	0 (0.0)
Relationship status	Partner	10 (71.4)
	Divorced	2 (14.3)
	Single	2 (14.3)

### Sexual complaints

Two patients (14%) suffered from lifelong premature ejaculation. Three patients complained about reduced libido, all as a consequence of their POIS complaints; none suffered from erectile dysfunction. The average scores of the different IIEF domains are given in Table 3. One patient refrains from sexual activity and did not fill in the questionnaire, while for eight others the IIEF was based on 1 sexual activity in the month before filling out the IIEF questionnaire. In Table 4 the influence of POIS's complaints on their sexuality, their partner and relationship are described.

### Laboratory tests

None of the urine dipstick tests (pH, protein, glucose, ketones, leukocytes, hemoglobin, nitrite, Bilirubin) revealed any abnormalities. Seven patients (50%) had a positive semen skin test of which 5 (35.7%) had Grade II (5–10 mm wheal or 11–20 mm erythema) and 2 (14.3%) had Grade III (21–30 mm wheal erythema).

All mean laboratory tests were in the normal range. One patient had high white blood cell count (13.2  $10^9/l$ ), which normalized 4 weeks later (<10  $10^9/l$ ). Eleven (78.5%) patients had slightly elevated total IgE with a mean of 40.5  $\pm$  24.7 kU/l (normal range <35). The IgE test 24 h after ejaculation showed no significant increase in four of the patients (mean 42.5  $\pm$  23.3 kU/l;  $p = 0.24$ ). The C-reactive protein and white blood cell count in the post-ejaculation investigation showed no significant differences ( $p > 0.05$ ).

**Table 2** Prevalence of POIS complaints in 14 patients according to the different clusters of complaints (all of the patients had more than one symptom).

Cluster	Complaint	N	%	Severity (Likert scale) Mean
General	Extreme fatigue/exhausted	9	64.2	7.5
	Palpitations	0		
	Problem finding words/ Dysarthria	1	7.1	6
	Difficult to concentrate	4	28.5	7
	Quickly irritated	2	14.3	7.5
	Photophobia/irritated by noise	2	14.3	6.5
	Depressed mood	3	21.4	7.5
Flu-like	Feverish/ shivery/ warmth	1	7.1	5
	Feeling sick/ill	4	28.5	7.25
	Feeling cold	1	7.1	6
Head	Headache	2	14.3	8
	Pressure or heavy	5	35.7	7.6
	Foggy	4	28.5	7
Eyes	Burning	2	14.3	7.5
	Blurred vision	1	7.1	8
	Irritating/ itching	1	7.1	6
	Sensitive/ painful	2	14.3	6.5
Nose	Congestion	5	35.7	6.5
	Watery/ runny	0		
	Sneezing	1	7.1	6.5
Throat	Bad taste/ Dry mouth	2	14.3	7
	Sore	2	14.3	7
	Cough	0		
Muscle	Hoarse voice	1	7.1	7
	Tension	3	21.4	7.7
	Weakness	2	14.3	7
	Pain	3	21.4	6.3
	Heavy legs	2	14.3	7.5

**Table 3** IIEF-domain scores of 13 out of 14 patients.

Domain	Score range	Mean $\pm$ SD	Patient's range
Erectile function	1–30	23.1 $\pm$ 5.6	18–27
Orgasmic function	0–10	5.8 $\pm$ 0.7	4–8
Sexual desire	2–10	7.1 $\pm$ 0.7	6–8
Intercourse satisfaction	0–15	6.9 $\pm$ 2.1	5–9
Overall satisfaction	2–10	4.2 $\pm$ 0.7	3–5

## Treatments

The flow diagram of the treatment modalities is presented in Fig. 1. All 14 patients started treatment with on-demand Silodosin 8 mg in which eight (57.1%) of them, although

**Table 4** Impact of POIS on sexuality and relationship.

Consequence of POIS	N	%
Reduced frequency of sexual activity	12	85.7
Avoidance of sexual activity	8	57.1
Abstinence	1	7.1
Loss of sexual pleasure	1	7.1
Need to plan sexual activity	8	57.1
Influence on partner's sexuality <sup>a</sup>	7/10	70
Loss of intimacy <sup>a</sup>	9/10	90
Change in nature of the relationship <sup>a</sup>	4/10	40

<sup>a</sup>Ten patients had a stable relationship with partner, the other 4 were single or divorced.

they complained about the need for planning, were satisfied with the results, with no ejaculation and without post-orgasmic complaints. One patient was suffering from a Silodosin side effect (dizziness) and discontinued with Silodosin. Seven patients (six unresponsive and one with side-effects of Silodosin) received Ibuprofen 400 mg with an improvement of their complaints in two of them (28.5%). Four of the five unresponsive patients to Ibuprofen (80%) who received Prednisone (third-line treatment) saw an improvement in their symptoms. One patient without improvement received supportive therapy.

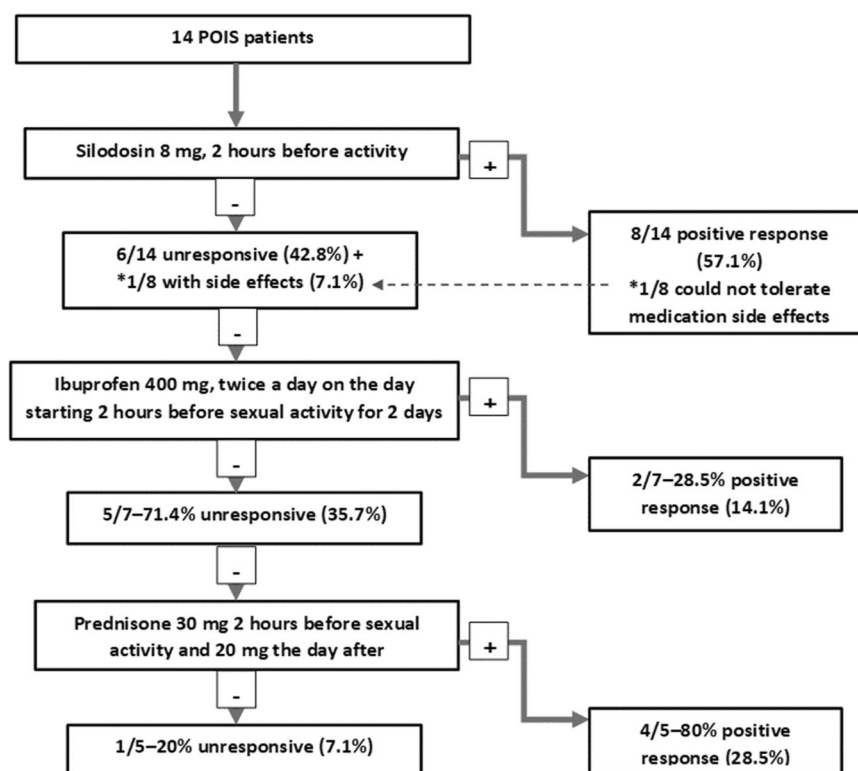
## Discussion

The National Institutes of Health Office of Rare Diseases recognizes POIS as a rare disorder [16]. Since first described in 2002, the literature contains only 57 reported cases of POIS while Internet forums contain more than 1000 members [17–19]. This difference can be explained by the fact that many health-care professionals are not aware of the disorder and POIS may be underdiagnosed and under-reported [3]. This observational study of highly selected clinical cases, according to defined preliminary diagnostic criteria, may contribute to our knowledge of this condition and to possible treatments reported so far.

In the current study of men who fulfilled four of the five diagnostic criteria, it appears that the presentation of POIS can be variable in the time to onset, duration and intensity of symptoms. The majority of the patients suffered from multiple symptoms distributed among the different clusters in accordance with previous reports [4, 5, 9]. Waldinger's patients reported extreme fatigue, concentration difficulties, being quickly irritated and feverishness as the most common symptoms (78.0–87%) compared to this study in which extreme fatigue, head pressure/heaviness, nose congestion, muscle tension, and difficulty concentrating were the most prevalent complaints (29–64%). One possible

**Fig. 1 Flow diagram of treatment modalities used.**

Numbers, percentage and (percentage of total) + Positive or – Negative effect on symptoms. Asterisk (\*) indicates patient could not tolerate silodosin side effects, received second line with Ibuprofen.



explanation for these differences is the younger age of the patients and therefore the shorter duration of POIS in this study, in comparison with Waldinger's report ( $34.07 \pm 7.5$  and 7 years vs  $43 \pm 13$  and 17 years, respectively). Younger age assumes more physical activity and therefore more muscle related complaints. The post-orgasmic symptoms started on average within 30 min of ejaculation and symptoms lasted for 3.5 days, which compares with previous reports [4, 5, 9].

The men in this study reported an emotional and psychosocial burden of their symptoms. A previous report noted that patients avoid masturbation and/or sexual activities and report dampening romantic prospects despite desiring to engage in these activities [3]. Some patients avoid romantic relationships altogether for fear of partner non-acceptance [2], and the physical symptoms that accompany any ejaculation may interfere with obligations such as work or study, forcing some patients to plan ejaculations to avoid disruption to their lives [7]. Nearly all men in this study reported a low quality of life (average Likert scale 5.78). To avoid symptoms, they had a decreased frequency or avoidance of sexual activity and the need to plan sexual activity. In this study we also asked about the influence of POIS on the partner and relationships. Ninety per cent (9 out of 10 patients with a partner) reported a loss of intimacy and 40% reported POIS influencing their partner's sexuality as well. Four patients reported a change in their relationship as a consequence of

the complaints. Waldinger et al. [4] reported that men were concerned about the relationship with their sexual partner and expressed feelings of guilt for having the disorder; 2 out of the 33 patients reported a divorce due to the patient's strategy of abstinence or avoidance of sexual activity. Other case reports emphasized that POIS caused a negative impact on the partners [7, 20]. One of the patients in this study was single and abstained from sexual activity for a period of 9 years, although he reported having desire.

The rate of premature ejaculation was 14%, which is much lower than the rate reported in a previous publication (56%) [4]. This is probably because we used the strict definition of PE according to the ISSM, of less than 60 s IELT. Given that the prevalence of premature ejaculation is not well defined, these values are within the range of other reported studies [21]. The IIEF scores as seen in Table 3, did not reveal sexual dysfunctions among this group of patients, except for low average scores on the IIEF-intercourse satisfaction and overall satisfaction domains. The IIEF questionnaire has been designed and validated for ED patients, and should be interpreted with care. In the absence of a questionnaire dedicated for POIS, we used the IIEF to exclude sexual problems.

Waldinger et al. [4] posited an immunological or autoimmune mechanism of POIS. This theory is supported by skin-prick test results that showed 88% of POIS patients in a sample of 33 reacting to diluted samples of injected autologous semen. The authors speculated that a Type I



(immediate type, related to antigen cross-linking with membrane bound IgE antibody of a mast cell or basophil) may involve in the pathogenesis of POIS [4, 8]. They did not show elevated levels of IgE in the test subjects; however, a similar study in Korean men [22] showed the existence of serum semen-specific IgE in their patient with POIS. The study by Waldinger [4] lacked the performing of the skin test with autologous semen in an age-matched control group of healthy men. To address this issue, Jiang et al. [5] performed a skin test in a patient with POIS and three healthy controls. 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].

In our patients, only four were known to have an allergy, in accordance with the finding of Strashny [9], and the mean total IgE level was not significantly elevated before and after ejaculation. It should be noted that IgE is an antibody produced during a Type I hypersensitivity reaction to an allergen. IgE antibodies are normally found in small amounts in the blood. A higher level than normal infers an allergic disorder may be present. A positive test result means sensitization to an allergen but a normal level of IgE may not exclude allergic disorders. Furthermore, the indicated level of IgE may not correlate with the extent or severity of symptoms when exposed to the allergen [23]. We can conclude that conclusive evidence to establish an aetiology of the syndrome remains elusive.

Given that POIS is a rare and poorly defined condition, there has not been adequate study to demonstrate the efficacy of treatments. Tested treatments include antihistamines and selective serotonin reuptake inhibitors (SSRIs), although these have had limited therapeutic value [7, 24]. Diclofenac improved up to 80% of symptoms in one case study [5]; however, it was shown to have no benefit in another [3]. Hyposensitization therapy, which has been used in the treatment of other forms of allergic, immunologic, and autoimmune disease, has also been pursued [8, 22]. Neither of these trials included a healthy male control. Although many other therapies, supplements and herbal remedies have been attempted, none of these have shown consistent efficacy. Previously the treatment protocol included the use of hyposensitization in the case of a non-response to other therapies and a positive skin test and elevated IgE. As a large number of the patients in this study had a negative skin test and no significant increase in IgE, hyposensitization was not used.

Silodosin, which considered to cause anejaculation [15], was chosen as the first-line therapy. Eight patients (57%) were able to be effectively treated with this approach, which is the first time this has been reported in POIS, and could be

considered as a possible treatment modality. Future randomized trials will need to determine the real efficacy of Silodosin for POIS patients.

The majority of patients (five out of seven) experienced no benefit from the use of a non-steroidal anti-inflammatory drug in accordance with previous findings [3]. These patients were treated with a glucocorticoid medication (Prednisone). Four out of five of our patients experienced some benefits for their complaint but the true efficacy will need to be verified in larger future studies.

This study had important limitations. As a retrospective observational study, the finding needs to be verified in large prospective data series and to be compared with a control group, which will determine whether hyperreactivity against semen is confined to POIS or to the general population. The diagnostic criteria applied were only once validated and should be validated in a large multicenter study with patients from different regions and age groups. Furthermore, there is a need for the development of a validated questionnaire and patients reported outcome scores to verify the effect of the therapies used, which were not available for this study.

## Conclusion

The current observational study describes a series of patients with POIS who were actively looking for medical help as POIS has a significant effect on patients and their partners. This rare condition deserves further investigations to gather an evidence-based definition and to elucidate its pathophysiology and possible treatment. As more data become available on POIS, this may increase awareness among health-care professionals and recognition by medical organizations in order to increase research support.

In this study, for the first time, anejaculation was described as a possible symptomatic treatment aiming at the possible source of the post-orgasmic symptoms. These findings need verification in large multicenter clinical trials, allowing much more progress in the diagnosis and management of POIS.

## Compliance with ethical standards

**Conflict of interest** The author declares that he has no conflict of interest.

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