



Andrology and fertility

## Successful treatment of Post-orgasmic illness syndrome with human chorionic gonadotropin

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### ABSTRACT

Post-orgasmic illness syndrome (POIS) is an uncommon condition in which men experience debilitating symptoms following orgasm, including anxiety, weakness, and lassitude. The etiology is unknown, and treatment challenging. We present a 25y man with POIS since puberty. He dreaded ejaculation due to his subsequent symptoms. Multiple prior treatments had failed. Blood tests revealed testosterone (T) deficiency. hCG was prescribed. At 6 weeks T levels normalized with near-complete resolution of symptoms. This successful result argues for hormonal investigation in men with POIS, and a trial of hCG or T therapy if total or free T is low or borderline.

### Introduction

Post-orgasmic illness syndrome (POIS) is a rare disorder in which affected men experience a cluster of bothersome symptoms following ejaculation, which may include severe fatigue, nasal congestion, burning eyes, concentration difficulties, irritability, depressed mood, and a flu-like state of generalized malaise.<sup>1</sup> Symptoms may last from one to seven days. To avoid these symptoms, men with POIS tend to minimize sexual activity, or attempt to avoid ejaculation when they do engage in sexual activity. The prevalence of POIS is unknown and difficult to determine, as it is likely that many affected individuals do not seek medical attention, and most physicians are unaware of the syndrome.<sup>2</sup> Due to lack of awareness of POIS as a medical entity, and with its component symptoms of anxiety, distress, and depressed mood, men with POIS may be first referred to a mental health professional, who also may be unfamiliar with this condition.

Waldinger and Schweitzer first described POIS in 2002, and proposed that POIS likely represented a "type 1 hypersensitivity disorder secondary to peptides from semen or urethra that contact the inner mucosal epithelium of the urethra to initiate a cascade of events of a hypersensitivity reaction".<sup>3</sup> Waldinger subsequently reported modest success delayed over many months with a hyposensitization protocol that included regular subcutaneous injections of diluted autologous semen.<sup>4</sup>

However, there is no consensus on the underlying etiology nor the optimal treatment of POIS, and we are unable to identify in the literature any absolute "cures" for POIS.

Treatment recommendations have included antihistamines, benzodiazepines, selective serotonin reuptake inhibitors, and CNS stimulants.

We here report a new and successful treatment of POIS by raising serum testosterone (T), in this case via subcutaneous injections of human chorionic gonadotropin (hCG).

### Results

A 25 year old single heterosexual man was seen for a chief complaint of anxiety, low energy and weakness following ejaculation, accompanied by mental fog and difficulty with word-finding. He avoided social contacts during his symptomatic period. Onset of symptoms could be immediate or delayed by 2–3 days, and would last 1–2 weeks. Symptoms began at 16 years with sexual maturity and continued to the present time, regardless of whether ejaculation occurred via masturbation or intercourse with a female partner. Symptoms interfered with studies and employment. For these reasons he avoided masturbation, and also attempted to avoid ejaculation when engaging in sex with a partner. At the time of presentation he was single and orgasm frequency was once every 2–3 months.

He had seen several physicians for these symptoms and performed extensive online research. He tried various diets, supplements, niacin, and antihistamines without benefit. An endocrinologist told him testosterone levels were low, but did not offer treatment. Adderall provided some benefit for the brain fog. He was under the care of a psychiatrist for anxiety, treated with propranolol. Alprazolam was prescribed as needed for POIS, but provided minor benefit. Trials of

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<https://doi.org/10.1016/j.eucr.2019.101078>

Received 11 November 2019; Accepted 21 November 2019

Available online 22 November 2019

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treatment for POIS with bupropion, and Vyvanse (lisdexamfetamine dimesylate) were unsuccessful. Laboratory blood tests from two years earlier included serum total T of 293 ng/dl and calculated free T of 33 pg/ml.

On examination height was 6 feet, weight 175 lbs, and BMI 23.7. He was normally virilized, no gynecomastia, flat abdomen, normal male genitalia including normal testicular volume. Vasa were palpable, and no varicoceles or hernias were noted. He was intelligent, a clear and reliable historian, affect was appropriate, and interpersonal skills were good. Blood tests revealed total T 374 ng/dl, free T (direct) 1.4 ng/dl, luteinizing hormone 4.7 mIU/L, and hematocrit 44.7%.

Treatment was initiated with hCG 1500IU injected subcutaneously three times per week. At six-week follow-up his symptoms had resolved completely, and he had discontinued use of alprazolam. He ejaculated more frequently, and experienced no weakness, anxiety, brain fog, or malaise afterwards. He noted improved mood, overall energy, and libido. Blood tests showed robust levels of total testosterone at 952 ng/dl and free T (direct) at 2.8 ng/dl. LH and FSH were below threshold limits. He reported this was the first time since he was 16y that he could experience orgasm without negative physical or emotional consequences afterwards. At six months of follow-up he continued hCG treatment, was happy, and masturbated several times per month. He still described mild POIS symptoms immediately following orgasm, but these resolved within 12 h and were not bothersome. Importantly, he no longer experienced dread with anticipated sexual activity.

## Discussion

POIS is a challenging clinical entity, causing considerable patient distress yet escaping easy definition, with unclear etiology and uncertain treatment.<sup>2</sup> The non-specific symptoms may often be dismissed as psychogenic, and in the absence of obvious physical causes it is reasonable to explore psychological issues triggered by sexual activity, such as guilt, religiosity, prior sexual abuse, or unacknowledged feelings of uncertainty regarding sexual orientation or gender identity. Pharmacological treatments may include antidepressants, anxiolytics, CNS stimulants and antihistamines, all of which were tried in our patient.

The largest POIS experience, involving 45 Dutch men, was reported by Waldinger and colleagues, who postulated the symptoms were due to an immune reaction to components of semen,<sup>1</sup> and reported limited and very delayed reduction in symptoms with subcutaneous injections of autologous diluted semen.<sup>4</sup> Successful hyposensitization was also reported by another group in one man.

Our success with hCG treatment raises the possibility that testosterone deficiency may be an underlying etiology in some cases, providing a possible new therapeutic approach. Our choice of hCG to raise serum T was based on the desire in this young man to preserve fertility and testicular volume,<sup>5</sup> however, we have no reason to believe exogenous T would have been any less effective.

## Conclusions

POIS is an uncommon condition without established etiology that can be difficult to treat. We here report the first successful treatment of POIS using hCG to elevate serum testosterone, resulting in prompt resolution of symptoms.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eucr.2019.101078>.

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