

MEN'S SEXUAL HEALTH

Sleep-Related Painful Erections—A Case Series of 24 Patients Regarding Diagnostics and Treatment Options



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ABSTRACT

Background: Patients with sleep-related painful erections (SRPEs) have deep penile pain during nocturnal erection that wakes them up and disturbs their nights of sleep. This rare parasomnia is poorly recognized by general practitioners and by urologists and sexologists.

Aim: To gain more insight into diagnostics and therapeutic options.

Methods: Data from a series of 24 consecutive patients who presented with SRPEs at the outpatient clinic from 1996 to 2015 were retrospectively analyzed. Additional questionnaires were completed to complement data and to obtain information about follow-up. Long-term treatment efficacy of baclofen was assessed using the Wilcoxon signed rank test.

Outcomes: SRPEs were not associated with urologic, surgical, or psychiatric history or with serum testosterone levels. The mean doctors' delay was 3.5 years. 14 of the 24 patients were treated with baclofen (10–75 mg). In 11 of them, complete remission was observed within a few weeks. 2 of the 3 remaining patients noticed a slight improvement of SPRE symptoms and only 1 patient experienced no effect at all. After an average follow-up of 4.5 years, only 41.6% of patients who had used baclofen were satisfied with their SRPEs. The others (58.4%) were dissatisfied, mostly owing to relapse of symptoms after the discontinuation of baclofen. Other treatment forms were applied sporadically, with strongly varying results.

Clinical Implications: This overview of SRPE contributes to a better clinical understanding and recognition of the phenomenon and provides new, more constructed advice about therapeutic implications, especially concerning the use of baclofen.

Strengths and Limitations: This study provides a systematic overview of a relatively large series of patients with SRPE, which provides substantiated treatment advice. However, treatment efficacy was based mainly on the patients' subjective perception and it was not possible to compare the results of baclofen with other forms of pharmacologic treatment, because these alternative drugs were applied only sporadically. Nevertheless, this study is directional for future research.

Conclusions: This study confirmed a long doctors' delay in patients with SRPE. There was no association between SRPEs and comorbidity and total serum testosterone levels. Treatment with baclofen proved successful and safe in the short term. Long-term feasibility needs further investigation. **Vreugdenhil S, Weidenaar AC, de Jong IJ, van Driel MF. Sleep-Related Painful Erections—A Case Series of 24 Patients Regarding Diagnostics and Treatment Options. Sex Med 2017;5:e237–e243.**

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Key Words: Sleep-Related Painful Erection; Rapid Eye Movement Sleep; Parasomnia; Humans; Baclofen

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INTRODUCTION

Patients with sleep-related painful erections (SRPEs) experience episodes of penile pain during nocturnal erections that frequently wake them up. SRPEs occur during rapid eye movement (REM) sleep. However, erections related to sexual activities are not painful and are normal in duration and rigidity and generally no penile anatomic abnormalities are found during

physical examination. Obviously, Peyronie's disease and phimosis can be present in some patients but they seldom explain the typical clinical presentation of SRPEs.¹

The intensity of pain and duration of the associated sleep deficit commonly increase during the second part of the night when REM sleep episodes become longer and more frequent.²

The underlying pathophysiologic mechanism and predisposing factors for SRPEs are not known. Treatment is still in an expert-based opinion phase and there is no consensus about how to treat this parasomnia. In addition, there is a lack of information about long-term follow-up. By documenting the symptomatology, diagnostic measurements, and treatment outcomes of our patients with SRPE, we aimed to gain a better understanding of the pathophysiology and to develop more substantiated advice about the diagnostics and therapeutic implications of SRPEs.

METHODS

Study Population

In this retrospective descriptive study, we collected data from all patients who presented with SRPE complaints at our outpatient clinic from 1996 to July 2015. 2 patients included in this study were previously described.² Patients who also had painful erotic erections or anatomic abnormalities (eg, Peyronie's disease and phimosis) were excluded. 2 patients who developed Peyronie's disease a couple of years after the onset of SRPE and patients with daytime painful non-erotic erections during follow-up were included. Information about demographics, symptomatology, psychosocial factors, findings at physical examination, and diagnostics were extracted from the patients' medical files.

Special attention was paid to the applied treatment modalities, their effectiveness, and their adverse event profile. Questionnaires (Appendix) about the subjective perception of short- and long-term results were sent to all patients. Classification of treatments was based on their answers (0 = no effect, 1 = partial remission, 2 = full remission). Satisfaction concerning the achieved effect was classified into 3 categories (0 = dissatisfied, 1 = moderately satisfied, 2 = satisfied).

Analysis

Data were analyzed using IBM SPSS Statistics Data Editor 23 (IBM Corp, Armonk, NY, USA). The primary end points of treatment efficacy in the short term (first 3 months of treatment) were change in frequency and duration of SRPEs as reported by the patient. Frequency was divided into 6 categories (0 = no SRPE, 1 = 0–1 time per night, 2 = 1–2 times per night, 3 = 2–3 times per night, 4 = 3–4 times per night, 5 = 4–5 times per night, 6 = >5 times per night). Duration was classified into 5 categories (0 = no SRPE, 1 = 1–15 minutes, 2 = 16–30 minutes, 3 = 31–60 minutes, 4 = >61 minutes). Differences in the average frequency and duration of SRPEs of patients treated with baclofen before vs (years) after treatment were estimated using the Wilcoxon signed rank test. All tests were 2-tailed and a

significant difference was defined as a *P* value less than or equal to .05. Effect size was interpreted according to Cohen. The baclofen group alone was large enough to be assessed in this manner. Participants who quit treatment prematurely because of side effects or for other reasons contributed to the average outcomes. Data of patients who did not return the questionnaire were disregarded for follow-up analysis.

RESULTS

Demographics

We included 24 patients with a median age of 53 years (range = 38–74) at the onset of SRPEs. 22 completed the questionnaires. All men were heterosexual and most were married for a longer period. 2 were in a divorce during the onset of SRPEs, 2 were single, and 1 had recently become a widower. Table 1 presents the medical or psychiatric history including urogenital, abdominal or spine surgery, chronic and psychiatric disease, and urologic illness.

Symptomatology

The median time from the onset of SRPEs to the first consultation with a urologist was 2.5 years (range = 0.5–20). The median frequency of nocturnal awakenings as result of a painful erection was 3 times a night (range = 1–10), and the erection persisted shorter than 15 minutes in 45% of patients. In 37% the duration was shorter than 60 minutes and in 4 (18%) the SRPEs persisted up to 1 hour. The pain was often described as stabbing, aching, and/or pressing. 12 of the 24 patients reported radiation to at least 1 adjacent area (Table 2).

After waking up from an SRPE, several maneuvers were applied to achieve detumescence (Figure 1). Urinating and walking around proved to be the most effective, respectively, in 54% and 50% of the 22 patients. There were different experiences concerning the effect of alcohol and eating before bedtime. However, all men reported that staying in bed maintained or even worsened the erection. 1 patient explicitly mentioned that marital issues and related stress were strongly influencing his complaints. After the divorce, he said, his SRPEs had disappeared spontaneously. Another patient noticed a relation between stress levels from his work and the severity of his complaints.

More than 80% reported sexual satisfaction to be unchanged since start of the symptoms. SRPEs appeared not to impair erectile function. However, sex drive decreased in 8 of the 24 men (33%). All patients complained about sleep deprivation and for nearly all of them this was the main reason why they had consulted a physician. Daytime sleepiness and fatigue were reported by 78.8%. In 25% (n = 6) daytime fatigue had forced them to partial or complete work absenteeism.

Diagnostics

In 22 of the 24 patients, serum testosterone levels were measured in the morning from 9 to 10 AM. The mean serum

Table 1. Patient characteristics: overview of medical history with special attention to surgical, urologic, and psychiatric histories

	Times reported, n	Explanatory memorandum
General history		
Cardiovascular disease	6	Hypertension 2×, supraventricular tachycardias 2×, atrial fibrillation 2×
Type 2 diabetes mellitus	3	Asthma, COPD, emphysema
Pulmonary disease	3	
Prolactinoma	1	
Multiple sclerosis	1	
Epilepsy	1	
Morbus Bechterew	1	
Hypothyroidism	1	
Morbus Steinert	1	Treated with CPAP
Osas	1	
Chronic fatigue syndrome	1	
Operations		
Abdominal	6	Appendectomy 3×, inguinal hernia correction 2×, epigastric hernia correction 1×
Urogenital	3	Scrotal surgery 2×, TUR of prostate 1×
Spine	2	Herniated nucleus pulposus operation 2×
Urologic history		
Luts	5	Treatment with α -blocker 3×, with anticholinergic + pelvic physiotherapy, with TUR of prostate
Premature ejaculation	1	Surgery needed
Varicocele	1	Surgery needed
Post-vasectomy syndrome	1	Drainage + injection of phenylephrine
Priapism	1	
Psychiatric history		
Mood disorder	2	Depression 2×, with anxiety disorder in 1

COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; LUTS = lower urinary tract symptoms; OSAS = obstructive sleep apnea syndrome; TUR = transurethral resection.

testosterone level was 16.4 nmol/L (SD = 5.07). 6 had a level below 14 nmol/L. The patient with a level of 5.6 nmol/L had a history of prolactinoma. None of the patients had a testosterone level above the upper limit.

Table 2. Pain radiation (n = 12)

Patient number	(Hemi) scrotum	Groins	Perineum	Glans penis	Lower abdomen
1 ^{*,†}	x			x	x
2	x				
3	x	x			
4	x				
5 ^{*,†}	x		x		
6 ^{*,†}			x		
7			x		
8 ^{*,†}			x		
9					x
10				x	
11 [*]	x	x		x	
12 [†]	x			x	
Total	7	2	4	4	2

*Patient also experienced painful non-erection erections during daytime.

†Patient also experienced lower urinary tract symptoms.

To visualize the duration and intensity of the SRPEs, 15 of 24 patients underwent nocturnal penile tumescence and rigidity (NPT-R) measurements. In 2 patients NPT-R was combined with polysomnography (PSG). According to the age-related criteria formulated by Burriss et al,³ NPT-R measurements were aberrant in 7 of these 15 patients and showed prolonged episodes with erection. One patient could not finish the NPT-R measurement because of pain and the other 7 showed a normal pattern. 1 of the 2 patients in whom PSG was performed showed typical characteristics: an increased percentage of REM sleep (25%) and all REM episodes accompanied by erection and subsequent awakening, resulting in sleep fragmentation and decreased sleep efficiency of 73%. Simultaneously performed electromyography of the pelvic floor muscles showed irregular increase of muscle tonus during REM sleep episodes. In the other patient, PSG showed no abnormalities.

In 8 men Doppler ultrasound of the cavernosal arteries showed an increased rest flow in 3 (0.26, 0.28, and 0.37 m/s, respectively). The others showed normal values.

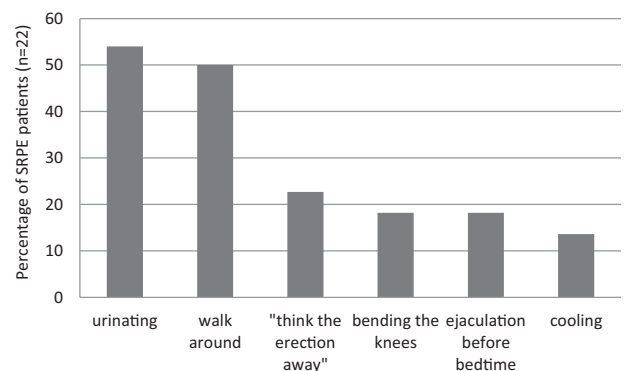


Figure 1. Maneuvers performed by patients to achieve detumescence.

Table 3. Treatment: overview applied treatment per patient with short- and long-term results and reported side effects

Age (years)	Treatment	Result (short term)*	Side effects
41	Baclofen 20 mg	1	None
44	Baclofen 10 mg	2	None
55	Baclofen 30 mg	1	Weight gain
66	Baclofen 20 mg	1	Debilitating headache
69	Baclofen 30 mg	1	None
53	Baclofen 10 mg + cyproterone acetate 50 mg	1	Loss of sex drive
71	Baclofen 20 mg + cyproterone acetate 50 mg	2	None
58	Baclofen 75 mg	2	None
	Cyproterone acetate 20 mg	0	Loss of sex drive, erectile dysfunction
40	Baclofen 20–30 mg	1	Myalgia with 30 mg, none with 20 mg
	Cyproterone acetate 50 mg	0	None
	Amitriptyline	0	Delusions, suicidal thoughts
	Pelvic physiotherapy	0	None
43	Baclofen 30 mg	0	Mild drowsiness
	Cyproterone acetate 10 mg+ amitriptyline 20 mg	0	Loss of sex drive, erectile dysfunction
	Cyproterone acetate 30 mg	0	Itching around genitals
47	Baclofen 30 mg	2	None
	Cyproterone acetate 10 mg	0	Fever?
	Amitriptyline	1	Drowsiness, mood swings
	Carbamazepine	0	None
	Pelvic physiotherapy	0	None
62	Baclofen 80 mg	1	None
	Cyproterone acetate 50 mg	0	None
	Amitriptyline 30 mg	1	None
	Tadalafil 5 mg	0	More erections
53	Baclofen 30 mg	1	Mild fatigue and lethargy (in morning)
	Carbamazepine 100 mg	1	None
53	Tadalafil 5 mg	?	None
	Baclofen 10 mg	2	Mild headache (sometimes)
47	Amitriptyline	0	None
	Pelvic physiotherapy	2	None
65	Tadalafil 5 mg + pelvic physiotherapy	2	None
58	Tadalafil 5 mg	2	None
47	Sexologist	1	None
49	Sexologist + venlafaxine	1	None
74	Sexologist + pelvic physiotherapy	2	None
38	—	0	—
41	—	1	—
50	—	2	—
55	—	0	—

— = no treatment.

*0 = unaltered; 1 = partial remission; 2 = full remission.

Treatment and Follow-Up

Before the initial visit to our outpatient clinic, different drugs had been tried by patients prescribed by several specialists, including benzodiazepines (clonazepam, nitrazepam, and oxazepam), opiates (tramadol and OxyContin), antiepileptics (carbamazepine and pregabalin), antidepressants (mirtazapine, paroxetine, venlafaxine, and amitriptyline), antihypertensives (β -blockers and clonidine), and β -agonists (terbutaline). Except for amitriptyline, none of these medications was effective (enough) and/or had caused too many disabling side effects.

After the first consultation at our clinic, 4 of the 24 patients refrained from further treatment. After extensive counseling on the off-label use, 18 of the remaining 20 patients were willing to try a pharmacologic treatment, with or without non-pharmacologic interventions such as pelvic physiotherapy and/or sexological counseling. 2 patients received only non-pharmacologic treatment. Table 3 presents data on the applied treatment per patient, its short-term effect, and reported side effects. In 22 of 24 patients, data were available on the long-term results of the treatment after a median follow-up of 5.0 years (range = 0.5–17.0).

Long-term treatment results of baclofen

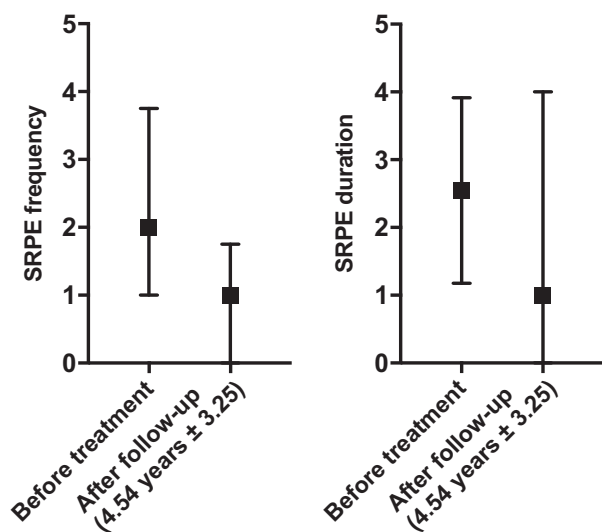


Figure 2. Long-term treatment results of baclofen. Median and interquartile range of SRPE frequency and duration before treatment compared with SRPE frequency and duration after long-term follow-up in patients treated with baclofen. SRPE = sleep-related painful erection.

Baclofen

Of the 18 patients receiving pharmacologic treatment, 14 were treated with baclofen (Lioresal; Medtronic, Fridley, MN, USA) starting with a dose of 10 mg at bedtime. Depending on the (side) effects, the patient was advised to increment the dose, initially up to a maximum of 40 mg. However, 2 men required a dosage of 75 and 80 mg, respectively, before adequate improvement was noticed. 5 of the 14 patients treated with baclofen (35.7%) experienced complete remission of symptoms after a few weeks, 8 (57.1%) noticed partial improvement, and baclofen in 1 (7.1%) was not effective at all. In general, baclofen was well tolerated. 2 patients used baclofen combined with cyproterone acetate (50 mg).

Long-term information was available for 12 of the 14 patients. We looked at the results of baclofen on frequency and duration of SRPEs after a mean follow-up of 4.5 years (SD = 3.25; Figure 2). The Wilcoxon signed rank test showed a statistically significant decrease of mean SRPE frequency in the entire series of patients treated with baclofen ($P = .026$), with a medium effect size ($Z = -2.232$, $r = -0.43$). The same was assessed for SRPE duration. The mean SRPE duration the entire series of patients using baclofen had decreased significantly ($P = .038$), with a medium effect size ($Z = -2.070$, $r = -0.43$).

4 patients (33.3%) were completely free of symptoms and 2 were still using baclofen. 2 (16.7%) experienced a partial remission about which 1 was completely satisfied in contrast to the other. In 6 patients (50%), SRPEs fully relapsed after discontinuation of baclofen. Only 3 patients were successfully

using baclofen after 0.5, 4.5, and 1 years, respectively, in the absence of any significant side effects.

Other Treatment Modalities

Other pharmacologic treatments included cyproterone acetate (Androcur; Bayer LPC, Reading, UK), an antiandrogen; tadalafil (Cialis; Eli Lilly, Indianapolis, IN, USA), a phosphodiesterase type 5 inhibitor; and amitriptyline (Sartex; Saertex GmbH & Co, Saerbeck, Germany), a tricyclic antidepressant.

Cyproterone acetate was used by 7 patients, dosages varied from 10 to 50 mg, and the drug was efficacious in only 1 patient who used cyproterone acetate 50 mg combined with baclofen 20 mg. The remaining patients reported no relieving effect whatsoever. Moreover, the drug caused debilitating side effects, including loss of sex drive and impaired sex-related erections.

Tadalafil 5 mg once a day was used by 4 patients and 2 of them experienced full remission (1 also had pelvic floor physiotherapy). This beneficial effect in the short term was sustained in the long term, but to a lesser extent after 5 years and 6 months, respectively, of treatment. The other 2 patients experienced no improvement or even aggravation of symptoms.

Amitriptyline was prescribed to 5 patients, of whom 1 used it combined with cyproterone acetate and the other 4 used it as monotherapy. 2 of these 5 reported partial remission, but the other 3 (including the 1 patient using combination therapy) experienced no remission whatsoever. Furthermore, 3 mentioned disabling side effects including drowsiness and mood disorders.

5 patients were referred to a pelvic floor physiotherapist. In 2 of them, the therapy was combined with tadalafil 5 mg or sexological counseling. In the remaining 3, pelvic floor physiotherapy was used as a last resort treatment option after several previously disappointing experiences with drugs. 2 patients experienced no remission of symptoms. The other 3 reported full symptom remission in the short term; 1 received simultaneous sexological counseling, 1 used tadalafil at the same time, and 1 tried pelvic floor physiotherapy as monotherapy.

Of the 4 patients using no treatment in any form, 1 was completely free of symptoms, 1 experienced partial remission, 1 had SRPEs without change, and in 1 data on this subject were not available.

DISCUSSION

To our knowledge, this series is the largest study describing patients with SRPEs with a relatively long follow-up. Data showed heterogeneity for age of onset (38–74 years) and medical background. In contrast, the symptomatology of SRPEs appeared to be remarkably similar in all patients. For most patients, SRPEs did not negatively affect their sex life. However, they caused significant sleep deprivation and a vast majority of patients (79%) had fatigue with considerable implications for daily life. We found no association between SRPEs and comorbidity.

Initially almost all patients treated with baclofen (10–75 mg) reported a substantial relief of symptoms. However, in the long term only 41.6% of baclofen users were satisfied with the treatment results, mostly because of relapse of symptoms after discontinuation.

Other different drugs were used, with variable results. More frequently used medicines, including amitriptyline ($n = 5$) and cyproterone acetate ($n = 7$), were discontinued at an early stage because of debilitating side effects. Moreover, in our patients, cyproterone acetate had little or no effect on SRPEs. This is remarkable because sleep-related erections depend more on androgen than erections related to sexual activities.^{4–6} Other pharmacologic treatment forms were used in only a small number of patients, which makes it impossible to draw any conclusions.

Baclofen is a muscle relaxant with spinal and central points of action. Rourke et al⁷ first reported on the use of oral nightly baclofen 40 mg in the management of recurrent priapism in patients with neurologic lesions. At the spinal level, baclofen inhibits mono- and polysynaptic reflex transmissions in the afferent terminal nerves. Theoretically, the efficacy of baclofen in patients with SRPEs also could be based on relaxation of the ischiocavernosus, bulbospongiosus, and other pelvic floor muscles. This probably proceeds through stimulation of γ -aminobutyric acid β -receptors, thus impeding the release of glutamic and aspartic acid. Stimulation of the γ -aminobutyric acid system has an inhibitory effect on the frequency of nocturnal erections.^{8,9} Some of our observations suggest that SRPEs might be related to hypertonia of the pelvic floor muscles. These include the radiation of penile pain to adjacent areas, the high concomitant occurrence of lower urinary tract symptoms, the relation with psychological stress, and the alternating increased pelvic floor muscle tone during REM sleep. In addition, we found positive long-term treatment results of pelvic floor physiotherapy in 3 of 5 patients.

There are some similarities between patients with SRPE and those with so-called stuttering priapism (also known as intermittent or recurrent priapism). The European guideline states that the etiology of stuttering priapism is similar to that of ischemic priapism, with sickle cell disease being the most common cause.¹⁰ According to the UK guidelines, stuttering priapism is often self-limiting or resolves after oral medication or conservative therapeutic maneuvers that patients develop (eg, waking up, going up and down stairs, or exercising).¹¹ In fact, the UK guidelines consider patients with stuttering priapism as a group with no obvious underlying risk factors who often present with self-limiting SRPEs; in other words, with erections lasting shorter than 1 hour. In contrast to the European guidelines, the UK guidelines do not confirm that stuttering priapism requires a period of erection of at least 4 hours.

Our results show a couple of differences between stuttering priapism and SRPEs. None of the patients with SRPE had a hematologic disease, which is the most common cause of stuttering priapism. Moreover, the duration of the last nocturnal

erection in patients with stuttering priapism often persists for 3 to 4 hours and in one third of all cases ends with ischemic priapism requiring emergency intervention.⁶ In contrast, the duration of SRPEs after awakening is often shorter than 1 hour and even shorter than 15 minutes in a large number of patients. Moreover, none of the patients with SRPE needed intervention other than cooling, micturition, walking around, or simply “thinking the erection away.” Although we describe 5 patients who developed painful non–sex-related erections during daytime, we could not diagnose stuttering priapism, because these erections disappeared within 4 hours. Moreover, in SRPE, there is complete erection; in stuttering priapism, the erection is limited to the cavernous bodies.

This study concerned a retrospective analysis of a limited population. For this reason, the results were mostly descriptively assessed. Furthermore, it was not possible to compare the effect of all treatment forms applied in our patient population, several drugs had already been applied before they visited our outpatient clinic, and the groups were too small. The interpretation of treatment results was strongly dependent on the patients’ subjective perceptions.

However, compared with previous studies, the systematic overview of symptomatology and impact of this parasomnia on daily life concerned a relatively large number of patients. In addition, this study provides a direction for future research, especially on the role of the pelvic floor muscles.

CONCLUSIONS

SPRE is a poorly recognized parasomnia that is difficult to objectify and has debilitating consequences for daily life. However, sex life is not impaired in most patients. Although the etiology and pathophysiology of SRPEs have not been clarified, our results suggest involvement of hypertonic pelvic floor muscles. According to our overview of the clinical presentation of SRPE, we believe that it differs substantially from stuttering priapism.

Ideally, standard diagnostics would include NPT-R measurement with simultaneous PSG and electromyography, but in practice this is very difficult to realize. Moreover, it would be interesting to aspirate blood from the cavernous body during an SRPE to exclude ischemia.

The results of this study suggest that relief of SRPEs and consequent improvement of sleep architecture might best be achieved by baclofen, rather than other treatment modalities. However, pelvic physiotherapy showed promising results in 3 of 5 patients and its role in the treatment of SRPE needs to be assessed further.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.esxm.2017.09.001>.