Contemporary best practice in the evaluation and management of stuttering priapism

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Abstract: Stuttering priapism is rare and under-investigated clinical entity. Although it shares similarities with ischaemic priapism, by definition, stuttering priapism has distinct characteristics that advocate for a different management in the clinical setting. Therefore, the management of stuttering priapism aims primarily to prevent recurrence rather than the resolution of spontaneous attacks. A multimodal approach and the individualization of each case are essential because of the diversity of the condition and the plethora of proposed therapeutic strategies. Understanding the underlying pathophysiology and familiarity with contemporary, past and emerging future agents and therapeutic options are required in order to provide an optimal solution for each patient. In addition, patient counselling and the option to combine therapeutic strategies and challenge second-line therapies are essential weapons in the armament of the urologist. Although further clinical trials and studies are mandatory in order to obtain solid data and provide recommendations, all therapeutic options are analysed, with specific interest in the potential advantages and disadvantages. A structured evaluation procedure is also described.

Keywords: erectile dysfunction, ischaemic, priapism, recurrent, sickle-cell disease, stuttering

Introduction

Priapism is one of the most challenging erectile disorders in terms of management. By definition, priapism is a prolonged, persistent and sometimes painful erection, which continues beyond or is even not associated with sexual stimulation.1 It constitutes a disorder in erection and detumescence mechanisms and physiology, which can potentially lead to permanent damage to the penile structures, causing permanent erectile dysfunction and subsequently impaired quality of life.2

A common classification widely used to differentiate manifestations of priapism divides the condition into two major categories, ischaemic (low flow, veno-occlusive) and nonischaemic (high flow, arterial) priapism. Both these categories have distinctly different etiologies, pathophysiology and clinical consequences, requiring different clinical management.3 A third category, stuttering priapism, has also been described, which manifests in recurring episodes of ischaemic priapism incidents of varying duration. Although many of these episodes are self-limited, they can increase in duration and incidence, leading to acute major ischaemic priapism events requiring emergency medical management.4

In 1914, recurrent priapic episodes of limited duration were observed, which were termed acute transitory attacks.5 The term ‘stuttering priapism’ was proposed by describing the recurrent episodes of priapism in patients with sickle-cell disease (SCD).6

Although stuttering priapism is rather uncommon, it is prevalent in certain populations and particular age groups. Stuttering priapism, as a distinct category or subdivision of ischaemic priapism, shares its etiology with the latter, including haematological disorders (mainly SCD), neurological conditions and idiopathic instances.7
In terms of management, the role of the urologist is more complex than with any other priapism category. Therefore, not only should any prolonged ischaemic attack be promptly and optimally treated in order to preserve the erectile function, but also the goal of the management strategy has to be the prevention of recurrence. Careful patient counselling is of high importance.

The scientific knowledge of stuttering priapism has grown rapidly with the evolution of molecular medicine in the last few years, leading to better understanding of the pathophysiology of the condition. The pathology of priapism and the pathophysiology of stuttering priapism have been thoroughly examined, leading to novel treatment modalities and potential future agents based on the evidence of basic science research.

Epidemiology and etiology
The incidence of priapism in men, regardless of age, is 0.3–1.5 per 100,000 yearly, with a peak in the fifth decade of age. Epidemiological data of stuttering priapism are not available, since most studies and reports are based on specific populations with a high prevalence of the condition, such as patients with SCD. The incidence of intermittent priapism in men with SCD has been reported to be 42%, whereas another report among children and adolescent males with SCD increases the incidence to 64%. The rate of erectile dysfunction as a result of priapism in this population exceeds 30%. In regard to age, there is a bimodal peak of prevalence, between 5 years and 10 years of age in children and 20 years and 50 years in adults. Nevertheless, by the age of 20, 89% of males with SCD will have experienced one episode of ischaemic priapism. The mean age of first occurrence is 12 years. In childhood, SCD accounts for more than 63% of all episodes, while in adults, it accounts for 23% of all cases of ischaemic priapism. In total, SCD-related priapism represents 28% of all cases.

Stuttering priapism shares the same etiological factors with ischaemic priapism. The most common causes are haematological conditions, with SCD being the most prominent, especially in children, whereas in adults, the condition is often idiopathic or in rare cases, due to neurological disorders. Toxin-mediated infections, neoplasms, metabolic disorders and medications, both vasoactive and nonvasoactive, prescribed or following an overdose, complete the sum of etiological factors for ischaemic priapism. It is important that men who have experienced a major ischaemic priapic incident present a higher risk for developing stuttering priapism, especially if the priapic event lasted more than 4 h. Stuttering priapism has also been described in newborns and there are also reports of nonischaemic stuttering priapic incidents.

Clinical manifestation and progression
The clinical manifestation of stuttering priapism resembles that of ischaemic priapism. Most of the literature reports are based on observations of continuous SCD-related incidents, whereas little is reported on the intermittent attacks that constitute the entity of stuttering priapism. Typically, the priapic events in stuttering priapism are self-limited, resolving in under 3 h, some lasting for only minutes before spontaneous resolution. It has been reported that 77% of the transitory attacks are sleep-related, 17% are associated with sexual activity, and that the mean duration is 125 min, with a peak incidence around 3.00 a.m. These episodes can occur in a wide range, from several daily to isolated incidents every few months, continuously or followed by periods free of incidents, of unknown duration, even months and years. In patients with SCD, these attacks are often unrelated to sickling crises, characteristic of the disease. Often these incidents start in childhood and they account for numerous visits to healthcare services, severe psychological impact, sexual performance anxiety, sleep disorders and impairment in the quality of life. Moreover, as it affects young men, even before the beginning of their sexual conformation, it may negatively impact their sexual maturity. It is believed that 28% of these patients will eventually progress to major ischaemic priapic episodes, whereas at least one stuttering priapic episode has been reported in 61% of patients with a major episode longer than 24 h. Generally, stuttering episodes manifest as engorgement of the corpora cavernosa (bicorporal priapic incident). Tricorporal involvement, including the corpus spongiosum and the glans penis, is regarded as a negative prognostic sign indicative of a possible infarction. It is well known that prolonged priapic incidents lasting more than 4–6 h can lead to corporal fibrosis, thus the duration of the attack is the most important predictor of the outcome, in terms of preserving erectile potency. It is believed that SCD-related priapism in prepubertal males has a more favourable prognosis, in contrast to postpubertal males.
who tend to present with more prolonged attacks.\textsuperscript{25} Although even self-limited priapic incidents have been associated with significant impairment in terms of quality of life and sexual maturity, it is of great concern that major and prolonged priapic events, if not treated promptly and accordingly, may result in severe irreversible erectile dysfunction. Therefore, the natural history and long-term consequences of major stuttering priapic events are similar to those of ischaemic priapism, constituting a medical emergency.

Pathophysiology

Although the pathophysiology of ischaemic priapism is not completely established, the result is the occlusion of venous return, the diminishing of arterial blood flow and the formation of a compartment-like syndrome in the corpora cavernosa. Grossly, this leads to hypoxia and metabolic acidosis preventing the initiation of detumescence mediated by smooth muscle contraction. A prolonged state of ischaemic priapism leads to irreversible structure damage and fibrosis.\textsuperscript{8}

Conventionally, it is widely agreed that haematological factors, such as enhanced blood viscosity in SCD, serve as the pathophysiological basis for priapism. Hinman proposed that the condition of venous stasis and hypoxia in the normal erection mediates erythrocyte sickling, inducing further congestion. Moreover, it has also been speculated that stuttering priapism is caused by damage to the neurological and endothelial detumescence mechanisms, due to ischaemia.\textsuperscript{3,26}

Today, it is well known that the pathophysiology of priapism is considerably more complicated, involving the dysfunction and imbalance between normal erection and detumescence mechanisms. It is believed that the molecular basis for stuttering priapism is shared with idiopathic ischaemic priapism, involving signalling molecules, nitric oxide (NO) metabolism, inflammatory response, endothelium factors and vascular reactivity.\textsuperscript{27,28} Specifically, a deficiency in endothelial NO causes downregulation in a cyclic guanosine monophosphate (cGMP)-dependent protein kinase and phosphodiesterase type 5 (PDE5), resulting in dysregulation in the corporal smooth muscle tone.\textsuperscript{28,29} Moreover, decreased NO availability decreases RhoA (Ras homolog gene family) and Rho-kinase, important factors for penile flaccidity, and disrupts adenosine signalling.\textsuperscript{30,31} As a result, lacking mechanisms to regulate cGMP in combination with reduced vasoconstrictive activity, the cavernosal smooth muscle tone is reduced, leading to increased and disproportionate responses to stimuli. Furthermore, the low point at which the smooth muscle is set remains, which potentially explains the intermittent nature of stuttering priapism.\textsuperscript{32} Moreover, adenosine, a vasodilator responsible for penile tumescence, has been found to be increased in conditions of stress, hypoxia and ischaemia, suggesting an important role in the pathogenesis of the priapic state.\textsuperscript{33–35} Other mediators, such as the recently described peptides, opiorphins, have been found to inhibit the function of endopeptidases, prolonging protein binding to receptors, and therefore promoting relaxation of the corporal smooth muscle.\textsuperscript{36,37} Finally haem oxygenase and carbon monoxide have also been proposed as potent signalling molecules in pathways involving the pathophysiology of ischaemic priapism\textsuperscript{38} and androgens have also been observed to have an association with priapism.\textsuperscript{39,40}

Evaluation

History

A full medical history is of the utmost importance. Medical conditions such as SCD and other haematological disorders, malignancies and specific medications have to be identified or ruled out in case of idiopathic priapism.\textsuperscript{1,7} Moreover, specific information on the duration of the acute incident and previous attacks, as well as the frequency and age of onset, can potentially reveal an underlying causative factor that has yet to be manifested. It is also important to collect information on methods of resolve that have been already tried by the patient, as well as medication for prevention that has been challenged in order to prevent recurrence, and invasive procedures in the past.\textsuperscript{25} An erections diary is also recommended in boys with SCD.\textsuperscript{41}

Physical examination

The physical examination must include the genitalia and perineum, as well as the lower abdomen. In ischaemic priapism, the engorgement involves the corpora cavernosa and the erection is usually painful. In some cases of corporal infarction, the glans penis and corpus spongiosum are also engorged. In cases of arterial priapism, the corpora cavernosa, although engorged, are not fully rigid.\textsuperscript{1,7} In addition, it has been
described that the application of pressure to the perineum results in penile detumescence. This piesis sign is indicative of arterial priapism and is mostly demonstrated in children.42

Laboratory evaluation
A complete blood count and a serum biochemistry profile are considered mandatory.43 The white blood count and differential, platelet count and haemoglobin iontophoresis might reveal haematological dyscrasias. The age of the patient, and in some cases the race or origin, might instruct further investigation due to the ethnicity-related high prevalence of specific haematological disorders. In case of a strong suspicion, screening for psychoactive drugs, both legal and illegal, through blood or urine toxicology might be performed. Further laboratory testing can be performed, in accordance with the medical history, the clinical examination and the first laboratory results.44 Blood gas evaluation, with corporeal blood aspiration, can easily distinguish between ischaemic and nonischaemic priapism, both by the macroscopic appearance (dark blood in low flow versus bright red in high flow), as well as by the end results (<30 mmHg pO2, >60 mmHg pCO2, pH <7.25 in ischaemic conditions, versus results similar to arterial blood gas in nonischaemic priapism).1,7

Ultrasonography
Colour duplex ultrasonography (CDU) can distinguish between ischaemic and nonischaemic priapism. The CDU can be performed as an alternative or in addition to corporeal blood gas analyses.7 Ultrasonography is capable of revealing the blood flow in the cavernosal arteries, which is little to nonexistent in the case of ischaemic priapism, whereas in nonischaemic cases, the blood flow velocity is normal or even high. General blood flow in the corpora can also be evaluated, revealing the absence of significant blood flow in cases of ischaemic priapism.1 The typical cavernosal arterial flow in ischaemic priapism is characterized by high resistance and low velocity, whereas some cases with high resistance and high velocity demonstrate negative end-diastolic velocity.45 Ultrasonography can also aid in the ongoing evaluation of the ischaemic incident, as in some cases, the resulting oedema can make the evaluation of detumescence difficult.12

Magnetic resonance imaging
Magnetic resonance imaging (MRI) can provide useful information about the viability of cavernosal smooth muscle, which can be a valuable predictor of the expected restoration of erectile function after the priapic incidence resolution. The sensitivity of the gadolinium-enhanced MRI evaluation has been reported to be as high as 100%. This information is particularly useful in the planning of invasive procedures such as shunts and patient counselling about long-term erectile function and the possibility of early penile prosthesis insertion.46

Management
The primary endpoint in the management of stuttering priapism is the prevention of recurrence. Nevertheless, each acute priapic event has to be regarded as a potential threat to normal erectile function, due to its correlation with ischaemic priapism and has to be dealt with accordingly.1 Both noninvasive measures as well as early minimally invasive intervention are capable of preventing ischaemic attacks from developing into a major priapic event. Systemic therapies have been found to be useful in terms of recurrence prevention. Finally, invasive procedures, ranging from minimally invasive procedures to penile prosthesis surgery, have been effective in resolving major prolonged ischaemic events.

Patient counselling
The goal of patient counselling is to provide patients suffering recurrent episodes with information about simple measures that can be taken in order to achieve resolution in cases of acute attacks, as well as to mobilize them to seek medical assistance, in cases of failure of these or prolonged attacks. Analgesia and the use of opioids have been found useful in achieving resolution of a priapic incident. Other practical measures, historically, include physical exercise, urination, ejaculation, fluid intake, cold baths, cold water enemas or cold packs.47 The latter can also serve as analgesic, vasoconstrictive and even cytoprotective for the smooth muscle, but also may induce priapism in the case of patients with SCD, and also reduce blood flow in a compromised area.48,49 All these conventional remedies lack evidence of efficacy.7
The use of intracavernosal injections (ICIs) with \(\alpha\)-agonists in ischaemic priapism is aimed at resolving priapic incidents, both as monotherapy in case of acute attacks, but also in the context of systemic therapies as an adjunct. \(^{50}\) Sympathomimetic agents have the ability to promote contraction, thus resulting in detumescence. \(^{51}\) Metaraminol, ephedrine, etilefrine, epinephrine, norepinephrine and phenylephrine have all been trialled and have been found potent in resolving ischaemic priapic events, also in addition to cavernosal blood aspiration and saline lavage. Sympathomimetic injection with or without irrigation has been found more potent than aspiration with or without irrigation in resolving ischaemic priapic events. No direct efficacy comparison between \(\alpha\)-agonists has been published.

The use of phenylephrine, a selective \(\alpha_1\)-agonist, is recommended by both the American Urological Association (AUA) and the European Association of Urology (EAU), as it lacks \(\beta\)-mediated effects, in concentrations of 100–500 \(\mu\)g/ml (AUA) or doses of 200 \(\mu\)g (EAU) every 5 min for 1 h. Lower concentrations for children or patients with severe cardiovascular conditions are advised. In all cases, caution must be taken because of the potential adverse effects and monitoring is recommended in high-risk patients. ICIs have been also described in the context of self-injection protocols. \(^{1}\) In addition, there is reference to the successful use of an implantation device, self-administering intracavernosal phenylephrine in a patient with stuttering priapism. \(^{52}\)

Oral \(\alpha\)-agonists, such as pseudoephedrine and etilefrine in a daily reduced dosage, have also been suggested as effective in the prevention of recurrence. \(^{53,54}\) ICIs result in the resolution of spontaneous attacks, rather than in the prevention of future episodes and therefore are not preferred over systemic therapies. \(^{1}\) The usage of \(\alpha\)-adrenergic agents should be limited to patients who cannot be treated with hormonal agents. Although self-injection protocols have been described, \(^{8,54–58}\) it is strongly recommended that the use of sympathomimetic agents is performed during and followed by medical observation and even monitoring in high-risk patients due to the known adverse effects of these agents. Moreover, patients should be informed and counselled regarding injection site, dosage, adverse effects and timing of administration, as well as taught the need to comply fully. \(^{1}\)

### Hormonal regulators

The primary goal of hormonal therapies is to suppress circulating testosterone levels. This has shown to be effective by the regulation of the pituitary gland using gonadotropin-releasing hormones (GnRH) agonists/antagonists, reducing testosterone production using ketoconazole, blocking receptors using antiandrogens (e.g. bicalutamide, flutamide and chlormadinone), inhibiting feedback by oestrogens using diethylstilbestrol (DES), and inhibiting conversion of testosterone to dihydrotestosterone using finasteride. \(^{11}\) Targeting the androgenic effect of the physiological pathway of erection may result in loss of libido, sexual maturity problems, contraceptive effects and growth abnormalities. Therefore, hormonal manipulation is not advised in prepubertal men or those wanting to conceive. \(^{2,41}\)

Both goserelin acetate and leuprolide have been used to prevent stuttering priapism with reports of successful outcomes. Side effects such as loss of libido, erectile dysfunction, gynecomastia and hot flashes have been reported. In general, GnRH agonists are considered effective and it is reported that despite the loss of libido most patients are able to engage in sexual activity. \(^{56,59}\)

Ketoconazole is an antifungal agent with the side effect of reducing testosterone levels and blocking the production of adrenal steroids. Thus, in the setting of a randomized clinical trial, it has been found to reduce postoperative erections. \(^{60}\) The use of ketoconazole and prednisone has been found to be effective and safe in the treatment of stuttering priapism, preserving sexual function, thus providing a potential valuable alternative for prepubertal men and preserving fertility. \(^{32,61}\) More clinical trials are needed to provide secure recommendations.

Antiandrogens have been reported to be effective in the treatment of stuttering priapism, additionally presenting with a more favourable safety profile than GnRH agonists and oestrogens. While libido is preserved, common side effects include hot flashes, gynecomastia and diarrhea. \(^{62–64}\) Again, further investigation is needed in order to investigate their role in the treatment of stuttering priapism.

DES is a synthetic oestrogen, which has been used successfully as a short-term therapy for stuttering priapism. In a randomized, placebo-controlled clinical trial, DES resulted in the termination of
the priapic incident in all cases, although 50% of the treated patients relapsed upon discontinuation of the therapy.\textsuperscript{65,66} On the other hand, due to the potential cardiovascular side effects, the loss of libido and erectile function, the gynecomastia and the associated life-threatening complications of DES, its use is not recommended in clinical practice. Ethinylestradiol has also been reported to be effective in treating idiopathic stuttering priapism.\textsuperscript{67}

Finasteride has been found to be effective in the treatment of stuttering priapism, reducing significantly the mean number of priapic events in patients with SCD, with minimal side effects. The success of 5α-reductase inhibitors challenges the belief that antiandrogens are the cornerstone of stuttering priapism management, as it seems that testosterone replacement therapy inhibits recurrence while preserving sexual function.\textsuperscript{68,69} More studies are needed to provide further recommendations.

The duration of treatment to achieve the desired effect varies. Whereas 2-week DES treatment has been reported to be effective, GnRH agonists and antiandrogens have been used for as long as 2 years. It has been hypothesized that the successful management of stuttering priapism for a given time can lead to no further recurrences, so that the patient can withdraw from therapy.\textsuperscript{7,11}

Digoxin
Digoxin is an inhibitor of the sodium-potassium pump, resulting in the regulation of smooth muscle tone and penile detumescence by increasing intracellular Ca\textsuperscript{2+} levels. \textit{In vivo} and \textit{in vitro} clinical studies have investigated its potential use in the treatment of stuttering priapism, with the subjective observation of a decrease in sexual desire and penile rigidity, and the \textit{in vivo} observation of impaired cavernosal smooth muscle relaxation.\textsuperscript{70} Its side-effect profile and the necessary blood-level monitoring do not advocate its use as a first-line treatment.

Baclofen
Baclofen is a γ-aminobutyric acid derivative, which can inhibit erection and ejaculation. It has been used to prevent reflexogenic erections in patients associated with neurological disorders and spinal-cord lesions. Studies have demonstrated that intrathecal rather than oral baclofen has a beneficial response in prolonged erections, although the type of priapism in not defined.\textsuperscript{71–73} Therefore, the relation between recurrent reflexogenic erections and stuttering priapism has to be assessed.

Gabapentin
Gabapentin is an analgesic and anticonvulsant agent used widely as an anti-epileptic. Although its mechanism of action remains unknown, it has been reported to result in reducing testosterone and follicle-stimulating hormone in rats, as well as inhibiting smooth muscle relaxation.\textsuperscript{74} These mechanisms both can explain its effectiveness in treating refractory priapism in a small series of patients, although further studies are needed in order to advocate its use.

Terbutaline
Terbutaline is a β2 agonist, which results in smooth muscle relaxation of the vasculature. In patients with SCD it promotes oxygenated arterial blood flow in the cavernosa, washing out stagnant sickle cells, therefore it may serve as an emerging therapy in the prevention of SCD-related recurrences. Both oral and subcutaneous terbutaline have proven to be effective in reported series in terms of erection resolution and recurrence inhibition. In a placebo-controlled clinical trial, terbutaline proved superior to pseudoephedrine and placebo in resolving prostaglandin E1–induced priapic incidents.\textsuperscript{53,75,76} Terbutaline is contraindicated in patients with diabetes, hypertension, hyperthyroidism and history of seizures. Although it has been demonstrated as an effective agent for pharmacologically induced priapism, its effectiveness in stuttering priapism has yet to be evaluated.

PDE5 inhibitors
Although PDE5 inhibitors are widely used as treatment for erectile dysfunction, scientific evidence has proven that they are effective in preventing stuttering priapism. The rationale is that the downregulation of PDE5 results in cGMP build up in the corpora cavernosa, prolonging smooth muscle relaxation and priapism.\textsuperscript{29} Both sildenafil citrate and tadalafil have been used successfully to reduce ischaemic priapic incidents in men with idiopathic and SCD-related priapism, without compromising normal erectile capacity.\textsuperscript{8,29,50,55,77–79} PDE5 inhibitors should be
first used under conditions of full detumescence and efficacy is obtained after 2–4 weeks of use. The results of the use of PDE5 inhibitors for the management of stuttering priapism have been encouraging so far, offering new treatment possibilities. Although investigational at the present time, ongoing larger scale clinical trials are under way to evaluate further their potential benefit and use.

SCD-related priapism
In cases of SCD-related priapism, the approach is similar to ischaemic priapism. Specific measures include intravenous hydration, narcotic analgesia, supplemental oxygenation and alkalinization with the use of bicarbonates. Furthermore, specific medication, such as hydroxyurea, an established treatment for SCD, has been reported to be successful in preventing recurrences of stuttering priapism. Hydralazine has also been reported to be effective in a case of SCD-related priapism. Moreover, chronic red-cell transfusion and exchange transfusion have also been suggested for prevention, with inconsistent effects and significant complication rates. Pentoxifylline has also demonstrated effectiveness in resolving SCD-related priapism by enhancing the rheological parameters or red blood cells. In vitro, nifedipine and verapamil have also been reported as capable in inhibiting the formation of irreversibly sickled cells. It is recommended that these therapies should not be considered for primary treatment.

Emerging therapies
The discoveries of basic science research in the pathophysiology of stuttering priapism and the molecular pathways involved have led to the proposal of many different preventive agents. Apocynin, an oxidative stress inhibitor, may favourably adjust NO levels. Theophylline, an adenosine receptor antagonist, has been shown to inhibit erections mediated by excess adenosine. Moreover, inhibitors targeting the upregulation of opiorphins may represent future agents for the prevention of recurrent priapism.

Surgical intervention
As a second-line treatment, surgical intervention in the form of penile shunts is recommended after the failure of conservative measures, cavernosal blood aspiration and/or lavage and ICI with sympathomimetic agents. The purpose of shunts is to relieve penile ischaemia and avoid fibrosis. Shunting is recommended for priapic events lasting 72 h or less by the International Society for Sexual Medicine. Distal shunts are recommended to be challenged first (percutaneous distal and open distal), with open proximal and vein shunts to be used as alternatives in case of failure of the first. The recovery of erectile function in adults after shunting procedures is controversial. Generally, priapic events lasting 36 h or more seem to impair irreversibly erectile function in adults. However, it is difficult to predict erectile dysfunction in children. Potency has been reported to have been regained after a shunting procedure in a 14-year-old with a 72-h priapic incident. Cavernosal smooth muscle biopsy during shunting can assist in decision making and further management.

In the context of surgical management, subcapsular orchidectomy has also been performed in cases of stuttering priapism refractory to oral therapy. This option, although obsolete in the era of GnRH agonists, can be a useful alternative for patients with contraindications or those suffering from side effects.

Conclusion
Despite the recent progress in understanding dysregulatory erection physiology and the mechanism involved in stuttering priapism, it largely remains an unsolved urological problem. Most proposed therapies and treatments have been described in the context of case reports and limited case series, thus preventing the making of firm recommendations. It is important to focus on the primary goal of the management of stuttering priapism, which
is prevention or recurrence, rather than resolution of acute priapic incidents. In the current literature, GnRH agonists and antiandrogens have been the most consistent successful treatments of stuttering priapism so far. Future agents, as well as PDE5 inhibitors, represent exciting novel therapeutic possibilities. Owing to the rarity and unpredictability of stuttering priapism, multicentre randomized clinical trials are needed in order to challenge all available treatment options and evaluate the trifecta of success: preservation of sexual potency, prevention of recurrence and optimal safety and tolerability.

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