Guidelines

European Association of Urology Guidelines on Priapism

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Abstract

Context: Priapism is defined as a penile erection that persists beyond or is unrelated to sexual interest or stimulation. It can be classified into ischaemic (low flow), arterial (high flow), or stuttering (recurrent or intermittent).

Objective: To provide guidelines on the diagnosis and treatment of priapism.

Evidence acquisition: Systematic literature search on the epidemiology, diagnosis, and treatment of priapism. Articles with highest evidence available were selected to form the basis of these recommendations.

Evidence synthesis: Ischaemic priapism is usually idiopathic and the most common form. Arterial priapism usually occurs after blunt perineal trauma. History is the mainstay of diagnosis and helps determine the pathogenesis. Laboratory testing is used to support clinical findings. Ischaemic priapism is an emergency condition. Intervention should start within 4–6 h, including decompression of the corpora cavernosa by aspiration and intracavernous injection of sympathomimetic drugs (e.g. phenylephrine). Surgical treatment is recommended for failed conservative management, although the best procedure is unclear. Immediate implantation of a prosthesis should be considered for long-lasting priapism. Arterial priapism is not an emergency. Selective embolization is the suggested treatment modality and has high success rates. Stuttering priapism is poorly understood and the main therapeutic goal is the prevention of future episodes. This may be achieved pharmacologically, but data on efficacy are limited.

Conclusions: These guidelines summarise current information on priapism. The extended version are available on the European Association of Urology Website (www.uroweb.org/guidelines/).

Patient summary: Priapism is a persistent, often painful, penile erection lasting more than 4 h unrelated to sexual stimulation. It is more common in patients with sickle cell disease. This article represents the shortened EAU priapism guidelines, based on a systematic literature review. Cases of priapism are classified into ischaemic (low flow), arterial (high flow), or stuttering (recurrent). Treatment for ischaemic priapism must be prompt in order to avoid the risk of permanent erectile dysfunction. This is not the case for arterial priapism.

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1. Introduction

Priapism is a pathologic condition representing a true disorder of penile erection that persists beyond or is unrelated to sexual interest or stimulation [1]. Overall, erections lasting up to 4 h are by consensus defined as prolonged (level of evidence [LE]: 4). Priapism may occur at all ages. Current data show that the incidence of priapism in the general population is low (0.5–0.9 cases per 100 000 person-years) [2,3]. In patients with sickle cell disease, which is an inherited disease that causes chronic haemolytic anaemia, the prevalence of priapism is up to 3.6% in patients <18 yr of age [4] increasing up to 42% in patients ≥18 yr of age [5–7].

2. Methodology

A systematic literature search of the Medline database was performed. The controlled vocabulary of the Medical Subject Headings database was searched using the term priapism. This search yielded 1199 articles (125 review articles, 404 original articles, and 670 case reports). The expert panel also identified critical problems and knowledge gaps, enabling priorities to be established for future clinical research. These European Association of Urology (EAU) guidelines on priapism were presented for the first time by the EAU Male Sexual Dysfunction Guidelines Panel.

3. Classification

3.1. Ischaemic (low-flow or veno-occlusive) priapism

Ischaemic priapism is a persistent erection marked by rigidity of the corpora cavernosa and by little or no cavernous arterial inflow [8]. The patient typically complains of penile pain, and the examination reveals a rigid erection. Resolution of ischaemic priapism is characterised by the penis returning to a flaccid nonpainful state. However, in many cases, persistent penile oedema, ecchymosis, and partial erections can occur that may mimic unresolved priapism.

When left untreated, resolution may take days, and erectile dysfunction invariably results.

3.2. Arterial (high-flow or nonischaemic) priapism

Arterial priapism is a persistent erection caused by unregulated cavernous arterial inflow [8]. The patient typically reports an erection that is not fully rigid and not associated with pain. Fully rigid erections under sexual stimulation may occur before returning to the previous state of penile tumescence. In this case, it is not associated with erectile dysfunction.

3.3. Stuttering (recurrent or intermittent) priapism

Stuttering priapism, also termed intermittent or recurrent priapism, is a distinct condition characterised by repetitive, painful episodes of prolonged erections. Erections are self-limited with intervening periods of detumescence [9]. The duration of the erectile episodes in stuttering priapism is generally shorter than in the low-flow ischaemic type [1]. The frequency and/or duration of these distressing priapic episodes may increase, and a single episode can sometimes develop into a major period of ischaemic priapic episodes.

4. Epidemiology and pathophysiology

4.1. Ischaemic (low-flow or veno-occlusive) priapism

Ischaemic priapism is the most common form of priapism, accounting for >95% of all priapism episodes [8,10]. In ischaemic priapism, there are time-dependent modifications in the corporal metabolic environment, progressively leading to hypoxia, hypercapnia, and acidosis.

Ischaemic priapism beyond 4 h is considered a compartment syndrome, characterised by pressure within the closed space of the corpora cavernosa that severely compromises circulation in the cavernous tissues. A compartment syndrome requires emergency medical intervention to minimise potential irreversible consequences such as corporal fibrosis and permanent erectile dysfunction [11,12]. The duration of priapism represents the most significant predictor of the maintenance of premorbid erectile function; in this context, interventions beyond 48–72 h since onset may eventually help relieve erection and pain, but they have little benefit in preserving erectile functioning. Histologically, by 12 h, corporal specimens show interstitial oedema, progressing to destruction of sinusoidal endothelium, exposure of the basement membrane, and thrombocyte adherence at 24 h. At 48 h, thrombi can be found in the sinusoidal spaces, and smooth muscle necrosis with fibroblast-like cell transformation is evident [12].

In terms of pathophysiology (Table 1), ischaemic priapism has been identified as idiopathic in most cases [8,13]. Moreover, ischaemic priapism has been associated with sickle cell anaemia, haematologic dyscrasias, neoplastic syndromes, and the use of several different medications. Ischaemic priapism occurs relatively often (0.4–35%) after intracavernous injections of papaverine, phentolamine, and/or prostaglandin E1 [8,14–16] (Table 1). However, most of these cases were treated with papaverine-based combinations; the prevalence of priapism is <1% in the case of prostaglandin E1 [15]. Since their introduction on the market, a few cases of priapism have been described in men who have taken phosphodiesterase type 5 inhibitors (PDE5-Is) [8]. Most of these men had histories of increased risk for priapism including sickle cell disease, spinal cord injury, combined administration of PDE5-I and intracavernosal injection of vasoactive agents, a history of penile trauma, abuse of narcotics or psychotropic medication, or taking PDE5-I for recreational purposes without a medical reason [8].

Sickle cell disease is the most common aetiology of ischaemic priapism in childhood, accounting for 63% of the cases. It is the primary aetiology in 23% of adult cases of priapism, with a lifetime probability of developing ischaemic priapism of 29–42% in men with sickle cell disease.
4.2. Arterial (high-flow or nonischaemic) priapism

Epidemiologic data on arterial priapism are almost exclusively derived from small case series [8,21,22]. The usual cause of high-flow priapism is blunt perineal trauma [23]. The injury results in a laceration in the cavernosal artery leading to a high-flow fistula between the artery and the lacunar spaces of the sinusoidal tissue [24]. This unregulated flow results in a persistent erection, probably via a mechanism that involves stimulation of endothelial nitric oxide synthase by the turbulent blood flow [25]. Partial erections are enhanced after sexual stimulation as the trabecular smooth muscle fully relaxes, activating the corporal veno-occlusive mechanism [26]. There is often a delay between the injury and the development of the priapism that may be up to 2–3 wk. This reflects either spasm or ischaemic necrosis of the injured artery with the fistula only developing as the spasm resolves or when the ischaemic segment blows out.

Occasional cases are associated with metastatic malignancy to the penis [27], with acute spinal cord injury [28], and following intracavernosal injections or aspiration [29,30].

4.3. Stuttering (recurrent or intermittent) priapism

Epidemiologic studies of stuttering priapism are lacking. Our current understanding of this stressful entity has been derived from observations in men with sickle cell disease in which the incidence of priapism is high [7,31]. Specifically, the incidence of recurrent episodes of priapism in men with sickle cell disease is between 42% and 64% [32,33]. In a multicentre study that involved 98 boys, adolescents, and young men with sickle cell disease, ranging in age from 5 to 20 yr, the incidence of priapism was 35%, of whom 72% had a history of stuttering priapism [7].

The aetiology of stuttering priapism is similar to that of ischaemic priapism. Sickle cell disease is the most common cause of stuttering priapism. The cause can also be idiopathic and may rarely be due to a neurologic disorder. Moreover, men who have experienced an acute ischaemic priapic event, especially one that has been long lasting (>4 h) may be at risk for developing stuttering priapism [34]. The underlining mechanism is similar to that of other types of ischaemic priapism: A deficiency of endothelial nitric oxide in the penis causes downregulation of its specific downstream effectors, a cyclic guanosine monophosphate (cGMP)-dependent protein kinase including the incorporation of stuttering priapism into the priapism, especially one that has been long lasting (>4 h) may be at risk for developing stuttering priapism [34]. The underlining mechanism is similar to that of other types of ischaemic priapism: A deficiency of endothelial nitric oxide in the penis causes downregulation of its specific downstream effectors, a cyclic guanosine monophosphate (cGMP)-dependent protein kinase including the incorporation of stuttering priapism into the priapism, especially one that has been long lasting (>4 h) may be at risk for developing stuttering priapism [34]. The underlining mechanism is similar to that of other types of ischaemic priapism: A deficiency of endothelial nitric oxide in the penis causes downregulation of its specific downstream effectors, a cyclic guanosine monophosphate (cGMP)-dependent protein kinase including the incorporation of stuttering priapism into the priapism, especially one that has been long lasting (>4 h) may be at risk for developing stuttering priapism [34].

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5. Diagnostic evaluation of priapism

5.1. History

A comprehensive history is the mainstay in priapism diagnosis [8,37]. Table 3 lists the key points in the medical history. The history can help determine the underlying type of priapism [Table 4]. Ischaemic priapism is associated with progressive penile pain, and the erection is rigid. Although most cases of ischaemic priapism are idiopathic, the patient history may reveal one of the causes listed in Table 1.

5.2. Physical examination

Physical examination of the genitalia, the perineum, and the abdomen must be included in the diagnostic evaluation of priapism [8,37]. In ischaemic priapism, the corpora are fully rigid and tender, but the glans penis is soft. In arterial priapism, the corpora are tumescent but not fully rigid.

Table 1 – Potential causative factors for ischaemic priapism

<table>
<thead>
<tr>
<th>Category</th>
<th>Potential Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td>*</td>
</tr>
<tr>
<td>Haematologic dyscrasias</td>
<td>(sickle cell disease, thalassemia, leukaemia; multiple myeloma, haemoglobin Omsted variant, fat emboli during hyperalimentation, haemodialysis, glucose-6-phosphate dehydrogenase deficiency, factor V Leiden mutation)</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>(ie, amyloidosis, Fabry disease, gout)</td>
</tr>
<tr>
<td>Neurogenic disorders</td>
<td>(ie, syphilis, spinal cord injury, cauda equina syndrome, autonomic neuropathy, lumbar disc herniation, spinal stenosis, cerebrovascular accident, brain tumour, spinal anaesthesia)</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>(metastatic or regional infiltration) (ie, prostate, urethra, testis, bladder, rectal, lung, kidney)</td>
</tr>
<tr>
<td>Medications</td>
<td>*</td>
</tr>
<tr>
<td>Vasoactive erectile agents</td>
<td>(ie, papaverine, phenolamine, prostaglandin E1/alprostadil, combination of intracavernous therapies)</td>
</tr>
<tr>
<td>α-Adrenergic receptor antagonists</td>
<td>(ie, prazosin, terazosin, doxazosin, tamsulosin)</td>
</tr>
<tr>
<td>Antianxiety agents</td>
<td>(hydroxyzine)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>(heparin, warfarin)</td>
</tr>
<tr>
<td>Antidepressants and antipsychotics</td>
<td>(ie, trazodone, bupropion, fluoxetine, sertraline, lithium, clozapine, risperidone, olanzapine, chlorpromazine, thioridazine, phenothiazines)</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>(ie, hydralazine, guanethidine, propranolol)</td>
</tr>
<tr>
<td>Hormones</td>
<td>(ie, gonadotropin-releasing hormone, testosterone)</td>
</tr>
<tr>
<td>Recreational drugs</td>
<td>(ie, alcohol, marijuana, cocaine [intranasal and topical], crack, cocaine)</td>
</tr>
</tbody>
</table>
Further laboratory testing should be directed by the history and clinical and laboratory findings. 

Ischaemic priapism is identified as idiopathic in the vast majority of patients; sickle cell anaemia is the most common cause in childhood. Ischaemic priapism occurs relatively often (up to 35%) after intracavernous injections of papaverine-based combinations, although it is rare (<1%) after prostaglandin E1 monotherapy. Priapism is rare in men who have taken phosphodiesterase type 5 inhibitors, with only sporadic cases reported. Arterial priapism usually occurs after blunt perineal trauma. The aetiology of stuttering priapism is the same as that for the ischaemic type. Although sickle cell disease is the most common aetiology of this entity, the cause can also be idiopathic and may rarely be due to a neurologic disorder.

Table 2 – Epidemiology and pathophysiology of priapism

<table>
<thead>
<tr>
<th>Ischaemic priapism</th>
<th>Arterial priapism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source pO2 (mmHg)</td>
<td>pCO2 (mmHg)</td>
</tr>
<tr>
<td>Normal arterial blood (room air)</td>
<td>&gt;90</td>
</tr>
<tr>
<td>Normal mixed venous blood (room air)</td>
<td>40</td>
</tr>
<tr>
<td>Ischaemic priapism (first corporal aspirate)</td>
<td>&lt;30</td>
</tr>
</tbody>
</table>

* Adapted from Broderick et al. [8].

6. Management of priapism

6.1. Management of ischaemic priapism

Acute ischaemic priapism is an emergency condition, and rapid intervention is compulsory in a stepwise approach (LE: 4). The aim of any treatment is to restore penile flaccidity, without pain, to prevent eventual chronic damage to the corpora cavernosa. In many cases, penile oedema may persist, with ecchymosis and partial erection that could eventually mimic unresolved priapism.

6.1.1. First-line treatments

First-line treatments in ischaemic priapism lasting >4 h are highly recommended before any surgical treatment (LE: 4).

Table 6 – Recommendations on the diagnosis of priapism

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>A comprehensive history is the mainstay in priapism diagnosis and can help to determine the underlying type of priapism.</td>
<td>B</td>
</tr>
<tr>
<td>Physical examination of the genitalia, the perineum, and the abdomen must be included in the diagnostic evaluation of priapism. It may help to determine the underlying type of priapism.</td>
<td>B</td>
</tr>
<tr>
<td>Laboratory testing should include complete blood count, white blood count with blood cell differential, platelet count, and coagulation profile. Further laboratory testing should be directed by the history and clinical and laboratory findings.</td>
<td>B</td>
</tr>
<tr>
<td>Colour duplex ultrasonography of the penis and perineum is recommended for the differentiation between ischaemic and arterial priapism and for localisation of the site of fistula in arterial priapism.</td>
<td>B</td>
</tr>
<tr>
<td>Magnetic resonance imaging of the penis can predict smooth muscle viability and erectile function restoration.</td>
<td>B</td>
</tr>
<tr>
<td>Selected pudendal arteriogram should be reserved for the management of arterial priapism when embolisation is undertaken.</td>
<td>B</td>
</tr>
</tbody>
</table>

GR = grade of recommendation.
Conversely, first-line treatments initiated beyond 72 h may have benefits in relieving the unwanted erection and associated pain, but they have little documented benefit in terms of potency preservation (LE: 4).

Several first-line treatments have been described historically including exercise, ejaculation, ice packs, cold baths, and cold water enemas [8]. However, there is a lack of evidence on the efficacy of such measures. The so-called simpler cases of drug-induced priapism are typically caused by a single intracavernosal administration of a drug such as alprostadil. The first step in treatment for this type of case can be the direct injection of a sympathomimetic agent (most often, phenylephrine or etilefrine), using a 30G needle, without prior aspiration of blood from the corpora cavernosa (LE: 4). However, these simpler cases can be successfully treated with blood aspiration alone without the need for a sympathomimetic agent (LE: 4).

Decompression of the corpora cavernosa usually promotes the recovery of intracorporal blood circulation, which should result in the relief of penile pain and counteract local acidic and anoxic metabolic derangements caused by the priapism itself. Blood aspiration may be performed with intracorporeal access through the glans or with a percutaneous needle access on either lateral aspect of the proximal penile shaft under local anaesthesia [42] (LE: 4). Overall, aspiration must be continued until fresh red oxygenated blood is aspirated (LE: 4).

Options for intracavernosal sympathomimetic agents include phenylephrine, etilefrine, ephedrine, epinephrine, norepinephrine, and metaraminol [8,43–49] (LE: 2b). Phenylephrine has been suggested as the drug of choice due to its high selectivity for the α1-adrenergic receptor, without concomitant β-mediated ionotropic and chronotropic cardiac effects (LE: 4) [44,45]. Phenylephrine is usually diluted in normal saline with a concentration of 100–500 μg/ml and given in 1-ml doses every 3–5 min directly into the corpus cavernosum, up to a maximum dosage of 1 mg for no more than 1 h (LE: 4). A lower concentration or volume is applicable for children and patients with severe cardiovascular disease and the potential for systemic cardiovascular side effects [8,43–46] (LE: 4). Vital signs (blood pressure and pulse) should be monitored every 15 min [47]. Potential treatment-related side effects of intracavernous phenylephrine (and other sympathomimetic agents) include headache, dizziness, hypertension, reflex bradycardia, tachycardia and palpitations, and irregular cardiac rhythms.

Patients with ischaemic priapism may not respond properly to conventional doses of phenylephrine due to the attenuated contractile response associated with hypoxia and acidosis [50]. Higher doses, up to a total cumulative dose of 50 000 μg, have been suggested to be of clinical benefit (LE: 3) [44,45].

The management of sickle cell disease–related priapism is similar to the approach previously described in other cases of ischaemic priapism [9,51] (LE: 4). However, other therapeutic practices may also need to be implemented [51]. Specific measures for sickle cell disease–related priapism include the administration of intravenous hydration and parental narcotic analgesia while preparing the patient for aspiration and irrigation. In addition, supplemental oxygen administration is required and alkalisation with bicarbonate [9,18]. Exchange blood transfusion has been also proposed, with the aim of increasing the tissue delivery of oxygen.

6.1.2. Second-line treatments

Second-line intervention typically refers to surgical intervention in the form of penile shunt surgery. In an acute situation, surgery for ischaemic priapism should be considered only when conservative management options fail, with the specific purpose of relieving penile ischaemia and the avoidance of corporal fibrosis (LE: 4) [8,43,52]. In 2009, the International Society for Sexual Medicine Standards Committee stated that shunting should be considered for priapism events lasting ≤ 72 h (LE: 4) [8].

In general, the type of shunt procedure chosen is suggested by the surgeon’s preference and familiarity with different techniques (LE: 4). However, it is preferable for distal shunt procedures to be tried first (LE: 4). Proximal shunting may be considered if distal procedures have failed to relieve the priapism (LE: 4). However, the efficacy of this treatment strategy is questionable, and cavernous biopsy may be considered to diagnose muscle necrosis.

Data are not unique regarding the postoperative recovery rates of erectile function in men submitted to shunt surgery for prolonged erections [53]. In this context, priapism events prolonged > 36 h appear to impair irreversibly erectile tissue both structurally and functionally [54]. Overall, it has been considered that in patients experiencing major ischaemic priapism lasting continuously for a prolonged duration (≥ 36 h), any shunt procedure may only serve to limit pain sensations without adequately preserving erectile functioning (LE: 4).

Four categories of shunt procedures have been reported [1,8,52]: These include the percutaneous distal (corporoglanular) shunts (by Winter, Ebbehoj, Lue), the open distal (corporoglanular) shunts (by Al-Ghorab, Burnett), the open proximal (corporospongiosal) shunts (by Quackles, Sacher), and the vein anastomoses/shunts (by Grayhack, Barry). It is not possible to say that one procedure is more effective than another due to the limited available data, particularly the lack of data allowing accurate predictions of outcome (LE: 4).

Intractable therapy-resistant acute ischaemic priapism or episodes lasting > 48–72 h usually result in complete erectile function impairment, along with possible major penile deformity. In these cases, immediate penile prosthesis surgery has been recommended because it seems to avoid the difficulty of surgery and the risk of complications (eg, urethral injury, tunical erosions, infection, and/or penile shortening) that may occur whenever surgery is performed some time later after long-term corporal fibrosis has already developed [55–58] (LE: 3). Potential complications that could compromise immediate penile prosthesis implantation include distal erosion and cavernositis [56,58], along with a mild rate of revision surgery [56]. Table 7 summarises the recommendations on the treatment of ischaemic priapism.
6.2. Management of arterial priapism

The management of high-flow priapism is not an emergency because the penis is not ischaemic. Definitive management can therefore be considered and should be discussed with the patient so he understands the risks and complications of treatment (LE: 3) [8,37].

Conservative management, which may include the use of ice applied to the perineum or site-specific perineal compression, has been reported to be successful [21,22,59]. It is an option in all cases, particularly children [60] (LE: 3). The fistula occasionally closes spontaneously. Even in those cases when it does not, the response to a sexual stimulus does allow for intercourse. Blood aspiration is not an option for the treatment of arterial priapism, and the use of α-adrenergic antagonists is not recommended due to potential severe adverse effects (eg, transfer of the drug into the systemic circulation).

Selective arterial embolisation can be performed using an autologous clot [61], gel foam, or sponge, or more permanent substances such as coils [62] or acrylic glue [63], with success rates up to 89% (LE: 3). The series reporting the efficacy of these different approaches are all uncontrolled and relatively small, so although the relative merits of the different substances can be debated, there are no robust data to demonstrate superiority.

The use of an autologous clot has some attractions, at least theoretically. It temporarily seals the fistula, but when the clot is lysed, the arterial damage has usually resolved and the blood flow of the penis can therefore return to normal. The use of a permanent device, such as a coil, would permanently block an artery and may lead to adverse effects upon spontaneous sexual function. Following percutaneous embolisation, a follow-up is appropriate within 1–2 wk. Assessment by clinic examination and by colour Doppler ultrasonography may be helpful in determining whether the embolisation has been successful [39]. Recurrence rates of 7–27% after a single treatment of embolisation have been reported [64] (LE: 3). In a few cases, repeat embolisation is necessary. Sexual function following embolisation can be adversely affected, although there is a full restoration of potency in approximately 80% of men [64] (LE: 3).

Embolisation in children, although reportedly successful, is technically challenging and requires treatment within a specialist paediatric vascular radiology department [65]. Surgical treatment consists of selective ligation of the fistula through a transcapsoreal approach under the guidance of colour Doppler ultrasound [1,66]. However, it is technically challenging and may pose significant risks, mainly erectile dysfunction due to accidental ligation of the cavernous artery instead of the fistula. Today, it is rarely performed and only in cases with pseudocapsular formation around the fistula (because this makes it easier to identify the fistula), contraindications for selective embolisation, no availability of the technique, or embolisation failure (LE: 4). Table 8 summarises the recommendations on the treatment of arterial priapism.

6.3. Management of stuttering priapism

The primary goal in the management of patients with stuttering priapism is the prevention of future episodes. This goal can usually be achieved pharmacologically. The management of each acute episode is similar to that for

| Table 7 – Recommendations on the treatment of ischaemic priapism |
|---------------------|------------------|
| **Recommendation** | **GR** |
| Ischaemic priapism is an emergency condition; rapid intervention is compulsory. | B |
| The specific aim of any emergent treatment is to retrieve penile flaccidity, without pain to prevent eventual chronic damage to the corpora cavernosa. | C |
| Management of ischaemic priapism should start as early as possible (within 4–6 h) and should follow a stepwise approach. Erectile function preservation is directly related to the duration of priapism. | B |
| The first step in the management of ischaemic priapism is decompression of the corpora cavernosa by penile aspiration until fresh red blood is obtained. In cases of drug-induced priapism after intracavernous injections of vasoactive agents for the treatment of erectile dysfunction, blood aspiration can be replaced by intracavernous injection of a sympathomimetic drug as the first step. | C |
| In the case of priapism recurrence after aspiration, the next step is intracavernous injection of a sympathomimetic drug. Phenytoin is the recommended drug due to its favourable safety profile on the cardiovascular system compared with other drugs. Phenytoin is usually diluted in normal saline with a concentration of 100–500 μg/ml and given in 1-ml doses every 3–5 min directly into the corpus cavernosum, up to a maximum dosage of 1 mg for no more than 1 h. Patients at high cardiovascular risk should be given lower doses. Patient monitoring is highly recommended. | B |
| In case of priapism recurrence after aspiration and intracavernous injection of a sympathomimetic drug, these steps should be repeated several times before considering surgical intervention. No clear recommendation for the highest phenylephrine dose can be given. | C |
| Ischaemic priapism due to sickle cell anaemia is treated in the same fashion as idiopathic ischaemic priapism. Other supportive measures are recommended (intravenous hydration, oxygen administration with alkalinisation with bicarbonates, blood exchange transfusions), but these should not delay initial treatment. | B |
| Surgical treatment is recommended only when blood aspiration and intracavernous injection of sympathomimetic drugs have failed or for priapism events lasting <72 h. | C |
| Distal shunt surgical procedures should be performed first followed by proximal procedures in case of failure. The efficacy of this treatment strategy is questionable, and cavernous biopsy may be considered to diagnose muscle necrosis. No clear recommendation of one type of shunt over another can be given. | C |
| In cases of priapism presenting >36 h after onset, or in cases for which all interventions have failed, erectile dysfunction is inevitable and the immediate implantation of a penile prosthesis is recommended. Implantation of penile prosthesis at a later stage can be difficult due to severe corporeal fibrosis. | B |

**GR** = grade of recommendation.
ischaemic priapism, namely aspiration/irrigation in combination with intracavernous injections of α-adrenergic agonists. Unfortunately, the efficacy and safety of the various treatment modalities reported in the medical literature have been poorly characterised [9,18,67].

The aim of hormonal manipulation is to smother circulating testosterone levels to suppress the action of androgens on penile erection [9,18,68]. This can be done through the use of gonadotropin-releasing hormone agonists or antagonists [69] (LE: 4). Potential side effects may include hot flushes, gynaecomastia, impaired erectile function, loss of libido, and asthenia. Antiiandrogens (ie, flutamide, bicalutamide) [70] and oestrogens [71] may also be efficacious (LE: 4). The 5α-reductase inhibitors (finasteride, dutasteride) block the conversion of testosterone to dihydrotestosterone. In a noncontrolled study of 35 patients with sickle cell disease, finasteride, 3 or 5 mg daily for 120 d, produced a significant decrease in the number of recurrent priapic episodes [72] (LE: 3). Finally, ketonazole, an antifungal agent that reduces adrenal and testicular androgen production, may also be a potential treatment for priapism [73] (LE: 4).

The duration of hormonal treatment for effective suppression of recurrent priapic events varies from weeks to years and depends on the type of agent and the investigator suggestions. Because this information has been derived from small case series in men with idiopathic stuttering priapism and patients with sickle cell disease, it is not possible to reach any clear conclusions. Hormonal agents have a contraceptive effect and interfere with normal sexual maturation. Caution is therefore strongly advised when prescribing hormonal treatments to prepubertal boys, adolescents, or those men who are trying to impregnate their female partner.

Studies of oral α-adrenergic agonists including pseudoephedrine and etilefrine (50–100 mg daily) have suggested that limited daily dosing with these agents is effective in up to 72% [74,75]. Drug therapy is generally prescribed at bedtime. Side effects have included tachycardia and palpitations.

Digoxin regulates smooth muscle tone through a number of different pathways leading to penile detumescence [9,18]. A small clinical double-blind placebo-controlled study using digoxin (0.25–0.5 mg daily) produced a decrease in sexual desire and excitement with a concomitant reduction in penile rigidity [76] (LE: 2b). Common side effects may include a decreased libido, anorexia, nausea, vomiting, confusion, blurred vision, headache, gynaecomastia, rash, and arrhythmia.

Terbutaline is a β-agonist that causes vasodilation, resulting in smooth muscle relaxation of the vasculature [18]. Oral terbutaline was suggested as a compound to prevent stuttering priapism with detumescence rates of 36% in patients with alprostadil-induced priapism [77] (LE: 3). In the only randomised placebo-controlled study in patients with pharmacologically induced priapism, detumescence occurred in 42% of the terbutaline-treated group compared with only 15% in the placebo-treated group [78] (LE: 1b). Side effects may include nervousness, shakiness, drowsiness, heart palpitations, headache, dizziness, hot flashes, nausea, and weakness.

Gabapentin is a drug with anticonvulsant, antinoceceptive, and anxiolytic properties. Its proposed mechanism of action is the inhibition of voltage-gated calcium channels, which in turn attenuates synaptic transmission. It is given at the dose of 400 mg four times a day up to 2400 mg daily, until a complete penile detumescence occurs, with subsequent maintenance administration of gabapentin 300 mg daily [79] (LE: 4). Side effects may include anorgasmia and impaired erectile function.

Baclofen is a γ-aminobutyric acid (GABA) derivative that can inhibit penile erection and ejaculation through GABA activity and is used to prevent recurrent reflexogenic erections or prolonged erections from neurologic diseases [18]. Intrathecal baclofen dosing is more effective than oral administration [9,80,81] (LE: 4). Side effects may include drowsiness, confusion, dizziness, weakness, fatigue, headache, hypotension, and nausea.

Hydroxyurea is an established treatment for ameliorating sickle cell disease in most patients and in improving their life expectancy [51]. For patients with sickle cell disease and recurrent priapism, there is limited evidence to suggest a medical prophylactic role for hydroxyurea (LE: 3) [82]. Potential side effects may be oligospermia and leg ulcers.

PDE5-Is act by increasing PDE5 function (ie, by increasing the concentration of cGMP in the smooth muscle in a nitric oxide dysfunctional state). This state occurs in priapism in association with the underlying disease state. It may result in a change in the nitric oxide pathway, producing downregulation of PDE5 in the penis and therefore preventing the complete degradation of cGMP in the corpora cavernosa [9,18]. Low doses of PDE5-1 (sildenafil 25 mg daily or tadalafil 5 mg three times weekly) have a paradoxical effect in alleviating and preventing stuttering priapism, mainly in patients with idiopathic and sickle cell disease–associated priapism [9,18,83,84] (LE: 3). Treatment should be started only when the penis is in its flaccid state, and there may be a delay of 1 wk before...
treatment is effective. There are no reported impairments in male sexual function (LE: 3). Table 9 summarises the recommendations on the treatment of stuttering priapism.

**Author contributions:** Konstantinos Hatzimouratidis had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Salonia, Hatzimouratidis, Wespes.

**Acquisition of data:** Salonia, Hatzimouratidis.

**Analysis and interpretation of data:** Salonia, Hatzimouratidis.

**Drafting of the manuscript:** Salonia, Hatzimouratidis.

**Critical revision of the manuscript for important intellectual content:** Salonia, Hatzimouratidis.

**Supervision:** Salonia, Hatzimouratidis, Wespes.

**Other (specify):** None.

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### References


7. Broderick GA, Kadioglu A, Bivalacqua TJ, Musicki B, Kutlu O, Burnett AL. New insights into the prevention of future episodes. They should not be used before sexual maturation is reached. Phosphodiesterase type 5 inhibitors have a paradoxical effect in alleviating and preventing stuttering priapism, mainly in patients with idiopathic and sickle cell disease-associated priapism. Treatment should be initiated only when the penis is in its flaccid state. Other systemic drugs (digoxin, α-adrenergic agonists, baclofen, gabapentin, terbutaline) can be considered, but data are even more limited. Intracavernosal self-injections at home of sympathomimetic drugs can be considered for the treatment of acute episodes on an interim basis until ischaemic priapism has been alleviated.

**Table 9 -- Recommendations on the treatment of stuttering priapism**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>GR</th>
</tr>
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<tbody>
<tr>
<td>The primary goal in the management of patients with stuttering priapism is the prevention of future episodes, which can generally be achieved pharmacologically. The management of each acute episode is similar to that for ischaemic priapism.</td>
<td>B</td>
</tr>
<tr>
<td>Hormonal therapies (mainly gonadotropin-receptor hormone agonists or antagonists) and/or antiandrogens may be used for the prevention of future episodes. They should not be used before sexual maturation is reached. Phosphodiesterase type 5 inhibitors have a paradoxical effect in alleviating and preventing stuttering priapism, mainly in patients with idiopathic and sickle cell disease-associated priapism. Treatment should be initiated only when the penis is in its flaccid state. Other systemic drugs (digoxin, α-adrenergic agonists, baclofen, gabapentin, terbutaline) can be considered, but data are even more limited. Intracavernosal self-injections at home of sympathomimetic drugs can be considered for the treatment of acute episodes on an interim basis until ischaemic priapism has been alleviated.</td>
<td>C</td>
</tr>
</tbody>
</table>

**GR** = grade of recommendation.


