Our experience in the treatment of priapism

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INTRODUCTION

Priapism (Hulseyism) is a rare pathologic condition characterized by abnormally long-lasting, usually painful erections not accompanied by sexual stimulation and arousal [1]. The word “priapism” is derived from the Roman and Greek god Priapus, famous for his enormous, continuous erections. A special feature of priapism is that the erect penis does not spontaneously return to its flaccid state.

There are two types of priapism – ischemic, owing to weak blood supply, and non-ischemic, owing to abundant blood supply. Ischemic priapism can develop due to sickle-cell anemia, thrombocytopenia, leukemia, anticoagulant intake, spinal injury, fat embolism, and antipsychotic (clozapine, chlorpromazine) drugs have been reported. It is necessary to remember a possibility of priapism appearance due to sildenafil, vardenafil, or tadalafil treatment. Non-ischemic priapism with abundant blood supply most often develops as a result of perineal trauma and injuries of the penis. In such cases, the presence of a communication between the artery and cavernous bodies is typical, as result penis is filled with blood under intense pressure and blood cannot be drained adequately.

Many causes of priapism still remain unknown.

OBJECTIVE

To analyze the etiology of priapism, contemporary approaches to its management and efficacy of one-sided cavernoglandular shunting after Winter in ischemic priapism treatment.

PATIENTS AND METHODS

The study enrolled 10 patients with priapism who were treated at our urological clinic between 2001 and 2009. Their age ranged 22-71 years. In six patients priapism developed after erectile dysfunction treatment. In two patients priapism occurred as a consequence of systemic intake of anticoagulants (low-weight heparin) due to serious vascular pathology (phlebothrombosis, thrombophlebitis). In another two patients no objective cause of priapism was detected, therefore idiopathic disease was determined.

We analyzed the frequency of priapism incidences depending on prescribed medicines in 120 patients with erectile dysfunction (ED), who were treated by intracavernous injections. Among the 10 patients with priapism, six cases appeared as a complication of ED treatment. Priapism as a complication developed in two (2.7%) among of 74 patients after intracavernous injection of 20 mcg of prostaglandin E1 (PGE-1), in 1 (5%) of 20 patients after consequent administration of 20 mcg of PGE-1 plus 0.5 mg of phentolamine, and also in 3 (8.3%) of 36 patients after administration of 2% papaverine solution. Patients in whom priapism developed after intracavernous injection of vasoactive substance, primarily reported to the sexological practice of Lviv Regional Consultative Ambulatory and the Chair of Urology of Danylo Halytsky Lviv National Medical University with complains of ED. All of them subsequently had a dopplerographic study of cavernous hemodynamics after pharmacological induction of erection for verification of the etiology of ED. The array of clinical and laboratory methods allowed to diagnose the primary cause of ED as psychogenic in all three patients with priapism after administration of PGE-1 solution. In three patients (aged 47, 51, and 58 years) with development of priapism due to injection of 2% papaverine solution, primary diagnosis was a mixed type of ED (a combination of psychogenic, vascular factors and manifestations of late hypogonadism). All patients with mixed ED were initially administered 0.7 ml of 2% papaverine solution, which did not cause an adequate erection and acceptable hemodynamic indices in the cavernous arteries (over 25 cm/sec), which is why 15 min after the first injection, 0.7 cc of 2% papaverine solution were administered to them additionally, which finally caused priapism.
For the treatment of priapism initially we used intracavernous injections of E-adrenoreceptor agonists, but such therapy was ineffective. Afterwards all of 10 patients with verified priapism were injected by ketamine hydrochloride 1 mg/kg body mass IV in the operating room, and also peridural anesthesia was performed 20-30 min later, which did not produce detumescence too. After that one-sided transcaputal punctures after Winter were performed (Fig. 1) in all patients, using a 16G needle (single-use IV catheter with an obturator was used) with heparin irrigation 5000-15000 IU during 30-45 minutes.

RESULTS

Results of treatment in 10 patients with priapism are presented in Table I.

In all of 10 patients shunting after Winter was effective in priapism elimination. It can be observed that in five cases the duration of priapism was insignificant (7-9 hours), since all patients were warned prior to injection of vasoactive substance about possible development of priapism and advised to seek immediately medical aid if this condition occurred. The short duration of priapism allowed to restore and to preserve the erectile function in all three patients with psychogenic erectile dysfunction, since there were no likely fibrotic changes in the cavernous tissue over 8 hours, and the difficulty of the intervention was insignificant. In three patients with a preliminary diagnosis of mixed erectile dysfunction (with an organic vascular component) it was not feasible to restore erectile function after shunting. The presence of endothelial dysfunction was possible in those patients prior to injection of a vasoactive substance, which necessitated seeking help for ED treatment. No other cases presented recurrences of priapism in the postoperative period. ED was not an actual problem for both patients receiving anticoagulant therapy. Both patients with idiopathic priapism reported absence of erections over several months of post-operative follow-up. Thus, it can be conferred that prolonged priapism often leads to irreversible dysfunction of endothelium with destructive and fibrotic changes in the cavernous tissue, which probably occur simultaneously [2]. Therefore, a retrospective review revealed a necessity to find new erection-safe methods for treatment of this disease.

DISCUSSION

There are such different therapeutic approaches to priapism treatment as mechanical (prolonged compression of perineum and application of ice packs), pharmacological (oral, intracavernous, and intravenous), radiological (selective embolization), and surgical (ligation of arteries or arteriovenous shunting) [3, 4]. In contradistinction to non-ischemic priapism, which does not require immediate intervention, protracted ischemic priapism is always associated with progressive fibrosis of the cavernosal tissues and erectile dysfunction [2, 5]. That is why all patients with priapism should be evaluated urgently in order to start treatment immediately in those patients with ischemic priapism. The aim of the treatment of all patients with priapism is to achieve detumescence as soon as possible to prevent future ED. In order to preserve erectile function, the first-line intervention should be mechanical and medical treatment (oral, intravenous, or intracavernous injections), following by a second-line shunting procedure if first-line fails [3, 6, 7].

Some urologists have considered that oral administration of medications such as pseudoephedrine (E-adrenoreceptor agonist, decongestant) or the asthma medication terbutaline (agonist of β-adrenoreceptors) can be used to treat ischemic priapism. However, only a few studies have shown a persuasive success of this type of treatment. Oral pseudoephedrine, 60-120 mg orally has been suggested as a conceivable therapy due to its alpha-agonist effect. The precise efficacy of this mediation’s oral use is not well studied [8]. The use of terbutaline orally, at a dose of 5-10 mg, followed by another 5-10 mg 15 minutes later, if required, produces detumescence in 36% of patients who had prostaglandin-induced priapism [9]. This treatment is appropriate when preparing the infusion. In the following study there is a report on oral administration of terbutaline (2.5-5 mg) in the treatment of recurrent idiopathic priapism [10].

Table 1. The results of treatment in patients with priapism

| Number of Patients/Priapism-Inducing Medication | Age (years) | Duration of priapism (hours) | Duration of One-sided shunting after Winter (minutes) | Recurrence of priapism | Persistent ED during 6-month monitoring |
|-----------------------------------------------|------------|------------------------------|---------------------------------------------|------------------------|----------------------------------------|
| 1/ low-weight heparin                         | 71         | 35                           | 45                                          | –                      | 1                                      |
| 1/ low-weight heparin                         | 64         | 21                           | 40                                          | –                      | 1                                      |
| 1/ idiopathic priapism                        | 37         | 24                           | 45                                          | –                      | 1                                      |
| 1/ idiopathic priapism                        | 52         | 18                           | 40                                          | –                      | 1                                      |
| 1/ PGE-1                                     | 22         | 7                            | 35                                          | –                      | –                                      |
| 1/ PGE-1                                     | 35         | 7                            | 30                                          | –                      | –                                      |
| 1/ PGE-1+ phentolamine                        | 26         | 7.5                          | 40                                          | –                      | –                                      |
| 1/ papaverine                                | 47         | 25                           | 40                                          | –                      | 1                                      |
| 1/ papaverine                                | 51         | 9                            | 35                                          | –                      | 1                                      |
| 1/ papaverine                                | 58         | 8                            | 40                                          | –                      | 1                                      |
In five patients priapism was completely cured during 30 minutes after administration of 5 mg terbutaline per os.

Also its must be remembered that beta-agonists should be prescribed with caution in individuals with severe angina pectoris, since subsequent acceleration of hemocirculation can cause depletion of potassium ($K^+$), which may later provoke tachycardia and pulmonary edema.

If after oral or intravenous medication use no detumescence occurs within 30 minutes, the next step is intracavernous vasoactive substances injections. Presently there are a few intracavernous vasoactive substances for the treatment of priapism: metaraminol or agonists of $E$-adrenoceptors – phenylephrine, norepinephrine, ethylephrine and epinephrine – all with a similar mechanism of action [9–13]. Alpha-agonists exert a vasoconstrictive action on smooth muscle tissue. The literature data demonstrate that for all patients with ischemic priapism, resolution occurred in 81% of cases treated with epinephrine, 70% with metaraminol, 43% with norepinephrine, and 65% with phenylephrine [14]. The complications of intracavernous injections could be the following: pain, hematoxia, infection, and fibrosis of the penis [13]. To prevent the occurrence of complications, the medication must only be injected into a fully erect penis [15]. Local application of above-mentioned medications can lead to systemic complications – increase of blood pressure up to 200 mmHg and hemorrhagic stroke [16, 17]. In patients with high risk of cardiovascular pathologies, electrocardiogram and blood pressure monitoring are strongly recommended during priapism medication.

There are recent works describing use of methylene blue (MB) in order to increase the efficacy and safety of non-invasive therapeutic procedures with minimal side effects and complications [18, 19, 20]. Methylene blue, a guanylate cyclase inhibitor, is a potential inhibitor of endothelial mediated cavernous relaxation and has been used for the treatment of priapism. Its efficacy for the treatment of priapism secondary to intracavernous drugs was generalized by Martinez H. et al. [19, 21]. This pharmacological agent counteracts relaxation of cavernous smooth muscle tissue, causing detumescence. A perspective option is intracavernous administration of MB in the treatment of priapism, since its toxicity and systemic influence is less than in $E$-adrenergic agents, which are widely used [20]. Using this method, DeHoll et al. first treated 11 patients with priapism by aspirating up to 200 ml cavernous blood and then injecting 50 mg of MB over 3 to 5 minutes [18]. The MB was then also aspirated and the penis was gently squeezed for over 5 minutes. In 67% of patients, immediate detumescence was noted. Thus, detumescence was found in 100% patients in whom priapism was caused by intracavernous injection therapy (prostaglandin E1). However, taking into consideration the data of the last research presented by Mejean et al., we do not recommend administration of MB in the presence of cavernous fibrosis, for example in patients with repeated priapism [22].

Priapism due to sickle-cell anemia is often successfully managed by rehydration, alkalization, analgesia, and hemodilution, which are the main treatment modalities in this case; however, in patients with a sickle-cell disease or hematologic malignancy, systemic treatment of the underlying disorder should not be undertaken as the only treatment for ischemic priapism. Ischemic priapism requires specific oral or intracavernous treatment, which should be administered concurrently with the systemic treatment for hematologic pathology [14]. So, if medical measures are not sufficient, surgical treatment should be performed in these cases [23, 24].

Studies on efficacy of gonadotropin-releasing hormone analogs have been conducted, including the use of an antiandrogenic substance (flutamide) in prolonged treatment of recurrent priapism [25].

Despite various pharmacological therapies available for priapism, surgical management is often required if medical therapy is ineffective. There are a large variety of operative treatment modalities:

- distal cavernoglanular shunting: shunting after Winter, shunting after Ebbehoj or Al-Ghorab technique – excising of a piece of the tunica albuginea at the tip of the corpus cavernosum [26];
- anastomosis between a cavernous body and a superficial femoral vein known as shunting after Grayhack;
- cavernous (porcoronospinosus) shunt (i.e. Quackels technique);
- proximal ligation of the internal pudendal artery;
- shunting of the dorsal cavernous vein, incisions;
- irrigation and drainage of cavernous sinuses;
- percutaneous blood aspiration from cavernous bodies;
- removal of pudendal nerves from the ischiocavernous muscle;
- amputation of the penis if priapism is related to a neoplasm of the penis, etc. [14, 27].

In our opinion, shunting after Winter is minimally traumatic among all the surgical methods of ischemic priapism treatment and is successful in the majority of cases. That is why we used this procedure in our patients.

A distal cavernoglanular shunt after Winter is most frequently performed, because this method is effective and creates a connection between, the glans penis and tunescous cavernous body [26]. The success rate of the procedure varies between 50% and 65% [28]. Complications after such kind of intervention include cavernitis with abscess formation, injury of urethra with stricture or external fistula formation, hematoma with or without thrombosis, and subsequent development of ED in 50% of patients [29].

Therefore, shunting should be performed only after failure of medical treatment [6]. Proximal shunting using Grayhack or Quackels technique may be performed if more distal shunting procedures have failed to achieve detumescence. The summary data presented by Montague D.K. et al. show resolution rates of 77% for Quackels, 76% for Grayhack, 74% for Al-Ghorab, 73% for Ebbehoj, and 66% for Winter procedures, but these rates significantly depend on patients selection. ED rates are less for distal shunts (approximately 25%) than for the proximal shunts, Quackels and Grayhack, (about 50%) [14]. If subsequent ED developed, the method of choice is a phalloplasty [30].

Repeated painful priapism always needs precision tactics. Taking into consideration frequent failures of open surgeries and their short-term effectiveness, Bastuba et al. have studied the efficacy of selective penile arterial embolization (SPEA) [16]. Using SPEA, normal erectile function was restored in 86% of patients during 5-months, depending on the duration of thrombus disintegration. The authors recommend application of SPEA as a successful surgery in cases of non-ischemic priapism that developed due to injury or arteriovenous fistulas.

CONCLUSIONS

1. Priapism is viewed as an emergency urological condition that requires a rapid and consistent therapeutic approach. In all cases, the treatment of priapism has to be initially pharmaceutical, which can be converted to surgical treatment as needed.

2. An obligatory condition of priapism management is definition as either ischemic (low flow) or non-ischemic (high flow) type because the treatment approaches and outcomes for these two types are significantly different.

3. According to our data, priapism as a complication after intracavernous administration of prostaglandin E1 occurs in 2.7% of patients, after additional administration of prostaglandin E1 and
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Phentolamine – in 5% patients, after administration of papaverine – in 8.3% patients.

4. Unilateral transcaputal puncture of cavernous body (shunting after Winter) in our patients with ischemic priapism allowed to achieve detumescence in 100% of cases without subsequent recurrence.

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