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CASE REPORT

Priapism – A rare side effect of alpha blockers: Report of 2 cases and literature review

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KEYWORDS
Alpha blocker;
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Abstract Priapism is a prolonged unintended erectile state unrelated to sexual stimulation or sexual desire. There is a very rare relationship between the use of alpha blockers and the development of priapism. Here, we describe 2 cases of alpha blocker induced priapism and a literature review. One of these cases is related to the use of silodosin and the other is related to the use of tamsulosin. So far, 18 alpha blocker induced priapism cases have been reported. We are presenting the first case of silodosin induced priapism and the eighth case of priapism secondary to tamsulosin. Despite silodosin having a much greater affinity for the α1-a receptor than the α1-b receptor, as represented in this case it can cause this rare side effect. Before starting alpha blocker treatment, side effects such as priapism, which may be very rare but may cause serious problems, should be kept in mind.

PALABRAS CLAVE
Alfabloqueante;
Priapismo;
Tratamiento LUTS

Priapismo – Un efecto secundario raro de los alfabloqueantes: informe de dos casos y revisión de la literatura

Resumen El priapismo es un estado eréctil prolongado no intencionado y no relacionado con la estimulación o el deseo sexual. Existe una relación muy infrecuente entre el uso de alfabloqueantes y el desarrollo de priapismo. Describimos aquí dos casos de priapismo inducido por alfabloqueantes y una revisión de la literatura. Uno de estos casos guarda relación con el uso de silodosina, y el otro con el uso de tamsulosina. Hasta el momento se han reportado 18 casos de priapismo inducido por alfabloquantes. Presentamos aquí el primer caso de priapismo inducido por silodosina y el octavo caso de priapismo secundario a tamsulosina. A pesar de que silodosina tiene mucha mayor afinidad por el receptor α1-a que el receptor α1-b, según lo representado

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en este caso, puede causar este efecto secundario raro. Antes de iniciarse tratamiento con alfabloquantes deben tenerse en cuenta los efectos secundarios, tales como priapismo, que pueden ser muy raros pero pueden causar problemas graves.

Introduction

Priapism is a prolonged unintended erectile state unrelated to sexual stimulation or sexual desire.[1] There are three types of priapism, depending on penile artery blood flow: ischemic, non-ischemic, and recurrent.[2] It could be idiopathic, medication induced, or secondary to trauma, hematologic disorders, infections, metabolic disorders, and neoplasms.[3] Alpha blockers are used in the treatment of hypertension at the beginning. They began to be used in lower urinary tract symptoms (LUTS) following studies implicating that alpha blockers play a role in prostate smooth muscle relaxation.[4] Common side effects of alpha blockers are dizziness, orthostatic hypotension, and headache.[5]

There is a very rare relationship between the use of alpha blockers and the development of priapism. In this article we aim to emphasize that this frequently used group of drugs should be used more carefully.

Method

The words ''alpha blocker'' and ''priapism'' were searched in PubMed and all articles were scanned. Only alpha blocker induced priapism cases were included.

Results and case presentations

Case 1: A 52-year-old male with no known medical history presented with LUTS. On digital rectal examination his prostate was firm and slightly enlarged. Urine analysis and hemogram were normal; prostate specific antigen (PSA): 1.3 ng/mL. Uroflowmetry was consistent with obstruction with qmax 8.7 mL/s and urinary ultrasound with prostate measuring 60 cc, post-voidal residual volume (PVR) 120 cc. He was started on silodosin 8 mg once a day for LUTS treatment, suggestive of benign prostate hyperplasia (BPH). In a week, he presented back with a 48-h unintended erection. The patient did not use any medications other than silodosin, and there was no history of trauma. The exam was consistent with priapism, and the emergent penile ultrasound showed decreased penile blood. Despite undergoing emergent corpus cavernosum aspiration and 0.1% adrenalin irrigation, tumescence persisted, requiring corpus cavernosum deep venous shunt with reversion of the prolonged erection on post-op follow-up. Within the first month following treatment, the patient developed erectile dysfunction. Subsequently, penile prosthesis implantation was performed. It was planned to implant an inflatable penile prosthesis, but a malleable penile prosthesis could be implanted due to corporeal fibrosis. (Before using silodosin International Index of Erectile Function [IIEF]-5 score: 21; post-shunt operation 1 month IIEF-5 score: 8).

Case 2: A 54-year-old with a history of hypertension on amlodipine presented with LUTS. On digital rectal examination his prostate was firm and moderately enlarged. Urine analysis and hemogram were normal, PSA: 1.5 ng/mL. Uroflowmetry was consistent with obstruction with qmax 7.5 mL/s and urinary ultrasound with prostate measuring 70cc, PVR 100cc. He was started on tamsulosin 0.4 mg once a day for LUTS treatment, suggestive of BPH. In 4 days, he presented with a 12-h unintended erection. The patient did not use any medications other than tamsulosin and amlodipine. He reported that he had no trauma. The exam was consistent with priapism, and an emergency penile ultrasound was performed. Ultrasonographic findings were consistent with ischemic priapism. Penile tumescence resolved after corpus cavernosum aspiration, and 0.1% adrenalin irrigation. Patient had no complications. (Before using tamsulosin IIEF-5 score: 25; after priapism 3 month IIEF-5 score: 20).

Discussion and literature review

There are three subtypes of the α1-adrenoceptor (α1a, α1b, and α1d); while α1a is the predominant α1-adrenoceptor subtype in the human prostate, α1b is mainly found in the cardiovascular system.[6] Older α1-blockers including alfuzosin, doxazosin and terazosin show little selectivity for the α1-adrenoceptor subtypes, and tamsulosin is moderately selective for the α1-a subtype. Silodosin has 162-fold greater selectivity for the α1-a over the α1-b subtype which is found in vascular smooth muscle and 50-fold greater selectivity for the α1-a over the α1-d subtype.[7]

So far, 18 alpha blocker induced priapism cases have been reported.[8–11] Prozasin and tamsulosin are more likely to cause this complication, and there is no case associated with silodosin.[8] We are presenting the first case of silodosin induced priapism and the eighth case of tamsulosin induced priapism. Despite silodosin having a much greater affinity for the α1-a receptor than the α1-b receptor which is mainly found in vascular smooth muscle,[7] as represented in this case it can cause this rare side effect.

Alpha blockers, which are widely used in the treatment of urological diseases and hypertension, rarely induce priapism. Alpha blockers inhibit sympathetic discharge and thus prevent detumescence. This effect is held responsible for causing priapism.[12] After prolonged priapism cases, cavernosal tissue damage and erectile dysfunction secondary

Table 1 Alpha blocker induced priapism cases.

Authors	Indication	Alpha Blocker	Age	Dose	Duration of Erection	Treatment	Result
Bhalla et al.	HT	Prazosin	43	20 mg OAD, first episode after 3 months	30 h	Treatment with ancrod (defibrinogenating agent) unsuccessful. Treated successfully with corpora drainage.	Erectile dysfunction developed after 4 months of follow-up
	HT	Prazosin	43	18 mg OAD, three episodes after 3 months	6 h	Spontaneous resolution	Did not recur after stopping the drug
Burke and Hirst	HT	Prazosin	33	20 mg OAD, first episode after 4 months	12 h	Discontinuation of the drug	Did not recur after stopping the drug
Bullock	HT	Prazosin	55	22.5 mg OAD, after 5 days of treatment presented with priapism	12 h	Cavernosospongiosum shunt was performed. The new attack after 3 months was treated with intracavernosal injection of metamizol(1 mg). Then prazosin was stopped.	Did not recur after stopping the drug; normal erectile function continued
Siegel et al.	HT	Prazosin	25	4 mg OAD, not enough data on how long it had been used	40 h	Corporoglanular shunt was performed and medication stopped	Did not recur after treatment; normal erectile function continued
Ylitalo and Pasternack	Not reported	Prazosin	Not reported	10 mg OAD, after 4 months of use	Not reported	Not reported	Not reported
Avisrror et al.	LUTS	Doxazosin	66	8 mg OAD, after 15 days of use	19 h	Cavernosal-glandular shunt was performed	Recovered normal sexual function
Qazi et al.	LUTS	Alfuzosin	56	10 mg OAD, three episodes after 2 weeks	72 h	Treatment with oral terbutaline, cavernosal aspiration and phenylephrine infusion was unsuccessful. Partial response with Winter's shunt	Erection function that allows penetration was achieved after 1 year of follow-up
Vaidyanathan et al.	Neurogenic bladder	Terazosin	20	2 mg OAD, 2 hours after the dose was increased from 1 mg to 2 mg	5 h	Spontaneous resolution and medication stopped	Did not recur after stopping the drug

Table 1 (*Continued*)

Authors	Indication	Alpha Blocker	Age	Dose	Duration of Erection	Treatment	Result
Sadegui-Nejad and Jackson	LUTS	Terazosin	42	5 mg OAD, not enough data on how long it had been used	17.5 h	Treatment with oral pseudoephedrine was unsuccessful. Treated successfully with corpora aspiration and intracavernosal infusion phenylephrine solution.	Developed erectile dysfunction
Dodds et al.	LUTS	Tamsulosin	58	0.4 mg OAD, after 4 days of use	7 h	Treated successfully with cavernosal aspiration and irrigation with phenylephrine solution. Then prazosin was stopped.	Did not recur after stopping the drug
Pahuja et al.	LUTS	Tamsulosin	56	0.4 mg OAD, after 2 weeks of use	28 h	Winter's procedure was performed	Developed corpora fibrosis
Yagoob	HT	Prazosin	24	1 mg OAD, after 4 days of use	12 h	Winter's procedure was performed	Developed erectile dysfunction
Spagnul et al.	LUTS	Tamsulosin	32	0.4 mg OAD, after first dose of the drug	40 h	Treated successfully with cavernosal aspiration and irrigation with adrenaline solution.	Returned to normal erectile function after 10 days
Kilinc et al.	LUTS	Tamsulosin	59	0.4 mg OAD, after 2 weeks of use	48 h	Proximal corpus cavernosal-spongiosum shunt was performed	Returned to normal erectile function after 3 months
Marconi et al.	Distal ureteral stone	Tamsulosin	45	0.4 mg OAD, after second dose of the drug	5 h	Treated successfully with cavernosal injection of phenylephrine solution.	Erectile function continued
Khater et al.	LUTS	Tamsulosin	61	0.4 mg OAD, after first dose of the drug	Not reported	Treated successfully with cavernosal aspiration and irrigation with phenylephrine solution.	Returned to normal erectile function after 3 months
	Distal ureteral stone and ureteral stent related LUTS	Tamsulosin	24	0.4 mg OAD, after 3 days of use	72 h	Treatment with cavernosal aspiration and irrigation with phenylephrine solution was unsuccessful. Then penoscrotal corporeal decompression was performed.	Complete loss of potency after 6 weeks of follow-up

Table 1 (*Continued*)

Authors	Indication	Alpha Blocker	Age	Dose	Duration of Erection	Treatment	Result
Unal et al.[a]	LUTS	Silodosin	52	8 mg OAD, after 1 week of use	48 h	Treatment with cavernosal aspiration and irrigation with adrenaline solution was unsuccessful, then Barry shunt was performed.	Developed erectile dysfunction and penile prosthesis implantation was performed
	LUTS	Tamsulosin	54	0.4 mg OAD, after 4 days of use	12 h	Treated successfully with cavernosal aspiration and irrigation with phenylephrine solution.	Erectile function continued

HT: hypertension, LUTS: lower urinary tract symptoms, OAD: once a day.
[a] This case reports.

to fibrosis may develop.[2] Of the priapism periods of the cases in the literature, the longest priapism periods were 72 h in the case reported by Khater U et al.[11] and 48 h in the case reported by Kilinc et al.[10] In the case of Khater et al., penoscrotal corporeal decompression was performed. Rigid erection improved, but potency had been completely lost on follow-up. In the case of Kilinc et al., proximal corpus cavernosal-spongiosum shunt was performed and the patient returned to normal erectile function after 3 months. Our case, with 48 h of priapism, is the second longest alpha blocker induced priapism case in the literature. In this case, we applied a corpus cavernosum deep dorsal vein shunt (barry shunt)[13] and applied a malleable penile prosthesis to the patient who developed erectile dysfunction in the early following period. During the application of the penile prosthesis, the stage of cavernosal dilatation was quite difficult due to the changes in cavernous tissues after ischemia. With these results, it will be appropriate to try shunt application after aspiration-irrigation and to apply the penile prosthesis in the early period if these other treatments fail.

Additionally, one case was reported by Marconi et al.: a 45-year-old male patient was started on tamsulosin 0.4 mg due to distal ureteral stones and experienced 5 h of priapism.[9] The final case was reported by Usama Khater et al.: a 24-year-old male patient was started on tamsulosin 0.4 mg due to stent-related LUTS and experienced 3 days of priapism.[11]

According to the results of this review, the probability of developing priapism after the use of an alpha blocker is higher in the young population. Only 2 patients were over 60 years of age (Table 1).

Alpha blockers are mainly used in LUTS treatment. LUTS is a common urologic problem in males 50 years or older. However, recently, tamsulosin administration has become a common practice in the treatment of patients with distal ureteral stones as medical expulsive therapy.[14] Since this patient group tends to be younger, and the risk of developing priapism is higher in the young population, it is possible to report more cases of priapism induced by alpha blockers in the future.

Conclusion

Before starting alpha blocker treatment, side effects such as priapism, which may be very rare but may cause serious problems, should be considered. Patients should be informed about possible side effects. Emergency treatment should be applied to patients developing priapism, when necessary.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Authors' contribution

All co-authors contributed to the preparation of this manuscript.

Ethical statement/informed consent

Our article is a case report. Ethics committee approval is not necessary.

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Conflict of interest

The authors declare no conflict of interest.

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