American Journal of Emergency Medicine 34 (2016) 222–224

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

Effect of phenylephrine and terbutaline on ischemic priapism: a retrospective review☆,☆☆

Colleen Martin [a,*], Craig Cocchio [b]

[a] Emergency Medicine, Nyack Hospital, Nyack, NY
[b] Emergency Medicine, Trinity Mother Frances Hospital, Tyler, TX

ARTICLE INFO

Article history:
Received 18 June 2015
Received in revised form 14 October 2015
Accepted 17 October 2015

ABSTRACT

Background: Ischemic priapism is the most common cause of priapism due to low blood flow. Current guidelines recommend penile aspiration and the use of intracavernous injection of vasoactive agents. The data to support these recommendations are limited and rely on expert consensus.
Objective: The objective was to determine the effectiveness of terbutaline and phenylephrine on detumescence of ischemic priapism.
Methods: This was a retrospective review of patients presenting to the emergency department with a chief concern of priapism who received oral or subcutaneous terbutaline or intracavernous phenylephrine. The primary outcome is successful detumescence. The secondary outcome is drug-related adverse drug events.
Results: A total of 31 cases of ischemic priapism were included, with 8 patients receiving terbutaline and 23 receiving phenylephrine. Of the cases treated with terbutaline, 25% had successful detumescence compared with phenylephrine with a 74% success rate. No drug-related adverse events were reported or identified.
Conclusions: Patients receiving intracavernous irrigation with phenylephrine were more likely to achieve successful detumescence than those treated with oral or subcutaneous terbutaline.

1. Background

Priapism is a prolonged erection that is unrelated or lasts beyond sexual stimulation [1]. Priapism is a relatively rare disorder, with a national incidence of priapism in the United States reported to be 0.73 per 100,000 male subjects per year [2]. Classification of priapism can be separated into ischemic, arterial, or stuttering. Ischemic priapism is the most common cause of priapism and is due to little or low cavernous arterial flow [1]. The pathophysiology of ischemic priapism has been identified as idiopathic, hematologic dyscrasias, neoplastic syndromes, and the use of several different medications [3]. Because ischemic priapism is an emergency condition, the goal of treatment is detumescence as soon as possible. Current guidelines recommend penile aspiration and the use of intracavernous injection of vasoactive agents [1,3]. The data to support these recommendations are limited and rely on expert consensus. Because of the available evidence of successful detumescence with terbutaline for intraoperative priapism and ease of use, it has been used for the treatment of ischemic priapism [4–6]. The current practice in the emergency department (ED) at this university teaching hospital ED is to treat ischemic priapism with oral or subcutaneous terbutaline, intracavernous phenylephrine, and/or irrigation.

2. Objective

The objective of this retrospective review was to determine the effectiveness of terbutaline and phenylephrine on detumescence of ischemic priapism in patients presenting to the ED.

3. Methods

3.1. Study design

This study was a retrospective medical record review performed at a tertiary care, academic medical center in New Jersey. The emergency department is a Level I trauma center with an annual census for the ED that exceeds 100,000 patients. Our institutional review board approved this study.

3.2. Patient selection

Patients were eligible for inclusion if they presented to the ED with a chief concern of priapism between January 1, 2012, and December 31, 2014. A diagnosis of ischemic or recurrent priapism was required to

☆ The authors report no financial disclosures and no conflicts of interest.
☆☆ At the time of this research, both Drs Martin and Cocchio were employed by Rutgers University, Ernest Mario School of Pharmacy.
* Corresponding author.
E-mail address: Colleenmartin13@gmail.com (C. Martin).

http://dx.doi.org/10.1016/j.ajem.2015.10.029
0735-6757/

be documented in the physician's note. Exclusion criteria included unavailable medical record or any missing data points.

3.3. Data collection, demographics, and outcomes

Baseline demographic data including age, duration of priapism, medical history, and recent medication use were collected through medical record review. Treatment drug, route, and frequency were collected as well as disposition from the ED. The primary outcome of detumescence was based on physician documentation. Reviewing physician and nurse documentation was used to evaluate for adverse drug events from treatment.

3.4. Data analyses

Descriptive statistics were generated including means and standard deviations, or medians and interquartile ranges. Categorical variables were analyzed using χ^2 and Fisher exact tests; and continuous variables, with Student *t* test.

4. Results

From January 1, 2012, through December 31, 2014, 29 patients with 38 visits were evaluated for inclusion in the study. Five cases had spontaneous resolution of priapism in the ED, 1 case had missing information, and 1 case did not receive a diagnosis of priapism by the provider (Figure). Thirty-one (N = 31) cases were included which was comprised of 22 patients. Of the cases of ischemic priapism treated in the ED, 8 were treated with terbutaline and 23 with intracavernosal phenylephrine. Seven of the 8 patients (87.5%) in the terbutaline group received a dose subcutaneously 1 time at a mean dose of 383 ± 129 μg, and 1 patient received a 5-mg dose by mouth. Phenylephrine for intracavernous irrigation was prepared to a final concentration of 100 μg/mL in a 10-mL syringe. A mean dose of 138 ± 85 μg was used. Baseline clinical characteristics are summarized in Table 1. No differences were found between treatment groups in terms of age, duration of priapism, and recent medication use. There were significantly more cases in the phenylephrine group of patients with a medical history including a risk factor for priapism.

The primary outcome of successful detumescence with initial treatment was statistically greater with phenylephrine compared with terbutaline (17/23 [74%] compared with 2/8 [25%]; risk ratio, 0.34; 95% confidence interval, 0.099-1.15; $P = .03$) (Table 2). Of the 6 treatment failures with terbutaline, 4 (67%) had successful detumescence with phenylephrine, and 2 (33%) required surgical intervention. All of the 6 treatment failures with phenylephrine went on to have surgical intervention followed by admission to the hospital. No adverse drug-related events were reported in the medical record.

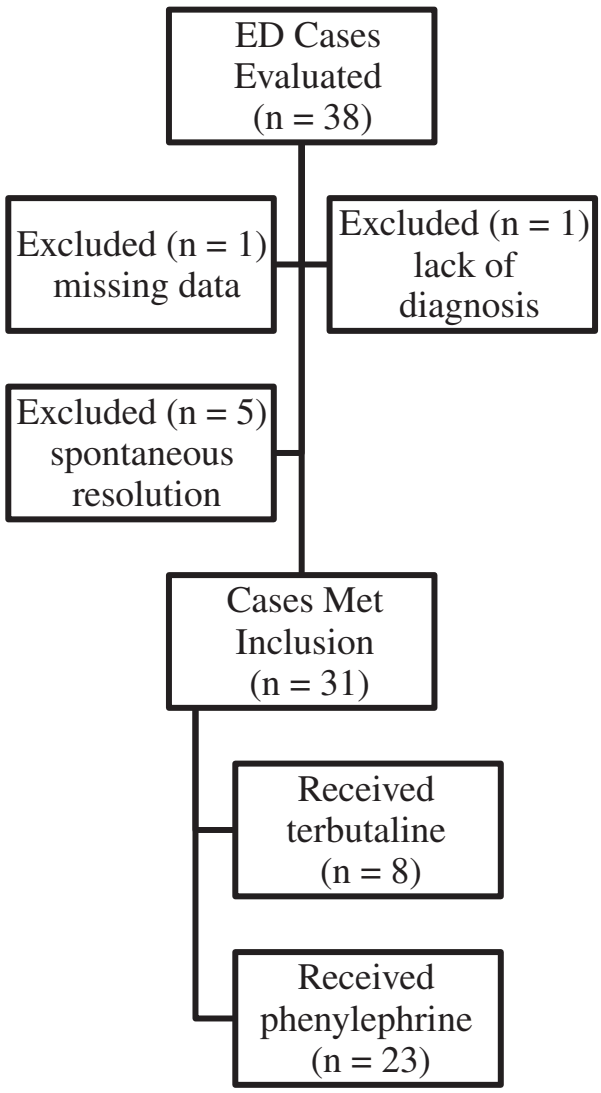

Figure. Patient selection.

4.1. Discussion

The primary outcome of this study illustrated a statistically significant difference in detumescence between intracavernous phenylephrine and oral or subcutaneous terbutaline with a corresponding number needed to treat of 2.This is an important finding because ischemic priapism with a duration lasting greater than 4 hours is considered a compartment syndrome of the corpus cavernosa. Subsequently, failure to relieve pressure may result in corporal fibrosis and permanent erectile dysfunction [7,8].

The treatment of priapism is based on recommendations that are limited by a paucity of evidence and rely on expert consensus. The European Association of Urology (EAU) recommends medical

Table 1
Baseline characteristics

	Terbutaline	Phenylephrine
Cases (n)	8	23
Patients (n)	8	14
Age (y), mean ± SD	39 ± 14	33 ± 11
Duration (h), mean ± SD	10 ± 11	14 ± 30
Medical history, n (%)[a]		
Sickle cell trait	1 (13)	9 (39)
Sickle cell anemia	1 (13)	7 (30)
None	6 (75)	6 (26)
Prostate neoplasm	0 (0)	1 (4)
Recent medication, n (%)[a]		
Cocaine	1 (13)	9 (39)
None	3 (38)	6 (26)
Tadalafil	0 (0)	3 (13)
Citalopram	1 (13)	1 (4)
Trazodone	1 (13)	1 (4)
Alprostadil	1 (13)	0 (0)
Alprostadil/papaverine/phentolamine[b]	1 (13)	0 (0)
Quetiapine	0 (0)	1 (4)
Ondansetron	0 (0)	1 (4)
Papaverine/phentolamine/ prostaglandin E1/forskolin[c]	0 (0)	1 (4)
Xanthoparmelia/*Cnidium*/yohimbine[Δ]	0 (0)	1 (4)

n = number of patients.
[a] Percentages calculated using number of cases.
[b] Trimix (alprostadil, papaverine, phentolamine).
[c] Quadmix (papaverine, phentolamine, prostaglandin E1, forskolin).
[Δ] Stamina Rx (*Xanthoparmelia*, *Cnidium*, yohimbe extracts).

Table 2
Treatment outcomes

	Terbutaline	Phenylephrine	*P* value
Success, n (%)[a]	2 (25)	17 (74)	.03
Resolved, discharged	1 (13)	16 (70)	.01
Resolved, admission	1 (13)	1 (4)	.46
Failure, n (%)[a]	6 (75)	6 (26)	.03
Surgery, discharged	1 (13)	0 (0)	.26
Surgery, admission	1 (13)	6 (26)	.64
Resolved, discharged	3 (38)	0 (0)	.01
Resolved, admission	1 (13)	0 (0)	.26

[a] Percentage calculated using number of cases.

management for ischemic priapism lasting between 4 and 72 hours before surgical treatment [3]. Nonmedical interventions are also recommended by the EAU including exercise, ejaculation, ice packs, cold baths, and cold-water enemas. The EAU recommended decompression of the corpus cavernosa by penile aspiration until fresh blood is aspirated indicating return of blood flow and reversal of local acidotic and anoxic metabolic derangements. In their view, sympathomimetic agents should be added to the irrigation solution when priapism is drug induced or recurs after irrigation alone.

The American Urological Association (AUA) recommends a stepwise approach to treatment initiating with intracavernous injection of an α-adrenergic sympathomimetic agent, with or without evacuation of old blood [1]. Phenylephrine is the sympathomimetic agent of choice for the AUA due to a more favorable cardiovascular profile. If this intervention is unsuccessful, AUA recommends a surgical shunting procedure.

The American College of Emergency Physicians does not have a formal policy for the treatment of priapism in the ED. The current practice at our institution is to treat ischemic priapism with oral or subcutaneous terbutaline, intracavernous phenylephrine, and/or irrigation due to recommendations from emergency medicine training [9,10].

Sympathetic agents that have been used for the treatment of priapism include epinephrine, norepinephrine, phenylephrine, ephedrine, and metaraminol. Although there are no published data comparing the agents, phenylephrine is the preferred agent due to α-agonism needed for resolution of priapism and absence of β-agonism resulting in adverse cardiac side effects. Phenylephrine is diluted to a concentration of 100 μg/mL and administered in 1-mL doses into the corpus cavernosum at our institution. In 2003, the AUA evaluated the literature to determine the rate of successful detumescence with different pharmacologic strategies [1]. Overall, phenylephrine resulted in resolution of priapism in 65% (66/101) of cases. The rate of detumescence was higher when used in conjunction with aspiration as compared to without, 78% (28/36) vs 58% (38/65), respectively. These data are similar to the results of this study, as 74% (17/23) of patients treated with intracavernous phenylephrine had resolution of priapism.

Terbutaline is a sympathomimetic β2-agonist with minor β1 effects. The proposed mechanism for use in priapism is that terbutaline relaxes the smooth muscles of the cavernous tissue, arteries, veins, and polsters in these vessels, allowing blood to drain from the penis [5]. In the same review in 2003 by the AUA, the success rate of oral terbutaline was determined to be 65% (15/23). The rate of resolution with terbutaline was much lower in this study, 25% (2/8). It can be speculated that the difference in results may be due to the fact that terbutaline was administered subcutaneously or that 21 of the published priapism cases reviewed by the AUA were due to pharmacologic penile injection.

Administration of sympathomimetic agents, regardless of route, requires monitoring for tachycardia, chest pain, and arrhythmias due to the mechanism of action of this class of medications. Sympathomimetic agents administered by the intracavernous route may also result in pain, burning, necrosis, and fibrosis [1]. These adverse effects were not identified during our retrospective medical record review.

4.2. Limitations

This retrospective review may suffer from selection bias, as patients were not prospectively randomized to treatment arms. This study included a small number of patients, with patients being counted more than once if they presented again during the study period; this limits the generalizability of the results. The safety of the interventions was difficult to determine because of the retrospective nature of the study. Adverse events may have occurred but were not identified as a response to treatment or were simply not documented. Phenylephrine was administered in conjunction with irrigation of the corpus cavernosum. As these interventions were done concomitantly, it is difficult to identify which resulted in resolution of priapism.

5. Conclusions

Patients who received phenylephrine for treatment of priapism in the ED had statistically better resolution of priapism compared with those who received terbutaline. This study may provide rationale for a prospective study comparing pharmacotherapeutic interventions for priapism in the ED. Based on the findings of this observational study, if pharmacologic intervention is required for the treatment of priapism, phenylephrine should be used.

Terbutaline may still have a role in treatment when patients are unwilling to have intervention by the intracavernous route or if there is a delay in therapy due to drug acquisition or arrival of urology consultant to the bedside.

References

[1] Montague DK, Jarow J, Broderick GA, Dmochowski RR, Heaton JP, Lue TF, et al. American Urological Association guideline on the management of priapism. J Urol 2003;170(4 Pt 1):1318–24.
[2] Roghmann F, Becker A, Sammon J, Ouerghi M, Sun M, Sukumar S, et al. Incidence of priapism at emergency departments in the United States. J Urol 2013;190(4):1275–80. http://dx.doi.org/10.1016/j.juro.2013.03.118.
[3] Salonia A, Eardley I, Giuliano F, Hatzichristou D, Moncada I, Vardi Y, et al. European Association of Urology guidelines on priapism. Eur Urol 2014;65(2):480–9. http://dx.doi.org/10.1016/j.eururo.2013.11.008.
[4] Shantha TR. Intraoperative management of penile erection by using terbutaline. Anesthesiology 1989;70(4):707–9.
[5] Shantha TR, Finnerty DP, Rodriquez AP. Treatment of persistent penile erection and priapism using terbutaline. J Urol 1989;141(6):1427–9.
[6] Priyadarshi S. Oral terbutaline in the management of pharmacologically induced prolonged erection. Int J Impot Res 2004;16(5):424–6.
[7] El-Bahnasawy MS, Dawood A, Farouk A. Low-flow priapism: risk factors for erectile dystunction. BJU Int 2002;89:285–90.
[8] Spycher MA, Hauri D. The ultrastructure of the erectile tissue in priapism. J Urol 1986;135:142–7.
[9] Nicks BA, Manthey DE. Chapter 96. Male genital problems. In: Tintinalli JE, Stapczynski JS, Ma OJ, Cline DM, Cydulka RK, Meckler GD, T, editors. Tintinalli's emergency medicine: a comprehensive study guide. New York, NY: McGraw-Hill; 2011. p. 7e.
[10] Heidenreich J. Chapter 39. Genitourinary emergencies. In: Stone C, Humphries RL, editors. Current diagnosis & treatment emergency medicine. New York, NY: McGraw-Hill; 2011. p. 7e.