A Case Report of Hypertensive Emergency and Intracranial Hemorrhage Due to Intracavernosal Phenylephrine

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Abstract

Background: Intracavernosal injection of phenylephrine is a commonly used therapy for ischemic priapism and is typically well tolerated with few severe adverse side effects. We report a case of intracranial hemorrhage related to hypertensive emergency due to intracavernosal phenylephrine. **Case Report:** A 43-year-old Caucasian man with history of hypertension, diabetes mellitus type I, end-stage renal disease status post a combination kidney-pancreas transplant, and recurrent idiopathic priapism presented to emergency department with an episode of priapism. His home medications were lisinopril, metoprolol tartrate, mycophenolate mofetil, prednisone, sulfamethoxazole-trimethoprim, and tacrolimus. After local injection of 2 rounds (1 hour apart) of 100 µg phenylephrine into each corpus cavernosa, priapism resolved. Within 5 minutes, the patient had headaches, dyspnea, and excruciating chest pain. His blood pressure (BP) was noted to be 240/130 mm Hg but normalized spontaneously within few minutes. During this period, he developed new-onset right arm and leg weakness and found to have intracranial hemorrhage in the midbrain. **Conclusion:** A careful review for pharmacologic interactions should be performed prior to intracavernosal phenylephrine administration, and close monitoring should occur after its administration.

Keywords

phenylephrine /adverse effects, hypertension /chemically induced, priapism

Introduction

The incidence of priapism has been reported to be between 0.73 and 1.50 per 100 000 men per year.^{1,2} Priapism can be ischemic (veno-occlusive) as seen in patients with sickle cell disease or nonischemic due to penile or perineal trauma. Ischemic priapism is usually treated with intracavernosal injection of a sympathomimetic, the most commonly utilized agent being phenylephrine. Ridyard et al reported that high dose intracavernosal phenylephrine resulted in detumescence in 86% of patients with ischemic priapism.³ Phenylephrine is a selective α_1 -adrenergic agonist and used as a vasopressor when systemically administered. Other routes of administration have reduced bioavailability and a low effect on blood pressure (BP). However, topical administration of phenylephrine has infrequently been described to be associated with hypertensive crisis or cardiovascular compromise.^{4,5} We report a case where intracavernosal injection of phenylephrine resulted in hypertensive emergency leading to intracranial hemorrhage.

Case Report

A 43-year-old Caucasian gentleman presented to the emergency department with a painful erection that had lasted more than 4 hours. His medical history was significant for hypertension, diabetes mellitus type I, end-stage renal disease status post a combined kidney-pancreas transplant, and recurrent idiopathic priapism treated with intracavernosal phenylephrine. He had no history of stroke or hypertensive emergency. His home medications were lisinopril, metoprolol tartrate (100 mg twice daily), mycophenolate mofetil, prednisone, sulfamethoxazole-trimethoprim, and tacrolimus. He did not have any history of penile or perineal trauma,

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Figure 1. Noncontrast head computed tomography demonstrating a hyperdense lesion involving the left pons, with extension inferiorly and laterally in the middle cerebellar peduncle.

recreational drug use, herbal medication use, hematologic disorders, or malignancy that can contribute to priapism. His vital signs upon presentation were within normal limits, including a BP of 121/78 mm Hg, pulse of 70 beats/min, and weight of 95 kg. His physical examination was unremarkable except for a fully erect penis.

After local injection of 2 rounds (1 hour apart) of 0.5 mL of 100 μ g phenylephrine (10 mg/mL phenylephrine diluted to a concentration of 200 μ g/mL) into each corpus cavernosa, priapism resolved rapidly. Within 5 minutes, the patient began experiencing headaches, dyspnea, and excruciating chest pain. He appeared diaphoretic, and his BP at that time was elevated to 240/130 mm Hg. His electrocardiogram showed new ST-segment depressions in the inferolateral leads. An immediate troponin returned at 0.05 ng/mL. Within 10 minutes of developing these symptoms, his BP normalized spontaneously to 138/79 mm Hg. On neurological examination, new-onset right arm and leg weakness (strength 3/5), right pronator drift, and partial left hemianopia were noted. A STAT noncontrast computed tomography (CT) showed hyperdense lesions in the midbrain involving the left pons with inferior and lateral extension in the middle cerebellar peduncle (Figure 1). Magnetic resonance imaging (MRI) of the brain 4 hours later demonstrated the same hemorrhage with mild surrounding edema (Figure 2). The hemorrhage had a tubular appearance on T2-weighted images. The CT angiography of the head, neck, and chest did not reveal evidence of aneurysms, arteriovenous malformations, or aortic dissection. His troponin elevation was attributed to

a type 2 myocardial infarction; troponin peaked at 0.69 ng/mL (4 hours from symptom onset) and then trended down, and his chest pain and Electrocardiogram (EKG) changes resolved after spontaneous normalization of BP.

The patient was admitted to intensive care unit for conservative management of hypertensive emergency and intracranial hemorrhage. Priapism recurred during hospitalization, necessitating a distal shunt placement, which resulted in detumescence. Patient was hospitalized for a total of 6 days during which his neurologic deficits progressively improved; however, mild diplopia and gait impairment persisted at discharge.

Case Discussion

Priapism occurs when the penis remains erect for hours in the absence of stimulation or after the stimulation has ended. Priapism is a urological emergency; untimely diagnosis and intervention can lead to penile fibrosis and ultimately erectile dysfunction. Diagnosis is made by history and physical examination; sometimes, blood gas analysis of the aspirated blood from the penis or ultrasound can be used to support the diagnosis.⁶ One of the common modality of treatment is intracavernosal injection of sympathomimetic agent especially phenylephrine because of the rapid onset and shorter duration of action.⁷⁻⁹

Use of intracavernosal phenylephrine is off-label, however recognized as standard of care. Systemic toxicity is rarely reported after intracavernosal injection of adrenergic agents.¹⁰⁻¹² In a case study by Muruve and Hosking, there

Figure 2. Magnetic resonance imaging of brain without contrast demonstrating the hemorrhage involving left pons with extension in middle cerebellar peduncle, with mild surrounding edema.

Table 1. Naranjo Adverse Drug Reaction Probability Scale.

Question	Response	Score
Are there previous conclusive reports of this reaction?	Yes	+1
Did the adverse event appear after the suspected drug was administered?	Yes	+2
Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	Don't know	0
Did the adverse reaction reappear when the drug was readministered?	Don't know	0
Are there alternative causes (other than the drug) that could on their own have caused the reaction?	No	+2
Did the reaction reappear when a placebo was given?	Don't know	0
Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	Don't know	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	Don't know	0
Did the patient have a similar reaction to the same or similar drug in any previous exposure?	No	0
Was the adverse event confirmed by any objective evidence?	Yes	+1

Note. Our patient had a score of 6 on Naranjo Scale making intracavernosal phenylephrine a probable cause of the hypertensive emergency.

were no observed changes in BP and heart rate after intracavernosal injection of phenylephrine among 9 patients.¹⁰ However, Roberts and Isenberg reported a case where intracavernosal epinephrine injection leading resulting in severe hypertension and angina pectoris in a 39-year-old with no significant past medical history.¹¹ Davila et al reported a case

where intracavernosal phenylephrine was associated with subarachnoid hemorrhage in a 23-year-old with history of sickle cell disease.¹² In our case, the patient had received intracavernosal phenylephrine, which caused hemorrhage in the midbrain with inferior and lateral extension in the middle cerebellar peduncle.

Phenylephrine causes vasoconstriction by activating the α_1 receptors which causes smooth muscle cell activation and contraction. Srivastava et al hypothesized that the chronotropic effect of the phenylephrine is due to its β_1 action.¹³ It is known that prolonged β -blocker use causes sympathetic hyperinnervation of the myocardium.¹⁴ We hypothesize a similar phenomenon may happen in the peripheral vessels, potentiating the action of phenylephrine in a patient with prolonged use of metoprolol.

We used the the Naranjo adverse drug reaction probability scale to determine the causality of the reaction.¹⁵ The scale contains 10 questions and scores for individual questions can range from -1 to +2. With a total score >9, the incident is considered be a definite adverse drug reaction and with a score of 5 to 8, the incident is considered to be a probable adverse drug reaction. Given the lack of another etiology and a Naranjo Scale score of 6 in our patient (Table 1), intracavernosal phenylephrine is a probable cause of this patient's hypertensive emergency and subsequent intracranial hemorrhage.¹⁵

Conclusion

A careful review for medication interaction with β -blockers and patient's risk of hypertensive crisis should be performed prior to intracavernosal administration of phenylephrine as it can lead to hypertensive emergency and associated complications. Patients should be closely monitored with frequent vital signs after administration of intracavernosal phenylephrine

Declaration of Conflicting Interests

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References

1. Roghmann F, Becker A, Sammon JD, et al. Incidence of priapism in emergency departments in the United States. *J Urol*. 2013;190(4):1275-1280. doi:10.1016/j.juro.2013.03.118.
2. Eland IA, van der Lei J, Stricker BH, Sturkenboom MJ. Incidence of priapism in the general population. *Urology*. 2001;57(5):970-972.
3. Ridyard DG, Phillips EA, Vincent W, Munarriz R. Use of high-dose phenylephrine in the treatment of ischemic priapism: five-year experience at a single institution. *J Sex Med*. 2016;13(11):1704-1707. doi:10.1016/j.jsxm.2016.09.010.
4. Son J-S, Lee S-K. Pulmonary edema following phenylephrine intranasal spray administration during the induction of general anesthesia in a child. *Yonsei Med J*. 2005;46(2):305-308. doi:10.3349/ymj.2005.46.2.305.
5. Abdelhalim AA, Mostafa M, Abdulmomen A, Othman EA. Severe hypertension and pulmonary edema associated with systemic absorption of topical phenylephrine in a child during retinal surgery. *Saudi J Anaesth*. 2012;6(3):285-288. doi:10.4103/1658-354X.101224.
6. Podolej GS, Babcock C, Kim J. Emergency department management of priapism [digest]. *Emerg Med Pract*. 2017;19(1 Suppl Points & Pearls):S1-S2.
7. Munarriz R, Wen CC, McAuley I, Goldstein I, Traish A, Kim N. Management of ischemic priapism with high-dose intracavernosal phenylephrine: from bench to bedside. *J Sex Med*. 2006;3(5):918-922. doi:10.1111/j.1743-6109.2005.00140.x.
8. Bruno D, Wigfall DR, Zimmerman SA, Rosoff PM, Wiener JS. Genitourinary complications of sickle cell disease. *J Urol*. 2001;166(3):803-811.
9. Montague DK, Jarow J, Broderick GA, et al. American Urological Association guideline on the management of priapism. *J Urol*. 2003;170:1318-1324.
10. Muruve N, Hosking DH. Intracorporeal phenylephrine in the treatment of priapism. *J Urol*. 1996;155(1):141-143.
11. Roberts J, Isenberg DL. Adrenergic crisis after penile epinephrine injection for priapism. *J Emerg Med*. 2009;36(3):309-310. doi:10.1016/j.jemermed.2007.10.024.
12. Davila HH, Parker J, Webster JC, Lockhart JL, Carrion RE. Subarachnoid hemorrhage as complication of phenylephrine injection for the treatment of ischemic priapism in a sickle cell disease patient. *J Sex Med*. 2008;5(4):1025-1028. doi:10.1111/j.1743-6109.2007.00715.x.
13. Srivastava RD, Kalitha M, Varma P, Bhatnagar VM. A mechanism of action of phenylephrine on heart. *Indian J Physiol Pharmacol*. 1977;21(3):167-174.
14. Clarke GL, Bhattacharjee A, Tague SE, Hasan W, Smith PG. β -adrenoceptor blockers increase cardiac sympathetic innervation by inhibiting autoreceptor suppression of axon growth. *J Neurosci*. 2010;30(37):12446-12454. doi:10.1523/JNEUROSCI.1667-10.2010.
15. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239-245.