Ketamine For Sickle Cell Priapism: A Case Report & Literature Review

Mohamad Bakir and Sharafaldeen Bin Nafisah

***Abstract*—Priapism is a urological emergency that requires swift intervention to prevent complications. Here, we present a case in which ketamine effectively induced detumescence in an adult patient suffering from priapism secondary to sickle cell disease. Our review explores the efficacy of ketamine for priapism from diverse causes beyond sickle cell disease, as well as its usein paediatric populations, while also assessing its safety profile. Based on the evidence, we recommend the use of ketamine for priapism in acute care settings. The valuable insights provided by our study encourage additional investigation and educated clinical judgment to improve patient outcomes in the treatment of this condition.**

***Index Terms*—Case Report, Ketamine, Priapism, Sickle Cell Disease**

I. INTRODUCTION

Sickle cell disease is responsible for a high proportion of adult priapism cases, with rates ranging from 40% to 80% [1]. Ischaemic priapism is generally the most prevalent type, whereby detumescence is delayed due to a failure to reverse the arterial relaxation and smooth muscle paralysisthat triggered the erection [1]. Ischaemic priapism accounts forover 95% of cases of sickle cell priapism. Patients with this disease might have a condition known as "stuttering priapism"
— a rare form of priapism that is recurrent and typically ischaemic in nature [2]. Mechanical venous blockage and malfunction cause high pressure in the corpora's venous channels; this reduces venous return and eventually causes corporal engorgement with little arterial inflow. This is comparable to compartment syndromes that affect any part of the body [1, 3].

Sufferers of sickle cell disease who experience priapism typically have a more severe form of the condition, with greater instances of cerebrovascular accident, chest pain, anda greater likelihood of haemolysis. The haemolysis generates free haemoglobin and arginine, both of which lower the levels of nitric oxide readily available in the body. In sickle cell patients, cyclic guanosine monophosphate (cGMP) and nitric oxide levels are frequently low - a phenomenon that would otherwise impede erections and lower the likelihood of priapism. However, the smooth muscle in the erectile tissueof the penis is thought to become overly responsive to nitric oxide and cyclic GMP; thus, even at levels that would not usually activate the phosphodiesterase enzymes that normally break down cyclic GMP, smooth muscle may be hypersensitive to them. This increased sensitivity may result in prolonged erections that last longer than is considered typical [4].

Despite the fact that priapism is typically described as an erection lasting 4 hours or longer, physiological modifications and microscopic tissue injury within the penis do not normally begin until about 6 hours after initiation [1, 3]. Trabecular interstitial oedema, which appears after 12 hours, is the first sign of lasting structural alteration of the corporal smooth muscle tissue. Within 24 hours, cellular injury manifests as sinusoidal endothelial breakdown, basement membrane skeletonization, and enhanced platelet adhesion. Within 36 hours, thrombus accumulation in the sinusoidal gaps and direct injury to the smooth muscle tissue of the cavernosa start to occur, resulting in fibrosis and permanent erectile dysfunction [5]. Up to 90% of men are unable to engage in regular sexual activity after experiencing priapism for longer than 24 hours [6], whereas long-term erectile dysfunction is typically avoided through prompt intervention [1].

Currently, several medications are used for the treatment of priapism, including ephedrine and phenylephrine, among others. Ketamine, although it has not attracted much attention, has been postulated as an effective treatment modality: the dissociative nature of this drug may prevent the subconscious cerebral response to peripheral penile stimulation [7]. According to one theory, priapism results from an autonomic imbalance brought on by intrinsic subconscious central stimulation" [7]. The arteries and veins of the corpora cavernosa possess luminal protrusions called "polsters", and it is the failure of the venous polsters to relax as the arterial polsters contract that is thought to be the cause of priapism. Theoretically, an imbalance in the autonomic system might impact the correct functioning of these polsters. Ketamine might suppress the stimulating brain signals; additionally, it stimulates the para- and sympathetic nervous systems [7].

Although the first reported case of ketamine-induced detumescence is dated to the 1970s, still the modality is little known and it is rarely mentioned as a management approach for priapism. In this paper, we explore the role of ketamine in a case of priapism in a 33-year-old patient with sickle cell disease who was treated successfully with such medication. We also explore the literature for the use of ketamine in priapism.

II. CASE PRESENTATION

A 33-year-old male patient, with a medical history of sickle cell anaemia and multiple episodes of priapism requiring frequent aspiration, presented to the emergency department with a painful prolonged erection that had lasted longer than

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2 hours. The use of ketamine was discussed and the side effects explained to the patient. A controlled, monitored setting was ensured for the duration of the procedure, and the patient's vital signs were monitored throughout. An injection of 38 mg ketamine, calculated at 0.5 mg/kg, was given intravenously at 9:07 am, over 1-3 minutes, during which the patient's vital signs remained stable. Following the administration of the ketamine, the patient experienced an emergence phenomenon, but did not require intervention and resolved spontaneously. The ketamine effectively resolved the priapism 12 minutes after commencing the injection, and the patient reported relief from the associated pain. He was observed for several hours inthe emergency department after the resolution of the episode, after which he was discharged home.

III. DISCUSSION

This article provides further evidence that ketamine is an effective and rapid method of managing priapism. Our findings provide new evidence for ketamine in such cases, built upon several previous studies. In 1972, the first case was described for the use of ketamine in priapism, where three cases of penile turgescence were effectively treated with 0.5 mg/kg ketamine hydrochloride. In two of these cases, an inhalation anaesthetic was also used [8].

In one study, a higher dose of 2.2 mg/kg was used, which demonstrated a positive effect [9]. On the other hand, another researcher employed a lower dose of 0.5 mg/kg, which yielded only partial detumescence, and had to be accompanied by physostigmine to achieve full flaccidity [7, 10]. In another study, erections were relieved in 7 out of 9 patients (77.8%) by using intravenous ketamine at doses ranging from 18 mg to 75 mg, the mean dose being 34.3 mg and the patients' mean weight 69 kg. Thus, the ketamine dose administered to the 9 patients ranged from approximately 0.26 mg/kg to 1.09 mg/kg, the mean dose being approximately 0.5 mg/kg [11].

The successful use of ketamine to treat priapism has been reported multiple times in the literature, including the treatment of adult priapism caused by general or spinal anaesthesia [12, 13]. In one particular case, priapism was observed in a patient as a side effect of risperidone, a dopamine antagonist medication. Successful resolution was achieved through the intravenous administration of ketamine at 0.5 mg/kg [14].The evidence provided in several case studies highlights the phenomenal efficacy of ketamine as a therapeutic option for priapism, even across a variety of causes — grounds for optimism in sickler and non-sickler patients alike.

In one study, the authors noted very rapid detumescence after ketamine treatment in priapism that had lasted 8 hours. However, in one instance the patient's priapism persisted beyond 14 hours and, after receiving ketamine, still required a phenylephrine injection and corporal irrigation to achieve detumescence [14]. Ketamine's effectiveness in refractory cases was challenged when a prolonged, 10-hour episode persisted despite administering 2.2 mg/kg initially, followed by two additional doses of 1.1 mg/kg which also proved ineffective, as did a penile dorsal nerve block. There was still no detumescence after spinal anaesthesia with 0.4% tetracaine (pontocaine); the following morning, the tumescence resolved on its own [8]. In another study, prolonged priapism of 12 hours was effectively treated with intravenous ketamine (2 mg/kg), neostigmine (1 mg), and diazepam (5 mg) [10]. An extremely hyperactive 15-year-old adolescent with priapism responded remarkably well to ketamine treatment: the 14-hour crisis, secondary to dexmethylphenidate, was resolvedby the rapid sedative effect of ketamine, ending the need for aspiration despite earlier unsuccessful therapies [15].

The use of ketamine for priapism in children requires elaboration. A case report described the use of intravenous ketamine hydrochloride (0.5 mg/kg) to manage priapism that arose during a hypospadias correction [16]. Intravenous ketamine was also used to induce rapid detumescence of idiopathic priapism in a 3.6-kg neonate [17]. A paper written to analyse and systematise the treatment approaches for priapism in minors noted that, for acute bouts of priapism, ketamine injections (0.5–1 mg/kg) were one of the options [18]. In a retrospective review of children with painful ischaemic priapism, ketamine was used as a bridge for corporal irrigation. The process involved the administration of intravenous ketamine to achieve procedural sedation, at a dose of 0.5 mg/kg, which was adjusted as needed during the treatment. After ketamine treatment, there was an almost instantaneous detumescence that lasted 8 hours. However, one patient with sickle cell disease experienced priapism for longer than 14 hours, necessitating corporal irrigation and phenylephrine injection following the ketamine treatment in order to achieve detumescence. Three patients responded to ketamine alone with no corporal irrigation, and the detumescence lasted throughout the night [14]. In another patient, an intramuscular dose of ketamine (4 mg/kg) quickly induced sedation, softening the phallus within 2 to 3 minutes and obviating the need for aspiration in a 15-year-old child with a complicated medical history. The patient's priapismwas successfully treated; he remained dormant throughout the next day's observation, although ketamine was used to treat hyperactivity [15].

Although it is not usual practice to prevent ketamine's side effects, one study employed fentanyl (1 g/kg) and midazolam (0.02 mg/kg) [11]. In another study, 10 mg diazepam was given intravenously, in divided doses [9]. If ketamine is given too quickly or at a high dose, there could be a brief,mild respiratory depression. The healthcare provider should therefore be prepared to carry out emergency intubation [19].

In our case, the patient experienced an emergence phenomenon; this side effect did not require any intervention and no midazolam was administered. Lowering the ketamine dose below a particular threshold might reduce the risk of such side effects. However, as demonstrated in the research by Gale [9] and Villalonga et al. [10], it is important to recognise that this strategy may also reduce the capacity of the drug to resolve priapism. Thus, it is vital to achieve the correct balance between minimising adverse effects and maintaining therapeutic outcomes. This necessitates additional study and careful review prior to adopting any dosage modifications.

IV. Conclusion

Ketamine appears to be effective and well tolerated for the treatment of priapism in an acute care setting. The advantage of such medication lies in its ability to achieve prompt detumescence, obviating the need for aspiration and procedural sedation, and its tolerability and positive patient experience hint towards its superiority. While its mechanism of action requires further investigation, the exact dosage that induces detumescence ranges from 0.5 mg/kg to 2.2 mg/kg. Overall, its efficacy appears to be consistent regardless of the condition causing the priapism, and across several age segments.

V. References

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