Outpatient penile aspiration and epinephrine irrigation for young patients with sickle cell anemia and prolonged priapism

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The optimal management of prolonged priapism for patients with sickle cell anemia (SCA) has not been established. We prospectively studied in an outpatient setting the efficacy and safety of a procedure that employs aspiration of blood from the corpora cavernosa and irrigation with a dilute epinephrine solution under local anesthesia to relieve priapism in young patients with SCA. If hydration and analgesics failed to produce detumescence or if priapism had lasted >4 hours, the protocol was activated in the emergency room or clinic. Fifteen patients with homozygous SCA (Hb SS) were treated on 39 occasions; 10 patients were treated once, 1 patient twice, 2 patients 3 times, 1 patient 6 times, and 1 patient 15 times. Median age of patients at first treatment was 14.3 years (range, 3.9-18.3 years). The procedure was successful in producing immediate detumescence on 37 of 39 occasions (95% efficacy, 95% confidence intervals (CI): 81%-99%). No serious immediate or long-term side effects were observed. None of the patients who demonstrated detumescence required hospitalization. The 2 patients whose priapism persisted after aspiration and irrigation presented with episodes lasting >24 hours. All evaluable patients whose priapism resolved after aspiration and irrigation self-reported normal erectile function at a median of 40 months (range, 3-58 months) after the last procedure. Thus, aspiration of the corpora cavernosa followed by irrigation with dilute epinephrine is effective in producing immediate and sustained detumescence and should be the initial therapy employed for patients with SCA and prolonged priapism. (Blood, 2000; 95:78-82)

Introduction

Priapism is a sustained, unwanted, and painful erection usually unrelated to sexual activity.[1] The prevalence of severe priapism in patients with sickle cell anemia (SCA), based upon review of hospital admissions, is 2% to 5%.[2] However, we recently estimated that the prevalence of priapism may be as high as 89%[3] in young males (by the age of 20 years) with homozygous SCA (Hb SS) or hemoglobin S-β^0 thalassemia. Retrospective studies of adults with SCA indicate that 30% to 45% have experienced priapism on 1 or more occasions.[4,5]

Prolonged priapism is a urologic emergency requiring urgent intervention to avoid irreversible ischemic penile injury, corporal fibrosis, and impotence.[6] Numerous therapeutic interventions, including hydration, analgesics, simple erythrocyte transfusion, exchange transfusion, vasodilators, and hormones,[7] have been used for the treatment of priapism associated with SCA. However, none of them is predictably effective in relieving priapism, and many may delay efforts or procedures that potentially allow reperfusion of the corpora cavernosa. In addition, some interventions have been associated with serious side effects,[8,9] and most if not all of these interventions require hospitalization.

Alpha adrenergic agents have been shown to be effective in the treatment of priapism resulting from intrapenile injections of vasoactive drugs (such as papaverine, phentolamine, or prostaglandin E1), which are used for the treatment of impotence.[10,11] Thus, we prospectively studied whether aspiration of blood from the corpora cavernosa and intrapenile irrigation with epinephrine, a potent α-agonist, is effective in terminating prolonged episodes of priapism in patients with SCA as well. Preliminary results with the use of this procedure from our center have been previously described.[12] Our overall and long-term experience with this therapeutic approach is described below.

Materials and methods

Management protocol

In January 1993 we established a prospective management protocol for the outpatient management of prolonged episodes of priapism. Patients with SCA who experienced priapism were advised to drink extra fluids, use oral analgesics, exercise gently, and attempt to urinate soon after development of the complication. When these measures failed or if an episode lasted longer than 2 hours, the patients were advised to seek medical attention at the emergency room of the Children's Medical Center of Dallas. When intravenous hydration and parenteral morphine failed to induce detumescence within 1 to 2 additional hours, the protocol was applied. Our goal was to perform the procedure within 2 hours of presentation to the emergency room and <4-6 hours from the beginning of the episode.

Procedure

After induction of conscious sedation with intravenous midazolam and/or morphine, the lateral side of the penis was thoroughly swabbed with povidone iodine. A 1% lidocaine solution (1/2 mL) was infiltrated under the skin and more deeply into the tunica albuginea. A 23-gauge needle was then inserted perpendicularly into the corpus cavernosum (ie, unilateral insertion), and as much blood as possible was aspirated into a dry 10-mL syringe

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through a 3-way stopcock. Another 10-mL syringe containing a 1:1 000 000 solution of epinephrine (ie, 1 mL of 1:1000 epinephrine diluted in 1 L normal saline) was then attached to the 3-way stopcock, and the corpora cavernosa were irrigated with the epinephrine solution. If needed, additional blood was aspirated until detumescence occurred. After withdrawal of the needle, firm pressure was applied by the urologist for 5 minutes (timed by the clock) to prevent hematoma formation, and the patient was discharged home if there was continued and/or sustained detumescence 30 minutes following the procedure.

Results

Between January 1993 and November 1998, 39 aspiration and irrigation procedures were performed on 15 patients (Table 1). All patients had homozygous SCA and all except 2 patients (Nos. 6 and 7) were known to us to have previously experienced brief and self-limited episodes of priapism. Ten patients were treated once according to the protocol, 1 patient twice, 2 patients 3 times, 1 patient 6 times, and 1 patient 15 times.

The median age of patients at first treatment was 13.7 years (range, 3.9-18.3 years). Two patients (Nos. 7 and 11) were <6 years of age. Although patients were advised to seek prompt medical attention, the procedure was performed after prolonged episodes of priapism (lasting 6 to 28 hours) on 12 occasions. Five patients (Nos. 1, 4, 5, 8, and 15) who had multiple (2 to 15) procedures always presented to the emergency room sooner after the second (or later) episode compared to the initial event.

The procedure was successful in producing detumescence within <1 minute on 37 of the 39 occasions (95% efficacy, 95% CI: 81%-99%).[13] Ten of 15 patients (67%) required only 1 aspiration and irrigation treatment, and all 7 patients with adequate follow-up (Nos. 3, 6, 9, 11, 12, 13, and 14) had no recurrences of severe priapism at a median follow-up of 39 months (range, 12-58 months).

The only immediate complication that occurred was formation of a small intrapenile hematoma on 2 occasions (Nos. 12 and 14). None of the patients whose priapism resolved required hospitalization. A 6-year-old boy (No. 14) whose priapism persisted after aspiration and irrigation did not present to the emergency room until 28 hours after his first episode of priapism. He underwent an emergency cavernosal-glanular shunt without response. His priapism finally resolved slowly following a simple red blood cell transfusion, 7 days of hydration, and parenteral analgesics. The second patient who failed to demonstrate detumescence, a 16-year-old boy (No. 4), also presented after an episode of priapism lasting 28 hours. He developed severe acute chest syndrome shortly after presentation and was admitted to the intensive care unit, where he underwent an automated exchange transfusion (Hb S of 30.6% at the end of the exchange). His priapism resolved within 48 hours. Notably, 18 months later, following another priapism episode of 6 hours duration, the patient demonstrated immediate detumescence in response to the aspiration and irrigation performed.

The patient who required aspiration and irrigation on 15 occasions (No. 1) returned to the emergency room 6 times within 72 hours with recurrent priapism requiring repeated aspiration and irrigation. After the patient was started on monthly intramuscular leuprolide therapy, he did not experience any priapism recurrences and therefore did not require further aspiration and irrigation procedures. No recurrences were seen within 72 hours following this last procedure (patient No. 1) and the remaining 33 procedures performed in the other 14 patients.

As of February 1999, 1 patient (No. 10) died from a cause unrelated to SCA (drowning), and 2 patients (Nos. 2 and 7) did not return to follow-up. The remaining 12 patients continue to be followed by us (Table 2). All 11 of the boys who underwent successful aspiration and irrigation, as well as patient No. 4, self-report normal erectile function. Direct questioning was done in person or by telephone at a median follow-up of 40 months (range, 3-58 months) after the last procedure. The 6-year-old boy (patient No. 14) who underwent emergency shunting has residual penile fibrosis, which was evident on physical examination performed 40 months after the procedure.

To attempt to prevent further recurrences of priapism, 7 patients who required aspiration and irrigation on 1 (Nos. 3, 9, 11, 12, 13, and 14) or more (No. 8) occasions take as-needed or scheduled oral pseudoephedrine at bedtime. Review of medical records and self-reporting by patients and their families suggest that oral pseudoephedrine decreases recurrences of both stuttering (ie, brief and self-limited) and major (ie, lasting >2 hours) priapism.

Two patients who required multiple aspiration and irrigation

Table 1. Initial results in 15 patients with SCA who underwent penile aspiration and epinephrine irrigation for prolonged priapism

Patient	Age at First Episode (years)	Duration of Episodes Prior to Aspiration (hours)	Prior Episodes of Priapism	Number of Procedures	Outcome	Complications
1	16.5	4	Yes	15	ID	None
2	14.7	5.5	Yes	1	ID	None
3	13.7	2	Yes	1	ID	None
4	16.2	28, 6	Yes	2	NR, ID	None
5	18.3	12, 11, 6	Yes	3	ID	None
6	15.2	9	No	1	ID	None
7	4.7	3	No	1	ID	None
8	10.3	9, 4, 4	Yes	3	ID	None
9	9.2	5	Yes	1	ID	None
10	12.1	4	Yes	1	ID	None
11	3.9	UN	Yes	1	ID	None
12	14.3	>24	Yes	1	ID	Penile hematoma
13	13.3	12	Yes	1	ID	None
14	6.6	28	Yes	1	NR	Penile hematoma
15	16	6-8	Yes	6	ID	None
Total number of aspiration/irrigation procedures performed				39		

UN, unknown; ID, immediate detumescence; NR, no response.

Table 2. Long-term follow-up of patients with SCA who underwent penile aspiration and epinephrine irrigation for prolonged priapism

Patient	Follow-up* (months)	Current Treatment	Outcome
1	40	Monthly IM leuprolide	Normal potency
2		Lost to follow-up	
3	58	Oral pseudoephedrine prn	Normal potency
4	41	None	Normal potency
5	48	Monthly IM leuprolide	Normal potency
6	51	None	Normal potency
7		Lost to follow-up	
8	3	Oral pseudoephedrine prn	Normal potency
9	39	Oral pseudoephedrine prn	Normal potency
10	46		Deceased
11	12	Scheduled oral pseudoephedrine	Normal potency
12	34	Oral pseudoephedrine prn	Normal potency
13	20	Oral pseudoephedrine prn	Normal potency
14	40	Oral pseudoephedrine prn	Residual penile fibrosis
15	48	Monthly IM leuprolide	Normal potency

*The duration of follow-up is from the last aspiration and irrigation procedure until February 28, 1999.

procedures (Nos. 1 and 5) and 1 patient (No. 12) who had a prolonged episode of priapism have received monthly intramuscular injections of leuprolide without further recurrences of severe priapism.

Discussion

Priapism is a painful and disabling vaso-occlusive complication of SCA.[1-7] Despite the high prevalence of priapism and its potentially devastating consequence, ie, impotence,[14,15] neither the natural history of priaspism nor its optimal therapy have been established. In addition, patients with SCA frequently do not associate priapism with their underlying disease and may delay seeking medical attention. For example, we recently ascertained that only 7% of boys diagnosed with SCA but without a known history of priapism knew what priapism was and were aware that it is a complication of SCA.[3]

Two clinical patterns of priapism have been described. Severe episodes lasting more than 2 to 3 hours often require medical intervention for pain control and to prevent ischemic injury to the penis. Shorter episodes, so called stuttering spells, last from a few minutes to 2 hours and resolve spontaneously, but they may recur and or be followed by prolonged events.[3] Although involvement of the corpus spongiosum and glans penis has been described in 1 series of adults with SCA and priapism (tricorporal priapism), the vast majority of cases in children, adolescents, and young adults are bicorporal, as was the case in our series.[16]

The underlying mechanism of priapism is the obstruction of venous drainage of the penis.[17,18] After abnormally long erections, blood trapped in the corpora cavernosa becomes deoxygenated, resulting in local acidosis and further sludging of sickled erythrocytes. This leads to increased intracavernous pressure. When the latter exceeds the mean arterial pressure for prolonged periods of time, the penis becomes ischemic,[17,18] possibly resulting in corporal fibrosis and impotence. Priapism often has its onset in the early morning hours during periods of rapid-eye-movement sleep. This time is normally associated with erections and the relative nocturnal acidosis and dehydration favor sickling of erythrocytes.[7]

Many interventions have been used to treat priapism in children and adults with SCA. Nonsurgical measures include oral or intravenous hydration, alkalinization to ameliorate acidosis, analgesics, and frequent urination.[7] Although all of these maneuvers have been credited with terminating episodes of priapism, they have not been carefully studied and are less likely to succeed after prolonged episodes.

Vasoactive agents, given either orally and by injection, have commonly been used to treat priapism. For example, terbutaline, a β_2-agonist, has been shown to be effective in the management of intraoperative penile tumescence and of pharmacologically induced priapism,[19-21] but it has not been formally studied in patients with SCA. A single case report describes the successful use of hydralazine, a vasodilator, in a patient with SCA and priapism.[22]

Rifkind and coworkers[23] first reported on the successful use of exchange transfusion in a 26-year old man with homozygous SCA who presented with a 3-day history of priapism. Although a small case series of patients successfully treated with this approach has been published,[24] exchange transfusion is not universally successful, and automated exchange transfusion may not be available. In addition, the procedure has been associated with the onset of severe neurologic complications known as ASPEN syndrome (association of SCA, priapism, exchange transfusion, and neurological events).[8,9] Although simple red cell transfusion therapy has been employed to treat priapism, the efficacy of this strategy (ie, immediate detumescence) has been unpredictable.[25,26] In addition, the risks of ASPEN syndrome described above apply to simple erythrocyte transfusions as well.[8,9]

Surgical management of priapism with a variety of shunt procedures, usually between the corpora cavernosa and glans penis[27-30] or saphenous vein,[31] has been successful in relieving severe and refractory priapism, with the objective of maintaining potency. But shunt procedures are limited by a high failure rate and frequent complications, such as skin sloughing, chordae, cellulitis, and urethral fistulas.[32] Thus, most urologists limit surgical shunts for priapism in those patients with SCA whose priapism persists after less invasive measures.

Interventions that have been used to prevent priapism include hormones and red cell transfusions. Hormonal interventions decrease the production of testosterone (eg, gonadotropin-releasing hormone analogues) or its action (eg, estrogens). Published experience includes 1 small randomized clinical trial using stilboestrol[33] and 1 case report and a single case series describing the successful use of gonadotropin-releasing hormone analogues.[34,35]

Sayer and Parsons[36] were the first to report the successful use of intracorporeal epinephrine in a 34-year old man with paranoid schizophrenia and priapism. Molina and coworkers[37] subsequently described the successful use of intrapenile injections of a dilute 1:1 000 000 epinephrine solution for the treatment of priapism in 18 patients. Although 6 patients had SCA, no specific details were provided, and long-term follow-up was lacking.[37] In that report, all aspiration and irrigation procedures were successful when the duration of priapism was $<$35 hours, while only 1 of 3 procedures was successful after longer episodes of priapism.[37] Dittrich and coworkers[11] have also described the use of intracavernous injections of phenylephrine in 36 patients with pharmacologically induced erections or priapism due to anesthesia, but none of their patients had SCA.

This report is, to the best of our knowledge, the first to date to demonstrate the safety and efficacy of this approach in an

outpatient population of young patients with SCA. Among 15 consecutive and unselected patients with homozygous SCA treated on 39 occasions, the procedure was 95% effective in producing immediate detumescence, with no serious complications. Most patients (10 of 15 or 67%) required only 1 aspiration and irrigation procedure, and 7 patients (Nos. 3, 6, 9, 11, 12, 13, and 14) had no further recurrences at a median follow-up of 39 months. None of the successfully treated patients required hospitalization, and immediate pain relief accompanied the treatment-induced detumescence in each case. All successfully treated patients with adequate follow-up maintain normal erectile function. Both patients whose priapism continued despite aspiration and irrigation were first presented to us following priapism episodes lasting more than 24 hours. Thus, although the number of patients who failed to demonstrate detumescence is small (n = 2), success of penile aspiration and irrigation with dilute epinephrine appears to be less in patients with extremely prolonged episodes of priapism.

Evidence-based guidelines for the prevention of recurrent priapism in patients with SCA do not exist, since none of the reported therapeutic interventions have been compared in a randomized fashion. We often prescribe 30 mg of oral pseudoephedrine at bedtime for SCA patients who required aspiration and irrigation for priapism. This agent appears to be successful in causing detumescence in patients with pharmacologically induced priapism, and most episodes of priapism occur at night.[11] Although oral pseudoephedrine appears to decrease the number of recurrent episodes of priapism, this observation has not been studied in a controlled fashion. For patients who fail to respond to oral pseudoephedrine or who require multiple aspiration and irrigation procedures, we have successfully employed injections of leuprolide, a gonadotropin-releasing hormone analogue that suppresses the hypothalamic-testicular axis and the production of testosterone. [35]

Our study has several limitations. First, since both aspiration of blood and irrigation of the corpora cavernosa with epinephrine were employed, it is unclear which of the 2 contributed most to the observed outcome. While simple aspiration of blood from the corpora cavernosa under spinal anesthesia was successful in producing rapid detumescence in a small patient series,[38] our initial experience suggested that mere aspiration usually led to refill of the corpora cavernosa and recurrent priapism until epinephrine was instilled. Thus, we elected to use both aspiration of blood and irrigation of the corpora cavernosa with epinephrine. Second, the long-term follow-up of some patients, especially older adolescents who were transitioned to adult SCA care, was not optimal, and 2 patients discontinued follow-up. Third, a single successfully treated patient (No. 1) represents 38% of our overall experience (15 of 39 aspiration and irrigation procedures), thus possibly overestimating the efficacy of the procedure. However, even if we estimate the efficacy of penile aspiration and irrigation by patient rather than by event, it remains highly effective, with 13 of 15 patients (87%) exhibiting immediate detumescence. Finally, potency at last follow-up was determined by self-reporting alone. Thus, the ultimate potency of young men with SCA who required aspiration and irrigation for priapism during childhood remains to be determined.

In conclusion, aspiration of blood from the corpora cavernosa followed by irrigation with a dilute 1:1 000 000 epinephrine solution is effective in inducing detumescence in young patients with SCA and prolonged episodes of priapism. This simple, safe, and readily available (following urologic consultation) intervention does not require hospitalization or regional or general anesthesia. Moreover, it is 95% effective. Multicenter, randomized, placebo-controlled trials are needed to better define the role of oral α-adrenergic agonists and other strategies in preventing recurrences of severe episodes of priapism in both children and adults with SCA.

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