Treatment of Recurrent Priapism in Sickle Cell Anemia With Finasteride: A New Approach

Daibes Rachid-Filho, Andre G. Cavalcanti, Luciano A. Favorito, Waldemar S. Costa, and Francisco J. B. Sampaio

OBJECTIVES To determine whether the use of finasteride controls recurrent priapism in patients with sickle cell anemia.

METHODS Thirty-five patients with recurrent priapism because of sickle cell disease received finasteride during 120 days. The initial dose was decreased every 40 days, from 5 mg/d to 3 mg and then to 1 mg of finasteride until the end of 120 days. Five groups (G) were created based on priapism episodes in a month: G0, no episode; G1, 1-15 episodes; G2, 16-30; G3, 31-45; and G4, >45 episodes.

RESULTS Records on day 0: G0, no patient; G1, 7 (20%); G2, 21 (60%); G3, 4 (12%); and G4: 3 (8%). After 40 days of using 5 mg/d finasteride we found the following results: G0, 5 patients (14%); G1, 19 (55%); G2, 8 (23%); G3, 3 (8%); and G4, none. At the end of the 40-day period, using 3 mg/d finasteride, the findings were as follows: G0, 19 patients (55%); G1, 14 (39%); G2, 2 (6%); G3, none; and G4, none. The findings after 120 days with 1 mg/d finasteride for the last 40 days were as follows: 16 patients (46%) and G1, 16 (46%). In 1 patient, the dose was increased to 3 mg and in 2 patients, to 5 mg, so as to achieve remission.

CONCLUSIONS To our knowledge, this is the first study demonstrating that the use of finasteride could decrease and control the number of priapism recurrences in patients with sickle cell anemia, with fewer side effects than other drugs currently used. UROLOGY 74: 1054–1057, 2009. © 2009 Elsevier Inc.

Priapism is a condition of painful, persistent penile erection in the absence of sexual desire. This condition is commonly associated with sickle cell disease. Sickle cell disease refers to various related disorders characterized by the predominance of sickle cell hemoglobin production.[1] Sickle cell disease causes microvascular occlusion, which is manifested in most organs and systems. The genitourinary tract is most commonly affected in sickle cell disease and priapism is a very frequent manifestation.[1]

The prevalence of priapism in patients with sickle cell disease has been reported to be 5%-45%.[2-4] Approximately 30%-45% of patients with sickle cell anemia will present at least 1 episode of priapism during their lifetime.[3,4]

Priapism may occur as prolonged or stuttering (recurrent brief episodes that resolve spontaneously). If priapism persists for 4 hours or more without detumescence, the patient is at risk for irreversible ischemic penile injury, which may result in fibrosis and erectile dysfunction.[1,5]

The treatment of recurrent priapism in sickle cell anemia has been in constant evolution.[6-8] Many different drugs have been used to treat recurrent priapism, including LH-RH analogs,[6] adrenergic agents,[7] phosphodiesterase-5 inhibitors,[8] antiandrogens,[9] digoxins,[10] and estrogens,[11] showing different outcomes and frequent side effects as hot flushes, gynecomasty, loss of libido, embolism, stroke, nausea, and vomiting, apart from the high cost of analogs and antiandrogens.

The objective of this study was to present finasteride as a new treatment modality to control recurrent priapism in patients with sickle cell anemia.

MATERIAL AND METHODS

From March 2001 to January 2007, 56 patients with recurrent priapism because of sickle cell disease had been using finasteride. Thirty-five patients used finasteride alone and the remaining 21 used it as adjuvant therapy. We analyzed only these 35 patients, without any previous treatment, according to the

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From the Souza Aguiar Municipal Hospital, and Urogenital Basic and Translational Research Unit, State University of Rio de Janeiro, Rio de Janeiro, Brazil

Reprint requests: Francisco J. B. Sampaio, M.D., Ph.D., Urogenital Basic and Translational Research Unit, Av 28 de Setembro, 87,FCM – térreo, Rio de Janeiro, RJ 22 051-030, Brazil. E-mail: sampaio@urogenitalresearch.org

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Table 1. Descriptive statistics of the number of priapism episodes related to finasteride dosage

	Interval				Difference Between Days of Treatment*		
Descriptive Statistics	D1	D40	D80	D120	D1-D40	D40-D80	D120-D80
Patients (n)	35	35	35	32	35	35	32
Mean	22.7	12.0	3.7	2.1	10.7	8.2	1.5
Standard deviation	10.9	9.3	5.0	2.6	3.9	6.0	4.3
Minimum	7	0	0	0	2	0	−4
Median	21	10	0	1	11	8	0
Maximum	48	35	18	9	18	21	13
					<0.001	<0.001	0.025

* Wilcoxon test was used to test the differences between days of treatment.

number of recurrences registered in a priapism records (number of episodes and duration of painful erection). Patient age was 15-53 years (mean 16), with a mean follow-up of 11 months (range 5-36).

All 35 patients started the treatment with 5 mg/d finasteride. We decreased the initial dose every 40 days, from 5 mg/d to 3 mg and then to 1 mg finasteride at 40 days before the end of 120 days. Five groups (G) were created based on the number of recurrences in a month: G0 = no recurrence, G1 = 1-15 recurrences, G2 = 16-30 recurrences, G3 = 31-45 recurrences, G4 = >45 recurrences.

Recurrent priapism was considered as an occurrence of at least 2 episodes a week, with >40 minutes duration. D1 was considered the beginning of the study with 5 mg finasteride daily; D40, a decrease to 3 mg; D80, a decrease to 1 mg; and D120, end of the study. All patients received finasteride free of charge, donated by our institution. This study was approved by the Institutional Review Board at our institution and all patients signed an informed consent form.

We used the Wilcoxon test for the descriptive statistics of recurrence based on time of finasteride dose change.

RESULTS

Priapism records showed on day 0 of treatment: G0 = no patient, G1 = 7 patients (20%), G2 = 21 patients (60%), G3 = 4 patients (12%), and G4 = 3 patients (8%). Findings after 40 days of treatment with 5 mg/d finasteride: G0 = 5 patients (14%), G1 = 19 (55%), G2 = 8 (23%), G3 = 3 (8%), and G4 = no patients. Sequentially, findings at the end of treatment with 3 mg/d finasteride, during 40 days: G0 = 19 patients (55%), G1 = 14 (39%), G2 = 2 (6%), G3 = no patient, and G4 = no patients. After 120 days of the study, with patients receiving 1 mg/d finasteride for the last 40 days, we observed that 16 patients (46%) were in G0, 16 (46%) in G1, and 3 patients needed dose increase to 3 mg (n = 1) and 5 mg (n = 2) because of recurrence of frequent priapism episodes. On day 1 of treatment, the mean of recurrent episodes was 22.7 and on day 120, it was 2.1. The difference of the mean of recurrences between days 1-40 was 10.7 episodes, days 40-80 was 8.2 episodes, and days 80-120 was 1.5 episodes. Twelve of 16 patients in G1 had <5 episodes per month at the end of the study.

No patient in this series presented acute priapism that required drug discontinuation or surgical or hematological procedures. Also, the patients did not present any significant side effects, with 6 patients presenting painless gynecomasty.

Table 1 shows the descriptive statistics of recurrence based on the time of decreasing the finasteride ingestion by the patients. Table 2 shows the comparison of recurrence based on the period that finasteride ingestion was reduced in patients.

COMMENT

There are 2 types of priapism—low-flow (ischemic) and high-flow (nonischemic)—with priapism in sickle cell anemia being the low-flow type. The stuttering priapism in patients with sickle cell disease is most frequently identified during sleep and sexual arousal, and these episodes in fact have no relationship to other vaso-occlusive events characteristic of sickle cell disease.[12]

Initial treatment of patients with sickle cell disease and priapism should include systemic therapies such as hydration and relief of pain and anxiety. Transfusional therapy has become a mainstay treatment for persistent sickle cell disease-related priapism.[13,14] Patients who do not respond to initial noninvasive procedures may need more aggressive intervention.[1] Recurrent priapism in young men is a devastating condition that may result in erectile dysfunction (ED) as a result of corpora cavernosa fibrosis in approximately 30% of cases.[5,15]

The pathologic aspects of penile structures in recurrent priapism, caused by ischemic effects within the penis, are equivalent to a compartment syndrome of an extremity and consist of erectile tissue necrosis and fibrosis, which will determine erectile dysfunction.[14] The natural history of priapism in sickle cell disease commonly involves recurrent episodes, which frequently herald a subsequent major episode; thus, the goal of the management of recurrent priapism is prevention of future episodes, avoiding the consequent erectile dysfunction.[1,15]

Many different medications have been used to treat recurrent priapism, but there is no consensus on the optimal drug to treat this condition. There are many side effects related to drugs used in treatment of recurrent priapism.[6-9] Stilbestrol, which blocks testosterone production, has been effective in treating and preventing future episodes of priapism; nevertheless, its use presents

Table 2. Comparison of recurrence in accordance with different periods (doses) by groups

			Recurrences on D40				
Recurrences on D1	Total		0	1-15	16-30	31-45	>46
0	0	0.0	0	0	0	0	0
1-15	7	20.0	4	3	0	0	0
16-30	21	60.0	1	16	4	0	0
31-45	4	11.4	0	0	4	0	0
>46	3	8.6	0	0	0	3	0
Total	35	100.0	5	19	8	3	0
			Recurrences on D80				
Recurrences on D40	Total		0	1-15	16-30	31-45	>46
0	5	14.3	5	0	0	0	0
1-15	19	54.3	14	5	0	0	0
16-30	8	22.9	0	8	0	0	0
31-45	3	8.6	0	1	2	0	0
>46	0	0.0	0	0	0	0	0
Total	35	100.0	19	14	2	0	0
			Recurrences at D120				
Recurrences on D80	Total		0	1-15	16-30	31-45	>46
0	19	54.3	13	6	0	0	0
1-15	11	31.4	3	8	0	0	0
16-30	2	5.7	0	2	0	0	0
31-45	0	0.0	0	0	0	0	0
>46	0	0.0	0	0	0	0	0
Total	32	91.4	16	16	0	0	0

important risks including gynecomastia and thromboembolic events.[16] The use of gonadotropin-releasing hormone analogs appear to be effective in controlling recurrent priapism; however, these hormone analogs reduce libido and are expensive.[14,17] Oral antiandrogens (flutamide) alone have been administered successfully for managing recurrent priapism in patients who did not tolerate injectable therapy, although its use was reported in a series with a limited number of patients.[1] The use of hydroxycarbamide has recently been reported in the prevention of recurrent priapism, but this study analyzed only one patient.[18] To the best of our knowledge, the present study is the first reporting the use of finasteride for treatment of recurrent priapism.

Finasteride belongs to the group of medicines called enzyme inhibitors. Finasteride is the first 5α-reductase inhibitor that has received clinical approval for the treatment of human benign prostatic hyperplasia and androgenetic alopecia (male pattern hair loss). These clinical applications are based on the ability of finasteride to inhibit the type II isoform of the 5α-reductase enzyme, which is the predominant form in human prostate and hair follicles. Also, finasteride can reduce testosterone to dihydrotestosterone.[19] Gynecomastia has been the most frequently reported condition and difficult adverse effect of this drug[20]; however, in our study, only 6 of the 35 patients had gynecomastia that was not painful.

In this study, we demonstrated that the use of finasteride could control the number of priapism recurrences in patients with sickle cell anemia, with fewer side effects than other drugs currently used. After the fourth month of the study, we observed that 16 patients (46%) were in group 0 (no recurrence) and other 16 patients (46%) were in Group 1 (1-15 recurrences). At the beginning of the treatment with finasteride, the mean of episodes of priapism per patient was 22.7 and after 4 months of treatment the mean was 2.1. These results show that finasteride can decrease and control the number of recurrent episodes of priapism. The optimal outcomes were found using 5 and 3 mg/d finasteride. When the finasteride dosage was decreased to 1 mg/d we observed few cases of recurrences.

We could not assess the long-term effects of treatment with finasteride on fertility. Because the population is young, the long-term effect of finasteride on fertility must be evaluated in future studies.

Further studies including randomized controlled trials assessing the effectiveness of specific interventions must be carried out to determine the real efficacy of finasteride in recurrent priapism associated with sickle cell anemia.

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