Trends in Sickle Cell Disease-related Priapism in U.S. Children's Hospitals

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OBJECTIVE To define rates of priapism diagnosis and inpatient admission among males with sickle cell disease (SCD).

PATIENTS AND METHODS We retrospectively reviewed the Pediatric Health Information System database for males aged <21 years treated 2004-2012. We identified patients with SCD and priapism based on the *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis codes. Logistic regression and generalized estimating equation models were used to control for confounding and to adjust for within-hospital clustering of similar patients.

RESULTS We identified 17,186 males who were admitted 137,710 times during the study period. Of these, 362 (2.1%) were diagnosed with priapism on 748 admissions. There was a significant decrease in the number of priapism admissions among patients with SCD over time (0.81% in 2004 to 0.44% in 2012, $P < .001$). The number of patients diagnosed with SCD-related priapism varied over time without a statistically significant trend (2.3% in 2004, 2.69% in 2008, 1.01% in 2012, $P = .34$). Rates of priapism admissions (0-4.4%) varied widely between hospitals. Older patient age was associated with an increased likelihood of a priapism admission in the multivariate logistic regression model after adjusting for treatment year, hospital region, and for hospital-level clustering of similar patients.

CONCLUSION From 2004 to 2012, the number of admissions for SCD-related priapism declined whereas the number of individual patients diagnosed with SCD-related priapism did not. Rates of priapism-related admissions in males with SCD vary widely among PHIS hospitals. UROLOGY 89: 118–122, 2016. © 2016 Elsevier Inc.

Priapism is a common urologic complication of sickle cell disease (SCD) and is often anecdotally cited as one of the more difficult clinical problems encountered by pediatric urologists. SCD is estimated to account for up to 65% of all priapism episodes occurring in children,[1,2] and up to 89% of men with SCD report experiencing at least one priapism episode before age 20.[3] The exact pathophysiology of priapism in SCD is unclear. However, the most likely etiology is dysfunction within the nitric oxide pathway that leads to hypoxia with sickling of erythrocytes and eventual sludging of blood within the corpora cavernosa.[1,4] Importantly, a significant portion of male patients with SCD will experience stuttering priapism at some point during their lifetime[3,5]; these children are at high risk of long-term morbidity, particularly erectile dysfunction.[6,7]

The aim of this study was thus to describe temporal trends in the diagnosis and treatment of priapism in males with SCD in U.S. children's hospitals.

PATIENTS AND METHODS

Data Source

Data for this study were obtained from the Pediatric Health Information System (PHIS) database, an administrative database that contains inpatient, emergency department, ambulatory surgery, and observation encounter-level data from over 44 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children's Hospital Association (Overland Park, KS). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the PHIS database are managed by Truven Health Analytics (Ann Arbor, MI). Data are de-identified at the time of data submission, and are subjected to a number of reliability and validity checks before being included in the database. We excluded hospitals without complete billing and pharmacy data throughout the entire course of the study; 10 hospitals were excluded for this reason. In total, complete data from 34 hospitals were included in this study.

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Patients and Outcomes

We identified all inpatient hospital encounters occurring between January 2004 and December 2012 (inclusive) for males under 21 years of age with an *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis code for sickle cell disease (282.41, 282.42, 282.5, 282.60-282.69). Priapism was defined in 2 different ways in this analysis:

(1) Patient-level analysis. Patients who had a diagnosis code for priapism (607.3) during the study period were defined as having a history of priapism beginning with their index admission with priapism at a PHIS hospital. For patients without a history of priapism, the index admission was defined as the first SCD admission at a PHIS hospital.
(2) Admission-level analysis. Because priapism is a dynamic state, priapism admissions were defined as occurring if the patient had a diagnosis code for priapism during that admission only. These data were then used to generate analysis of temporal trends in priapism diagnoses among patients with SCD.

Approximate resource utilization was estimated based on hospital billing records. Of note, PHIS data include hospital charges only; physician reimbursements (both within the hospital and within the clinic) are not necessarily captured. Pharmacy data were obtained via review of pharmacy billing codes based on use during inpatient admissions, ambulatory medical or surgical short-stay visits, or emergency department visits, but not during routine outpatient clinic visits.

Statistical Methods

Initial bivariate tests of association were performed using Fisher's exact test, Cochran-Armitage trend, or Wilcoxon rank-sum tests as appropriate based on data characteristics and distribution. These were performed on both a per-patient and per-admission basis. Based on these results, logistic (priapism episodes) and negative binomial (charge and length of stay) regression models were constructed to further examine trends after adjusting for possible confounding effects. Model covariates were chosen based on biological plausibility and/or a bivariate *P* value of .2 or less on initial bivariate analysis. Other covariates entered into our final model included patient age, year of admission, U.S. census region, and the individual hospital at which a patient was treated. Model diagnostics revealed no significant violations of regression assumptions. Generalized estimating equations were used to adjust for hospital- and patient-level clustering. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). All tests were two-sided and *P* values of less than .05 were considered significant.

This study was deemed exempt from review by our institutional review board, and administrative approval was obtained from PHIS prior to data collection or analysis.

RESULTS

Cohort Demographics

We identified 17,186 males with SCD who were admitted to 34 PHIS hospitals a total of 137,710 times between 2004 and 2012 (median 9 admissions to PHIS hospitals per patient, range 1-180). Ten hospitals were excluded for incomplete billing data during the study period. The mean (standard deviation) age at first SCD admission to a PHIS hospital was 7.9 (±6.1) years. Table 1 shows the demographic characteristics of the cohort by priapism history.

Table 1. Patient demographics

Characteristics	Priapism	No Priapism	*P* Value
Number of patients	362	16,824	
Age in years (mean, SD)	10.2 (5.3)	7.9 (6.1)	<.001*
Patient age by category (years)			<.001†
0-1	7 (2%)	1592 (9%)	
1-3	12 (3%)	2123 (13%)	
3-6	25 (7%)	2420 (14%)	
6-12	89 (25%)	4268 (25%)	
12-18	158 (44%)	4664 (28%)	
18-21	71 (20%)	1757 (10%)	
Treatment year			.21†
2004-2007	76 (21%)	4014 (24%)	
2008-2011	286 (79%)	12,810 (76%)	
Hospital region			.01†
Northeast	41 (11%)	1799 (11%)	
Midwest	125 (35%)	4629 (28%)	
South	168 (46%)	9130 (54%)	
West	28 (8%)	1265 (8%)	
Length of stay (median, IQR)	2 (1-4)	1 (1-3)	<.001‡
Charges (median, IQR in U.S. dollars)	8397 (3323-22,804)	6358 (2122-15,067)	<.001‡

IQR, interquartile range; SD, standard deviation.
* *P* value from *t* test.
† *P* value from chi-square test.
‡ *P* value from Wilcoxon rank-sum test.

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