Journal of Pediatric Surgery 49 (2014) 91–94

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Vesicoureteral reflux and febrile urinary tract infections in anorectal malformations: A retrospective review

Sabrina Sanchez, Robert Ricca, Byron Joyner, John H.T. Waldhausen *

Seattle Children's Hospital University of Washington School of Medicine

ARTICLE INFO

Article history:
Received 17 September 2013
Accepted 30 September 2013

Key words:
Vesicoureteral reflux
Anorectal malformation
Urinary tract infection
Voiding cystourethrogram

ABSTRACT

Background: Multiple studies document a correlation between anorectal malformations (ARMs) and vesicoureteral reflux (VUR), development of urinary tract infections (UTIs), and subsequent renal disease. We aimed to determine which patient characteristics are associated with VUR and UTI in this population.
Methods: A retrospective review of ARM patients at a free-standing children's hospital from January 1996 to December 2011 was performed. Logistic regression was used to investigate the associations between VUR and UTI and ARM classification and co-morbid diagnoses.
Results: Of 190 patients, 41 (31%) received a diagnosis of VUR. Thirty-one of the 190 patients had at least one febrile UTI (16%). Of these, only 16 (51%) had a diagnosis of VUR. On multivariable logistic regression, the only patient variable associated with VUR was having an ectopic kidney ($p = 0.026$). Similarly, the presence of GU malformations was the closest variable associated with developing a UTI ($p = 0.073$).
Conclusions: In ARM patients, VUR as well as UTIs are associated with the presence of GU malformations. Thus, voiding cystourethrogram (VCUG) testing should be pursued when there are other caudal and GU abnormalities, regardless of fistula location. Antibiotic prophylaxis for UTI should be considered in children with ARM and any GU malformation, not only VUR.

Anorectal malformations (ARMs) have a high incidence of associated genitourinary (GU) anomalies, ranging from 25% to 50% [1–3]. This significant association has led to routine diagnostic imaging to determine the presence of renal anomalies and vesicoureteral reflux (VUR). VUR has been reported in 20%–47% of children with ARMs [4]. Children with ARMs previously described as having "high" malformations have an increased risk of VUR ranging from 33% to 39%. Children with "low" malformations have a slightly lower incidence, reported at 20%–37% [4,5]. The presence of VUR increases the risk of developing febrile urinary tract infections (UTIs) which may ultimately lead to renal scarring and subsequent renal dysfunction [6,7]. Traditionally, all patients with VUR have been placed on prophylactic antibiotics in order to prevent complications secondary to febrile UTIs.

The data regarding the benefits of antibiotic prophylaxis in children with VUR are mixed. A Cochrane review analyzing the results of 20 randomized controlled trials, including 2234 children, concluded that compared to no treatment, prophylactic antibiotics in the setting of VUR did not significantly reduce the number of recurrent febrile UTIs in children, although it did reduce the number of children developing new or progressive renal damage [8]. These children represent a heterogeneous group with multiple comorbidities and congenital anomalies making it difficult to apply these data to a single population. Even with this limitation, there has been a trend towards not treating patients with documented low-grade VUR with prophylactic antibiosis [9]. There have been many reports documenting the association of non-fistulous GU anomalies with ARM, including VUR [10]. In this study we aimed to review all the children with ARM treated at our institution over the last 15 years to determine which characteristics in ARM patients are associated with VUR and/or UTI diagnoses to better define who would benefit from voiding cystourethrogram (VCUG) testing and/or UTI prophylaxis.

1. Methods

We performed a retrospective review of infants at a free-standing children's hospital from January, 1996 to December, 2011 (IRB approval #13904). We included all male and female infants with a primary diagnosis of ARM including those with a cloacal anomaly. Exclusion criteria included cloacal exstrophy, conjoined twins, patients expiring within the first 3 months of life, or those who had their initial surgical management at an outside institution. Demographic and clinical variables were obtained by chart review and included age, gender, ARM classification according to the initial operating surgeon during the index admission, performance and results of VCUG on index admission with regards to presence of VUR, co-morbid diagnoses recorded during index admission, surgical

* Corresponding author. Division Chief Pediatric Surgery Fellowship Program Director Seattle Children's Hospital Seattle WA 98105, USA. Tel.: +1 206 987 1177; fax: +1 206 987 3925.
E-mail address: john.waldhausen@seattlechildrens.org (J.H.T. Waldhausen).

0022-3468/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jpedsurg.2013.09.031

Table 1
Clinical and demographic characteristics of 190 study subjects.

		N	Percent
Gender	Male	101	53.16%
	Recto-perineal fistula	54	53.47%
	Recto-urethral fistula	19	18.81%
	Recto-vesical fistula (bladderneck)	3	2.97%
	Imperforate anus without fistula	25	24.75%
	Female	89	46.84%
	Recto-perineal fistula	29	32.58%
	Recto-vestibular fistula	24	26.97%
	Cloacal anomaly	33	37.08%
	Imperforate anus without fistula	3	3.37%
Procedures performed related to anorectal malformation	Diverting colostomy	98	51.58%
	Anoplasty	183	96.32%
	Cecostomy/Appendicostomy	23	12.11%
Co-morbid diagnoses	Congenital heart defect	41	21.58%
	Tracheoesophageal fistula	10	5.26%
	Tethered cord	13	6.84%
	Spina bifida	6	3.16%
	Vertebral anomaly	36	18.95%
	Genetic syndrome	13	6.84%

operations performed related to the diagnosis of ARM, occurrence of febrile UTI, and use of prophylactic antibiotics for UTI prevention. Of note, a subject was considered to have had a febrile UTI when they had a urine culture growing at least 10^5 bacteria per ml of a single organism in addition to being symptomatic with fever, suprapubic, or back pain, and requiring organism-targeted antibiotic treatment.

For the purposes of this study ARMs were classified according to gender and fistula location. Co-morbid diagnoses included tracheoesophageal fistula (TEF), congenital heart defect, vertebral anomalies, tethered cord, spina bifida, and genetic syndromes. GU anomalies included any recorded anomaly of the genital or urinary tract. Ectopic kidney included any diagnosis of ectopically located kidneys, including horseshoe kidney. Dysplastic kidney included any type of dysplasia, including hypoplasia and cystic malformations. Urinary tract system duplications included kidney, ureteral and urethral duplications. Female genital system anomalies included duplications or absence of the uterus, cervix, or vagina, bicornuate uterus, obstructed uterine horns, and vaginal atresia, among others. Male genital system anomalies include any deformities of the testicles, scrotum or penis, such as undescended testicle, penile chordee, bifid scrotum, and penoscrotal transposition. Urethral anomalies included epispadias, hypospadias, urethral atresia, and duplicate urethra. Other GU anomalies included rare anomalies in our cohort that could not be included in any of the previous categories, including ureteral anomalies, uretero-pelvic junction obstruction, and bladder anomalies.

Descriptive statistics were used to describe the demographic and clinical characteristics of the study subjects. Simple logistic regression was used to investigate the associations between VUR and the patient variables measured. We then constructed a multivariable logistic regression model with VUR as the outcome of interest including all variables associated with VUR with $p \leq 0.1$ in the previously performed bivariate analyses. Simple logistic regression was also used to model the associations between UTI occurrence and patient demographic and clinical characteristics. We again incorporated all the variables associated with UTI with $p \leq 0.1$ as well as variables considered to influence UTI occurrence in a multivariable logistic regression model with UTI as the outcome of interest. The statistical software STATA 10.0 (College Station, TX) was used for all analyses; statistical significance was set at $p \leq 0.05$. Continuous measures are presented as mean $\pm$ standard deviation and categorical variables are summarized by percentages.

2. Results

One hundred and ninety patients were included in this study. Table 1 summarizes the clinical and demographic characteristics of our subjects. The average age of our subjects at the completion of the study was 93.43 $\pm$ 52.05 months and median 4.04 years (22 days–15.5 years). Table 2 focuses on the GU diagnoses of our study population. Out of the 190 patients studied, 133 (70%) had a VCUG performed during their index admission and of these, 41 (30.83%) received a diagnosis of VUR. Median follow up for these patients was 5.63 years (120 days–14.71 years) and only 2 of these patients were lost to follow up prior to resolution of their VUR. Of the 41 children with VUR, 56% had a VUR grade of III or greater, and almost all (39, 95.12%) were placed on prophylactic antibiotics to prevent UTIs. Sixteen of these 41 went on to develop at least one febrile urinary tract infection (39.02%). Of these 16 patients with VUR and a UTI, 11 (68.75%) had VUR of grade III or above. Of the two patients who were not treated with prophylactic antibiotics, one had grade III reflux and to date has not developed a UTI. The other had grade IV reflux and did develop a febrile UTI.

The results of simple logistic regression analyses exploring the association between a diagnosis of VUR and measured clinical variables, controlling for performance of a VCUG at birth and gender as appropriate are summarized in Table 3. A multivariable logistic regression model was then constructed to investigate these predictor variables and their association with a diagnosis of VUR. This model included all variables with $p \leq 0.1$ on simple logistic regression as well as fistula location as a variable presumed to affect the likelihood of being diagnosed with VUR. In this model, only a diagnosis of ectopic kidney remained associated with having a diagnosis of VUR (OR = 13.263, p = 0.026, 95%CI = 1.354–129.92).

In total, 31 (16.32%) patients from the 190 included in the study developed a febrile UTI. Of these, 16 (51.61%) had a diagnosis of VUR. Only 5 of them (16.13%) were not diverted with a sigmoid end

Table 2
Urogenital diagnoses and initial VCUG evaluation results of the study population.

		N	Percent
Genitourinary anomaly	Any GU malformation	69	36.32%
	Solitary kidney	13	6.84%
	Dysplastic kidney	10	5.26%
	Ectopic kidney	12	6.32%
	Urinary tract system duplication	6	3.16%
	Female genital anomaly	25	28.09%
	Male genital anomaly	18	17.82%
	Urethral abnormalities	16	8.42%
	Other	13	6.84%
VCUG on initial evaluation		133	70%
	Male	74	73.27%
	Recto-perineal fistula	30	40.54%
	Recto-urethral fistula	19	25.68%
	Recto-vesical fistula (bladderneck)	3	4.05%
	Imperforate anus without fistula	22	29.73%
	Female	59	66.29%
	Recto-perineal fistula	9	15.25%
	Recto-vestibular fistula	20	33.90%
	Cloacal anomaly	27	45.76%
	Imperforate anus without fistula	3	5.10%
Vesicoureteral reflux		41	30.83%
	Male	17	22.97%
	Recto-perineal fistula	6	35.29%
	Recto-urethral fistula	4	23.53%
	Recto-vesical fistula (bladderneck)	1	5.89%
	Imperforate anus without fistula	6	35.29%
	Female	24	40.67%
	Recto-perineal fistula	3	12.5%
	Recto-vestibular fistula	9	37.5%
	Cloacal anomaly	11	45.83%
	Imperforate anus without fistula	1	4.17%