Journal of Pediatric Urology (2015) 11, 280.e1–280.e6

Impact and frequency of extra-genitourinary manifestations of prune belly syndrome

G.M. Grimsby [a], S.M. Harrison [a], C.F. Granberg [b], I.H. Bernstein [d], L.A. Baker [a,c]

[a]Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA

[b]Department of Urology, Mayo Clinic, Rochester, MN, USA

[c]McDermott Center for Human Growth and Development, University of Texas Southwestern Medical Center, Dallas, TX, USA

[d]Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX, USA

Correspondence to: L.A. Baker, Children's Medical Center, 2350 Stemmons Freeway, Suite F4300, Dallas, TX 75207, USA, Tel.: +1 214 456 7974; fax: +1 214 648 3800

gwen.grimsby@gmail.com (G.M. Grimsby)
sharrison6@partners.org (S.M. Harrison)
granberg.candace@-mayo.edu (C.F. Granberg)
ira.bernstein@utsouth-western.edu (I.H. Bernstein)
linda.baker@childrens.com (L.A. Baker)

Keywords
Prune belly syndrome; Orthopedic; Gastrointestinal; Constipation; Scoliosis; Cardiopulmonary

Received 8 April 2015
Revised 29 May 2015
Accepted 23 June 2015
Available online 9 July 2015

Summary

Introduction
Prune belly syndrome (PBS) extra-genitourinary (extra-GU) manifestations are serious comorbidities beyond the genitourinary (GU) anomalies of this disease. We hypothesized an underestimation of the reported frequency and understated impact on quality of life (QOL) of extra-GU comorbidities in PBS survivors beyond the newborn period. To assess this, the frequencies of extra-GU manifestations of PBS in a contemporary cohort of living patients were compared to compiled frequencies from published literature. Second, the impact of extra-GU PBS manifestations on patient/family QOL was assessed via a non-validated open-ended survey.

Material and methods
From 2010 to 2013, PBS survivors were prospectively recruited locally or at three PBS Network National Conventions. The family/subject was asked to complete a detailed PBS questionnaire, non-validated QOL survey, and provide medical records for review. Clinical data were extracted from medical records for local patients. The frequencies of extra-GU manifestations were compared between the contemporary, living cohort and a published literature cohort derived from PubMed.

Results and discussion
Seven of 706 published studies met criteria for frequencies tabulation of extra-GU PBS manifestations. This largest reported living PBS patient cohort ($n = 65$) was 99% male with mean age 10 years (1 month-45 years). The living PBS cohort had a statistically significantly higher incidence of gastrointestinal (63%), orthopedic (65%), and cardiopulmonary (49%) diagnoses compared to the compiled published cohort ($n = 204$).

Eleven PBS males and 32 family members completed the QOL survey. Of these, 47% listed at least one non-GU problem (i.e. lung disease, skeletal problems, constipation) as negatively affecting their QOL; 42% listed at least one GU problem (i.e. self-catheterization, recurrent UTIs) as negatively affecting their QOL; 56% reported musculoskeletal surgery and 21% reported gastrointestinal surgery/medication as positively impacting their QOL.

Conclusions
In this large contemporary series, surviving individuals with PBS had a significantly higher incidence of orthopedic, gastrointestinal, and cardiopulmonary diagnoses than previously reported in PBS publications. From the patient/family QOL perspective, non-GU PBS manifestations negatively impact their QOL and treatment of these non-GU conditions improves their lives. As urologic surgeons for these medically complex patients, it is extremely important to be aware of and prepare for the high incidence of non-GU PBS comorbidities directly impacting the medical and surgical treatment and QOL of PBS patients and their families.

http://dx.doi.org/10.1016/j.jpurol.2015.06.005

Introduction

Prune belly syndrome (PBS) is classically characterized by three cardinal features: bilateral undescended testicles, a dilated urinary tract, and deficient abdominal wall musculature [1]. Unfortunately, the syndrome has high morbidity, with 20—30% of affected children dying within the first few months of life [2]. Despite advances in prenatal care and neonatal resuscitation, a 2010 publication reported that the US perinatal death rate remains high at 29% [3].

Pediatric urologists are infrequently consulted to evaluate and treat the fetus with PBS or the neonate that succumbs to PBS. More frequently, they care for the surviving child. For children with PBS, pediatric urologists are one of the more frequently visited surgical specialists, as these children ultimately require bilateral orchiopexy as well as urinary tract reconstruction and, often, abdominoplasty. As the understanding of genitourinary (GU) manifestations has improved, pediatric urologists have recognized that PBS represents a spectrum of abnormalities ranging from partial absence of abdominal wall musculature with bilateral cryptorchidism and mild urinary tract dilation, to the patient with renal dysplasia/chronic kidney disease, massive hydronephrosis, high-grade VUR, and severe bladder dysfunction. However, extra-GU manifestations affecting the gastrointestinal, orthopedic, and cardiopulmonary organ systems can also have high morbidity [1], and many chronic extra-GU disorders, such as constipation and asthma, may directly affect the medical and surgical care that urologists provide these children. It is likely that contemporary providers under-appreciate the prevalence of these comorbidities, as publications tabulating the frequency of extra-GU manifestations of PBS are hampered by small sample sizes, reliance on autopsy studies, and being >20 years old [1,2,4—8].

It was hypothesized that there are underestimations of the reported frequency and impact on quality of life (QOL) of extra-GU comorbidities in children with PBS who survive the newborn period. To assess this, the present study compared the extra-GU manifestations of PBS in a contemporary cohort of living people who had survived the newborn period to those that had previously been described in the literature. Second, it assessed the impact of extra-GU manifestations of PBS on the QOL of these people and their families via a non-validated open-ended survey.

Materials and methods

Historical prune belly syndrome cohort

A PubMed search using the terms 'prune belly syndrome', 'PBS', and 'Eagle—Barrett syndrome' was performed to identify studies during the period 1967—2013 that described the frequency of extra-GU manifestations in people with PBS of all ages — living and deceased. The decision to review a paper was based on a review of the study abstract. Publications that exclusively reported urologic data, surgical outcomes, or newborn subjects were excluded. The overall frequency of each extra-GU manifestation of PBS was calculated by averaging the individual frequencies of each manifestation from all identified studies to derive the historical cohort data.

Contemporary, living prune belly syndrome cohort

With IRB approval, living people with PBS from 2010 to 2013 were prospectively recruited into our local DNA/tissue repository or at three PBS Network National Conventions. Deceased people with PBS and those who did not survive the newborn period (defined as the first 30 days of life), and non-English speakers were excluded. The family/person with PBS completed a comprehensive PBS medical health questionnaire (available on request) and provided medical records for retrospective review of the person with PBS. Clinical data on the frequency of extra-GU manifestations of PBS were extracted and calculated from the questionnaire, external medical records, for non-local subjects and internal medical records for local subjects. The clinical information that was reported in the questionnaires was crossed referenced with external hospital records, when possible, to ensure accuracy.

To document which aspects of PBS negatively affect QOL in people with PBS and their families, an open-ended non-validated prune belly syndrome quality of life (PBSQOL) survey was created and administered to those with PBS and their family members at the August 2013 national meeting of the Prune Belly Syndrome Network in St. Louis, MO, USA. The PBSQOL survey posed three open-ended questions requiring anonymous, unbiased, free-text responses about how the disease and medical care affected their QOL (Appendix). The PBSQOL survey was distributed to PBS survivors and PBS family members over the age of 10 years and completed anonymously in private; it was hoped that this would remove any potential bias of the providers directly asking questions. Each question was on a separate sheet of paper, which allowed documentation of as many lines of free-text responses to each question that were required. The responses were reviewed and categorized into thematic domains and expressed as a percentage of responders.

Statistical analysis

The frequency of extra-GU manifestations was compared between the historical and contemporary, living cohorts with Fischer's exact test via GraphPad statistical software (GraphPad Software, Inc, La Jolla, CA, USA).

Results

Of the 706 identified publications on PBS, seven historical studies met inclusion criteria and tabulated the frequency of extra-GU PBS manifestations (Table 1). One contemporary study by Routh et al. was reviewed but excluded from the analysis as it only studied newborns with PBS [3]. The selected studies for review were published a mean of 30 years ago (19—39 years). When combined, the seven publications included a total of 204 PBS subjects ranging from newborns to adult survivors. Combining these studies, the historical cohort of PBS subjects had the following average frequency of extra-GU comorbidities: 36% gastrointestinal