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Early pyloric stenosis: a case control study

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Abstract

Objective Pyloric stenosis (PS) is rare in the first 2 weeks of life, often leading to delays in diagnosis and treatment. We conducted a case control study to delineate the characteristics of patients with early PS (EPS). In addition, we tested the hypothesis that patients with EPS present with a smaller pylorus than older patients.

Methods A database of all patients presenting with PS to a children's hospital over a 5-year period (2002–2006) was obtained. Each patient admitted during the first 2 weeks of life (subject) was matched to a patient admitted after 4 weeks of age (control), with the same gender, electrolyte status, and treating surgeon. A single pediatric radiologist, blinded to patient age, reviewed all available ultrasounds retrospectively. Demographic, clinical, diagnostic, therapeutic, and outcome data were compared.

Results During the study period, 278 pyloromyotomies were performed for PS. Sixteen patients (5.8%) presented with EPS between 2 and 14 days of life. EPS patients had a higher prevalence of positive family history (31 vs. 0%, $P = 0.043$), and breast milk feeding (75 vs. 31%, $P = 0.045$). Sonographic measurements showed a pylorus that was of significantly less length (17.1 ± 0.6 vs. 20.5 ± 0.9 mm, $P = 0.006$) and muscle thickness (3.5 ± 0.2 vs. 4.9 ± 0.2 mm, $P < 0.001$) in patients with EPS. Hospital stay was significantly longer for EPS patients (4.3 ± 0.9 vs. 2.0 ± 0.1 days, $P = 0.19$)

Conclusions Babies presenting with EPS are more likely to be breast fed and to have a positive family history. EPS is associated with a longer hospital stay. Use of sonographic diagnostic measurements specific to this age group may prevent delays in diagnosis and treatment, and improve outcomes.

Keywords Pyloric stenosis · Early · Ultrasound · Diagnosis · Pyloric muscle

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Introduction

Infantile hypertrophic pyloric stenosis (PS), first described by Hirschsprung [1], occurs in approximately 3 of every 1,000 livebirths [2], making it the most common indication for surgical intervention in infancy. It is characterized by hypertrophy and thickening of the circular and longitudinal muscle of the pylorus, leading to a gastric outlet obstruction. The typical presentation is projectile, non-bilious vomiting occurring between 3 weeks and 3 months of age. Failure to diagnose the condition often results in weight loss, dehydration, and metabolic abnormalities. In experienced hands, the clinical diagnosis can be made by

palpation of the thickened pylorus, or “olive”, in the right upper quadrant. However, in the twenty-first century, this has been largely replaced by sonographic diagnosis [3]. Sonographic diagnostic criteria include a muscle thickness of at least 3–4 mm and a pyloric channel length of at least 14–17 mm [3–13]. However, there is no consensus on whether these measurements are influenced by age, size, or prematurity [5–10, 12, 13]. There are also no defined parameters for diagnostic measurements in the youngest patients, those presenting in the first 2 weeks of life. This, in addition to the perception that PS is rare in the first 2 weeks of life, often leads to symptom misinterpretation, further diagnostic imaging, and delayed diagnosis.

To our knowledge, there are no reports in the literature on patients with early pyloric stenosis (EPS), which we defined as those presenting in the first 2 weeks of life. We conducted a case–control study of these patients, to delineate their demographic, clinical, therapeutic, and outcome characteristics. In addition, we tested the hypothesis that patients with EPS present with a smaller pylorus than their older counterparts.

Patients and methods

The study was performed at Miller Children’s Hospital, Long Beach, California. The hospital is affiliated with the University of California, Irvine School of Medicine and serves as the pediatric tertiary care institution for the greater Long Beach, northern Orange County, and southern Los Angeles County regions. A database of all the patients presenting with PS during a 5-year period (2002–2006) was obtained from the hospital medical records department using ICD-9 code 750.5 (congenital pyloric stenosis), and CPT code 43520 (pyloromyotomy). Each patient diagnosed with pyloric stenosis during the first 14 days of life (subject, EPS) was matched to a patient diagnosed after 30 days of age (control, PS). Matching was controlled for gender, electrolyte status, and treating surgeon. Other than the three matching criteria, no data were known or collected prior to initiating the chart reviews.

All pyloromyotomies during the study period were performed by three board-certified pediatric surgeons. One surgeon used a right upper quadrant approach, a second used a peri-umbilical approach, and the third initially used a peri-umbilical approach, but switched to a laparoscopic approach in late 2005. Approximately half the patients were transferred from outside institutions with a presumptive diagnosis of pyloric stenosis. In those cases, initial imaging was completed at the referring facility, and sent with the patient. Sonograms performed at Miller Children’s Hospital were initially read by pediatric or general, radiologists. However, in the study design, a single

pediatric radiologist (SN), blinded to patient age, reviewed all available ultrasounds retrospectively.

Demographic, clinical, diagnostic, therapeutic, and outcome data were compared between the two groups by *t* tests, or Fisher’s exact test, as appropriate. A *P* value <0.05 was considered significant. Continuous data are reported at mean ± standard error of the mean. The study was approved by the Memorial Health Services Institutional Review Board (400-06CR).

Results

During the study period, 278 pyloromyotomies were performed for PS. Sixteen patients (5.8%) presented with EPS between 2 and 14 days of life. Average age was 11.3 ± 0.8 days for subjects and 42.8 ± 3.1 days for controls. In each group, 86% were males, and 13% presented with metabolic alkalosis. There were no significant differences in any of the demographic data (Table 1). The clinical characteristics data is shown in Table 2. EPS patients had a significantly higher prevalence of positive family history (5 patients, 31%). Three patients had an affected parent and 2 patients had an affected sibling. The prevalence of breast milk feeding was also significantly higher in EPS patients (12 patients, 75%). Nine of the twelve patients were fed a combination of formula and breast milk, while three were fed exclusively breast milk.

Ultrasound was the first imaging test performed in 81% of subjects and controls alike. Upper gastrointestinal study

Table 1 Demographics

	EPS <i>N</i> = 16	PS <i>N</i> = 16	<i>P</i>
Firstborn (%)	63	69	NS
Premature (%)	6	13	NS
C/section delivery (%)	38	44	NS
Gestational age (weeks)	39.6 ± 0.4	38.8 ± 0.4	NS
Gestational weight (grams)	3555 ± 141	3178 ± 194	NS

EPS early pyloric stenosis, PS pyloric stenosis, NS not significant

Table 2 Clinical characteristics

	EPS <i>N</i> = 16	PS <i>N</i> = 16	<i>P</i>
Positive family history (%)	31	0	0.043
Breast milk feeding (%)	75	31	0.045
Duration of emesis (%)	3.1 ± 0.5	13.5 ± 3.3	0.004
Projectile emesis (%)	88	94	NS
Co-morbidities (%)	12	12	NS
Weight (grams)	3459 ± 120	4049 ± 156	NS

Table 3 Sonographic measurements

	EPS N = 11	PS N = 13	P
<i>Longitudinal view</i>			
Pyloric channel length (mm)	17.1 ± 0.6	20.5 ± 0.9	0.006
Range	15.0–20.0	14.6–27.0	
Pyloric wall thickness (mm)	3.5 ± 0.2	4.9 ± 0.2	<0.001
Range	2.7–4.5	3.7–5.9	
<i>Cross-sectional view</i>			
Pyloric wall thickness (mm)	2.8 ± 0.2	4.6 ± 0.2	<0.001
Range	2.0–3.5	3.5–6.0	

(UGI) was the first test in 3 patients in each group. All the patients eventually received at least one US during the work-up. US was diagnostic in 50% of subjects and 81% of controls, *P* = 0.06. Repeat US and/or UGI was employed to establish the diagnosis in the remainder. Ultrasounds were available for blinded retrospective review for 11 subjects and 13 controls. Sonographic measurements showed significantly shorter and thinner pylori in patients with EPS versus their older counterparts (Table 3). Sonographic shouldering was seen in 73% of subjects and 92% of controls. The difference was not statistically significant. Failure to pass gastric contents was noted on all ultrasounds.

Therapeutic and outcome data are shown in Table 4. Despite a similar incidence of metabolic alkalosis in the two groups, duration between admission and operation was significantly longer for subjects. The longer duration to full feeds in subjects did not reach statistical significance. However, duration between operation and discharge, and total hospital stay were significantly longer in subjects. One subject, operated through a peri-umbilical incision at 9 days of age, developed a wound infection and positive *S. aureus* blood cultures, requiring 10 days of intravenous antibiotics and 13-day hospitalization. There were no other complications.

Discussion

Congenital hypertrophic pyloric stenosis is the most common etiology of infantile intestinal obstruction, occurring

Table 4 Therapeutic and outcome data

	EPS N = 16	PS N = 16	P
Admission to operation (days)	1.1 ± 0.2	0.6 ± 0.1	0.047
Operation to full feeds (days)	2.1 ± 0.4	1.4 ± 0.1	NS
Operation to discharge (days)	3.4 ± 0.8	1.4 ± 0.1	0.015
Hospital stay (days)	4.3 ± 0.9	2.0 ± 0.1	NS
Complications (%)	6	0	NS

in 2–5/1,000 live births per year [2, 3]. The overwhelming majority of patients (>95%) present between 3 and 12 weeks after birth [2]. However, reports have documented cases of early onset PS, including presentation at birth [14, 15]. In addition, there is evidence that the age at which PS is diagnosed is steadily decreasing [16]. This trend was evident, even before the introduction of ultrasound, signifying a possible epidemiologic shift in age at presentation [16]. In our study, 6% of the patients presented in the first 2 weeks of life, a rate twice that found in a large epidemiologic study from California published a decade ago [2].

Early presentation, occurring during the first 14 days of life, presents the clinician with several challenges. First, the symptoms are often confused with gastroesophageal reflux, an almost ubiquitous condition in the first 2 weeks of life. Second, the clinical impression that PS is unlikely to present early often adds to delay in diagnosis. Finally, the lack of established sonographic criteria for the smallest patients commonly produces equivocal imaging results.

Our study was designed to elucidate the epidemiologic, clinical, diagnostic, and outcome characteristics of patients with EPS through a case control design, eliminating the major confounding factors of electrolyte imbalance, surgical approach, and treating clinician. Our results show that early presenting patients are more likely to have a positive family history than older patients. Almost 1 in 3 patients with EPS has an affected first-degree relative. This duplicates the finding of the only other study in the literature on early presenting pyloric stenosis, where patients younger than 21 days were found to have a 32% prevalence of positive family history versus 8% prevalence in older infants [17]. Anecdotally, we discovered that the parents and siblings of our subjects with positive family history presented at approximately the same age as the probands. The etiology of PS, still mysterious, undoubtedly includes genetic and environmental components [18–21]. In an elegant, prospective study, Rollins et al. [21] demonstrated that, in a population of 1,400 infants, none of the nine patients who subsequently developed PS had an abnormal pylorus at birth. It appears that genetics may play a stronger role in the etiology of EPS.

Another remarkable finding in our study is the significantly higher prevalence of breast milk feeding in EPS patients. To our knowledge, the only other report of potential association between breast milk and PS comes from an Italian report of two cases [22]. Davanzo et al. [22] postulated that cow’s milk protein allergy, transmitted through breast milk, was an etiologic factor in two babies with PS. To the contrary, although not statistically analyzed, Zhang et al. [23] found a lower prevalence of breast feeding in PS patients.

In 1977, Teele and Smith [24] published the first report on the utility of US in the diagnosis of PS. Since then, the speed, facility, safety, and non-invasiveness of US have established it as the test of choice for the diagnosis of PS. In our region, few radiologists use the UGI study to evaluate possible PS. Rather, the UGI is used following equivocal ultrasound results, or when gastroesophageal reflux is the suspected etiology for emesis. Approximately one-third of EPS patients in our study received an UGI, not significantly higher than the control group, but three times as high as our overall PS population (<10%). Four of the five UGI studies in the EPS group were performed as the first imaging modality because the assessing clinician felt the child was too young to have PS (2, 12, 13, and 13 days). In those 4 patients, ultrasounds were performed after the UGI, and 3 were still interpreted as equivocal despite the positive UGI. The fifth was performed after an equivocal ultrasound in a 12-day-old baby. Interestingly, the prevalence of projectile emesis was not significantly lower in EPS patients, establishing the symptom as a reliable predictor of PS in all age groups.

There has been significant controversy in the literature regarding what measurements of pyloric muscle thickness (PMT) and pyloric muscle length (PML) are consistent with PS [3–13]. The most accepted measurements confirming PS are a PMT ≥ 4 mm, and a PML ≥ 17 mm, but threshold PMT and PML vary between 3.0–4.5 mm and 14–20 mm, respectively [3]. Accepting the lower limits may increase the false positive rate, while accepting the higher ones may increase the false negative rate. In one of the earlier reports, dell’Agnola et al. [4] alluded to the notion that younger babies may have less thickened muscle, although their study did not include any patients younger than 3 weeks. Kofoed et al. [5] concluded that no correlation with age and weight exist, but again did not study the youngest patients. In one of the few studies looking at younger patients, Lamki et al. [7] found that PMT was significantly less in children less than 30 days old, but there was no difference in PML. They suggested a diagnostic PMT value of 3 mm in children less than 1 month of age [7]. Hernanz-Schulman et al. [8] agreed with this finding, and again set a lower limit of 3 mm for PMT. However, they did not investigate any patients less than 2 weeks of age [8]. Haider et al. [10] found that decreased PMT was strongly correlated with weight, but not age. Most recently, Australian investigators added to the controversy by reporting no significant correlation between sonographic measurements and age, weight, or prematurity [13]. They recommended using the same criteria (PMT ≥ 3 mm and PML ≥ 17 mm) for all the patients [13]. However, once again, age data were not clearly reported in the study [13].

Noticing a significant decrease in the age of the patients presenting to our service with PS over the last 10 years, and frequent difficulty in making a sonographic diagnosis in the youngest patients, we concentrated our study on patients presenting in the first 2 weeks of life. We hypothesized that EPS patients have shorter and thinner pylori than their older counterparts. Our study demonstrated that, after blinded retrospective review of the ultrasounds, EPS patients had significantly decreased PMT and PML measurements, confirming our hypothesis. When the PMT was measured longitudinally, all but two of the eleven EPS patients whose ultrasounds were available for review had values less than 4 mm. In the cross-sectional view, 7 of the 11 patients had PMT values less than 3 mm, and none reached the 4-mm threshold. In the control group, cross sectional and longitudinal PMT measurements were consistent. We believe that, in EPS, the pylorus may be heterogeneous in thickness, and cross-sectional measurements may represent false sampling. Therefore, we recommend the pyloric muscle be always measured at the thickest point in the longitudinal view. Although shouldering was not universally demonstrated, all patients showed failure to pass a gastric feed. This emphasizes a conclusion from a comprehensive review by Hernanz-Schulman [3]. “The actual numeric value is less important than the overall morphology of the canal and the real-time observations.” [3] Ultrasound, therefore, should remain the imaging modality of choice for patients, of any age, suspected of having PS. We feel it would be advantageous for an experienced pediatric radiologist to perform the ultrasound for patients presenting early, whenever possible. In the setting of projectile or persistent emesis in a baby less than 2 weeks old, the sonographic triad of PMT ≥ 2.5 mm, PML ≥ 14 mm, and failure to pass gastric contents is diagnostic of PS. Palpation should always remain an important part of the clinician’s armamentarium, and in fact can resolve the diagnostic dilemma arising from equivocal imaging. UGI studies should be rarely required, if at all.

We found that EPS patients spent approximately twice as much time in the hospital before proceeding to operation, despite controlling for metabolic alkalosis in the analysis. Although difficult to ascertain, the delay was most likely due to the diagnostic dilemmas in this age group. We also found a significantly increased duration between operation and discharge, as well as overall longer hospital stay in the youngest patients, despite no significant statistical difference in the period required to achieve full feeds. This persisted after excluding the EPS patient with wound infection and bacteremia from the analysis, and likely represents clinicians’ reluctance to discharge these neonates early. Despite this, all PS patients in our study,

regardless of age, had the expected excellent outcomes associated with this disease.

Our study has some obvious limitations. Since the numbers of subjects and controls are small, differences in positive family history and incidence of breast milk feeding may not have been significant if a few more patients in the control group had a positive family history or were breast fed. A case control design was chosen to minimize confounding variables with respect to outcome measurements, but had little effect on epidemiologic and diagnostic parameters. The latter may have been better analyzed through comparing patients with EPS to the rest of the patients. However, we did not believe that comparing 16 patients to 262 would have been statistically sound. Ultrasounds were available for blinded review for the majority of patients, but not all. Although this may have caused some alterations in the average pyloric measurements, it is unlikely to have led to different conclusions, given the narrow standard errors and high statistical significance.

Conclusions

In this pilot study of patients presenting with pyloric stenosis during the first 2 weeks of life, we found an increase in genetic predisposition and breast milk feeding. We also demonstrated that the pylori in these patients, although stenotic, often do not meet the accepted sonographic criteria for patients in the typical age range. Recognizing that PS can present very early, performing a careful history and physical examination, and employing a sonographic triad of longitudinal muscle thickness ≥ 2.5 mm, muscle length ≥ 14 mm, and gastric outlet obstruction, can achieve a prompt diagnosis, avoid unnecessary additional imaging, and improve outcomes in patients with EPS. The findings noted here can be further confirmed through a properly designed prospective study that attempts to correlate age and weight with epidemiologic and sonographic parameters.

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