Original research article

Assessment Of The Predictive Factors For Time To Full Enteral Feeding After Pyloromyotomy For Infantile Hypertrophic Pyloric Stenosis: Observational Study

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Abstract

Aim: the aim of this study to evaluate the predictive factors for time to full enteral feeding after pyloromyotomy for infantile hypertrophic pyloric stenosis**.**

Materials and methods: This is a retrospective study conducted in the Department of Paediatrics surgery Patna Medical College and Hospital, Patna, Bihar, India and Sushrut Child Surgery Centre, Patna, Bihar from October 2016 to January 2020. All children underwent pyloromyotomy were include in this study. Inclusion criteria were diagnosis of isolated IHPS and isolated pyloromyotomy operation. The diagnosis of IHPS was based on clinical symptoms and ultrasound findings. Parameters in demographics and in the preoperative and postoperative period were evaluated against TFEF (hours) using linear regression models.

Results: Total 200children's were included in this study. Out of 200, 160 (80%) boys, with a mean corrected age of 39±15 days, a mean weight of 3897 g, 31 (15.5%) of which were premature, and 17 (8.5%) of which had a severe underlying disease. Median duration of symptoms was 4.2 days (IQR: 8); 151 patients (75.5%) experienced weight loss; and increased bilirubin was seen in 25 patients (12.5%). Mean TFEF was 48±42 hours and mean length of postoperative hospital stay was 67±51 hours. The majority of children (89.5%) were fed according to a feeding schedule. No child required intravenous nutrition. There were 11 children (5.5%) presented with postoperative complications, of which 7 required reoperation. In the univariate analysis, age, weight, severe underlying disease increased bilirubin level, and duration of symptoms were found to affect TFEF. In the multivariate analysis, only age (B: −0.63 (−1.15 to −0.21), p=0.005). and severe underlying disease (B:26.64(3.41 to 51.52),p=0.021)remained as variables significantly affecting TFEF. Hence, for every day of age, the time to fully fed decreased with 0.7 hour, and the presence of an underlying disease increased the time to fully fed with over 1 day. TFEF did not seem to be affected by prematurity, preoperative weight loss, symptom duration, preoperative acid/base balance or electrolyte values, surgical method, or method of postoperative feeding (table 3 and 4).

Conclusion: we conclude that the time to full enteral feeding decreased with higher age and increased in children with a severe underlying disease.

Introduction

Hypertrophic pyloric stenosis (HPS) is a condition affecting infants, in which the pyloric portion of the stomach becomes abnormally thickened and manifests as obstruction to gastric emptying. The infant presents in the first 2 to 12 weeks of life with forceful or projectile nonbilious vomiting after feeding. With protracted vomiting, the emesis may become blood-tinged because of gastritis. Jaundice occurs in about 2% of infants with HPS secondary to defective hepatic glucuronyl transferase activity, which resolves after surgery.[1] The incidence of HPS is about 2 to 4 per 1000 live births in Western populations,[2] but it is less common in African and Asian populations, with a male-to-female ratio of approximately 4:13. The basis for higher male susceptibility is unknown. There is evidence both for and against an increased incidence in the first-born child, and there is familial clustering of HPS, but not in a Mendelian pattern.[3] HPS appears to be more common in bottle-fed infants,[4] in rural populations,[2] and in the summer months (Langer and coworkers, unpublished data). The first clinical description of HPS was by Fabricious Hildanus in 1627, but Harald Hirschsprung's seminal article in 1888 led to our modern understanding of the condition.[5] Although HPS is the most common surgical condition producing emesis in infancy,[1] its etiology is unknown. Whether the condition is congenital or acquired is debated.[6] Neonatal HPS does exist but is very rare.[3] Variations in HPS incidence, trending over time, suggest that unknown environmental factors have an impact.[2] The mechanism underlying the narrow window of diagnosis between approximately 2 and 12 weeks is obscure, but may reflect normal postnatal physiology, such as introduction of enteral feeding, acting on abnormal pyloric tissue.[3] Deficiency of nerve terminals, markers for nerve-supporting cells, peptide containing nerve fibers, mRNA production for nitric oxide synthase and interstitial cells of Cajal have all been found in the muscular layer of the pylorus,[7,8] as well as increased insulin-like and platelet-derived growth factors.[9] This abnormal innervation is postulated to lead to failure of relaxation of the pylorus muscle, increased synthesis of growth factors, and subsequent hypertrophy. It is likely that a spectrum of genetic mutations involving the production of nitric oxide may be responsible for many cases of HPS.[10]

Materials and methods

This is a Retrospective study conducted in the Department of Paediatrics surgery Patna Medical College and Hospital, Patna, Bihar, India and Sushrut Child Surgery Centre, Patna, Bihar from October 2016 to January 2020.

Methodology

All children underwent pyloromyotomy were include in this study. Inclusion criteria were diagnosis of isolated IHPS and isolated pyloromyotomy operation. The diagnosis of IHPS was based on clinical symptoms and ultrasound findings. The postoperative feeding was initiated by the operating surgeon and started 3–4hours after surgery with either free feeding or according to a schedule. The specific feeding schedule started with 20% of the full amount (150mL/kg), and increases with 20% for every meal; if significant vomiting occured, the same amount would be given again at the next meal.

Primary outcome was duration (hours) to full enteral feeding. This was defined by the time from operation to journal notes either stated 'fully fed' or describing correct amount of food intake without emesis. Independent variables were preoperative parameters such as demographical data, type of feeding (breastmilk/ formula), symptoms and blood tests; surgical data such as method of operation; and postoperative parameters including method of feeding and complications. Children with congenital heart disease (CHD) requiring surgery and syndromes were included in the 'severe underlying disease' group. The cut-offs used for ultrasound were pyloric muscle thickness of 4mm or more, and pyloric channel length of 16mm or more.[11] In infants small than 3 weeks the cut-off for thickness was 3.5 mm.[12] Blood samples were taken from venous blood to perform analysis of sodium, potassium, chloride, base excess pH, pCO2 , pO2 , hemoglobin, and liver function tests including alanine transaminase, aspartate transaminase, alkaline phosphatase, gamma-glutamyl transpeptidase, and bilirubin (total). Reference intervals for all analyses were age specific and followed international standards.[13]Thereferenceintervalsfor(total)bilirubin were:<2days of age:<100µmol/L;2–6daysofage:<200µmol/L;7–20 days of age: <100 µmol/L; 21–29 days:<50 µmol/L;and>1 month of age: <22 µmol/L. Complications included were postoperative infection and reoperation.Length of postoperative hospital stay (hours) was counted from operation until discharge.

Statistical analyses

Statistical analyses were performed using IBM SPSS Statistics for Mac, V.24 (IBM). Continuous variables were presented as median or interquartile range (IQR) (no normal distribution) or mean±SD (normal distribution). Normal distribution was tested by evaluation of skewness and kurtosis. Dichotomous variables were presented as the absolute number and percentage of patients. The primary outcome of full enteral feeding was treated as a continuous parameter and different parameters were tested as independent variables, first in a univariate and then in a multivariate linear regression model. The results were presented as beta (B) with 95% confidence interval (CI). Reoperations and complications were also added to the regression analysis since they might have an impact on feeding. Collinearity between the continuous parameters was evaluated. If moderate to strong correlation existed, the final regression model would be tested with and without the different variable(s). A p value <0.05 was considered to be statistically significant.

Results

Total200children's were included in this study. Out of 200,160 (80%) boys, with a mean corrected age of 39±15 days, a mean weight of 3897g, 31 (15.5%) of which were premature, and 17 (8.5%) of which had a severe underlying disease. Median duration of symptoms was 4.2days (IQR: 8); 151 patients (75.5%) experienced weight loss; and increased bilirubin was seen in 25 patients (12.5%). (table 1). Mean TFEF was 48±42hours and mean length of postoperative hospital stay was 67±51 hours. The majority of children (89.5%) were fed according to a feeding schedule. No child required intravenous nutrition. There were 11 children (5.5%) presented with postoperative complications, of which 7 required reoperation (table 2). In the univariate analysis, age, weight, severe underlying disease increased bilirubin level, and duration of symptoms were found to affect TFEF (table 3). In the multivariate analysis, only age (B: −0.63 (−1.15 to −0.21), p=0.005). and severe underlying disease (B:26.64(3.41 to 51.52),p=0.021) remained as variables significantly affecting TFEF (table 4). Hence, for every day of age, the time to fully fed decreasedwith0.7hour, and the presence of an underlying disease increased the time to fully fed with over 1 day. TFEF did not seem to be affected by prematurity, preoperative weight loss, symptom duration, preoperative acid/base balance or electrolyte values, surgical method, or method of postoperative feeding (table 3 and 4). The correlation between the different continuous parameters was overall weak (Spearman's correlation coefficient (r_S) between−0.1and0.1), except the correlation between age and weight (r_S:0.41). The final regression model was tested with and without the weight included and there was little difference in the beta for age (−0.63,95% CI−1.15 to−0.21 and−0.60,95% CI−0.97to−0.21,respectively).When checking for heteroscedasticity, the residuals of the final regression model seemed to have constant variance.

Table 1: Demographics, preoperative data and surgical method in 200 children with infantile hypertrophic pyloric stenosis

Gender (male)	160(80%)
Age (days)	39±15
Breast feeding	141 (70.5%)
Gestational age	39+4 (27+4 to 42+1)
Premature	31 (15.5%)
SGA	17 (8.5%)
Weight (g)	3873±884*
Weight loss	151 (75.1%)†
Severe underlying disease	17 (8.5%)

Increased bilirubin	25 (12.5%)	
Bilirubin (μmol/L)	46 (175)	
Duration of symptoms (d)	4.2days	
Acid base balance	First	Last
Metabolic acidosis	3 (1.5%)	3 (1.5%)
Metabolic alkalosis	60 (30%)	0 (0%)
Base excess	4.8 (−8.2 to 22.5)	0.8 (−7.5 to 9.2)
CO_2	5.9 (1.5)	5.6 (1.1)
Electrolyte balance	First	Last
Hyponatremia	22 (11%)	12 (6%)
Chloride	102 (51)	112 (56)
Lactate	3 (1.5)	3 (1.5)
Preoperative LOH (days)	2 (1)	
Operation		
Umbilical incision	120 (60%)	
Right upper quadrant incision	83 (41.5%)	

Values presented as absolute numbers and percentage of patients; n (%), mean±SD, median (min to max) or as median (IQR)

Table 2: Postoperative data and outcome in 175 children operated for infantile hypertrophic pyloric stenosis

Method of feeding	
Ad libitum	21 (10.5%)
Scheduled	179 (89.5%)
Time fully fed (hours)	48±42
Complications	11 (5.5%)
Reoperation	7 (3.5%)
Postoperative LOH (hours)	67±51
Readmission (<30 days)	7(3.5%)

Values presented as absolute numbers and percentage of patients; n (%) and mean±SD

Table 3: Univariate regression of demographics, preoperative and postoperative data and the effect on time in hours to full enteral feeding

Parameter	**B (95% CI)**	**P value**
Gender (male)	−13.7(−25.37 to 1.41)	0.070
Corrected age (days)	−0.66(−0.92 to −0.37)	**<0.001**
Breast feeding (yes)	−2.7 (−14.5 to 8.51)	0.612
Premature (yes)	7.4(−7.32 to 20.95)	0.325
SGA (yes)	15.5 (−4.5 to 35.19)	0.185
Weight (kg)	−4.8 (−9.41 to −0.52)	**0.004**
Weight loss (yes)	−1.6 (−13.18 to 9.88)	0.789
Severe underlying disease (yes)	34.4 (14.97 to 53.5)	**0.001**
Increased bilirubin (yes)	20.7 (7.28 to 35.54)	**0.003**
Bilirubin (μmol/L)	−0.03 (−0.172 to 0.121)	0.754
Duration of symptoms	−0.78 (−1.55 to −0.042)	**0.041**

pH	−5.7 (−79.7 to 68.77)	**0.865**
Base excess	0.57 (−0.68 to 1.87)	**0.332**
pCO2	4.4 (−0.43 to 9.27)	**0.071**
First electrolyte balance		
Sodium (mmol/L)	0.94 (−1.05 to 2.91)	0.332
Chloride (mmol/L)	0.37 (−0.57 to 1.28)	0.412
Lactate (mmol/L)	−1.8 (−6.48 to 3.04)	0.487
Operation (umbilical)	−1.4 (−11.77 to 8.95)	0.712
Method of feeding	14.6 (−1.31 to 31.26)	0.076
Reoperation (yes)	0.12 (−33.1 to 33.15)	0.985
Complication (yes)	2.17 (−22.5 to 26.4)	0.821

Linear regression presented as beta (B) with 95% CIs. Signifcant p-values (<0.05) in bold.SGA, small for gestational age

Table 4: Multivariate linear regression of variables predicting longer time in hours to full enteral feeding in 200 children operated for infantile hypertrophic pyloricstenosis

Parameter	**B (95% CI)**	**P value**
Gender (male)	−9.86 (−26.12 to 6.51)	0.212
Corrected age (days)	−0.63 (−1.15 to −0.21)	**0.005**
Breast feeding (yes)	−2.31 (−15.16 to 10.46)	0.729
Premature (yes)	12.08 (−10.08 to 34.24)	0.256
SGA (yes)	4.27 (−23.53 to 32.05)	0.778
Weight (kg)	−2.1 (−3.4 to 0.56)	0.821
Weight loss (yes)	−1.13 (−14.35 to 12.12)	0.833
Severe underlying disease (yes)	26.64(3.41 to 51.52)	**0.021**
Increased bilirubin (yes)	4.32 (−11.73 to 20.37)	0.587
Duration of symptoms (hours)	−0.10 (−1.07 to 0.91)	0.841
First acid base balance		
pH	36.51 (−151.41 to 224.25)	0.745
Base excess	0.43 (−2.17 to 3.04)	0.722
pCO_2	2.81 (−6.85 to 12.41)	0.563
First electrolyte balance		
Sodium (mmol/L)	1.14 (−1.22 to 3.51)	0.324
Chloride (mmol/L)	−0.58 (−5.99 to 4.83)	0.887
Lactate (mmol/L)	−1.02 (−5.73 to 2.51)	0.624
Operation (umbilical incision)	−2.39 (−13.51 to 8.82)	0.687
Method of feeding (schedule)	7.41 (−9.66 to 25.47)	0.312
Reoperation (yes)	−15.24 (−39.16 to 41.2)	0.522
Complication (yes)	0.854 (−39.2 to 41.8)	0.936

Linear regression presented as beta (B) with 95%CIs. Significant p-values (<0.05) in bold. SGA, small for gestational age

Discussion

In children who underwent pyloromyotomy for IHPS, a higher age decreased TFEF, while presence of underlying disease was associated with increased duration. There is a significant value in evaluating preoperative factors as predictors for worse postoperative outcome. Such evaluations improve preoperative and postoperative information to caregivers; they also provide away to improve preoperative and postoperative care. Further, being able to stratify patients in different risk groups would be of great importance in future studies evaluating different surgical methods or different postoperativefeedingregimens,asdescribedearlier.[14] We evaluated several parameters of patient characteristics, preoperative symptoms and signs of dehydration, including laboratory values, feeding method and operation method, but only two of these parameters appeared to affect TFEF. Our hypothesis that metabolic alkalosis and/or hypochloremia at admission, and symptom duration, would increase the duration of reaching goal feeds was not supported. In addition, neither prematurity, preoperative weight loss, other preoperative acid/base balance or electrolyte values, surgical method, nor method of post operative feeding had an effect on TFEF. The finding of higher age decreasing and severe underlying disease increasing TFEF is not unexpected. Unfortunately, these parameters also cannot be influenced and we therefore cannot modify our preoperative or postoperative management of children with IHPS based on this study. The strength of this study is that all children were treated at the same center and that the management of children with IHPS, besides operation technique, did not change during the study period. Another strength is the full evaluation of several parameters and a multivariate analysis which in comparison with the literature is sparsely conducted before.

A few studies before the present one have tried to evaluate how different preoperative parameters affect postoperative outcome, either defined as emesis, time to goal intake, or length of postoperative hospital stay. A prospective study found that the degree of hypokalemic, hypochloremic, and metabolic alkalosis correlated with the number of postoperative emesis episodes and TFEF.[15]The authors also concluded that the duration of dehydration and failure to thrive was correlated with poor outcome since there were inverse correlations between the number of episodes of postoperative emesis and time to goal intakes with weight at admission. Results from a randomized trial found that low chloride levels increased TFEF.[16] Our results do not support either of these results despite roughly the same number of included patients; hence the present study was in that sense not under powered. The parameters found to cause longer time to full goals in previous studies[15,16] were mainly laboratory values that should be less affected by our retrospective design. On the other hand, the primary outcome of TFEF was in the present study extracted from charts and could of course be subject to the disadvantages of a retrospective design. Other studies have found a correlation of post- operative emesis or longer hospital stay (not specifically TFEF) with weight[17] and age at surgery,[18,19] symptom duration[20,21]and pyloric thickness onultrasound.[18] None of these results were supported by our study. However, none of these retrospective studies included a multivariate analysis and the results could therefore be questioned. A severe underlying disease, defined in our study as CHD requiring surgery, or a syndrome, was also associated with increased risk of longer TFEF. A study of IHPS comparing postoperative outcomes between patients with and without CHD showed that a comorbidity lengthened hospital stay.[22] In isolated cases of IHPS, time until full feed of ten equals length of hospital stay, but it seems harder to distinguish the two when a comorbidity is the evaluated factor. We believe that this is due to other treatment requirements which may prolong or hinder the advancement of reaching goal feeds. Children with CHD may also need extra calories. All children did not have the same post operative feeding regimen which was known to affect times to full enteral feeds.[23,24]

Conclusion

We conclude that the time to full enteral feeding decreased with higher age and increased in children with a severe underlying disease.

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