PAPERS

Paediatric gastro-oesophageal reflux: prognostic indicators from pH monitoring

K Varty, D Evans, L Kapila

Abstract

The original diagnostic 24 hour pH monitoring data in 57 children with gastro-oesophageal reflux (GOR) were retrospectively reviewed after a minimum of one year follow up. The tracings of children who responded to medical treatment were compared with those who failed to respond and required a fundoplication. Children with GOR secondary to oesophageal atresia/tracheo-oesophageal fistula and neurological conditions (n=12) were analysed separately from those with primary GOR (n=45). Children with primary GOR requiring a fundoplication (n=9) had increased daytime reflux. The percentage time pH<4 was the best discriminator (21% v 7%) with a threshold of 18% giving a 92% specificity and a 70% sensitivity. For children with secondary GOR the percentage time pH<4 at night was significantly higher (29% v 3.7%) in those requiring a fundoplication (n=5). A threshold of 18% gave an 80% specificity and an 86% sensitivity. These results show that both daytime and night time pH monitoring data can be of prognostic value in different subgroups of children with GOR. A percentage time pH<4 of greater than 18% was a useful threshold to apply when evaluating the pH monitoring data. (Gut 1993; 34: 1478-1481)

The diagnosis of gastro-oesophageal reflux (GOR) using prolonged (12-24 hours) pH monitoring was first reported in adults by Miller and colleagues¹ in 1964, and in children by Jolley and co-workers² in 1978. With modern portable systems ambulatory recording has become more acceptable to children and reflux can be seen during 'normal' activities, postures, and diet. As a result, 24 hour pH monitoring has become the standard technique for the diagnosis of GOR in children. In addition to a diagnostic role it has been suggested that pH monitoring may also be of predictive value identifying patients unlikely to respond to medical treatment. No clear prognostic indicators have emerged, however, with varying reports suggesting that a continuous pattern of reflux,³ night time reflux,⁴ and the number of episodes of reflux⁵ may all have a predictive value. Our own initial experience with a small number of patients suggested an overall 24 hour reflux index may even be of some predictive value.⁶ The aim of this study was to further assess the predictive value of pH

monitoring in children with GOR by correlating pH monitoring data with clinical outcome.

Patients and methods

From 1 March 1987 to 28 February 1990, 24 hour ambulatory oesophageal pH monitoring was performed on 95 children with symptoms suggestive of GOR. Monitoring failed in four cases because of technical problems and 25 children had normal recordings (26%). Complete pH monitoring data and clinical follow up data were available for 57 of 66 children with abnormal recordings (86%) and analysis of these data formed the basis for this study. Thirty six (63%) of these children were referred from their own general practitioner, 14 (24%) were referred from local paediatric outpatient clinics, and seven (13%) were tertiary referrals from other centres.

Oesophageal pH monitoring was performed using a 6 French gauge glass pH probe (Graph probe, Zinetics) and a Flexilog 1010 24 hour ambulatory pH recorder (both supplied by Oakfield Instruments, Eynsham, Oxon, UK). The pH electrode was positioned in the oesophagus 5 cm above the gastro-oesophageal junction using the pH profile on withdrawal from the stomach. The position was confirmed with a chest x ray. A standard silver chloride surface electrocardiograph electrode was used as a reference electrode. Monitoring was continued for 24 hours with a normal diet. Events, the time spent asleep, and posture were recorded using the event button on the recorder. The recording was analysed on an IBM computer using the Flexilog analysis program (Oakfield Instruments, Eynsham, Oxon). Table I shows the pH monitoring criteria used to diagnose GOR. These were derived from studies in adults as we have not, for ethical reasons, performed extended pH monitoring on asymptomatic children. Our criteria do not differ greatly, however, from those recommended in other centres.⁷ A reflux episode was defined as any drop in pH to below 4 for at least 20 seconds' duration. A diagnosis of GOR was made if two or more of the above criteria were abnormal.

TABLE I Twenty four hour pH monitoring criteria used to diagnose gastro-oesophageal reflux

Variable	Day	Night
% Time pH<4	6.3	1.2
No of episodes	24	6
No of episodes >5 minutes' duration	3	0
Longest episode (mins)	9.2	4.5

Department of Paediatric Surgery, Queens Medical Centre, Nottingham
K Varty
D Evans
L Kapila

Correspondence to:
Mr K Varty, Department of Surgery, Clinical Sciences Building, Leicester Royal Infirmary, Leicester LE2 7LX.

Accepted for publication
10 March 1993

TABLE II Primary gastro-oesophageal reflux. Comparison of age, sex, and presenting features between medical and surgery groups. Figures in parentheses are percentages

	Medical (n=36)	Surgery (n=9)
Median age (months)	6.5	12
Range	1-48	1-60
M:F	19:17	7:2
Presenting features		
Vomiting	26 (72)	8 (88)
Haematemesis	3 (8)	3 (33)
Failure to thrive	3 (8)	1 (11)
Weight loss	5 (14)	3 (33)
Abdominal pain	5 (14)	3 (33)
Dysphagia	4 (11)	1 (11)
Respiratory	12 (33)	2 (22)

TABLE III Secondary gastro-oesophageal reflux. Comparison of age, sex, and presenting features between medical and surgery groups. Figures in parentheses are percentages

	Medical (n=7)	Surgery (n=5)
Median age (months)	24	6*
Range	12-84	3-60
M:F	3:4	2:3
Presenting features		
Vomiting	2 (29)	3 (60)
Haematemesis	1 (14)	1 (20)
Failure to thrive	0 (0)	5 (100)*
Weight loss	1 (14)	4 (80)
Abdominal pain	1 (14)	0 (0)
Dysphagia	2 (29)	0 (0)
Respiratory	4 (57)	4 (80)

*= $p < 0.05$ Wilcoxon's rank sum test and χ^2 test.

A barium meal examination or oesophago-scopy was performed in 88% of cases and showed no important underlying abnormalities – that is, partial thoracic stomach, large hiatus hernia. Oesophageal biopsy was restricted to those children with severe GOR to confirm the presence of oesophagitis before surgery. None of the children had previously received treatment for GOR. In 12 cases GOR was secondary to either severe neurological impairment (6) or post-oesophageal atresia and tracheo-oesophageal fistula repair (6). These children were considered separately from the children with primary GOR (n=45) when analysing the results.

All children received an initial course of medical treatment consisting of upright posture and milk thickening agents in infants, Gaviscon 5 ml four times daily (or infant Gaviscon sachets where appropriate) and cimetidine 20–30 mg/kg daily in three divided doses. Where the clinical response to treatment was poor at six weeks, additional treatment with prokinetic agents was used. Metoclopramide (1 mg twice or thrice daily according to age) was used in the early part of the study, and cisapride (0.2 mg/kg thrice daily) more recently. Eight children were treated initially with cisapride and Gaviscon for six weeks as part of a trial running simultaneously with this study, and non-responders at six weeks were switched to our normal treatment regimen. Medical treatment was continued while symptoms improved and gradually withdrawn when symptoms were controlled.

The clinical data were retrospectively reviewed after a minimum follow up of one year (median 27 months). The children were divided into two groups; responders to medical treatment

(medical group) and non-responders requiring a fundoplication (surgery group). Tables II and III show the ages, sex, and presenting features of these two groups subdivided into primary and secondary GOR. The selection of children for fundoplication was based on clinical criteria combined with the results of oesophagoscopy showing uncontrolled oesophagitis and was not based on the results of the original diagnostic pH monitoring tracing. These tracings were therefore analysed in this study to look for any prognostic indicators of the response to medical treatment that might be of value in the future. The day and night time periods of these tracings were analysed separately.

STATISTICS

The pH monitoring scores and ages were compared using the Wilcoxon rank sum test. Differences in the presenting features between the groups of children were tested using χ^2 analysis. Prognostic thresholds were derived from the data using receiver operating characteristic curves.

Results

Nine of the children with primary GOR required a fundoplication (20%). There was no significant difference in age or presenting features between the children in the medical and surgery groups (Table II). One child in the surgery group had pH monitoring performed on two occasions before starting treatment and both these recordings were used for analysis giving a total of 10 sets of data for this group. Table IV summarises the pH monitoring data. The children in the surgery group had significantly higher daytime scores for all the variables analysed. The overall percentage time pH<4 was the best discriminator (21% v 7%) with a threshold of 18% giving a 92% specificity and a 70% sensitivity for predicting failure to respond to medical treatment. There was no significant difference in night time scores between the two groups.

Five of the children with secondary GOR required a fundoplication (42%), three with neurological impairment and two after tracheo-oesophageal fistula repair. Younger age and presentation with failure to thrive were significantly more common in the surgery group (Table III). Respiratory symptoms were more common in all of these children compared with those with primary reflux. Table V summarises the pH

TABLE IV Primary gastro-oesophageal reflux. Comparison of pH monitoring scores for surgery (n=9) and medical (n=36) groups. Values are medians with interquartile ranges in parentheses

	Daytime		Night time	
	Surgery	Medical	Surgery	Medical
% Time pH<4	21 (9-33)	7* (4-11)	6 (2-18)	4 (1-8)
Longest episode (mins)	21.4 (9-30)	9** (4-14)	8.6 (3-20)	10 (2-23)
No of episodes	30 (15-35)	17** (7-21)	3.5 (1-5)	2 (1-6)
No of episodes >5 minutes' duration	4 (2-6)	1.5** (0-2)	1 (0-1)	1 (0-2)

*= $p < 0.01$, **= $p < 0.05$ Wilcoxon's rank sum test.

TABLE V Secondary gastro-oesophageal reflux. Comparison of pH monitoring scores for surgery (n=5) group and medical (n=7) group. Values are medians with interquartile ranges in parentheses

	Daytime		Night time	
	Surgery	Medical	Surgery	Medical
% Time pH<4	15.6 (13–23)	4.8 (3–14)	29 (22–32)	3.7** (1–9)
Longest episode (mins)	11 (9–24)	4.3 (4–8)	30 (13–41)	2.6 (1–6)
No of episodes	9 (6–12)	11 (9–15)	6 (2–6)	2 (1–6)
No of episodes >5 minutes' duration	3 (2–4)	0 (0–3)	1 (1–4)	0 (0–1)

**=p<0.05 Wilcoxon's rank sum test.

monitoring data. The percentage time pH<4 at night was significantly higher in the surgery group. The duration of the longest episode at night was also higher but just failed to reach statistical significance with this small number of cases. A threshold of 18% for the night time pH<4 gave an 80% specificity and an 87.5% sensitivity for predicting failure to respond to medical treatment. There was no significant difference in daytime scores between the two groups.

Discussion

Two different patterns of reflux have emerged in this study associated with a poor response to medical treatment. Prolonged daytime reflux occurred in children with primary reflux who came to surgery whereas night time reflux was more severe in children with reflux secondary to neurological conditions and tracheo-oesophageal fistula who required surgery.

The importance of night time (sleep) reflux in association with respiratory symptoms is now well recognised.^{8,9} The high incidence of respiratory symptoms in children with reflux secondary to neurological disorders and tracheo-oesophageal fistula is also well reported.^{10–13} The findings in the secondary reflux group in this study highlight both of these associations. Eighty per cent of the children with severe reflux presented with respiratory symptoms and had a prolonged night time reflux. An important component of this prolonged night time reflux was the increased length of the reflux episodes resulting in a prolonged ZMD (mean duration of reflux episode)⁸ in every case. Jolley and co-workers noted a delayed clearance of single reflux episodes in children with nocturnal reflux suggesting an impaired pharyngo-oesophageal mechanism may be the underlying disorder.⁹ Such a disorder of peristalsis has been reported in children with tracheo-oesophageal fistula¹⁴ and Sondheimer has suggested that central damage to vagal nuclei or oesophageal ischaemia, or both, as a result of birth asphyxia may result in a similar disorder of peristalsis in children with cerebral palsy.¹⁵ In children with nocturnal GOR this coincides with arousal periods when inappropriate lower oesophageal sphincter relaxations occur.¹⁶ Children with neurological disorders frequently have a low lower oesophageal sphincter pressure, which exacerbates this problem.¹⁵ A combination of inappropriate lower oesophageal

sphincter relaxations and deranged oesophageal peristalsis results in the pattern of reflux we have seen in the children with secondary GOR requiring surgery. Sondheimer found that lower oesophageal sphincter pressure was higher in neurologically impaired children who responded to medical treatment, though overall these children as a group have a poor response to medical treatment.¹⁵

The pattern of reflux was very different in children with primary reflux. Such a clear association between daytime reflux and outcome has not been previously described. Few studies have presented, however, an analysis of subgroups of children based on cause as in this study. Combining the data from the primary and secondary groups in this study would have masked the separate significance of the day and night time reflux in each group. In particular our results in the primary reflux group differ from the findings of Colson and colleagues who carried out a similar study but in a very heterogeneous population of children.⁴ They found sleep reflux and acid clearing time to be the most useful predictors of a poor response to medical treatment. An analysis of a subgroup of children excluding those with neurological conditions and after tracheo-oesophageal fistula repair still found sleep reflux to be the best predictor of outcome though daytime reflux was also significantly different in the two groups. These groups were poorly matched for age, however, and a number of children had had a Nissen fundoplication with a recurrence of GOR. A comparison with our population of generally younger children all before surgery is therefore difficult to make. A more homogeneous population of children with primary GOR was studied by Cucchiara and colleagues¹⁷ who found that oesophagitis was not associated with nocturnal reflux. It has been suggested that feeding is a potential cause of GOR in these children with daytime reflux and analysis of postprandial tracings is a sensitive method for detecting this.¹⁸ In our experience we have not found such an analysis of tracings to be helpful (data not shown) and do not routinely perform this. Interestingly Cucchiara also found that postprandial analysis of tracings was unhelpful.¹⁷

In conclusion, increasing emphasis has been placed on night time reflux because of its association with serious respiratory problems in children¹⁸ and with oesophagitis in adults.¹⁹ But this viewpoint has been challenged by other studies showing a correlation between daytime reflux and oesophagitis in both adults²⁰ and children.¹⁷ While there remains uncertainty on this subject one possible conclusion is that both daytime and night time reflux can be of importance in different subgroups of patients with GOR as shown in this study.

We are grateful to the staff of the Department of Surgery, University Hospital, Nottingham for performing the pH monitoring.

- 1 Miller FA, Dovale J, Gunther T. Utilization of the inlying pH probe for evaluation of acid-peptic diathesis. *Arch Surg* 1964; 89: 199–203.
- 2 Jolley SG, Johnson DG, Herbst JJ, Pena AR, Garnier RC. An assessment of gastroesophageal reflux in children by extended pH monitoring of the distal esophagus. *Surgery* 1978; 84: 16–23.

- 3 Jolley SG, Johnson DG, Herbst JJ, Matlak ME. The significance of gastroesophageal reflux patterns in children. *J Pediatr Surg* 1981; **16**: 859-75.
- 4 Colson DJ, Campbell CA, Wright VA, Watson BW. Predictive value of oesophageal pH variables in children with gastro-oesophageal reflux. *Gut* 1990; **31**: 370-3.
- 5 Ramenofsky ML, Powell RW, Curreri PW. Gastroesophageal reflux: pH probe directed therapy. *Ann Surg* 1986; **203**: 531-5.
- 6 Evans DF, Haynes J, Jones JA, Stower MJ, Kapila L. Ambulatory esophageal pH monitoring in children as an indicator for surgery. *J Pediatr Surg* 1986; **21**: 221-3.
- 7 Boyle JT. Gastroesophageal reflux in the pediatric patient. *Gastroenterol Clin North Am* 1989; **18**: 315-35.
- 8 Halpern LM, Jolley SG, Tunnell WP, Johnson DG, Sterling CE. The mean duration of gastroesophageal reflux during sleep as an indicator of respiratory symptoms from gastro-oesophageal reflux in children. *J Pediatr Surg* 1991; **26**: 686-90.
- 9 Jolley SG, Herbst JJ, Johnson DG, Matlak ME, Book LS. Esophageal pH monitoring during sleep identifies children with respiratory symptoms from gastroesophageal reflux. *Gastroenterology* 1981; **80**: 1501-6.
- 10 Sondheimer JM, Morris BA. Gastroesophageal reflux among severely retarded children. *J Pediatr* 1979; **94**: 710-4.
- 11 Wesley RJ, Coran AG, Sarahan TM, Klein MD, White SJ. The need for evaluation of gastroesophageal reflux in brain damaged children referred for feeding gastrostomy. *J Pediatr Surg* 1981; **16**: 866-71.
- 12 Dudley NE, Phelan PD. Respiratory complications in long term survivors of esophageal atresia. *Arch Dis Child* 1976; **51**: 279-82.
- 13 Jolley SG, Johnson DG, Roberts CG, Herbst JJ, Matlak ME, McCambs A, *et al.* Patterns of gastroesophageal reflux in children following repair of esophageal atresia and distal TOF. *J Pediatr Surg* 1980; **15**: 857-62.
- 14 Shepart R, Fenn S, Siber WK. Evaluation of esophageal function in postoperative esophageal atresia and trache-oesophageal fistula. *Surgery* 1966; **59**: 608-15.
- 15 Sondheimer JM, Morris BA. Gastroesophageal reflux among severely retarded children. *J Pediatr* 1979; **94**: 710-4.
- 16 Werlin SL, Dodds WJ, Hogan WJ, Arndorfer RC. Mechanisms of gastroesophageal reflux in children. *J Pediatr* 1980; **97**: 244-51.
- 17 Cucchiara S, Staaiano A, Casali LG, Paone FM. Value of the 24 hour intraoesophageal pH monitoring in children. *Gut* 1990; **31**: 129-33.
- 18 Orenstein SR, Orenstein DM. Gastroesophageal reflux and chronic respiratory disease in children. *J Pediatr* 1988; **112**: 847-54.
- 19 Robertson D, Aldersley M, Shepherd H, Smith CL. Patterns of acid reflux in complicated oesophagitis. *Gut* 1987; **28**: 1484-8.
- 20 De Caestecker JS, Blackwell JN, Pryde A, Heading RC. Daytime gastro-oesophageal reflux is important in oesophagitis. *Gut* 1987; **28**: 519-26.