Original Paper

Usefulness of ultrasound as a diagnostic method of pathological acid reflux in comparison with esophageal pH measurement

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Abstract

Introduction: the gold standard for diagnosis of acid reflux in paediatric patients is 24-hour pH monitoring. Ultrasound is a non-invasive technique and few studies have compared it with pH monitoring.

Methods: prospective, observational and analytical study. We performed an ultrasound examination in patients in whom pH monitoring was indicated before performance of the latter test. We analysed the sonographic variables proposed by the Ultrasound Group of the SEGHNP (modified Gomes 1991 criteria), with 2 or more abnormal sonographic parameters indicating the presence of pathological acid reflux.

Results: the study included 32 patients, 68.8% (*n* = 22) male, aged 1 month to 13 years. The results of pH monitoring were pathological in 59.3% (*n* = 19). We did not find an association between the sonographic diagnosis of reflux according to the criteria proposed by SEGHNP and the diagnosis of reflux based on pH monitoring (*p* = 0.169). We found a sensitivity of 60% and a specificity of 61.5% with the use of ultrasound, with a positive predictive value (PPV) of 70.58% and a negative predictive value of 53.3%. When we compared each ultrasound variable separately to the presence of reflux determined by pH monitoring, we did not find any significant associations. However, we found a statistically significant association between the combination of an angle of His in the pathological range and an abdominal oesophagus length of less than 1.3 cm on ultrasound and the detection of acid reflux by pH monitoring (*p* = 0.033), with a high PPV, positive likelihood ratio and pre-test probability (88.9%, 5.47 and 89.1%, respectively) and a low false-positive rate (7.7%).

Conclusion: in our sample, we did not find an association between the detection of pathological acid reflux by pH monitoring and the ultrasound parameters proposed by the SEGHNP, but we did find an association with the combined presence of an abdominal oesophagus length of less than 1.3 cm and an angle of His greater than 110°.

Key words:
- Abdominal ultrasound
- Oesophageal pH monitoring
- Gastroesophageal reflux
- Gastroesophageal reflux disease

Utilidad de la ecografía como método diagnóstico de reflujo ácido patológico en comparación con la pHmetría esofágica

Resumen

Introducción: el *gold standard* para el diagnóstico de reflujo ácido en Pediatría es la pHmetría 24 horas. La ecografía ha demostrado ser una técnica incruenta y existen pocos estudios que la comparen con la pHmetría.

Métodos: estudio prospectivo, observacional y analítico. Se realizó estudio ecográfico a pacientes con indicación de pHmetría, y previa a esta. Se determinaron variables ecográficas propuestas por el grupo de ecografía de la SEGHNP (Gomes 1991 modificado), considerando la presencia de reflujo ácido patológico si tenía dos o más parámetros alterados.

Resultados: se incluyeron 32 pacientes, 68.8% (*n* = 22) varones, entre 1 mes y 13 años. Tenían pHmetría patológica el 59.3% (*n* = 19). El diagnóstico de reflujo por ecografía según lo propuesto por la SEGHNP no se relacionó con el diagnóstico de reflujo ácido por pHmetría (*p* = 0.169). La ecografía presentó una sensibilidad de 60% y una especificidad del 61.5%, con valor predictivo positivo (VPP) de 70.58% y valor predictivo negativo de 53.3%. Al analizar cada variable ecográfica y compararla con la presencia de reflujo por pHmetría no hubo datos significativos. Sin embargo, un ángulo de His patológico y una longitud del esófago abdominal menor de 1.3 cm se asociaron estadísticamente con reflujo ácido por pHmetría (*p* = 0.033), obteniendo un VPP, cociente de probabilidad positivo y probabilidad preprueba positiva altos (88.9%; 5.47; 89.1%, respectivamente), con proporción de falsos positivos bajo (7.7%).

Conclusión: en nuestra población estudiada, los criterios ecográficos propuestos por la SEGHNP no se relacionan con pHmetría patológica, pero sí la presencia de un esófago abdominal menor de 1.3 cm junto a un ángulo de His mayor de 110°.

Palabras clave:
- Ecografía abdominal
- Enfermedad por reflujo gastroesofágico
- pHmetría
- Reflujo gastroesofágico

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INTRODUCTION

Gastro-oesophageal reflux (GOR) is one of the most frequent gastrointestinal complaints in children. It consists of the retrograde passage of gastric contents to the oesophagus through the lower oesophageal sphincter, with or without regurgitation or vomiting.[1,2] However, when this occurs with sufficient frequency and intensity to overwhelm the defences of the oesophageal mucosa and cause disease manifesting with different possible symptoms, typical or atypical, overt or silent, the term gastro-oesophageal reflux disease (GORD) applies.

Gastro-oesophageal reflux disease elicits considerable anxiety in families and is a frequent reason to seek paediatric medical care, but its actual prevalence is unknown. In most typical cases of GORD, especially in older children, a detailed history and physical examination suffice to make the diagnosis. However, and based on the most recent guideline on the management of GORD published in collaboration by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN),[1] performance of pH monitoring as part of the diagnostic evaluation of pathological acid reflux is indicated for the purpose of establishing an association between symptoms suggestive of GOR and episodes of gastric reflux, in patients with GOR that does not respond well to appropriate treatment and to assess the effectiveness of treatment, be it medical or surgical.

Intra-oesophageal measurement of pH with 24-hour monitoring is an invasive technique that is not available in every facility consisting of the insertion of a feeding tube to the distal end of the oesophagus guided by imaging and recording of pH values at the site for 18-24 hours. This test assesses different variables, most importantly the reflux index (IR). This index corresponds that the time in which gastric acid can be found in the distal oesophagus, and is considered pathological from 10% in infants and 5% from 1 year of age. The threshold for a pathological IR in preterm infants has been established at 5%. Another aspect assessed in pH monitoring is the symptoms that are associated with acid reflux, giving rise to the symptom index (SI), considered pathological from 50%, and the symptom sensitivity index (SSI), considered pathological from 10%.[3]

On the other hand, ultrasound is a painless, non-invasive and radiation-free technique, so it is very useful in the context of paediatric gastrointestinal disease. During a GOR episode, the retrograde passage of gastric contents to the oesophagus produces a pattern of bright linear echoes, representing microbubbles of air, that fills the lower oesophagus.[4] This technique offers the advantage of not exposing the patient to irradiation, and allows ruling out distal obstruction. It is not widely used to assess GOR, and recent guidelines do not recommend its routine performance, but note that in experienced hands it could be useful for screening and establish a series of measurements of the abdominal oesophagus, the angle of His, the clearance of the oesophagus and the number of reflux episodes as variables to document for the purpose of establishing the diagnosis by ultrasound.[5] Fallahi *et al* conducted a study in 56 cases and 50 controls using ultrasound, pH monitoring and endoscopy and found that ultrasound offered a sensitivity of 76% and a specificity of 100% for diagnosis of GORD.[6] Pezzazi *et al*.[7] conducted another study in preterm infants with performance of ultrasound examinations and pH monitoring and found that ultrasound offered a low sensitivity of 38% but a high specificity and positive predictive value of 100% in this subset of patients.

Furthermore, point-of-care ultrasound may be useful and relevant in the practice of paediatrics at the primary care level, as it could contribute to improving care in terms of effectiveness and efficiency and to simplifying paediatric management protocols while reducing iatrogenesis.

Thus, our aim was to establish the usefulness of ultrasound for diagnosis of acid reflux in the paediatric population compared to oesophageal pH monitoring.

MATERIAL AND METHODS

Design and objectives

We conducted an observational descriptive and analytical study in which we compared the results of the ultrasound scan of patients with suspected acid reflux disease to the results of oesophageal pH monitoring in order to establish the usefulness of ultrasound in the management of this disease.

Inclusion criteria

We included every case in which distal oesophageal pH monitoring was requested to rule out acid reflux disease between April 2017 and January 2019, recruiting patients from the paediatric gastroenterology, neonatology and paediatric inpatient care departments of a regional hospital. Before including patients in the study, we informed the parents and obtained their signed consent.

Study variables and data collection

Once patients were included in the study, we filled out a data collection form that included demographic, somatometric and clinical data. All patients underwent a detailed history-taking and comprehensive physical examination. Later on, sonographic data was collected either at the clinic or in the inpatient ward (if the patient was hospitalized) before the pH monitoring, so the sonographic findings were interpreted before pH monitoring. We collected pH data after analysing the results (*Digitrapper*).

After interpreting the results of testing in the patients included in the study, we notified those that required medical intervention. We also made a statistical analysis of the data.

Oesophageal pH monitoring

Patients were admitted to the hospital to undergo 24-hour pH monitoring. The catheter with the probe was inserted while monitoring the patient until reaching the distal third of the oesophagus, and correct placement verified by imaging. The ideal depth of insertion was calculated with the following formula:

$$\text{Height (cm)} \times 0.24 + 5.2$$

Subsequently, the probe was connected to a static memory data storage system similar to a Holter monitor programmed to identify different situations (whether the patient is eating, lying down, standing) and events (coughing, regurgitation, irritability, desaturation...). Before starting the test, the presence of intercurrent disease was ruled out and discontinuation of reflux medication scheduled for at least 48 hours before the test and antacid medication (ranitidine, omeprazole) 72 to 96 hours before. We recorded data for the following variables: reflux index or percentage of the total time with an oesophageal pH less than 4, total number of reflux episodes, number of reflux episodes lasting longer than 5 minutes, duration of longest reflux episode, symptom index (SI) and symptom sensitivity index (SSI). We considered an IR > 10% in infants and an IR > 5% in newborns, preterm infants and children 1 year and older indicative of pathological reflux. We also considered an SSI value > 50% and an SI > 10% indicative of a causal relationship between the event under study and the presence of acid reflux.

Ultrasound of the gastro-oesophageal junction

The oesophageal and gastric ultrasound examination was performed with a full stomach and before placement of the pH probe and interpretation of pH monitoring results (blinded assessment). All the examinations were performed by the same observer and prior to the obtention of pH monitoring results. The sonographic variables assessed in the evaluation were the parameters proposed by the Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica (Spanish Society of Gastroenterology, Hepatology and Paediatric Nutrition, SEGHNP) in the protocol for the ultrasound diagnosis of GOR,[5,10] according to which patho-

logical reflux was defined as the presence of 2 or more abnormal sonographic parameters.

Ultrasound measurements[5]: length of abdominal oesophagus (LAbO), 1.5 to 3.5 cm depending on age; shape of the cardias (CS), abnormally short or funnel-shaped canal; angle of His (AH), normal if acute/straight, pathological if obtuse/flat/greater than 110°; number of GER episodes in 10 minutes, abnormal if > 3; distal oesophageal clearance time, abnormal if > 0 seconds; closure of the cardia (CC), complete or incomplete.

Statistical analysis

The necessary sample size was calculated with the EPIDAT software (over a population with performance of 30 pH monitoring tests a year, approximately 50% of which had pathological results). To detect significant differences with a power of 80% defining statistical significance as a *p*-value of less than 0.05, the necessary sample size was 27 patients.

We collected data in a Microsoft Office Excel 2010 spreadsheet. To analyse associations, the data were subsequently processed with the software SPSS 22.0 (IBM). We assessed the distribution of continuous data by means of the Shapiro-Wilk test, as the sample size was less than 50. We used the χ^2 test to compare dichotomous data and the Fisher exact test in case the expected frequency was less than 5 in any of the variables under study. We compared continuous variables with the Student *t* test if the data followed a normal distribution, and otherwise with the Mann-Whitney *U* test. We defined statistical significance as $p < 0.05$. We assessed the correlation between continuous variables with the Spearman test since the data for some of the variables did not follow a normal distribution. We also applied a critical appraisal skills programme tool to assess the diagnostic tests (calculator available at CASPe.org).

Ethical considerations

The study was approved by the research ethics committee of the hospital. Patient data was kept confidential, accessible only to the research team. We assigned each child a numerical code for identification in order to protect their identity.

Limitations

We experienced a series of limitations in performing the study. Having to perform al ultrasound taking measurements that require a minimum duration of 15 minutes to ensure visualization of the sonographic structures in a quiet environment and a calm patient turned the test into a subjective and observer-dependent measure, and the data cannot be extrapolated to populations different from the one under study. We also found a high pre-test probability of a positive result (prevalence of disease of nearly 60% in our setting and performance of testing in cases of high suspicion), which could lead to overestimation of definitive positive results and thus a bias in favour of the intervention.

On the other hand, this is the first study to assess the correlation between 24-hour pH monitoring and ultrasound for the diagnosis of GOR applying the criteria proposed by the SEGHNP. We did not find similar studies in the previous literature, and the studies on this disease that used ultrasound are widely heterogeneous and applied different criteria.

RESULTS

The study included a total of 32 patients, of who 68.8% (*n* = 22) were male and 31.3% (*n* = 10) female, aged between 1 month and 13 years, with 84.4% younger than 1 year (*n* = 27), 50% with a history of preterm birth (*n* = 16) and a mean age of 14.66 months (standard deviation [SD]: 38.17). None of the patients in the initial sample met the exclusion criteria.

There was variation in the reason for ordering the test. Most patients had typical symptoms of GOR, such as regurgitation, choking while feeding, arching of the torso, food refusal or crying or coughing during feeding, and fewer presented with atypical

symptoms such as apnoeic episodes, desaturation or bradycardia associated with feedings, asthma, rumination or supraventricular tachycardia (SVT).

The results of pH monitoring were pathological in 59.3% of the patients (n = 19), with evidence of a potential association between the event under consideration and the presence of pathological acid reflux (choking/desaturation in 7 cases, nighttime cough in 1). The pH results were pathological in 69.2% (n = 9) of patients with desaturation episodes and in 75% (n = 3) of patients with bradycardia, as well as in the patient that reported rumination and 2 of the patients that reported poorly controlled asthma. The patient with a history of SVT had normal oesophageal pH values.

We did not find a significant association between diagnosis of GORD based on the sonographic criteria proposed by the SEGHNP and the diagnosis of GORD based on pH monitoring (p = 0.169). When it came to ultrasound, we found a sensitivity (Sen) of 63.2% and a specificity (Spe) 61.5% for diagnosis of pathological acid reflux, with a positive predictive value (PPV) of 70.6% and a negative predictive value (NPV) of 53.3%. When we compared each individual sonographic parameter with the presence or absence of GORD based on pH monitoring, we did not find a statistically significant association for any of the parameters (p > 0.05).

However, when we compared the presence of both an abnormal angle of His and an abdominal oesophagus length of less than 1.3 cm on the ultrasound examination with the detection of pathological reflux by pH monitoring, we did find a significant association (p = 0.033), with a Spe of 92.3% and a PPV of 88.9% for diagnosis of reflux based on the combined presence of the 2 sonographic features. We also found a high positive likelihood ratio (LR+) and pre-test probability (5.47 and 89.1%, respectively), as well as a low percentage of false positives (7.7%) for diagnosis of GORD (**Tables 1** and **2**).

DISCUSSION

Gastro-oesophageal reflux is common in young children, and sometimes it is not detected because the symptoms are not significant, a reluctance to subject children to more invasive testing, like pH monitoring, or normal results of testing.

Based on the findings of our study, with a high PPV, LR+ and pre-test probability and a low false positive rate, for the combination of a length of the abdominal portion of the oesophagus of < 1.3 cm and an abnormal angle of His in the ultrasound examination, it would be possible to dispense with the use of pH monitoring as the initial diagnostic

Table 1. Comparison of diagnosis by gastro-oesophageal reflux based on 2 sonographic features (AH and LAbO) and pH monitoring

		GER detected by pH monitoring			
		No	Yes	Total	
AH in pathological range + LAbO ≤ 1.3 cm	No	12	11	23	p = 0.033
	Yes	1	8	9	
	Total	13	19	32	

AH: angle of His; **LAbO:** length of abdominal portion of oesophagus.

Table 2. Characteristics of ultrasound examination and 2 sonographic variables (AH and LAbO) for diagnosis of reflux

	Abnormal ultrasound (SEGHNP criteria)	LAbO <1.3 cm + pathological angle of His
Sensitivity	60%	42.1 %
Specificity	61.5%	92.3%
PPV	70.5%	88.9%
NPV	53.3%	52.2 %

AH: angle of His; **LAbO:** length of abdominal oesophagus; **NPV:** negative predictive value; **PPV:** positive predictive value.

test in these patients. This is a novel and preliminary result obtained in a small sample with an observer-dependent technique, so we will continue to recruit patients to confirm our findings.

For now, the way in which these findings may be applied to clinical practice is to contemplate forgoing invasive testing in children with clinically significant GOR with a LAbO of less than 1.3 cm and an angle of His in the pathological range. However, normal findings in these sonographic parameters do not allow ruling out the presence of GOR, and in this case performance of pH monitoring would be necessary for confirmation.

This is the first study that analyses the correlation between the results of 24-hour pH monitoring and of ultrasound for diagnosis of GOR based on the criteria proposed by the SEGHNP, so additional studies are required to confirm our findings.

CONCLUSION

Although oesophageal pH monitoring continues to be the gold standard for diagnosis of acid reflux, ultrasound is a harmless technique that can guide decisions regarding the use of more invasive methods, such as pH monitoring. Although the criteria for diagnosis of reflux proposed by the SEGHNP did not appear to be significant, the combination of a short abdominal portion of the oesophagus and an abnormally wide angle of His corresponded to a high positive predictive value for acid reflux in the sample under study.

Since ultrasound is a non-invasive technique that is widely available, its use may be considered in the primary care setting for a more direct and earlier approach to this disease in paediatric patients, thereby improving the quality of care.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose in relation to the preparation and publication of this article.

The study was presented as a brief oral communication ("Utilidad de la ecografía como método de diagnóstico de reflujo ácido patológico en Pediatría") at the XXVI National Congress of the Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica held May 16-18 May, 2019 in Santander, Spain.

FUNDING

The project received a 2000 euro grant from the Fundación Bienvenida Navarro-Luciano Trípodi, which allowed the purchase of a bedside ultrasound scanner to perform the study.

ABBREVIATIONS

ESPGHAN: European Society for Paediatric Gastroenterology Hepatology and Nutrition • **GOR:** gastro-oesophageal reflux • **GORD:** gastro-oesophageal reflux disease • **LOS:** lower oesophageal sphincter • **NASPGHAN:** North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition • **NPV:** negative predictive value • **PPV:** positive predictive value • **RI:** reflux index • **SD:** standard deviation • **SI:** symptom index • **SSI:** symptom sensitivity index.

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