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Diagnostic accuracy of a pH stick, modified to detect gastric lipase, to confirm the correct placement of nasogastric tubes

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ABSTRACT

Objective The correct placement of a nasogastric feeding tube is usually confirmed by establishing that an aspirate is acidic using a pH stick. However, antacid medication and achlorhydria can cause false negative pH tests that may delay feeding and increase resource use. The purpose of this study was to evaluate a modified pH stick designed to detect gastric lipase and therefore reduce false negative tests.

Methods In this prospective observational study, a convenience sample of adult patients who had either gastric and oesophageal samples taken during routine diagnostic gastroscopy (n=97) or bronchial and saliva samples taken during a bronchoscopy (n=106). The samples were tested by blinded observers using the modified and standard pH sticks. The sensitivities and specificities of the two pH sticks in identifying gastric and non-gastric aspirates were compared using the pH cut-off ≤5.5.

Results The sensitivities of a pH≤5.5 to correctly identify gastric samples were 66% (95% CI 56 to 75) and 68% (95% CI 57 to 77) for the modified and the standard pH, respectively. The specificities were 81% (95% CI 76 to 85) and 79% (95% CI 74 to 84). There were no significant differences in the distribution of the discordant results between the paired gastric and non-gastric samples for both the modified and standard pH sticks at pH≤5.5 (both McNemar's tests, p≥0.05).

Conclusions There were no significant differences between the paired modified and standard pH tests for the gastric samples. Due to the limited accuracy of pH sticks, further research is required to identify accurate and cost-effective bedside methods to confirm the correct placement of nasogastric tubes.

Summary box

What is already known about this subject?

- Current guidelines recommend that the first-line test to confirm nasogastric tube (NGT) position is that the pH of a gastric aspirate is ≤5.5.
- Patients on antacid medications more often have false negative pH tests (>5.5), which delays feeding and increases the number of chest X-rays (second-line test) to confirm NGT position.
- A previous study found that modified pH sticks, coated with triglyceride to detect human gastric lipase (HGL), were more sensitive to correctly identify NGT position than standard pH sticks.

What are the new findings?

- There were no significant differences between the paired modified and standard pH tests to differentiate gastric from non-gastric samples taken from fasting patients at pH≤5.5.
- The accuracy of pH remained unchanged, regardless of whether patients were taking antacid medication or not.

How might it impact on clinical practice in the foreseeable future?

- Further refinement of the modified pH stick to accurately detect NGT placement is required, including investigation of the stability of tributyrin coated on different types and makes of sticks and of HGL activity in different patient populations.

INTRODUCTION

The pH of an aspirate cut-off ≤5.5 is commonly used as the first-line test to confirm that the nasogastric tube (NGT) is correctly positioned in the stomach.[1] However, it has been reported that false negative pH tests (>5.5) can occur in patients who secrete less gastric acid, because they receive antacid medications, achlorhydria or buffering by NGT feeds.[2–4] This can lead to significant delays to feeding and greater use of chest X-rays to visually confirm the NGT position.[5] However, misinterpretation of X-rays can lead to significant feeding errors.[6]

A proposed solution to check non-acid gastric aspirates is by using stomach specific enzyme-based diagnostic tests for NGT confirmation. Human gastric lipase (HGL) is mostly secreted from the gastric fundus and is considered to be one of the most acid stable stomach enzymes.[7] HGL is able to hydrolyse dietary triglycerides that results in the release of butyric acid and alcohol.[8] Therefore, the

presence of lipase might be measured through detecting the acid derived from the breakdown of triglycerides.[9] However, the HGL activity is only stable between pH 3.0 and 7.0 and is inactive at very acidic (pH≤2.0) and alkaline pH values (pH>8.0).[7 9 10] Therefore, a combined test that measures both pH and HGL activity has been hypothesised to be more accurate than the pH test in isolation.[9] Modified pH sticks that detect HGL (pH stick supplied by Merck, New Jersey, USA, Ref: 1095840001), which is coated with tributyrin (Ingenza, Roslin, Scotland), were also found to be more sensitive to correctly identify NGT placement than standard pH sticks (97% (95% CI 85 to 100) vs 66% (95% CI 48 to 81)).[9] However, the sample size was small, including only 36 patients who had aspirates taken from NGTs.

The aim of this study was to compare the diagnostic accuracy of pH measurements using modified HGL and standard pH stick results on aspirates obtained during gastroscopy or bronchoscopy at the recommended pH cut-off of ≤5.5.

METHODS

This study was carried out as part of a broader study of the accuracy of pH testing to distinguish gastric aspirate from aspirates from other sites, which has been previously published.[11]

Participants

In this prospective observational study, a convenience sample of adults (≥16 years) who were referred for a first elective diagnostic gastroscopy or bronchoscopy in two UK teaching hospitals between 1 November 2014 and 20 December 2016 were eligible for the study. Eligible patients had data regarding the use of antacid medication or conditions/surgery that might affect the pH of any aspirate results. Patients were excluded if they were having follow-up procedures, if they lacked mental capacity or the specimens were considered high risk, including known tuberculosis, blood or airborne viruses.

Data collection

Two aspirates were taken per patient during either gastroscopy (gastric and oesophageal samples) or bronchoscopy (bronchial and saliva samples). Each operator followed site-specific guidance for the collection of gastric, oesophageal and bronchial samples. Patients undergoing bronchoscopy were also asked to spit salvia into labelled containers prior to the procedure. Between 5 and 10 mL of each type of aspirate were placed into universal containers, which were immediately put on ice to preserve any HGL activity in the gastric fluid for up to 2 hours.[10] The reference standard was direct confirmation of the type of aspirate confirmed by the operator undertaking the procedure.

The standard CE-marked pH stick was supplied by Enteral UK, North Duffield, UK. A biochemist coated the same pH test paper with tributyrin (Ingenza, Roslin, Scotland, patent W02011068891A1). It was hypothesised that both sticks would be able to detect hydrochloric acid if present in the stomach (pH≤5.5). However, if there was no hydrochloric acid but HGL was present in the stomach, the HGL would break down the tributyrin on the modified stick to produce butyric acid providing an acidic response.[9] Both the standard and modified pH sticks were stored at room temperature in a cool dry place away for direct sunlight, as per the pH stick manufacturers' instructions, with a minimum expiration date of 3 years. The pH stick scale ranges from 2.0 to 9.0 with three colour blocks in intervals of 0.5 pH units.

The research nurses tested one of each of the samples with the two visually identical pH sticks, one standard and one modified to test HGL, within 2 hours of the sample being collected from the patient. The research nurses were blind to the type of stick used and each of the pH sticks were given a code, so they could not be identified when testing the specimens. The research nurses followed a standard operating procedure to ensure that each specimen was pipetted from the container to cover the two different types of pH stick (modified and standard) separately to prevent cross-contamination of samples. The colour of the sticks was compared after 60 s with that on the container. Although visual colour impairment was not formally tested, the research nurses all indicated they had normal colour vision.

Patient involvement

No patients were involved in the design or implementation of this study.

Analyses

Demographic categorical data are presented as percentages, the median (IQR), frequencies and 95% CI. In order to identify the sensitivity, specificity, positive/negative predictive values (PV) and the positive/negative likelihood ratios (LR) for the standard and modified pH tests, the cut-off values were aligned to the clinically agreed standards for testing pH, that is, ≤5.5 was classified as acidic sample whereas >5.5 was classified as non-acidic sample. All data analyses were performed using Statistical Analysis System Institute, SAS V.9.4, Cary, North Carolina, USA.

The sample size of 100 for each sample was estimated based on the 95% CIs and the majority of gastric aspirates having a pH≤5.5. However, the sample size could vary depending on how many patients have gastric secretions with a pH>5.5, as this was unknown we arbitrarily chose 4% where pH might misclassify the samples. We expected no false positives samples when testing saliva or bronchial aspirate, which would give specificity of 100% (95% CI 97 to 100). Therefore, we estimated that 200 patients each having two different samples each tested with the two types of pH sticks, taken during either gastroscopy (gastric and oesophageal samples) or bronchoscopy (bronchial and saliva samples) procedures would be required, providing a total of 800 (400 modified and 400 standard) pH tests.

Table 1 The participant characteristics based on whether they had a gastroscopy (n=97) or bronchoscopy (n=106)

	Gastroscopy		Bronchoscopy		Total	
	n	%	n	%	n	%
Male	39	40	56	53	95	47
Female	58	60	50	47	108	53
Antacid medication	42	43	41	39	83	41
Proton pump inhibitor H_2	39	40	40	38	79	39
Antagonist/combination	3	3	1	1	4	2
Previous gastric surgery	1	1	8	8	9	4
Pernicious anaemia	2	2	1	1	3	1
Total n of participants	97	100	106	100	203	100

RESULTS

A total of 203 patients were included, 97 (48%) had gastroscopy and 106 (52%) a bronchoscopy. Table 1 shows 95 (47%) patients were male; 83 (41%) were taking antacid medication prior to the gastroscopy (42/97, 43%) or bronchoscopy (41/106, 39%); and 3 (1%) had known pernicious anaemia, but these factors did not differ significantly between those who had a gastroscopy or bronchoscopy. Significantly more patients who had bronchoscopy (8/106, 8%) had previous gastric surgery than those who had a gastroscopy (1/97, 1%) (Fisher's Exact test, p=0.04). There were 390 samples tested with the standard stick and 379 with the modified pH stick (figure 1).

The median standard and modified pH were similar for each of the different types of samples at pH≤5.5, both in the presence and absence of prior use of antacid medication and/or other confounding factors (table 2). The sensitivity of a pH≤5.5 to correctly identify gastric samples was 66% (95 CI 56 to 75) and 68% (95% CI 57 to 77) for the modified and standard pH sticks, respectively. The specificities were 81% (95 CI 76 to 85) and 79% (95% CI 74 to 84) for modified and standard pH sticks. There appeared to be no differences in the positive and negative PVs and LRs between the two types of pH stick (table 3).

The gastric pH was similar in those patients receiving antacid medications (median pH=2.0, IQR 2.0–6.6) compared with those who were not (median pH=2.3, IQR

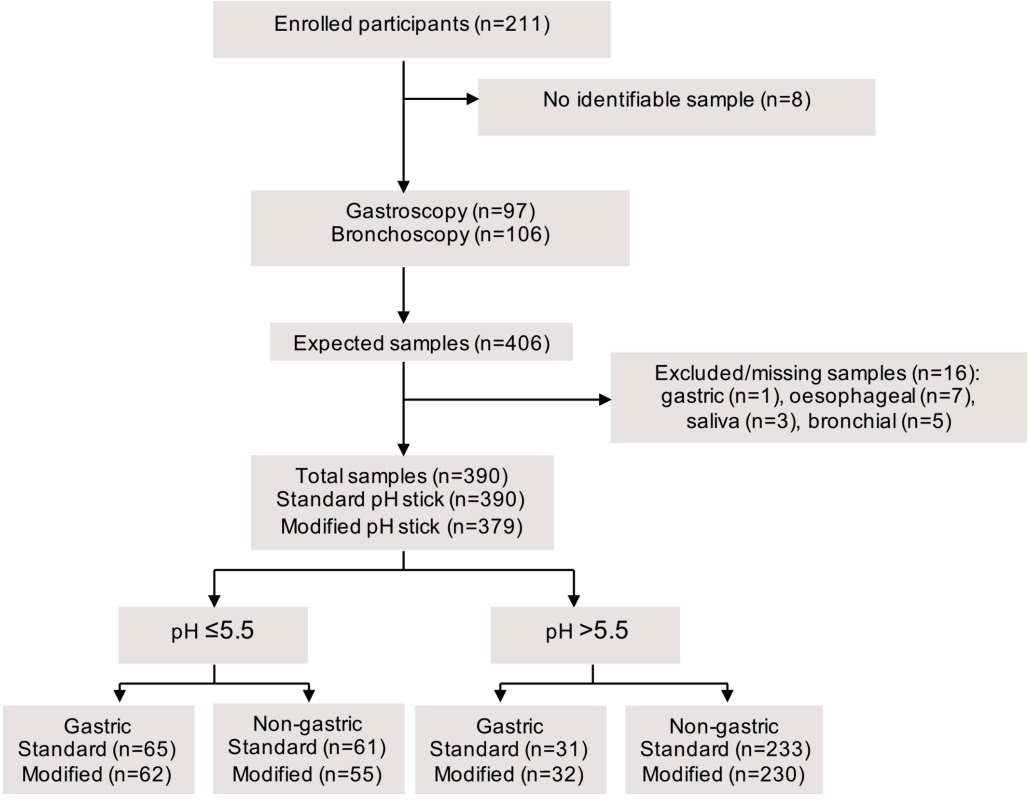

Figure 1 STAndards for the Reporting of Diagnostic accuracy studies (STARD) diagram reporting the flow of participants through the study.

Table 2 The proportion of samples from different sources with pH≤5.5 in the presence and absence of antacid medication

Sample	pH stick	Median (IQR)	All	Antacid medication	No antacid medication	All confounding factors*
			Number with pH≤5.5/n (%)			
Gastric	Standard	2.5 (2.0–6.5)	65/96 (68)	30/42 (71)	35/54 (65)	32/44 (73)
	Modified	2.5 (2.0–6.5)	62/94 (66)	28/42 (67)	34/52 (65)	30/44 (68)
Oesophageal	Standard	5.0 (2.0–6.5)	59/90 (66)	26/41 (63)	33/49 (67)	26/42 (62)
	Modified	5.5 (2.5–6.5)	53/89 (60)	22/40 (55)	31/49 (63)	22/41 (54)
Saliva	Standard	7.0 (7.0–7.5)	2/101 (2)	2/40 (5)	0/61 (0)	2/43 (5)
	Modified	7.0 (7.0–7.5)	2/97 (2)	1/37 (3)	1/60 (2)	1/41 (2)
Bronchial	Standard	7.0 (6.5–7.5)	0/103 (0)	0/41 (0)	0/62 (0)	0/45 (0)
	Modified	7.0 (7.0–7.5)	0/99 (0)	0/41 (0)	0/58 (0)	0/44 (0)

*Confounding factors included antacid medication, pernicious anaemia and/or gastric surgery.

2.0–6.5), regardless of the type of pH stick. In patients on antacids, the sensitivity of the pH of gastric samples (pH ≤5.5) was 67% (95 % CI 51 to 80) for the modified and 71% (95% CI 55 to 84) for the standard pH stick (table 3). The sensitivity of gastric samples remained similar when patients with pernicious anaemia (n=3) or had previous gastric surgery (n=9) were included in the analyses: modified stick=68% (95% CI 52 to 81) and standard stick=73% (95% CI 57 to 85).

Overall, there were no significant differences in the distribution of the discordant results between the paired gastric (McNemar's test=0.50, p=0.5) and non-gastric (McNemar's test=2.13, p=0.1) samples for both modified and standard sticks at pH≤5.5.

DISCUSSION

In this study, the modified and standard pH sticks' sensitivity was low in terms of correctly identifying gastric aspirate, regardless of whether patients were on antacids or had other confounding factors. It has been previously reported that standard pH testing can have sensitivity ranging between 66%-90% and the differences between results may depend on the type and make of pH indicator stick.[3 9 11–13] It was surprising that the modified pH stick did not demonstrate higher sensitivities similar to those reported by the previous study, particularly in patients with a pH>5.5.[9] We found that a third of the gastric samples had a pH>5.5 suggesting a high prevalence of

Table 3 The diagnostic accuracy of the modified and standard pH stick tests for all gastric samples compared with non-gastric samples tested at the pH≤5.5, including the absence or presence antacid medication

Diagnostic test	pH stick	All	Antacid medication	No antacid medication	All confounding factors*
		Gastric pH≤5.5 versus all other samples (95% CI)			
Sensitivity %	Standard	68 (57 to 77)	71 (55 to 84)	65 (51 to 77)	73 (57 to 85)
	Modified	66 (56 to 75)	67 (51 to 80)	65 (51 to 78)	68 (52 to 81)
Specificity %	Standard	79 (74 to 84)	77 (69 to 84)	84 (74 to 86)	79 (70 to 85)
	Modified	81 (76 to 85)	81 (72 to 87)	81 (70 to 87)	82 (74 to 88)
PPV %	Standard	52 (45 to 58)	52 (42 to 61)	53 (44 to 62)	53 (44 to 62)
	Modified	53 (46 to 59)	55 (44 to 65)	57 (46 to 67)	57 (46 to 67)
NPV %	Standard	88 (85 to 91)	89 (83 to 93)	90 (84 to 93)	90 (84 to 93)
	Modified	88 (84 to 90)	87 (81 to 91)	88 (83 to 92)	88 (83 to 92)
PLR	Standard	3.3 (2.5 to 4.2)	3.1 (2.1 to 4.5)	4.0 (2.7 to 5.9)	3.4 (2.3 to 4.9)
	Modified	3.4 (2.6 to 4.5)	3.4 (2.2 to 5.2)	3.4 (2.5 to 4.2)	4.0 (2.4 to 5.7)
NLR	Standard	0.4 (0.3 to 0.5)	0.4 (0.2 to 0.6)	0.4 (0.3 to 0.6)	0.4 (0.2 to 0.6)
	Modified	0.4 (0.3 to 0.6)	0.4 (0.3 to 0.6)	0.4 (0.3 to 0.6)	0.4 (0.3 to 0.6)
Overall agreement %	Standard	76 (72 to 81)	76 (68 to 82)	77 (71 to 82)	77 (70 to 83)
	Modified	77 (73 to 81)	77 (70 to 83)	77 (71 to 83)	78 (71 to 84)

*Confounding factors included antacid medication, pernicious anaemia and/or gastric surgery.
NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.

hypo/achlorhydria, which is likely to be more common in patients undergoing scope investigations.[14] It was also predicted that patients taking antacid medication would have higher pH values than those not receiving antacid medications.[2] However, in the current study, the accuracy of pH remained unchanged, regardless of whether patients were taking antacid medication or not. This may be a result of patients being required to fast for up to 4 hours and/or having stopped their antacid medication prior to the procedure, which can increase gastric acid rebound hypersecretion.[15 16]

A strength of the current study was the large number of aspirates that were obtained from patients undergoing routine gastroscopy and bronchoscopy. NGT placement cannot be controlled and it would be unethical for patients to have unnecessary chest X-rays.[17] Furthermore, aspirates cannot be obtained directly from NGTs in up to 46% of patients.[5] Although pH appears to be a cost effective first-line approach to confirm NGT,[18] studies have shown that the accuracy of pH sticks remains mixed due to testers' ability to obtain aspirate and visually differentiate the colorimetric results.[5 11 19] Previous studies have reported that misreading pH sticks can be influenced by a number of factors, including testers who have colour vision deficiency, time factors and poor lighting conditions.[5 19] However, there is a lack of evidence that the use of more expensive pH meters improves the accuracy to confirm correct NGT placement.[3] Therefore, redesigning pH sticks to potentially reduce errors caused by visual inspection should be further investigated.[5 11]

It is unclear why this large study did not confirm the encouraging results of a similar smaller study.[9] One explanation might be that different types of pH sticks were used, although both were prepared by the same laboratory. Studies comparing the different makes and types of pH stick have been found to either overestimate or underestimate pH in known buffer solutions.[19 20] Although pH sticks with multiple colour blocks used in this study are considered to be more accurate than single colour blocks when testing the pH of buffer solutions,[20] it was important to determine their performance with different aspirates taken from patients. Second, lipases may also originate from the tongue and the pharynx (lingual lipase); however, studies have found that gastric lipase is the predominant preduodenal enzyme in humans, with only trace amounts of lingual lipase activity detected from the small number of lingual serous glands compared with the larger stomach area.[7 21 22] These results were recently corroborated in a study that found no detectable lipase activity from saliva samples (unpublished data) and found that it was not present in lung aspirates.[9] Third, in this study, the patients had been fasting prior to their procedure, which will reduce the production of gastrin that stimulates both HGL and hydrochloric acid secretion in the stomach.[23] In the fed state, the conditions are more likely to be favourable for HGL, particularly at elevated pH levels between pH 3.0 and 7.0.[24] If this was indeed the case, HGL may be reduced or not present in the stomach and the modified pH stick would be unable to correct false negative results. Fourth, there may have been variability between methods used to obtain the samples during the procedure. It is not possible to confirm whether the gastroscopic procedure could inadvertently result in alkaline duodenal fluid to be sampled or mixed the gastric secretions, particularly when the patients are in the supine position.[25 26] However, there is conflicting evidence whether contamination of gastric contents with bile salts, increases or decreases HGL activity.[27] Finally, several conditions in humans, including pancreatitis, gastritis, cystic fibrosis and alcoholism, have significantly lower HGL activity when compared with healthy subjects.[27] In this study, the specimens were deidentified as the aim was to compare the accuracy of both pH sticks on the different types of aspirate, therefore it was not possible to follow-up patients to confirm diagnosis postprocedure. Furthermore, the population undergoing scope procedures may not be generalisable to those requiring nasogastric feeding. Indeed, the NGT position requires to be checked prior to and after feeding and/or giving medications that will result in variable HGL activity.

Implications for practice and conclusion

Overall, the sensitivities of the modified and standard pH tests were low, but both were able to rule out all of the bronchial samples (100% specificity) at the pH cut-off ≤5.5. The implications for practice based on the findings from this study suggest further refinement of the modified pH stick is required, including investigation of the stability of HGL at very low and high pH values; the optimal shelf-life and storage of the tributyrin coated on different types and makes of pH sticks and the HGL activity in different patient populations, including fasting and feeding status and conditions that are associated with lipase insufficiency. Due to the limited accuracy of current colorimetric pH sticks, further research is urgently needed to determine more accurate methods that would reduce NGT misplacement and delays in feeding and would be safe, cost-effective, easy to use and improve patient outcomes.

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Competing interests None declared.

Patient consent Not required.

Ethics approval Written informed consent was obtained from all respondents. This study received prior approval from the Lothian NHS research ethics committee (REC: 13/SS0184; R&D: 20130299).

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Data sharing statement The deidentified dataset will be made available on request to the lead author.

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