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Correspondence

Optimization of upper gastrointestinal endoscopy: Value of real-time gastric juice analysis

Dear Editor,

Upper gastro-intestinal endoscopy (EGDS) has limitations in identifying microscopic lesions [1]. Unfortunately, microscopic lesions are frequent in patients undergoing EGDS and often represent pre-neoplastic conditions. Hence the need for biopsies and histological evaluation which, however, do not ensure total protection from diagnostic errors.

In addition, in patients without focal lesions, endoscopists often take only a few antral samples or do not perform biopsies at all [2]. Consequently, omission errors may increase.

A possible solution to the problem is the prediction of gastric health during endoscopy (i.e., in real-time). This way, the endoscopist could be alerted to the presence of abnormalities and select the most appropriate diagnostic approach.

A potential method of predicting gastric health may be the examination of the gastric juice; two reliable indicators of gastric health are gastric pH and ammonium concentration, the former reflecting the capability to produce acid [3], and the latter, the presence of *Helicobacter pylori* and, indirectly, of gastritis [4].

Table 1
Histological findings. The results of complete histological evaluation (two antral + two fundic biopsies, stained with both haematoxylin-eosin and immunohistochemical techniques) were taken as the gold standard to which the six diagnostic strategies were compared.

Pathological conditions		Strategy 1 all pts	Strategy 2 hypochl. pts	Strategy 3 all pts	Strategy 4 hypochl. pts	Strategy 5 all pts	Strategy 6 hypochl. pts
Antral glandular atrophy	no. lesions detected (%)	4/19 (21.1%)	11/19 (57.9%)	19/19 (100%)	11/19 (57.9%)	19/19 (100%)	11/19 (57.9%)
Oxyntic glandular atrophy	no. lesions detected (%)	4/25 (16%)	4/25 (16%)	4/25 (16%)	24/25 (96%)	25/25 (100%)	24/25 (96%)
Antral intestinal metaplasia	no. lesions detected (%)	0/20 (0%)	15/20 (75%)	20/20 (100%)	15/20 (75%)	20/20 (100%)	15/20 (75%)
Oxyntic intestinal metaplasia	no. lesions detected (%)	0/9 (0%)	0/9 (0%)	0/9 (0%)	9/9 (100%)	9/9 (100%)	9/9 (100%)
Other (adenocarcinoma, lymphoma)	no. lesions detected (%)	3/3 (100%)	3/3 (100%)	3/3 (100%)	3/3 (100%)	3/3 (100%)	3/3 (100%)
Total non-endocrine lesions	no. lesions detected (%)	11/76 (14.5%)	33/76 (43.4%)	46/76 (60.5%)	62/76 (81.6%)	76/76 (100%)	62/76 (81.6%)
Antral G cell hyperplasia	no. lesions detected (%)	0/17 (0%)	0/17 (0%)	0/17 (0%)	0/17 (0%)	0/17 (0%)	15/17 (88.2%)
ECL cell hyperplasia	no. lesions detected (%)	0/20 (0%)	0/20 (0%)	0/20 (0%)	0/20 (0%)	0/20 (0%)	19/20 (95%)
Total endocrine lesions	no. lesions detected (%)	0/37 (0%)	0/37 (0%)	0/37 (0%)	0/37 (0%)	0/37 (0%)	34/37 (91.9%)
Total gastric mucosal lesions	no. lesions detected (%)	11/113 (9.7%)	33/113 (29.2%)	46/113 (40.7%)	62/113 (54.9%)	76/113 (67.3%)	96/113 (85%)
Helicobacter pylori colonization	no. cases detected (%)	0/107 (0%)	102/107 (95.3%)	105/107 (98.1%)	104/107 (97.2%)	107/107 (100%)	104/107 (97.2%)
Total pathological conditions	no. conditions detected (%)	11/220 (5%)	135/220 (61.4%) °	151/220 (68.6%) °	166/220 (75.5%) §	183/220 (83.2%) #	200/220 (90.9%) *

Hypochl, hypochlorhydric; pts, patients; ECL cell, enterochromaffin-like cell; G-cell, gastrin cell.
* $p < 0.001$ vs. strategy-1, 2, 3, 4, and 5.
# $p < 0.05$ vs. strategy-4; $p < 0.001$ vs. strategy-1, 2, and 3.
§ $p < 0.001$ vs. strategy-1, 2.
° $p < 0.001$ vs. strategy-1.

On the basis of these considerations, we performed a retrospective analysis of a prospective cohort of 216 patients referred for diagnostic EGDS [2], in order to evaluate the usefulness and efficacy of real-time gastric juice analysis (GJA) in diagnostic upper endoscopy.

Endoscopic pattern, histological features, and real-time GJA were performed in all patients. The parameters evaluated were: *H. pylori*, glandular atrophy, intestinal metaplasia, enterochromaffin-like cells, and gastrin-producing cells. A detailed description of patients features and methods adopted is reported elsewhere [2].

Real-time GJA was carried out employing a new device (*Endofaster)* that, interposed between the endoscope and the suction system, performs a real-time determination of the pH and ammonium concentration of gastric juice, allowing the detection of hypochlorhydric conditions and *H. pylori* infection [2].

After data collection six different diagnostic scenarios were simulated, each including only part of the overall investigations employed (endoscopy, histology, GJA). Specifically, EGDS alone (1), EGDS with antral biopsies (H&E staining) in hypochlorhydrics (2) or in all patients (3), EGDS with antral and fundic biopsies (H&E staining) in hypochlorhydrics (4) or in all patients (5), EGDS with antral and fundic biopsies (H&E + immunohistochemical staining) only in hypochlorhydrics (6).

Finally, considering the complete histological evaluation (2 antral + 2 fundic biopsies, stained with both H&E and immunohistochemical stains) as the gold standard, we determined the diagnostic performance of these 6 strategies by evaluating how many of the pathological conditions identified on histology would have been detected by each strategy.

The data obtained are reported in the Table 1. In total, 220 pathological conditions were identified and 85% of them were detected in hypochlorhydric patients (comprising 25% of the study population). A correlation ($r = 0.67$; $p < 0.01$) was found between hypochlorhydria and histological lesions (glandular atrophy, intestinal metaplasia, endocrine cell hyperplasia), as well as between high ammonium levels and *H. pylori* infection ($r = 0.69$; $p < 0.01$).

On the whole, these results demonstrated that EGDS without biopsies (strategy n.1) is inadequate for reliable diagnosis because *H. pylori* and microscopic lesions cannot be detected.

Among the remaining strategies, those employing real-time GJA and performing biopsies only in hypochlorhydric patients showed diagnostic performance similar to or better than strategies involving biopsies for all patients, despite the four-fold lower number of biopsies performed.

Performing biopsies in all patients and in both regions certainly reaches the best diagnostic performance (either considering or not endocrine cell hyperplasia), but that represents the gold standard. In all the remaining cases (that embrace the most commonly used endoscopic approaches), the use of GJA highly increases the diagnostic accuracy because of its capacity of focusing on at-risk patients. Moreover, it results also in cost and time savings and does not require additional efforts for the endoscopist.

Conflict of interest

None declared.

References

[1] Carpenter HA, Talley NJ. Gastroscopy is incomplete without biopsy: clinical relevance of distinguishing gastropathy from gastritis. Gastroenterology 1995;108:917–24.

[2] Tucci A, Bisceglia M, Rugge M, et al. Clinical usefulness of gastric juice analysis in 2007, the stone that the builders rejected has become the cornerstone. Gastrointestinal Endoscopy 2007;5:881–90.

[3] Andersen J, Strom M. A technique for screening of achlorhydria and hypochlorhydria during upper gastrointestinal endoscopy. Scandinavian Journal of Gastroenterology 1990;25:1084–8.

[4] Kearney DJ, Ritchie K, Peacock JS. Gastric juice ammonia assay for diagnosis of *Helicobacter pylori* infection and relationship of ammonia concentration to gastritis severity. American Journal of Gastroenterology 2000;95:3399–403.

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High prevalence of hepatitis B non-immunity in paediatric non-alcoholic fatty liver disease patients

Dear Editor,

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in both adults and children in the United States today [1]. While achieving a healthy weight is optimal management of NAFLD and non-alcoholic steatohepatitis (NASH), equally important is preventing secondary damage to the liver that might accelerate liver fibrosis. Hepatitis B is one such preventable cause of secondary liver damage and therefore prevention of hepatitis B has been a public health priority. As this is most effectively done with vaccination against hepatitis B, hepatitis B vaccination is part of the universal vaccination schedule for infants and children. Unfortunately, obesity has been identified as a predictor of poor serologic antibody development after hepatitis B vaccination [2,3]. The objective of this study was to determine the sero-prevalence of immunity against hepatitis B in a cohort of consecutively evaluated paediatric NAFLD patients. We hypothesized that positive hepatitis B surface antibody (HBsAb) sero-prevalence would be low in children with NAFLD, despite universal immunization practices in place against hepatitis B.

We conducted a retrospective review of prospectively collected clinical and histological data obtained from children and adolescents, age 6–18, enrolled in an IRB-approved single centre NAFLD registry at the Cincinnati Children's Hospital Medical Centre, Cincinnati, Ohio. The registry collected anthropometric data, laboratory assessments for other causes of chronic liver disease, and liver biopsies. Enrolment criteria included chronically elevated liver enzymes after exclusion of other liver diseases including: hepatitis B, hepatitis C, alpha 1 antitrypsin deficiency, Wilson disease, autoimmune hepatitis, and iron indices for hemochromatosis. The presence of HBsAb was used as a surrogate for immunity after vaccination. The absence of HBsAb after vaccination indicated a decreased immunogenic response. Patients were grouped into non-immune and immune groups and analyzed for demographic, and biochemical differences.

All 200 subjects had negative HBsAg levels and negative hepatitis B core antibody levels, indicating no past or active hepatitis B infection. Of 200 subjects, 96 (48%) had no documented HBsAb serology and had not been evaluated for hepatitis B immunity. No significant clinical differences in age, body mass index (BMI), aspartate aminotransferase (AST), alanine aminotransferase (ALT) or gender were found between those with documented HBsAb and