Do Pediatricians Apply the 2009 NASPGHAN-ESPGHAN Guidelines for the Diagnosis and Management of Gastroesophageal Reflux after Being Trained?

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Short running title: 2009 GER international guidelines training modalities

Abbreviations: ESPGHAN European Society for Pediatric Gastroenterology, Hepatology, and Nutrition - GER gastroesophageal reflux - GERD gastroesophageal reflux disease - NASPGHAN North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition - PPI proton pump inhibitor - US ultrasonography

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ABSTRACT

Aim: According to a recent survey, the 2009 NASPGHAN-ESPGHAN GER guidelines are poorly adhered to by European primary care pediatricians. The main issue raised from the survey was the prescription of unnecessary acid suppressive medications, especially in infants. No inquiry into the reasons was made. The primary objective of the present study was to assess the applicability of the guidelines in European primary care pediatricians undergoing specific trainings.

Methods: One hundred pediatricians involved in the previous survey agreed to participate and were randomly divided into 2 groups: one group was trained in the guidelines through an online podcast and the other group through a synopsis. During the following 3 months, each involved pediatrician was asked to enroll every consecutive infant, child or adolescent with suggestive reflux symptoms. For every enrolled patient pediatricians filled-in a report concerning their diagnostic and therapeutic choices.

Results: A total of 382 patients (M/F: 186/196, infants/children/adolescents: 194/123/65) were enrolled by pediatricians. Infants with unexplained crying and/or distressed behavior who were prescribed PPIs were 3.7% compared to 45.2% of the survey data obtained before the training (p<0.05). Infants with uncomplicated recurrent regurgitation and vomiting who were prescribed PPIs were 4.5% against 37.1% of the baseline survey data (p<0.05). The overall rate of children managed in full compliance with the guidelines was 46.1% after the training compared to 1.8% before the training (p<0.05). No significant differences were seen between pediatricians from podcast and synopsis group.

Conclusions: NASPGHAN-ESPGHAN GER guidelines have a good applicability, despite they are currently poorly adhered to by European primary care pediatricians. Simple, inexpensive trainings were proven to be effective in increasing adherence by pediatricians. The increase in compliance clearly favors the role of continuous medical education through simple educational tools and subsequent assessment of practice.

Key words: gastroesophageal reflux disease, guidelines
STUDY HIGHLIGHTS

1. WHAT IS CURRENT KNOWLEDGE

- GERD is a common and costly condition in childhood.
- Knowledge and implementation of guidelines among pediatricians are poor.
- The most relevant violation of the guidelines recommendations concerns the prescription of unnecessary acid suppressive medications.

2. WHAT IS NEW HERE

- The latest NASPGHAN-ESPGHAN reflux guidelines have a good applicability on clinical practice.
- Simple, inexpensive training approaches are effective in increasing adherence to guidelines by primary care pediatricians.
- The overall rate of PPIs inappropriate prescriptions can be dramatically reduced when guidelines are implemented.
INTRODUCTION

Gastroesophageal reflux disease (GERD) is a common condition, defined by the passage of gastric contents into the esophagus causing troublesome symptoms and/or complications, affecting up to 3.3% of the pediatric population (1). In October 2009 the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) jointly published new clinical practice guidelines for the diagnosis and management of reflux in the pediatric population, updating and unifying the previous ESPGHAN and NASPGHAN guidelines as a means of improving uniformity of practice and quality of patient care (2).

According to a recent survey, the 2009 NASPGHAN-ESPGHAN reflux guidelines are poorly adhered to by European primary care pediatricians (3). One of the most frequent deviations from NASPGHAN-ESPGHAN recommendations concerns the use of diagnostic tools. The majority of the involved pediatricians did not perform specific testing to diagnose GERD and relied on the clinical history even in young children and infants, although not supported by the guidelines. The other major violation of the guidelines pertains to the therapeutic approach to GER. Data from the survey confirmed the overuse of proton pomp inhibitors (PPIs), previously highlighted by other studies (4-7), especially for infants with unexplained crying and distressed behavior or with uncomplicated recurrent regurgitation and vomiting (physiologic GER).

Unfortunately, the findings of the survey did not allow any comment on the reasons for the European pediatricians’ failure to comply with recommendations and could not suggest specific interventions. To date no study has been performed to evaluate why the large majority of pediatricians are not practicing according to the guidelines.

The main objective of the study was to assess the applicability of the guidelines in European primary care pediatricians undergoing specific trainings. The secondary objective was to evaluate the efficacy of two different training approaches.
METHODS

The study was designed as an open, prospective, multicentric, randomized, intervention trial. The intervention consisted of training on the management of children with gastroesophageal reflux symptoms based on the major recommendations of the 2009 NASPGHAN-ESPGHAN clinical guidelines. The first randomly selected 100 European pediatricians who had been involved in the previous survey on the implementation of the guidelines and agreed to participate in the study were randomly allocated into 2 groups (3). One group of pediatricians (group A) was trained through a 30-minute lasting podcast including slide sets in the form of a PowerPoint presentation. The other group of pediatricians (group B) was trained through a synopsis they were asked to read about the essentials of the guidelines sent by email. Questionnaires were completed by pediatricians of both groups at the end of the training in order to assess their understanding.

During the 3 months following the training, pediatricians from both groups were asked to enroll every consecutive infant, child or adolescent who presented in their unit with suggestive reflux symptoms, such as regurgitation, vomiting, heartburn, chest pain, weight loss or poor weight gain, irritability in infants, ruminative behavior, hematemesis, dysphagia, odynophagia, wheezing, stridor, cough and hoarseness (as reported in the guidelines). For every enrolled patient pediatricians filled-in a report concerning their diagnostic and therapeutic management choices.

The national data obtained from the reports were collected by an ESPGHAN coordinator for each country and than sent for analysis to the Italian study coordinator. The study period was from October 1st, 2012 to April 30th, 2013. The current applicability of 2009 NASPGHAN-ESPGHAN reflux guidelines was evaluated based on children managed in full compliance with the guidelines recommendations by trained pediatricians and a comparison was made with the management shown by the same pediatricians before being trained.

The study was approved by the Independent Ethics Committee of the University of Naples Medical School and was conducted in accordance with the Declaration of Helsinki and Guidelines.
for Good Clinical Practice. Data were entered into Excel (Microsoft, Redmond, WA) and analyzed with SPSS software, version 8.0 (SPSS, Chicago, Illinois). Results are expressed as percentages. Statistical analyses included determination of means, t test, $\chi^2$ test, and Fisher's exact test, with significance accepted at the 5% level. The sample size has been computed with the SPSS Multivariate Anova (power 95%; alpha 0.05; first type error 0.05).

RESULTS

One hundred pediatricians who took part in the European survey were actually trained, half through the podcast and half through the synopsis. All pediatricians showed a good understanding of the guidelines recommendations when tested after the training. During the following 3 months, a total of 382 children (males/females: 186/196, mean age: 65 months, age range: 0-210 months) with symptoms suggestive of gastroesophageal reflux were seen by pediatricians. Of them, 194 were infants, 123 were children, and 65 were adolescents. All these children were enrolled in the study, 202 by pediatricians from group A and 180 by pediatricians from group B (Figure 1). The main baseline features of children, such as age, sex, and complained symptoms, were similar in both groups (Table 1). The main symptoms complained by the enrolled children were regurgitation (52.9%), vomiting (39%) and heartburn (24.6%). The main reported symptoms for each age group are listed in Table 2.

The overall rate of children who were managed in full compliance with the guidelines by trained pediatricians, as for both diagnostic and therapeutic choices, was 46.1% (176/382) compared to 1.8% of the survey data obtained before the training ($p<0.05$) (Figure 2). The remaining 53.9% (206/382) of the enrolled children were managed not completely adhering to the guidelines recommendations. Furthermore, a significant reduction in the PPI prescription rate was observed following the training. It should be noted however that even after the training 4.5% infants with uncomplicated recurrent regurgitation and vomiting and 3.7% infants with unexplained
crying and/or distressed behavior were prescribed PPIs, 21.7% children were prescribed ranitidine as first choice treatment for GERD, 7.4% were diagnosed GERD based on ultrasonography (US) imaging. Moreover, 20.3% children younger than 8 years of age were prescribed PPIs based on clinical grounds (vomiting and heartburn) whereas 43.9% adolescents were diagnosed GERD only after specific procedures, such as upper GI endoscopy and esophageal pH-monitoring. Considering the overall PPIs prescriptions done by trained pediatricians, 29.4% exceeded the guidelines indications for PPIs use (Figure 3).

Comparison data between the management of children with symptoms suggestive of GER shown by pediatricians before (data gathered from the previous survey) and after the training are reported in Table 3. No statistically significant differences were found between group A and group B pediatricians about their choices when making decisions about GER symptomatic children (data not shown). The overall rates of children managed in full compliance with the guidelines were similar in both groups (45.9% vs. 46.4%, respectively).

DISCUSSION

GER is a common condition in childhood and carries a correspondingly high burden of problems and costs for both families and national health systems. Optimal management of GER should be a priority for all pediatricians in their clinical practice. Following a recent survey showing a very low rate of adherence to the latest international guidelines by primary care pediatricians, this randomized controlled study evaluated the applicability of such guidelines on the global management of children with GER.

Our study was based on two simple, inexpensive training modalities. The approach taken was similar to that used in a previous study examining the applicability and efficacy of acute gastroenteritis (GE) (8). In our study, primary care pediatricians showed a significantly higher
adherence to the guidelines recommendations after being trained compared to the management shown before the training.

A detailed analysis of our results allows for speculation on the impact of guidelines knowledge on the most common attitudes and decisions made by pediatricians disregarding the international recommendations for best clinical practice. The most relevant source of concerns highlighted by the survey among untrained pediatricians was the prescription of unnecessary acid suppressive medications (PPIs), especially in infants. The same issue was recently addressed by several studies, which highlighted the lack of efficacy of both lansoprazole and omeprazole in infants treated for presumed GERD, recommending a serious effort to curtail their empiric use (9-11). In our study, most trained pediatricians showed an overall significant reduction in the use of PPIs for the treatment of symptoms for which they are proved to have a lack of efficacy. Interestingly, the rates of healthy infants with uncomplicated recurrent regurgitation and vomiting or with unexplained crying and distressed behavior who were prescribed PPIs dropped dramatically after the training.

Untrained pediatricians committed frequent guidelines violations when surveyed on reflux diagnostic modalities. Even though the guidelines conclude that symptom description is unreliable and non-specific in children younger than 8-12 years of age, almost half (48%) of them based GERD diagnosis in this age group on clinical grounds. After being trained on the proper diagnostic tools, this percentage decreased significantly and a higher rate of pediatricians asked for tests searching for an excessive frequency or duration of reflux events, esophagitis, or a clear association of symptoms and signs with reflux events in the absence of alternative diagnoses, as recommended by the guidelines. Conversely, the reported use of US to confirm GERD diagnosis didn’t vary significantly between trained and untrained pediatricians, showing a deeply embedded reliance on the use of such a simple and inexpensive but equally inappropriate tool (2, 12, 13).

Intriguingly, a non-negligible rate of untrained pediatricians prescribed ranitidine as first choice long-term treatment for GERD rather than a PPI, even if the occurrence of tachyphylaxis is
an acknowledged drawback to its chronic use (14). This rate was found slightly increased after the training, probably as an improper response to the attempt at curtailing PPI use.

In this study, there is an unavoidable potential bias related to the so-called “Hawthorne effect” (15). According to this effect, physicians could have performed better because they were under observation, and the effect of the intervention could be transient and limited to the study period. We can only acknowledge the fact that the Hawthorne effect may have influenced our results; however, the same effect should have disclosed in the same fashion within the baseline survey, the data of which have been used for comparisons.

In conclusion, this is the first study to have examined the applicability of the 2009 NASPGHAN-ESPGHAN guidelines for optimal GER management on clinical practice. Our results show that simple, inexpensive training approaches are effective in increasing adherence by pediatricians. This finding complements the process of guideline production and implementation in that it provides validation of their applicability.

In our opinion, the main breakthrough arising from the study concerns the decrease in PPIs inappropriate use by trained pediatricians. Considering the overall prescribing attitudes of untrained pediatricians, an amazingly high proportion (82%) was shown to prescribe PPIs in situations that did not concur with the recommended use in the NASPGHAN-ESPGHAN guidelines. Increasing primary care physician awareness by the use of the results referenced herein, pointing out the response of uncomplicated infant reflux to non pharmacologic management, and education of parents as part of anticipatory guidance to reset expectations has been proven to be effective in reducing this percentage to a much more acceptable rate.

We acknowledge that guidelines address the average situation and the evaluation of individual patients may reveal reasons for opening criteria for exceptions. However, even taking this into account, the increase in compliance clearly favors the role of continuous medical education through simple educational tools and subsequent assessment of practice. Future widespread educational efforts may be considered in order to optimize the management of GER, mainly
focusing on the appropriate use of health care resources and on the struggle against the inappropriate drug use in otherwise healthy infants and children.

REFERENCES


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FIGURE LEGENDS

Figure 1. Flow of pediatricians and children participating in the study

Figure 2. Overall rates of children managed in full compliance with the guidelines

Figure 3. Rates of PPIs over-prescription (according to the guidelines indications for prescription)
Guarantor of the article

Prof. Annamaria Staiano

Specific author contributions

Paolo Quitadamo - Dr. Quitadamo conceptualized and designed the study, coordinated and supervised data collection, drafted the initial manuscript, and approved the final manuscript as submitted.

Alexandra Papadopoulou - Dr. Papadopoulou coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Vaidotas Urbonas - Dr. Urbonas coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Enriqueta Roman - Dr. Roman coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Rok Orel - Dr. Orel coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Daniela Jojkić Pavkov - Dr. Jojkić Pavkov coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Jorge Amil Dias - Dr. Amil Dias coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Aco Kostovski - Dr. Kostovski coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Erasmo Miele – Dr. Miele conceptualized and designed the study, coordinated and supervised data collection, and approved the final manuscript as submitted.

Alberto Villani - Dr. Villani coordinated and supervised data collection at one of the sites, critically reviewed the manuscript, and approved the final manuscript as submitted.

Annamaria Staiano - Dr. Staiano conceptualized and designed the study, coordinated and supervised data collection, and approved the final manuscript as submitted.
Table 1. Baseline features of children in group A and group B

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>98 (48.5)</td>
<td>88 (48.9)</td>
<td>NS</td>
</tr>
<tr>
<td>F</td>
<td>104 (51.5)</td>
<td>92 (51.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Age, months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>68.1</td>
<td>62</td>
<td>NS</td>
</tr>
<tr>
<td>F</td>
<td>65.5</td>
<td>64.6</td>
<td>NS</td>
</tr>
<tr>
<td>Number of infants (%)</td>
<td>100 (49.5)</td>
<td>94 (52.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of children (%)</td>
<td>63 (31.2)</td>
<td>60 (33.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of adolescents (%)</td>
<td>39 (19.3)</td>
<td>26 (14.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Presence of warning signals (only infants), %</td>
<td>17</td>
<td>13.8</td>
<td>NS</td>
</tr>
</tbody>
</table>
Table 2. Main reported symptoms by the enrolled patients for each age group

<table>
<thead>
<tr>
<th></th>
<th>INFANTS</th>
<th>%</th>
<th>CHILDREN</th>
<th>%</th>
<th>ADOLESCENT</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitation</td>
<td>85</td>
<td></td>
<td>Heartburn</td>
<td>27.6</td>
<td>Heartburn</td>
<td>73.8</td>
</tr>
<tr>
<td>Vomiting</td>
<td>50.5</td>
<td></td>
<td>Vomiting</td>
<td>26</td>
<td>Vomiting</td>
<td>26</td>
</tr>
<tr>
<td>Irritability</td>
<td>38.7</td>
<td></td>
<td>Regurgitation</td>
<td>23.6</td>
<td>Cough</td>
<td>20</td>
</tr>
</tbody>
</table>
Table 3. Comparison data between trained and untrained pediatricians

<table>
<thead>
<tr>
<th></th>
<th>Untrained pediatricians</th>
<th>Trained pediatricians</th>
<th>$\chi^2$</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants with uncomplicated recurrent regurgitation and vomiting who were prescribed PPIs, %</td>
<td>37.1</td>
<td>4.5</td>
<td>74.02</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Infants with unexplained crying and/or distressed behaviour who were prescribed PPIs, %</td>
<td>45.2</td>
<td>3.7</td>
<td>109.7</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>GERD diagnoses based on ultrasonography imagings, %</td>
<td>9.7</td>
<td>7.4</td>
<td>1.27</td>
<td>NS</td>
</tr>
<tr>
<td>Use of ranitidine as first-choice treatment for GERD, %</td>
<td>16.9</td>
<td>21.7</td>
<td>1.5</td>
<td>NS</td>
</tr>
<tr>
<td>Children younger than 8 years of age who were prescribed PPIs based on clinical grounds (without specific testing), %</td>
<td>48</td>
<td>20.3</td>
<td>55.18</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Adolescents who were diagnosed GERD only after specific procedures, such as upper GI endoscopy and esophageal pH-monitoring, %</td>
<td>33</td>
<td>43.9</td>
<td>3.51</td>
<td>NS</td>
</tr>
</tbody>
</table>
Group A
Podcast-trained pediatricians
(n=50)

Group B
Synopsis-trained pediatricians
(n=50)

Enrollment of GER-symptomatic children

Children managed by Group A pediatricians
(n=202)

- Children managed according to the guidelines
  - Group A (n=93)
  - Group B (n=84)

Children managed by Group B pediatricians
(n=180)

- Children managed in disagreement with the guidelines
  - Group A (n=109)
  - Group B (n=96)
Figure 2.

![Bar graph showing the comparison between untrained and trained pediatricians. The graph indicates that 46.4% of the pediatricians are trained, while only 1.8% are untrained.](image-url)

- **Untrained pediatricians**: 1.8%
- **Trained pediatricians**: 46.4%
Figure 3.

Untrained pediatricians

Trained pediatricians

82% 29.4%