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Dysphagia and Quality of Life May Improve with Mometasone Treatment in Patients with Eosinophilic Esophagitis: A Pilot Study

Henrik Bergquist, MD, PhD¹, Helén Larsson, MD², Leif Johansson, MD, PhD³, and Mogens Bove, MD, PhD²

Abstract

Objective. The treatment of adult patients with eosinophilic esophagitis remains challenging. The aim was to assess dysphagia and health-related quality of life (HRQL) using validated scales and questionnaires before and after treatment with mometasone furoate.

Study Design. Case series with planned data collection.

Setting. University hospital and secondary referral hospital.

Subjects and Methods. Newly diagnosed patients with eosinophilic esophagitis were included and given 200 µg of orally administered topical mometasone furoate 4 times daily. Questionnaires incorporating the Watson Dysphagia Scale (WDS), the European Organization for Research and Treatment of Cancer Quality of Life–Oesophageal Module 18 (EORTC QLQ-OES18), and the Short Form–36 (SF-36) were completed before the initiation of treatment and after 2 months of treatment.

Results. Thirty-one consecutive patients (23 men; mean age, 45 years; range, 18-89 years) completed the trial. At inclusion, the mean scores of the WDS, the EORTC QLQ-OES18 dysphagia scale, the eating scale and choking item, and the global health and social functioning dimensions of the SF-36 were 21.3, 20.4, 35.0, 38.6, 71.1, and 82.3, respectively. Post-treatment, these scores improved to 8.9 (P < .0001), 4.6 (P < .00001), 17.8 (P < .001), 16.0 (P < .01), 76.1 (P < .05), and 91.9 (P = .0001), respectively. Except for 1 case of oral candidiasis, no significant side effects were reported.

Conclusion. The dysphagia and impaired HRQL found in untreated patients with eosinophilic esophagitis improved significantly after 2 months of mometasone furoate treatment. A randomized placebo-controlled trial is warranted to assess causality. The scales and questionnaires used are sensitive instruments appropriate for symptom surveillance in individuals with eosinophilic esophagitis.

Keywords
dysphagia, allergy, esophagitis, quality of life, treatment

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Eosinophilic esophagitis (EoE) is a relatively new disease entity associated with chronic or intermittent dysphagia, esophageal bolus impaction events, and reflux-like symptoms.¹ ² The prevalence in the general population may be as high as 1%, but the true incidence still remains uncertain.³ The typical adult patient is a man from 20 to 40 years old who suffers from some other allergic diathesis, such as asthma, allergic rhinitis, and/or atopic eczema. Characteristic endoscopic features of the esophagus include linear furrowing, white plaques or exudates, “crêpe-paper mucosa,” and concentric rings or strictures. Diagnosis is established by histological examination of mucosal biopsies, and >20 eosinophils per high-power field (×400) is considered a cutoff for diagnosis in scientific research.¹

Although much is still unknown about the true etiology and pathogenesis of the disease, several treatment modalities have been proposed and applied with various results.⁴–⁶ These include medical treatment with antihistamines, leukotriene receptor antagonists, proton-pump inhibitors, systemic corticosteroids, and endoscopic dilatation. However, the current

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first-choice treatment, orally administered aerosolized topical corticosteroids, was recently advocated by the American Gastroenterological Association (AGA) in a consensus report. Although this treatment has been studied in several trials, a lack of adequate evaluation of the effects on dysphagia still exists. The impact of the disease and its treatment regarding patients’ health-related quality of life (HRQL) also remains unclear. Using validated scales and self-assessment questionnaires, the present study aimed to establish baseline characteristics regarding dysphagia and HRQL in newly diagnosed patients with EoE and, second, to survey the outcome after treatment with topical corticosteroids.

Materials and Methods

Patients newly diagnosed with EoE and dysphagia were eligible for inclusion. The diagnosis of EoE was established according to the recommendations by the AGA Institute. At inclusion, demographic data and duration of symptoms were recorded, and questionnaires (as below) were administered. The patients were then prescribed aerosolized mometasone furoate 50 µg per spray, 4 sprays per dose taken 4 times daily. The doses were to be administered orally after each meal (breakfast, lunch, and dinner) and before bedtime, and the patients were not allowed to eat or drink for 30 minutes after using the drug. Follow-up was completed 2 months after inclusion. At this time, the patients were interviewed regarding compliance and the effects of the treatment, including side effects and adverse events. In addition, the patients filled out the questionnaires once more. The administration and duration of the treatment followed the recommendations suggested by the AGA Institute, with the exception that mometasone furoate was used instead of fluticasone or budesonide but with an equivalent dosage.

Questionnaires

To measure dysphagia and HRQL, the following scales and questionnaires were used:

1. The Watson Dysphagia Scale (WDS) gives a score ranging from 0 (no dysphagia) to 45 (severe dysphagia) on a 9-item scale (from liquids to solid food). The presence of any dysphagia for each liquid or solid substance is determined and scored by the patient on a 3-point Likert scale (1 = always, 0.5 = sometimes, and 0 = never). This score is then multiplied by a factor for each substance, and the scores for all substances are summed. The scale has been validated and used in several studies incorporating patients with esophageal dysphagia.

2. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Oesophageal Module 18 (EORTC QLQ-OES18) was originally designed to investigate problems due to esophageal cancer location and treatment. However, because the majority of the questions are not cancer specific, the questionnaire has been extensively used in different HRQL studies, and its cross-cultural validity and psychometric properties are considered satisfactory. The questionnaire comprises 4 scales: the dysphagia, eating, reflux, and local pain scales. The scores are calculated according to the EORTC scoring manual. The questions are scored by the patient on a 4-point Likert scale (not at all, sometimes, most of the time, and always), and the 4 points are transformed into scores from 0 to 100, where a high score represents a high level of symptoms/problems.

3. The Short Form–36 (SF-36) questionnaire is a multipurpose, self-administered general health survey consisting of 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically based physical and mental health summary measures. The questionnaire has been used in numerous studies, and its validity is well documented. The patient scores the questions using a 2-, 3-, 5-, or 6-grade Likert scale, respectively, and a 4-week time frame is used. The scores are transformed into a score from 0 to 100, where a high score represents a high level of functioning/well-being.

Statistics and Ethics

The mean, median, standard deviation, and range were used for descriptive purposes, and the Wilcoxon matched-pairs signed-rank test was used to compare the questionnaire scores before and after medical treatment.

The study was performed in accordance with the Declaration of Helsinki and was approved by the Regional Ethical Committee at the University of Gothenburg. Informed consent was obtained from each participant.

Results

During the 12-month study period from January 2009 to December 2009, 31 consecutive, newly diagnosed patients with EoE attending medical care at the Sahlgrenska University Hospital or the NÅL Medical Centre Hospital were included. No patients eligible for inclusion during the study period declined participation in the study. Seventy-four percent (n = 23) were men, and the mean age was 45 years (median, 45; range, 18-89 years). All of the patients suffered from dysphagia of some degree, either intermittent or constant, with a duration ranging from 1 year to 25 years. Forty-five percent (n = 14) had a previous episode of esophageal bolus impaction requiring endoscopic removal. Other atopic diatheses were common, including asthma (29%, n = 9), allergic rhinoconjunctivitis (32%, n = 10), and eczema (6%, n = 2). Three patients (10%) were diagnosed with gastroesophageal reflux disease (GERD) as a concomitant disorder, and hypertension was observed in another 3 patients (10%).

All of the patients completed the questionnaires both at inclusion and at the 2-month follow-up; missing data were rare (~5%). The results of the WDS, the EORTC QLQ-OES18, and SF-36 are presented and depicted in Table 1 and Figures 1 and 2. All of the patients reported dysphagia of some degree.
at inclusion, and improvements after the treatment were seen for several dysphagia-related scales and items, including the overall WDS score, the EORTC QLQ-OES18 dysphagia and eating scales, and problems with choking. In addition, HRQL improvements after treatment according to the SF-36 included improvement in the levels of bodily pain, global health, social functioning, and mental health. The only item score that deteriorated after treatment was trouble with coughing.

The interviews at the follow-up visits indicated that the treatment was well accepted and that compliance was high. Only 1 patient experienced side effects from the mometasone furoate treatment; this patient developed oral candidiasis 2 weeks after the initiation of the treatment. This mild infection responded well to topical antifungal medication (amphotericin B), and the patient then continued the corticosteroid treatment throughout the study period with a favorable outcome with regard to dysphagia relief. No other adverse events were reported during the trial or at the follow-up visits.

**Discussion**

The present study investigated the baseline characteristics regarding dysphagia and HRQL in newly diagnosed patients with EoE, and our results support previous indications of a favorable effect of topical steroid treatment. This assessment was made using validated, self-administered scales and questionnaires. A novel type of corticosteroid for the treatment of EoE, mometasone furoate, was used in this study. This is the first study to our knowledge where EoE patients’ HRQL was surveyed before and after treatment. The high levels of statistical significance obtained despite the limited sample size (n = 31) indicate that the sensitivity is sufficiently high for the scales and questionnaires to be considered valuable instruments for the surveillance of symptom control in patients with EoE.

The value of using validated questionnaires to assess symptoms and HRQL, not only in research but also as a tool in clinical practice, has been emphasized by many. Some authors even suggest that the outcome of HRQL questionnaires better outlines a patient’s disease state than does what the patient actually tells the doctor. The questionnaires used in our study were not completed during a face-to-face interview, in which the patient may want to please the doctor, but were filled out in private and returned anonymously with a return rate of 100%. Analyzing the scores of the various symptom scales implies the possibility of comparing the findings with those of other patient groups and evaluating different treatment regimens. For instance, the mean score of the WDS in our set of patients was somewhat better compared with that previously reported in patients with esophageal strictures or achalasia cardiae but worse compared to the scores of patients with GERD.

The fact that the outcomes of various treatment regimens in patients with EoE need further investigation was recently emphasized by a Cochrane review. In this analysis, the authors concluded that, because of the rarity of relevant studies, there is a limited capacity to compare the pros and cons of the

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Inclusion, Mean ± SD</th>
<th>2 Months, Mean ± SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watson Dysphagia Scale</td>
<td>21.3 ± 10.1</td>
<td>8.9 ± 9.3</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>EORTC QLQ-OES18</td>
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<tr>
<td>Dysphagia scale</td>
<td>20.4 ± 22.1</td>
<td>4.6 ± 9.3</td>
<td>&lt;.00001</td>
</tr>
<tr>
<td>Eating scale</td>
<td>35.0 ± 27.7</td>
<td>17.8 ± 22.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Reflux scale</td>
<td>21.5 ± 26.6</td>
<td>15.0 ± 18.4</td>
<td>.14</td>
</tr>
<tr>
<td>Local pain scale</td>
<td>18.9 ± 19.5</td>
<td>12.1 ± 16.5</td>
<td>.06</td>
</tr>
<tr>
<td>Trouble swallowing saliva</td>
<td>16.1 ± 29.7</td>
<td>8.5 ± 21.0</td>
<td>NS</td>
</tr>
<tr>
<td>Problems with choking</td>
<td>38.6 ± 28.8</td>
<td>16.0 ± 24.1</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>19.3 ± 28.2</td>
<td>22.6 ± 34.9</td>
<td>NS</td>
</tr>
<tr>
<td>Problems with taste</td>
<td>11.8 ± 27.9</td>
<td>5.4 ± 19.4</td>
<td>NS</td>
</tr>
<tr>
<td>Trouble with coughing</td>
<td>2.1 ± 8.2</td>
<td>11.8 ± 25.2</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Trouble with speaking</td>
<td>5.4 ± 15.1</td>
<td>8.6 ± 24.3</td>
<td>NS</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Physical functioning</td>
<td>89.3 ± 16.4</td>
<td>90.9 ± 13.2</td>
<td>NS</td>
</tr>
<tr>
<td>Role–physical</td>
<td>79.8 ± 37.3</td>
<td>90.8 ± 20.2</td>
<td>NS</td>
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<tr>
<td>Bodily pain</td>
<td>74.6 ± 24.6</td>
<td>81.8 ± 22.1</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>General health</td>
<td>71.1 ± 25.4</td>
<td>76.1 ± 22.0</td>
<td>&lt;.05</td>
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<td>Vitality</td>
<td>62.4 ± 23.0</td>
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<tr>
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<td>.0001</td>
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<td>Role–emotional</td>
<td>81.7 ± 35.3</td>
<td>85.6 ± 24.3</td>
<td>NS</td>
</tr>
<tr>
<td>Mental health</td>
<td>73.4 ± 22.8</td>
<td>81.6 ± 15.7</td>
<td>&lt;.01</td>
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</tbody>
</table>

Abbreviations: EORTC QLQ-OES18, European Organization for Research and Treatment of Cancer Quality of Life–Oesophageal Module 18; NS, not significant; SF-36, Short Form–36.
Medical interventions currently used for treating EoE. The first and only randomized placebo-controlled trial on topical corticosteroid treatment in adolescents and adults was just presented by Straumann et al; the results of this study provide additional evidence of the beneficial effect of this treatment (budesonide 1 mg twice daily). However, in that study, which included 36 patients, the primary end point was histological findings, and dysphagia relief was estimated using a nonvalidated scale. In addition, no assessment of the patients’ HRQL was performed. Another recent study that accentuates the need for further investigations was presented by Peterson et al. In that trial, EoE patients (n = 25) were randomized to receive treatment either with a topical corticosteroid (fluticasone 440 µg twice daily) or with a proton-pump inhibitor (esomeprazole 40 mg once daily). Perhaps somewhat unexpectedly, no significant differences with respect to dysphagia relief were found between the 2 treatment arms; however, an apparent limitation of the study was the low number of patients enrolled and the lack of use of a validated instrument for the assessment of dysphagia. The authors hypothesized that GERD might be important in the pathogenesis of adult EoE; however, the increased sensitivity to acid found experimentally to be experienced by EoE patients would be an equally probable explanation of their findings.

An obvious and significant limitation of the present study is the lack of a placebo control group. This prohibits a firm statement that the improvements observed during treatment could be attributed purely to the effect of mometasone furoate itself. Several potential confounders exist, including spontaneous improvement of symptoms without treatment, expectancy effects, the absence of blinding, and a regression toward the mean, which must be considered when interpreting the results. However, the symptom improvement according to the EORTC QLQ-OES18 was not general, as might have been expected in the case of pure placebo causation. Instead, this improvement occurred selectively, significantly influencing the most relevant and expected symptoms such as the dysphagia scale, the eating scale, and the problems with choking item. Furthermore, the importance of the meal as an opportunity to gather and meet people and the associated negative consequences of dysphagia were highlighted by the impaired social functioning dimension (according to the SF-36), which normalized after treatment.

The absence of objective findings to further confirm the improvement after treatment could be considered another relative limitation of the study. Initially, reevaluation with endoscopic examination and biopsy gathering was performed in a few patients (n = 5); however, because the macroscopic and microscopic findings improved in all of these patients and previous studies already have confirmed this effect of topical steroids, we decided to omit the routine of reendoscopies and focus on adding new information on the burden of illness as evaluated by
valid questionnaires. Yet, to better survey the long-term effects and generalizability of the treatment, future studies should strive to incorporate longer follow-up times, larger populations, and more participating medical centers.

Relief of dysphagia and improvement of HRQL would be sufficient reason to treat EoE; however, the fact that Aceves et al. observed considerable fibrosis of the esophageal wall of children and reported that this fibrosis may be prevented by steroid treatment might be an even more important reason to treat. Whether this result with respect to fibrosis applies to adults has not been established, but in the current situation in which there is a lack of knowledge, this medical treatment could be recommended. The good compliance and rare, mild side effects seen in our study incorporating treatment with mometasone furoate further support the use of this approach. Future research should aim at optimizing the doses and duration of therapy, as well as exploring new and more specific treatment modalities, including food elimination strategies, cytokine inhibitors, and allergen immunotherapy.

In summary, we conclude that the use of 3 validated scales and questionnaires in adult patients with newly diagnosed EoE allows a thorough description of their symptomatology, not only regarding dysphagia and its equivalents but also regarding important aspects of their HRQL. The questionnaires appear to be clinically useful instruments for surveillance over time and for detection of changes in symptoms between the treated and untreated disease state. The dysphagia and impaired HRQL found in the untreated patients improved significantly after 2 months of mometasone furoate treatment with a very low rate of side effects. A randomized placebo-controlled trial is warranted to assess causality.

Author Contributions
Henrik Bergquist, conception and design, acquisition of data, analysis and interpretation of data, drafting of article, final approval; Helén Larsson, analysis and interpretation of data, revising the article critically, final approval; Leif Johansson, analysis and interpretation of data, revising the article critically, final approval; Mogens Bove, conception and design, acquisition of data, analysis and interpretation of data, drafting of article, final approval.

Disclosures
Competing interests: Henrik Bergquist has worked as a consultant and lecturer for MSD and AstraZeneca. Mogens Bove has worked as a consultant and lecturer for AstraZeneca, and Leif Johansson has worked as a lecturer for MSD. The authors have no other financial interests in companies and no other conflicts of interest to disclose.

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