Pharyngolaryngeal reflux in outpatient clinical practice: personal experience

La malattia da reflusso faringolaringeo nella pratica clinica ambulatoriale: nostra esperienza

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Parole chiave
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Summary
Proximal pharyngolaryngeal reflux now appears to be strictly related to symptoms and clinical patterns frequently encountered in clinical ORL practice and which are, more often than not, differentiated from classical gastro-oesophageal reflux disease. The aim of the study was to evaluate the incidence of the symptoms and clinical signs of gastro-oesophageal reflux disease, together with the symptomatologic response to a cycle of acid suppression treatment with proton pump inhibitors in a non-selected population comprising consecutive patients coming to the outpatient unit of the Laryngology Clinic of Università Cattolica of Rome between June and December 2001, all of whom had been examined by the same practitioner. Of the 1300 patients evaluated, 52 presented a clinical history and chronic pharyngolaryngeal symptoms strongly indicative of gastro-oesophageal reflux disease. All selected patients were prescribed a two-month regimen of acid suppression therapy (20 mg Omeprazole twice daily, sufficient to confirm the clinical suspicion of pharyngolaryngeal reflux ex adiuvantibus (Omeprazole test), at the same time obtaining a satisfactory response in the symptomatology, as laid out in the guidelines emerging from the 1997 Consensus Conference Report on pharyngolaryngeal reflux. The same patients were later interviewed by telephone to evaluate the effectiveness of treatment, exclusively in terms of improvement in the symptoms. Analysis of the data from the 33 who answered the telephone questionnaire revealed a complete symptomatologic response in 24 (72.7%), partial response in 4 (12.1%) and no response in 5. The Authors stress that, despite the known limits of this treatment, linked to proton pump inhibitors resistance, the “Omeprazole test”, on account of excellent tolerability, lack of adverse effects and, above all, non-invasive nature, is feasible in the preliminary evaluation to confirm clinical suspicion of gastro-oesophageal reflux disease in outpatients, especially when a large-scale pH-metric multielectrode investigation is not possible. Furthermore, despite the many epidemiological, aetiopathogenetic, clinico-diagnostic and therapeutic aspects which remain to be clarified, there is no doubt that gastro-oesophageal reflux disease on account of the particular clinical features, directly involves the ORL specialist not only in the diagnostic, but also in the therapeutic phase.

Riassunto
Il reflusso prossimale faringo-laringeo sembra essere, ormai, strettamente connesso a sintomi e quadri clinici che si riscontrano frequentemente nella pratica clinica ORL e che, il più delle volte, risultano svincolati dalla malattia da reflusso gastroesofageo classica. Gli Autori hanno voluto valutare l’incidenza, ancora incerta in letteratura, della sintomatologia e dei segni clinici della malattia da reflusso prossimale faringo-laringeo e la risposta sintomatologica ad un ciclo di trattamento di soppressione acida con inibitori della pompa protonica, in una popolazione non selezionata costituita dai pazienti afferiti consecutiveamente presso l’ambulatorio divisionale della Clinica Otorinolaringoiatrica dell’Università Cattolica di Roma nel periodo compreso tra giugno e dicembre del 2001 e visitati dallo stesso operatore. 52/1300 pazienti analizzati presentavano una storia clinica ed una sintomatologia cronica faringo-laringea fortemente indicative di malattia da reflusso prossimale faringo-laringeo. A tutti i pazienti selezionati è stata prescritta una terapia medica di soppressione acida che prevedeva la doppia somministrazione giornaliera, per un periodo di due mesi, di 20 mg di omeprazolo, sufficiente per confermare ex adiuvantibus il sospetto diagnostico di reflusso prossimale faringo-laringeo (test all’omeprazolo) ed al contempo ottenere una soddisfacente risposta sintomatologica, come previsto dalle linee guida emerse dal Consensus Conference Report sul reflusso prossimale faringo-laringeo (1997). Successivamente gli stessi pazienti sono stati sottoposti ad un questionario telefonico per valutare la risposta alla terapia, esclusivamente in termini di miglioramento sintomatologico. Dei 33 che hanno risposto al questionario, l’analisi dei dati acquisiti ha evidenziato una risposta sintomatologica completa in 24 (72,7%), parziale in 4 (12,1%) ed assente in 5. Gli Autori sottolineano che, nonostante i limiti già noti relativi alla resistenza al trattamento con IPP, il “test all’omeprazolo”, in considerazione dell’ottima tollerabilità, dell’assenza di reazioni avverse e soprattutto di invasività, può rappresentare una buona indagine preliminare per confermare il sospetto clinico di malattia da reflusso prossimale faringo-laringeo nei pazienti ambulatoriali, soprattutto ove non sia possibile il ricorso, su larga scala, all’indagine pH-metrica multielettrodo. Concludono, infine, evidenziando che, nonostante numerosi aspetti epidemiologici, etiopatogenetici, clinico diagnosticici e terapeutici restino ancora da chiarire, è ormai indiscutibile che la malattia da reflusso pro-
Introduction

Alongside the well-defined picture of the classic gastro-oesophageal reflux disease (GERD), a new clinical entity has been taking shape, in a progressively distinct and often autonomous way: pharyngolaryngeal reflux disease (PLRD).

It includes a combination of supra-oesophageal signs and symptoms affecting, in particular, the otorhinolaryngologic area and which may manifest independently of the classic GERD features, such as pyrosis, retrosternal burning, oesophagitis, sialorrhoea, and burping. Proximal gastro-pharyngolaryngeal reflux, in fact, appears to be strictly related to symptoms frequently encountered in clinical ORL practice, such as dysphonia, vocal asthenia, dysphagia, pharyngodynia, hoarseness, pharyngeal globus, chronic cough, and disorders such as chronic sinusitis, laryngitis and pharyngitis, chronic oedema of the vocal folds, glottic contact ulcer, laryngeal granulomas, subglottic stenosis, tooth caries, tongue base hypertrophy, precancerous lesions and pharyngolaryngeal neoplasms.

This myriad of clinical manifestations continues to place the ORL specialist before epidemiological, aetiopathogenetic, clinico-diagnostic and therapeutic problems which still remain to be fully elucidated. In particular, unequivocal data are lacking regarding the incidence of PLRD, both in the general population and in ORL outpatient practice. Furthermore, the therapeutic regimen in these cases has not yet been standardised.

Aim of the present investigation was to evaluate the incidence of the symptoms and clinical signs of PLRD as well as the response to a cycle of PPI (proton pump inhibitor) acid suppression treatment in a non-selected population comprising consecutive patients attending the outpatient unit of our clinic between June and December 2001, all of whom had been examined by the same practitioner.

Patients and Methods

An analysis has been carried out on a group of 1300 patients who consecutively underwent evaluation, by the same specialist, in our outpatient clinic, between June and December 2001. From this group, those patients were selected suffering from chronic pharyngolaryngeal symptoms not correlated to subacute or chronic infections and unresponsive to earlier routine topical and systemic anti-inflammatory and anti-ca-
Table I. Correlation between endoscopic data and pharyngolaryngeal symptoms in 33 patients who underwent Omeprazole Test.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Posterior laryngitis n. patients</th>
<th>Tongue base hypertrophy n. patients</th>
<th>Pharyngitis n. patients</th>
<th>Granuloma (VC) n. patients</th>
<th>Negative objectivity n. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagging cough</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>33.3%</td>
</tr>
<tr>
<td>Pharyngodynia</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>24.2%</td>
</tr>
<tr>
<td>Foreign-body sensation</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td>36.4%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>6.1%</td>
</tr>
<tr>
<td>Dysphonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

% 72.7 6.1 9.1 3 9.1 100

77 years, whose pharyngolaryngeal symptoms could be presented as: foreign-body sensation and hoarseness (36.4%), nagging cough (33.3%), pharyngodynia (24.2%) and dysphagia (6.1%) (Table I). Within this subgroup, an objective examination showed that 92% presented clinical signs typical of PLRD, such as chronic posterior laryngitis (80%), chronic pharyngitis (10%), tongue base hypertrophy (6.7%) and vocal cord granuloma (0.3%), thus further confirming the initial clinical suspicion. Analysis of the data obtained from the telephone questionnaire revealed that the symptomatologic response to acid suppression treatment was complete in 24/33 (72.7%), partial in 4/33 (12.1%) and absent in 5 (15.2%) of the cases (Tables II, III).

Discussion

PLR, also known as extra-oesophageal reflux, is the backward flow of gastric contents into the pharynx and is a pathological picture with which the ORL specialist is well acquainted, in clinical practice, and which is often distinct from the classic GERD. Two forms of pharyngolaryngeal pathologies may be correlated with the reflux: a simple one, presenting oedema and engorgement of the arytenoid and retrocricoid mucosa, at times associated with hypertrophy of the posterior laryngeal commissure (posterior laryngitis), and a complicated one that is, instead, characterised by clearly pathological situations, such as subglottic stenosis, arytenoid vocal process granulomas, hyper-
motility of the vocal chords, and precancerous pharyngolaryngeal lesions and carcinomas. It has been reported in the literature, in fact, that 4-10% of ORL outpatients and about 50% of those with voice disorders and/or dysphagia present PLR and only a percentage <35% of the latter, instead also present typical signs and symptoms of GERD, particularly, retrosternal pyrosis and oesophagitis. Furthermore, both the pattern and the mechanism with which reflux occurs contribute to a more marked differentiation between the two situations, with considerable aetiopathogenetic, diagnostic and therapeutic implications. In particular, PLR, unlike classical GERD, occurs mainly during the day, during orthostatism, is not associated with oesophagitis or retrosternal pyrosis and does not interfere, except minimally, with oesophageal motor function, which is preserved or, at least, less impaired than in patients with GERD. Moreover, while a physiological reflux exists which is well tolerated by the oesophagus, thanks to protective intrinsic and extrinsic mechanisms, such as bicarbonate secretion, peristalsis and salivary bicarbonates which can restore the neutral pH after such episodes, the mucosa of the pharyngolaryngeal area, instead, lacks these protective acid clearance mechanisms and is, therefore, extremely susceptible to peptic damage. It is precisely for this reason that pharmacological proton pump inhibitory action is so effective, also in PLRD: by blocking the H+/K+ ATP-ase enzyme, the key enzyme in acid production in the gastric wall cells, and, consequently, activation of pepsin, so exposure of inflamed pharyngolaryngeal tissue to complex peptic damage is completely eliminated or reduced. Besides this direct harmful mechanical and chemical activity, a second aetiopathogenetic mechanism has been proposed, namely, activation of vagal reflexes in the distal oesophagus by the reflux matter, which is thought to manifest with chronic cough and frequent need to clear the throat, manifestations which are, in turn, considered responsible for the pharyngolaryngeal symptoms and signs observed clinically. Despite numerous reports on this issue appearing over the last few years, there is, however, still much controversy regarding the aetiologic role of PLR in the onset of supra-oesophageal clinical manifestations (variability of endoscopic laryngeal findings, failure to respond, in a high percentage of cases, to conventional antireflux therapy) and, indeed, the exact incidence of the same.

Over the last few years, the 24-hour pH-metric multielectrode investigation has greatly contributed to the diagnostic work up. This test enables direct, objective measurement of the reflux episodes to be made also in the pharynx, thus confirming the clinical suspicion of PLRD. It is, however, a minimally invasive examination and is not always available in outpatient practice; when it is not available or not suitable for all outpatients presenting symptoms suspicious for PLRD, the Omeprazole test has been proposed as an initial screening measure. This consists in the administration of high doses of Omeprazole in refracted doses for a period of at least 2-3 weeks thus allowing identification of responsive cases warranting continued treatment and/or further diagnostic investigation. Also in the present study, it was decided to use the ex adiuvantibus criterion of the Omeprazole response to evaluate the incidence of PLRD in patients coming to the outpatient Unit of our clinic. In agreement with reports in the literature, we observed that about 4% of these individuals presented symptoms or signs that could be correlated with supra-oesophageal acid reflux. This sample group underwent PPI (Omeprazole) therapy for two months and patients were later contacted by telephone to establish whether there was any improvement in their symptoms. Complete disappearance of symptoms after PPI therapy was observed in 72.7% of cases, while the remaining 27.3% reported a partial response or no response at all. This percentage is in keeping with preliminary data (varying between 19 and 42%) emerging from the literature with regard to resistance to treatment with high doses of PPI in patients with PLRD. The reasons for this oscillation remain to be elucidated (pharmacological tolerance, insufficient 24-hour gastric acid suppression, need to associate other classes of drugs in the treatment, such as prokinetics and/or H2-antagonists, in cases of partial response) and constitute the principal limit of this diagnostic test requiring multielectrode pH-metric investigations to confirm the working diagnosis in non-responsive patients. Despite these limits, however, in our opinion, the “Omeprazole test”, in consideration of the excellent tolerability, absence of adverse effects, and especially of invasive techniques, may be considered a feasible preliminary examination in the presence of clinical suspicion of PLRD in outpatients, especially in those cases in which large-scale use of multielectrode pH-metric evaluation is not available. Furthermore, in our opinion, it is mandatory that all selected patients be later submitted to instrumental examination to exclude other underlying gastro-oesophageal disease, the evolution of which could be masked by, exclusively, empirical and symptomatologic treatment. The present protocol, therefore, includes in symptomatic patients with endoscopic signs of PLRD, X-ray of the oesophagus to evaluate the lumen, oesophageal morphology and the possible presence of hiatal hernia, together with oropharyngo-oesophageal scintiscan. The latter exam is well tolerated, easy to perform and requiring a low dosage; in particular, besides offering functional and dynamic evaluation of the gastro-oesophageopharyngeal area, it also reveals both direct
GERD phenomena and indirect evidence of inflammation and/or oesophagitis through adhesion of the tracer to the areas explored. In this way, it is possible to differentiate, by means of a non-invasive technique, those requiring gastroenterological and endoscopic evaluation (oesophago-gastroduodenoscopy) from those presenting strictly laryngeal features. The latter may, in turn, undergo multielectrode pHi-metric investigation to confirm the presence and modalities of pharyngolaryngeal reflux and better understand the aetio-pathogenetic mechanisms or be submitted to pharmacological treatment.

In conclusion, despite the numerous epidemiological, aetio-pathogenetic, clinico-diagnostic and therapeutic aspects which remain to be clarified, it is now clear that PLRD should be considered a nosologic entity which on account of the particular characteristics, often completely differentiated from those of classic GERD, directly involve the ORL specialist in a role that is not only diagnostic, but also therapeutic.

References