Review article: laryngopharyngeal reflux – the ear, nose and throat patient

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SUMMARY

Laryngopharyngeal reflux is commonly encountered in UK ENT clinics. This paper describes the diagnosis and management of this condition in a district general hospital setting. Invasive investigations are usually reserved for cases which are diagnostically difficult, who do not respond well to medical treatment or where antireflux surgery is contemplated. New techniques which are less invasive are described. Symptoms should be documented using the Reflux Symptom Index at each visit. Standard medical treatment is described.

INTRODUCTION

Laryngopharyngeal reflux (LPR) is now a common diagnosis in UK ENT practice, although acceptance of the disease continues to attract a degree of controversy. The term was first used by Koufman in 1991.[1] It differs from classical gastro-oesophageal reflux disease (GERD) in several respects. Gastro-oesophageal reflux (GER) produces classical symptoms of heartburn and regurgitation, whereas LPR may present with a spectrum of throat symptoms.

GER is characterised by abnormal acid clearance times in the oesophagus (<5% is physiological). This leads to oesophagitis, which can be detected easily at upper gastrointestinal endoscopy. In LPR, oesophageal acid clearance is often normal, with brief 'flashes' of reflux reaching to the upper oesophageal sphincter and beyond, into the laryngopharynx. These reflux episodes may consist of mainly gas carrying an aerosol of gastric contents, rather than a large volume liquid bolus.[2] The upper aerodigestive tract is much more sensitive to the presence of refluxate than the oesophagus.

Refluxate contains both hydrochloric acid and enzymes, notably pepsin. Activated pepsin is probably the causative agent for mucosal inflammation in LPR, rather than acid alone.[3] In an animal model, it has been shown that reflux episodes lasting for 30 s three times per week are sufficient to cause significant mucosal damage. This is in stark contrast to GERD, where the oesophagus can withstand the presence of refluxate for up to 5% of each 24 h period.

While LPR and GERD may exist independently, evidence is growing that as severity increases, it is more likely that features of both will be present.[4] This article will describe current practice in diagnosis and treatment of LPR patients in a UK ENT out-patient clinic.

Diagnosis

In UK practice, most patients are diagnosed following a thorough clinical assessment. This begins with taking a careful case history. LPR symptoms are listed in Table 6. A patient completed questionnaire to quantify symptoms is an important part of the initial work-up, to aid in diagnosis and to set a baseline, which can be used later to assess response to treatment. The Reflux Symptom Index (RSI), described by Belafsky *et al.*,[5] is the most commonly used tool.

An ENT examination is then performed, with particular attention being paid to the larynx and pharynx. Indirect laryngoscopy with a mirror is not adequate in this setting: rigid or flexible laryngoscopy is essential, preferably using a digital system with video recording and still image capture. Features of LPR on examination are listed

in Table 7. These may be quantified using the Reflux Finding Score (RFS), for the same purposes as the RSI described above.

Most UK patients do not undergo further investigations at this stage. Any further tests are reserved for those who do not respond well to treatment, or in whom the diagnosis is unclear. LPR investigations are listed in Table 8.

Barium swallow is no longer routinely used to diagnose reflux disease, although it still has an important role if pharyngeal pouch is suspected. The Bernstein acid perfusion test is mainly of historical interest, but has been used recently in research into reflux-related cough. Upper gastrointestinal endoscopy is valuable in the diagnosis of GERD, but is often normal in LPR. Oesophageal manometry may not be directly helpful in the diagnosis of LPR, but it is necessary to determine the position of upper and lower oesophageal sphincters to guide the correct placement and spacing of electrodes for pH monitoring, and is very useful in the assessment of oesophageal dysmotility, which may be contributing to symptoms.

The 24 h dual channel pH monitoring, with electrodes in the distal oesophagus and at or just above the upper sphincter, has been the mainstay for diagnosis of LPR.[6] Single channel pH recordings can diagnose GERD, but may miss LPR. Some authors have considered that any episodes of reflux reaching the pharynx are abnormal, although others feel that ≥4 episodes in 24 h are needed to make the diagnosis. More recently, multichannel intraluminal impedance measurement has been added to pH monitoring (MII-pH) and may improve diagnostic accuracy, particularly for weakly acidic or non-acidic reflux events,[7] although again there is variation in the interpretation of normative data. Both techniques are invasive (involving transnasal insertion of catheter), expensive to perform, and are poorly tolerated by some patients. Protocols which require the patient to come off their antireflux medication for a period prior to the test can result in a worsening of symptoms. For patients where surgical intervention for LPR is being considered, physiological confirmation of the condition by pH monitoring or MII-pH is normally required.

A non-invasive test that gives rapid results would be very helpful in patient management, rather than waiting for the results of pH monitoring or MII-pH. One non-invasive procedure which has recently become available (Peptest, RD Biomed Limited, Hull, UK) uses a pepsin immunoassay applied within a lateral flow device for sampling pharyngeal secretions: if pepsin is detected, then the patient probably suffers from LPR.[8] Another minimally invasive procedure involves monitoring airway pH in the pharynx to detect aerosolised reflux (Restech, Respiratory Technology Corp., San Diego, CA, USA).[9] In ventilated patients, measurement of pH in exhaled breath condensate may be valuable.[10]

One study has found that in patients with cough related to LPR, which did not respond to standard medication, that some patients were found to be positive for *Helicobacter pylori*, and improved following eradication of the organism.[11]

It must be borne in mind that although LPR is a possible cause of laryngopharyngeal inflammation, it is by no means the only cause. Other causes of laryngeal inflammation are listed in Table 9.

Treatment

Treatment of LPR consists of dietary and behaviour modification for all patients, with pharmacotherapy for many, and surgery for a small number. The basic treatment algorithm used in our unit is shown in Figure 20.

Dietary and behaviour modification has been shown to be very effective in the management of LPR. An

Table 6 | Laryngopharyngeal reflux symptoms

(i) Dysphonia
(ii) Swallowing difficulty ('pseudodysphagia')
(iii) Globus/feeling of lump in throat (FLIT)
(iv) Throat clearing/tickle in throat
(v) Cough/choking
(vi) Thick mucus in throat 'Post Nasal Drip' or 'Catarrh'
(vii) Laryngospasm/cough syncope
(viii) Sore throat

Table 7 | Laryngopharyngeal reflux examination findings

(i) Erythema/hyperaemia, 3 point inflammation (both arytenoids and base of epiglottis)
(ii) Posterior commissure hypertrophy
(iii) Granuloma
(iv) Pseudosulcus
(v) Vocal cord oedema
(vi) Thick intralaryngeal mucus
(vii) Ventricular obliteration
(viii) Extra laryngeal signs: red mucosa in nasopharynx, lingual tonsil
(ix) Hypertrophy

advice sheet is normally given to the patient, along with an explanation of the condition and how to manage it. The main principles include avoiding fatty foods, fizzy drinks (especially cola) and fruit juices. Food should not be taken late in the evening. Smoking should be avoided, and alcohol (particularly spirits, white and rose wine) will aggravate the condition. Patients prone to supine reflux will benefit from using extra pillows or propping up the head of the bed, and sleeping on the left side rather than the right may reduce the tendency to reflux. Vigorous exercise such as jogging or circuit training may exacerbate symptoms. Obesity and tight clothing will also make matters worse.

A reflux advice session from a trained therapist may improve compliance, and voice therapy for those patients with hoarseness can improve outcomes.

Liquid alginate preparations have been shown to be effective in treatment of LPR symptoms, either alone[12] or in combination with proton pump inhibitors (PPI).[13] They have the advantage of being a nonsystemic medication. If used as sole treatment, they should be given after each meal and last thing at night: nothing should be taken by mouth after the nocturnal dose.

H2 receptor antagonists have largely been superseded by PPIs, which are more effective at blocking gastric acid secretion, although they may have a role in those patients who suffer from nocturnal acid breakthrough despite twice daily PPI.

Proton pump inhibitor drugs currently available on the UK market are shown in Table 10, along with their equivalent doses. Omeprazole and lansoprazole are available as generic preparations: rabeprazole, esomeprazole and pantoprazole are still proprietary drugs. All PPIs act for 12–14 h, so in LPR they need to be taken twice daily to give full 24 h protection given the sensitivity of the upper aerodigestive tract to refluxate. A period of 2–3 months is necessary to establish benefit from the medication. Although there has been controversy regarding the use of PPIs in LPR,[14] more recent research has shown evidence of benefit.[15] If patients do not respond to the first drug chosen, or if they suffer unacceptable side effects, it is worth trying another drug as some patients respond better to one PPI than another. Most patients require treatment for approximately 6 months, and then should be gradually weaned from the drug to minimise the possibility of PPI rebound.[16] Figure 21 illustrates a PPI dosage reduction schedule based on my own experience in using rabeprazole.

Proton pump inhibitor drugs are at best an indirect treatment for LPR, helping to reduce the activation of pepsin. At present there are no drugs which directly oppose the action of pepsin.

Prokinetic agents such as domperidone or metoclopramide can be helpful in GERD, especially when there is oesophageal dysmotility, but they are usually unhelpful in LPR. Newer agents that protect against transient lower oesophageal sphincter relaxation are in development,

Table 8 | Laryngopharyngeal reflux investigations

(i) Usually none: clinical diagnosis
(ii) Barium swallow
(iii) Acid perfusion test (Bernstein)
(iv) Oesophagoscopy
(v) Manometry
(vi) Oesophageal pH monitoring
(vii) Oesophageal impedance (MCII-pH)
(viii) Pepsin testing (Peptest)
(ix) Airway pH monitoring (Restech)
(x) Exhaled breath condensate pH monitoring

Table 9 | Causes of laryngeal inflammation

(i) Reflux
(ii) Smoking/inhaled irritants
(iii) Alcohol
(iv) Allergy
(v) Virus infections
(vi) Voice abuse

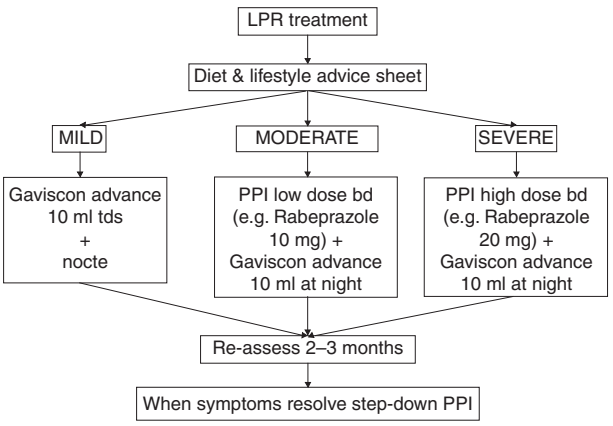

Figure 20 | Laryngopharyngeal reflux treatment algorithm.

Table 10 | Proton pump inhibitor equivalent doses

Equivalent PPI doses		
Drug	Low dose	High dose
Rabeprazole	10 mg	20 mg
Lansoprazole	15 mg	30 mg
Omeprazole	20 mg	40 mg
Esomeprazole	20 mg	40 mg
Pantoprazole	20 mg	40 mg

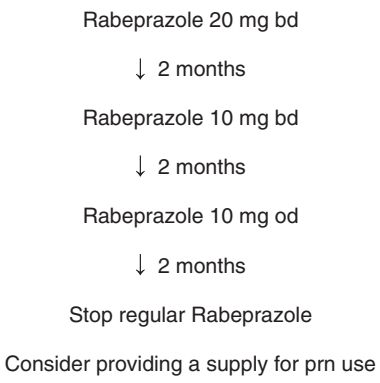

Figure 21 | Proton pump inhibitors dose reduction schedule. Most patients do not need to be on long-term PPIs: only a small number need maintenance therapy. Gaviscon Advance and dietary advice are more suitable long-term measures in the treatment of reflux disease.

including $GABA_B$ agonists,[17] and metatropic glutamate receptor 5 antagonists.[18]

In the longer term, most patients can manage their condition by dietary and lifestyle modification, supplemented by a liquid alginate at night. Some patients also find it helpful to have an 'as required' PPI available.

A small number of patients either fail to respond to medical treatment or require long-term high-dose PPI to control their symptoms. If it is confirmed following investigation that LPR is present after 24 h dual channel pH monitoring or MCII-pH, then laparoscopic fundoplication has been found to be effective.

CONCLUSION

Laryngopharyngeal reflux is a commonly diagnosed condition in UK ENT clinics. Most patients are treated on the basis of a clinical diagnosis, with invasive investigations being reserved for patients where the diagnosis is uncertain or treatment proves difficult. New less invasive techniques (e.g. Peptest, Restech) may be of greater value in UK practice. The majority of cases respond to dietary and lifestyle modification, and medical treatment, with only a small proportion going on to receive antireflux surgery.

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