

An Observational Study to Evaluate the Association of Magnesium Supplement in Laryngopharyngeal Reflux Disease

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Received: 19-07-2023 Revised: 12-08-2023 / Accepted: 25-08-2023

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to evaluate the association between Mg intake and the risk of reflux disease and that the addition of magnesium supplements should be considered and added to the LPRD treatment protocol for adults in accordance with the dietary reference intake (DRI).

Methods: This was a hospital based prospective study done over a period of 2 years in the Department of ENT in patients presenting with symptoms suggestive of LPR of the age group 18-65 years. A total of 200 patients were included in the study.

Results: Out of total 200 cases, 120 (60%) were females and 80 (40%) were males. Out of 120 female patients, 25% (n=30) were below 30 years, 62.50% (n=75) were within 30 to 50 years and 12.50% (n=15) were above 50 years. Out of 80 male patients, 25% (n=20) were below 30 years, 60% (n=48) were within 30 to 50 years and 15% (n=12) were above 50 years. The mean RSI score in each of these age groups for females were 17.4, 18.6 and 16.4 respectively and for males were 12.8, 14.6 and 14.2. Similarly the mean RFS for females were 13.3, 14.4 and 12.6 and for males were 10.2, 13.4 and 12.3 respectively. Foreign body/sticky sensation in throat was the foremost presenting complaint found in 70% of the study population, followed by excessive throat mucus (64%) and constant throat clearing (48%). Hoarseness of voice was seen in 7% of the patients. Dysphagia and dyspnea were the least common symptoms noticed 6% and 3% respectively.

Conclusion: Addition of magnesium supplements along with the regular treatment for LPRD, can improve LPRD symptoms and should be considered in the treatment protocol of LPRD.

Keywords: Laryngopharyngeal reflux disease, Magnesium supplements, GERD, Reflux treatment

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Introduction

Laryngopharyngeal reflux (LPR) is an inflammatory condition of the upper aero digestive tract tissues caused by the direct and indirect effects of gastroduodenal content reflux, which may induce morphologic changes in the interested tract. [1] Common laryngeal findings are arytenoid and vocal cord erythema, posterior commissure hypertrophy, and arytenoid oedema. [2-4] Patients with LPR often experience hoarseness, globus sensation, throat clearing, cough, excess throat mucus, and postnasal drip. [4] LPR is associated with a poor quality of life and a significant healthcare cost. [1,4] Although the prevalence of LPR is still unclear due to a lack of a gold standard for its diagnosis, it was estimated that LPR represents up to 10% of otorhinolaryngologists' consultations. [5,6] Additionally, an increase in the number of medical visits because of reflux, either LPR or gastro esophageal reflux disease (GERD), and in the number of anti-reflux prescriptions has been

observed over the last decades [7], suggesting that reflux is an increasingly spread health issue.

The major factors responsible for GERD are the lower esophageal sphincter dysfunction and the dysfunction of the stomach emptying mechanism. Normally the esophageal mucosal barrier has protective mechanisms against aggressive factors of the stomach content and it remains intact when a physiological reflux occurs, which normally happens at night. Laryngeal and pharyngeal mucosa do not possess these protective mechanisms and acido-peptic activity of the stomach content quickly leads to mucosal lesions in the larynx and pharynx. Mild or new cases of GERD/LPRD respond well to diet and lifestyles changes with/without medications; however, more serious GERD cases may require intensive therapies, medications and/or surgical interventions that can interfere with nutrient absorption, transport and/or utilization. [8] Gastroesophageal reflux is not the only cause of LPR, but rather it is a multifactorial syndrome with

a vast clinical representation and with complications, so it requires a multidisciplinary approach.

Mg helps relieve GERD and consequently LPRD by two mechanisms. Mg plays a major role in regulation of muscle contraction and it helps smooth muscles to relax. It plays a role in the action of pyloric sphincter. When the digestion of food in the stomach is complete, the pyloric sphincter relaxes, thereby allowing food to enter the small intestine for further digestive process. In case of magnesium deficiency, the pyloric sphincter fails to relax as often as it should, which impair gastric emptying. When the food remains in the stomach for a longer time, it creates pressure on the LES, causing it to open upwards and thereby causing acid reflux.

The aim of the present study was to evaluate the association between Mg intake and the risk of reflux disease and that the addition of magnesium supplements should be considered and added to the LPRD treatment protocol for adults in accordance with the dietary reference intake (DRI).

Materials and Methods

This was a hospital based prospective study done over a period of 2 years in the Department of ENT at Netaji Subhas Medical College and Hospital, Bihta, Patna, India in patients presenting with symptoms suggestive of LPR of the age group 18-65 years. A total of 200 patients were included in the study. After obtaining informed verbal consent, they were interviewed with predetermined questionnaire of reflux symptom index (RSI). Then video laryngoscopy was done in each of the patients and reflux finding score (RFS) was obtained. A RFS score above 7 and RSI above 13 were considered suggestive of LPRD. Data was analysed for age and sex distribution.

The data was collected prospectively by questionnaire and clinical examination. All the

patients presenting with symptoms like feeling of lump on the throat, changes in voice, difficulty in swallowing, chronic cough, excess throat mucus, heartburn and breathing difficulty were first clinically examined including examination with 70 degree Karl Storz endoscope.

Exclusion criteria were habit of smoking or tobacco-chewing, recent history of upper respiratory tract infection, history of any systemic inflammatory disease, voice abuse, thyroid mass, laryngeal tumours and vocal nodules and polyps and RFS below 7.

Questionnaire for RSI

It included name, date and the question: within the last month, how did the following problems affect you? (0-5 rating scale with 0=no problem and 5=severe). Normative data suggests that a RSI of greater than or equal to 13 is clinically significant. Therefore a RSI>13 may be indicative of significant reflux. Prior informed consent was signed by all the participants enrolled as per guidelines and standards of research using human beings. The study was given approval by the institutional ethics committee of the hospital.

The patients were followed up at 1 month and 3 months from initiation of medication and review scoring of RSI and RFS were done. Data was analyzed to ascertain the role of magnesium glycinate. The patients, who were under adequate treatment and following lifestyle modifications properly for at least 2 months but showing no improvement, were advised to follow a specially formulated reflux induction diet habit for 2 weeks and followed up to find out its impact.

The data was analyzed descriptively with Microsoft excel and statistical package for the social sciences (SPSS) version 21 using appropriate tests

Results

Table 1: Prevalence of LPRD by sex

Sex	Prevalence (%)
Females	120 (60)
Males	80 (40)

Out of total 200 cases, 120 (60%) were females and 80 (40%) were males.

Table 2: Prevalence of LPRD by age groups in both sexes

Sex	Age group (years)	Prevalence (%)
Females	<30	30 (25)
	30-50	75 (62.50)
	>50	15 (12.50)
Males	<30	20 (25)
	30-50	48 (60)
	>50	12 (15)

Out of 120 female patients, 25% (n=30) were below 30 years, 62.50% (n=75) were within 30 to 50 years and 12.50% (n=15) were above 50 years. Out of 80 male patients, 25% (n=20) were below 30 years, 60% (n=48) were within 30 to 50 years and 15% (n=12) were above 50 years.

Table 3: Mean RSI and RFS over both sexes in different age groups

Sex	Age group(years)	MeanRSI	Mean RFS
Females	<30	17.4	13.3
	30-50	18.6	14.4
	>50	16.4	12.6
Males	<30	12.8	10.2
	30-50	14.6	13.4
	>50	14.2	12.3

The mean RSI score in each of these age groups for females were 17.4, 18.6 and 16.4 respectively and for males were 12.8, 14.6 and 14.2. Similarly the mean RFS for females were 13.3, 14.4 and 12.6 and for males were 10.2, 13.4 and 12.3 respectively.

Table 4: Symptoms among patients with LPRD

Symptoms	N (%)
Foreign body sensations	140 (70)
Excessive throat mucous	128 (64)
Throat clearing	96 (48)
Chronic cough	34 (17)
Dysphagia	12 (6)
Dyspnoea	6 (3)
Hoarsness of voice	14 (7)
Heart burn	48 (24)

Foreign body/sticky sensation in throat was the foremost presenting complaint found in 70% of the study population, followed by excessive throat mucus (64%) and constant throat clearing (48%). Hoarseness of voice was seen in 7% of the patients. Dysphagia and dyspnea were the least common symptoms noticed 6% and 3% respectively.

Table 5: Endoscopic findings among patients with LPRD

Endoscopic findings	N (%)
Erythema/Hyperemia	200 (100)
Diffuse laryngeal edema	144 (72)
Subglottic edema	20 (10)
Vocal fold edema	130 (65)
Ventricular obliteration	16 (8)
Posterior commissure hypertrophy	200 (100)
Granuloma/Granulation	200 (100)
Thick endolaryngeal mucus	80 (40)

Among the laryngeal signs of LPRD, granular pharynx, laryngeal erythema and posterior commissure hypertrophy were present in all the cases. 72% of the cases had diffuse laryngeal oedema and thick endolaryngeal mucus ('positive string sign') was noted in 40% cases. Subglottic edema and ventricular obliteration were rare findings, found only in 10% and 8% cases respectively.

Discussion

Laryngopharyngeal reflux disease (LPRD) is one of the highly prevalent diseases seen in the clinical

practice of an otorhinolaryngologist and general physician. It is one of the most common upper gastrointestinal disorder encountered in the general population. According to Sataloff, laryngopharyngeal reflux (LPR) incorporates a complex set of abnormalities. [9] In healthy individuals, there are four barriers to reflux: the lower esophageal sphincter, the upper esophageal sphincter, esophageal peristalsis and epithelial resistance factors. Dysfunction in any of the above may lead to symptoms of LPR. The Merck manual (2020) defines gastroesophageal reflux disease (GERD) as the "incompetence of the lower

esophageal sphincter (which) allows reflux of gastric contents into the esophagus". When reflux occurs over a prolonged period of time, it leads to complications including inflammation of the esophagus (esophagitis), abnormal scarring, and stricture, and is also associated with LPRD that causes feeling of lump in the throat, vocal irritation, or respiratory complications. [10,11]

Out of total 200 cases, 120 (60%) were females and 80 (40%) were males. Out of 120 female patients, 25% (n=30) were below 30 years, 62.50% (n=75) were within 30 to 50 years and 12.50% (n=15) were above 50 years. Out of 80 male patients, 25% (n=20) were below 30 years, 60% (n=48) were within 30 to 50 years and 15% (n=12) were above 50 years. The mean RSI score in each of these age groups for females were 17.4, 18.6 and 16.4 respectively and for males were 12.8, 14.6 and 14.2. Similarly the mean RFS for females were 13.3, 14.4 and 12.6 and for males were 10.2, 13.4 and 12.3 respectively. Foreign body/sticky sensation in throat was the foremost presenting complaint found in 70% of the study population, followed by excessive throat mucus (64%) and constant throat clearing (48%). Hoarseness of voice was seen in 7% of the patients. Dysphagia and dyspnea were the least common symptoms noticed 6% and 3% respectively. Since magnesium plays a major role in the regulation of smooth muscle contraction by relaxing the pyloric sphincter and enhancing gastric emptying, thereby decreasing the pressure on the LES, and further reflux of gastric contents to the esophagus and the result of hypomagnesemia following prolonged usage of PPIs, a hypothesis was made that adding magnesium supplements along with the regular treatment for LPRD, can improve LPRD symptoms, and our study proves the same. [12] A prospective multicentre study conducted in 2014 concluded that pantoprazole magnesium dehydrate 40 mg once daily for 4 weeks significantly improves GERD symptoms and that it is a safe, effective and well tolerated drug. The fact that pantoprazole magnesium has a prolonged elimination half-life compared with pantoprazole sodium is likely due to the slow dissolution of the magnesium-containing tablets in the stomach, resulting in reduced solubility which may result in longer gastric acid suppression for day-time and night-time symptom control. [13]

McGlashan et al. conducted a RCT on 49 patients comparing the efficacy of a liquid alginate suspension (Gaviscon® Advance) to placebo in reducing LPR signs and symptoms. [14] They found a superiority of the alginate for LPR symptoms as measured by the RSI both at 2 and 6 months. A significant reduction of the RSI was reported also by Tseng et al. in a RCT comparing alginates (Alginos) to placebo after 8-weeks of treatments in 80 patients with LPR, although it did not significantly differ to the RSI reduction of the placebo. [15] Another study

compared the effect of the alginate (Gaviscon® Advance) alone to the efficacy of the alginate as an add-on treatment to PPIs in 72 patients with LPR. [16] A significant number of patients had overlap of two or more symptoms. Among the laryngeal signs of LPRD, granular pharynx, laryngeal erythema and posterior commissure hypertrophy were present in all the cases. 72% of the cases had diffuse laryngeal oedema and thick endolaryngeal mucus ('positive string sign') was noted in 40% cases. Subglottic edema and ventricular obliteration were rare findings, found only in 10% and 8% cases respectively.

A prospective multicenter study conducted in 2014 concluded that pantoprazole magnesium dehydrate 40 mg once daily for 4 weeks significantly improves GERD symptoms and that it is a safe, effective and well tolerated drug. The fact that pantoprazole magnesium has a prolonged elimination half-life compared with pantoprazole sodium is likely due to the slow dissolution of the magnesium-containing tablets in the stomach, resulting in reduced solubility which may result in longer gastric acid suppression for day-time and night-time symptom control. [17] Since the diagnostic tools like 24 hour ambulatory double-probe pH monitoring and detection of pepsin in throat sputum by immunoassay are not readily available in our centre, LPR was diagnosed clinically by assessing RSI and RFS. A RSI greater than 13 and RFS score greater than 7 have been used as clinical diagnostic criteria. Laryngeal erythema was seen to be diminishing with increasing severity of the disease but is not a reliable marker. Laryngeal edema and PCH were found to be a consistent marker of disease severity. A study conducted in rats show that orally administered L arginine and L glycine are highly effective against acid reflux esophagitis. [18] However its role in humans has to be studied and the role of magnesium glycinate combination needs to be evaluated. An Ireland population based study indicated that high intake of Mg may protect against reflux esophagitis and Barrett's oesophagus. The protective effect of Mg may be particularly pronounced in the context of a low Ca: Mg ratio intake. [19]

Conclusion

Adding magnesium supplements along with the regular treatment for LPRD, can improve LPRD symptoms, and should be considered in the treatment protocol of LPRD. Future studies including cohort studies and clinical trials are necessary to confirm our findings. Our findings, if confirmed, will have important public health significance.

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