

A Hospital Based Prospective Study the Assessing the Role of Magnesium Supplement in Laryngopharyngeal Reflux Disease**Satyabrata Dash****Associate Professor, Department of ENT, Gauri Devi Institute of Medical Sciences and Hospital, Durgapur, West Bengal, India****Received: 11-06-2023 / Revised: 09-07-2023 / Accepted: 10-08-2023****Corresponding author: Dr. Satyabrata Dash****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 1 year in the Department of ENT at Gauri Devi Institute of medical Sciences and Hospital, Durgapur, West Bengal, India in patients presenting with symptoms suggestive of LPR of the age group 18-65 years. A total of 100 patients were included in the study.

Results: Out of total 100 cases, 62 (62%) were females and 38 (38%) were males. Out of 68 female patients, 24.19% (n=15) were below 30 years, 61.29% (n=38) were within 30 to 50 years and 14.52% (n=9) were above 50 years. Out of 38 male patients, 23.68% (n=9) were below 30 years, 57.89% (n=22) were within 30 to 50 years and 18.43% (n=7) 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 69% 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. 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. 70% 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.

Conclusion: The use of magnesium supplements in conjunction with standard therapy for laryngopharyngeal reflux disease (LPRD) has the potential to enhance LPRD symptomatology and warrants consideration within the treatment regimen for LPRD.

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

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Introduction

Gastroesophageal reflux disease (GERD) is one of the most frequent gastrointestinal diseases.[1] It is defined on the basis of both esophageal and extra-esophageal symptoms, and/or lesions resulting from the reflux of gastric contents into the esophagus. GERD symptoms can be typical, such as heartburn and regurgitation, and atypical, such as chest pain, chronic cough, laryngeal burn, globus, and hoarseness. Therapy is commonly based on proton pump inhibitors (PPIs) and alginates as add on therapy. PPIs are effective in healing lesions and improving symptoms in most cases.[2] However, there is a significant proportion of patients, ranging from 10 to 40%, whose symptoms do not adequately respond to PPI therapy.[3-6]

Both genetic and environmental factors appear to influence the presence of GERD. Numerous studies have shown that obesity, weight gain, and increasing body mass index (BMI) are associated with GERD. Hiatal hernia is also a risk factor for GERD symptoms. Studies indicate that individuals with large hiatal hernias have shorter and weaker lower esophageal sphincters (LES), increased amount of reflux, less-efficient acid clearance, less-effective peristalsis, and increased severity of esophagitis compared with individuals with small or no hiatal hernia.[7] Research also indicates that smoking, excess alcohol consumption, irritable bowel syndrome, and a family history of upper GI disease are risk factors. Pharmaceutical usage such as anticholinergics, antidepressants, and inhaled

bronchodilators are also related to the disease. The study also associated lack of education and manual work with the presence of GERD.[8] Additional studies have suggested that increased intake of table salt, sweets, or white bread is also a risk factor. Exercise and diets high in fruit and dietary fiber appear to be protective against the condition.[9,10] However, high-intensity exercise has been shown to decrease LES pressure and induce GERD symptoms in otherwise asymptomatic individuals.[11] Caffeine ingestion also decreases LES pressure and decreases distal esophageal mean amplitude of contractions and peristaltic velocity, which can increase reflux.[12]

Magnesium is the most abundant intracellular divalent cation in the body. It plays an essential role in several physiological and biochemical processes. 50-60% of total magnesium is stored in the bones, about 40% is intracellular (mainly in muscles) and only 1% is found in extracellular fluid.[13] Approximately one third of the average daily magnesium (Mg) intake (about 360 mg; 15 mmol) is absorbed in the small intestine through both a saturable transport system and passive diffusion, while another 20 mg (0.8 mmol) is absorbed in the large bowel. Conversely, almost 40 mg (1.7 mmol) of magnesium is excreted in intestinal secretions.[13,14] 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 impairs 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 1 year in the Department of ENT at Gauri Devi Institute of medical Sciences and Hospital, Durgapur, West Bengal, India in patients

presenting with symptoms suggestive of LPR of the age group 18-65 years. A total of 100 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	62 (62)
Males	38 (38)

Out of total 100 cases, 62 (62%) were females and 38 (38%) were males.

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

Sex	Age group (years)	Prevalence (%)
Females	<30	15 (24.19)
	30-50	38 (61.29)
	>50	9 (14.52)
Males	<30	9 (23.68)
	30-50	22 (57.89)
	>50	7 (18.43)

Out of 68 female patients, 24.19% (n=15) were below 30 years, 61.29% (n=38) were within 30 to 50 years and 14.52% (n=9) were above 50 years. Out of 38 male patients, 23.68% (n=9) were below 30 years, 57.89% (n=22) were within 30 to 50 years and 18.43% (n=7) were above 50 years.

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

Sex	Age group (years)	Mean RSI	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	69 (69)
Excessive throat mucous	64 (64)
Throat clearing	48 (48)
Chronic cough	16 (16)
Dysphagia	6 (6)
Dyspnoea	3 (3)
Hoarseness of voice	7 (7)
Heart burn	24 (24)

Foreign body/sticky sensation in throat was the foremost presenting complaint found in 69% 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. A significant number of patients had overlap of two or more symptoms.

Table 5: Endoscopic findings among patients with LPRD

Endoscopic findings	N (%)
Erythema/Hyperemia	100 (100)
Diffuse laryngeal edema	70 (70)
Subglottic edema	10 (10)
Vocal fold edema	64 (64)
Ventricular obliteration	8 (8)
Posterior commissure hypertrophy	100 (100)
Granuloma/Granulation	100 (100)
Thick endolaryngeal mucus	40 (40)

Among the laryngeal signs of LPRD, granular pharynx, laryngeal erythema and posterior commissure hypertrophy were present in all the cases. 70% 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.[15] 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.[16,17]

Out of total 100 cases, 62 (62%) were females and 38 (38%) were males. Out of 68 female patients, 24.19% (n=15) were below 30 years, 61.29% (n=38) were within 30 to 50 years and 14.52% (n=9) were above 50 years. Out of 38 male patients, 23.68% (n=9) were below 30 years, 57.89% (n=22) were within 30 to 50 years and 18.43% (n=7) 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 69% 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.[18] 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.[19]

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.[20] 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.[21] 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.[22] 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. 70% 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.[23] 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.²⁰ 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.²¹

Conclusion

The use of magnesium supplements as an adjunct to conventional therapy for laryngopharyngeal reflux disease (LPRD) has the potential to ameliorate LPRD symptoms, hence warranting consideration within the treatment regimen for LPRD. Further research is required to validate our results by the implementation of future studies, such as cohort studies and clinical trials. If our results are validated, they will have significant implications for public health.

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