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Original Research Article

The role of magnesium supplement in laryngopharyngeal reflux disease

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ABSTRACT

Background: Laryngopharyngeal reflux disease (LPRD) is one of the most prevalent upper gastrointestinal disorder encountered in clinical practice and its optimal treatment is not standardized. The role of magnesium in the human body functions is often underestimated. Since magnesium (Mg) 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, it was hypothesized that adding magnesium supplements along with the regular treatment for LPRD, can improve LPRD symptoms. Magnesium has a neutralizing action on the gastric acid and therefore, it may be pertinent to achieve optimal Mg intakes in patients with LPRD.
Methods: This is a prospective study done over a period of 1 year conducted in a tertiary care hospital in central India in patients presenting with LPRD of the age group 18-65 years.
Results: The study patients were divided into two groups-one treated with esmoprazole 40 mg capsules and alginate syrup and the other with esmoprazole capsules, alginate syrup and magnesium glycinate (250 mg) supplement. Both the groups showed appreciable improvement in their mean reflux symptom index (RSI) and reflux finding score (RFS) at 1 month and 3 months follow-up. Females showed a higher preponderance than males in the disease, symptoms and the mean RSI and RFS score.
Conclusions: 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

INTRODUCTION

Laryngopharyngeal reflux disease (LPRD) is one of the highly prevalent diseases seen in the clinical practice of an otorhinolaryngoligist 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.[1] 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 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.[2,3]

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

acidopeptic 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.[3,4]

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.

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 inextracellular fluid.[5]

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.[5,6]

Overall, approximately 100 mg (4.1 mmol) of magnesium is absorbed and magnesium balance is maintained by urinary excretion. As the body cannot readily mobilize magnesium stores (in fact, equilibration with bone stores takes place after several weeks), alterations in magnesium intake are balanced by changes in urinary magnesium reabsorption.[5,7]

Hypomagnesimia is often underestimated and it can cause non-specific symptoms like fatigue, weakness and nausea and major complications like cardiac arrhythmias, neurological disturbances, seizures and secondary electrolyte imbalances. Mg deficiency can develop due to gastrointestinal and/or renal diseases. Long term PPI therapy is associated with hypomagnesemia.[8,9]

The major food sources of Mg are nuts, whole-grain foods, legumes, green leafy vegetables and deep-ocean fish.[10]

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.

Another mechanism by which Mg helps relieve GERD is by its neutralizing action on the gastric acid.

Therefore, it may be pertinent to achieve optimal Mg intakes in patients with LPRD.

The primary aim of this 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 is a hospital based prospective study done over a period of 1 year between February 2020- February 2021 conducted in a tertiary care hospital in central India in patients presenting with symptoms suggestive of LPR, attending the ear, nose and throat (ENT) out-patients' department (OPD),of the age group 18-65 years.

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.

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) (Table 1). Then video laryngoscopy was done in each of the patients and reflux finding score (RFS) (Table 2) was obtained. A RFS score above 7 and RSI above 13 were considered suggestive of LPRD. Data was analysed for age and sex distribution.

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.

Table 1: Complaint.

Complaint	Score					
Sensations/something sticking in your throat	0	1	2	3	4	5
Throat clearing	0	1	2	3	4	5
Excess throat mucous/postnasal drip	0	1	2	3	4	5
Difficulty swallowing food, liquids or pills	0	1	2	3	4	5
Hoarseness/change in voice	0	1	2	3	4	5
Coughing after you ate or after lying down	0	1	2	3	4	5
Breathing difficulties/choking	0	1	2	3	4	5
Chronic cough	0	1	2	3	4	5
Heart burn, chest pain, indigestion, or stomach acid coming up	0	1	2	3	4	5
Total						

Table 2: Finding.

Finding	Score
Erythema/hyperemia	2=arytenoids only; 4=diffuse
Diffuse laryngeal edema	1=mild; 2=moderate; 3=severe; 4=obstructing
Subglottic edema	2=present; 0=absent
Vocal fold edema	1=mild; 2=moderate; 3=severe; 4=polypoid
Ventricular obliteration	2=partial; 4=complete
Posterior commissure hypertrophy	1=mild; 2=moderate; 3=severe; 4=obstructing
Granuloma/granulation	2=present; 0=absent
Thick endolaryngeal mucus	2=present; 0=absent

Data was analyzed for age and sex distribution. Both male and female were divided in 3 age groups - less than 30 years, 30 to 50 years and above 50 years. In each group, mean RSI and RFS were correlated between same age groups. The presenting symptoms and signs were analyzed for their relative percentage. The study population was then divided into 3 groups based on RSI score (group A: score below 13, group B: score 13-20, group C: score above 20). In each group, the mean value of different signs were calculated and analyzed for their correlation with disease severity.

Finally the study population was divided into 3 groups based on RFS score (8 to 10, 11 to 14 and above 14). In each group, patients were randomly assigned to two groups- one to be treated with esmoprazole 40 mg capsules and alginate syrup and the other with esmoprazole 40 mg capsules, alginate syrups and magnesium glycinate 250 mg supplement. All patients were thoroughly counselled for lifestyle modifications.

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

Out of total 200 cases, 121 (60.5%) were females and 79 (39.5%) were males. So female: male ratio was 1.53:1. Out of 121 female patients, 25.6% (n=31) were below 30 years, 62.8% (n=76) were within 30 to 50 years and 11.6% (n=14) were above 50 years. Out of 79 male patients, 22.7% (n=18) were below 30 years, 58.2% (n=46) were within 30 to 50 years and 19% (n=15) were above 50 years.

Table 3: Prevalence of LPRD by sex.

Sex	Prevalence (%)
Females	121 (60.5)
Males	79 (39.5)

The mean RSI score in each of these age groups for females were 16.7, 17.9 and 15.2 respectively and for males were 13.8, 15.6 and 14.2. Similarly the mean RFS for females were 12.7, 13.3 and 11.4 and for males were 11.4, 13.4 and 12.3 respectively.

Table 4: Prevalence of LPRD by age groups in both sexes.

Sex	Age group (years)	Prevalence (%)
Females	<30	31 (25.6)
	30-50	76 (62.8)
	>50	14 (11.6)
Males	<30	18 (22.7)
	30-50	46 (58.2)
	>50	15 (19)

Table 5: Mean RSI and RFS over both sexes in different age groups.

Sex	Age group (years)	Mean RSI	Mean RFS
Females	<30	16.7	12.7
	30-50	17.9	13.3
	>50	15.2	11.4
Males	<30	13.8	11.4
	30-50	15.6	13.4
	>50	14.2	12.3

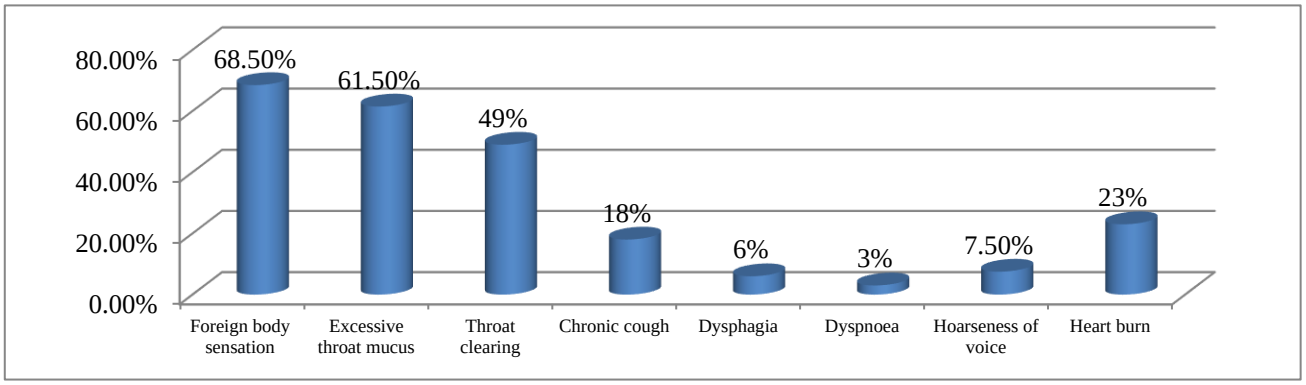

Figure 1: Symptoms among patients with LPRD.

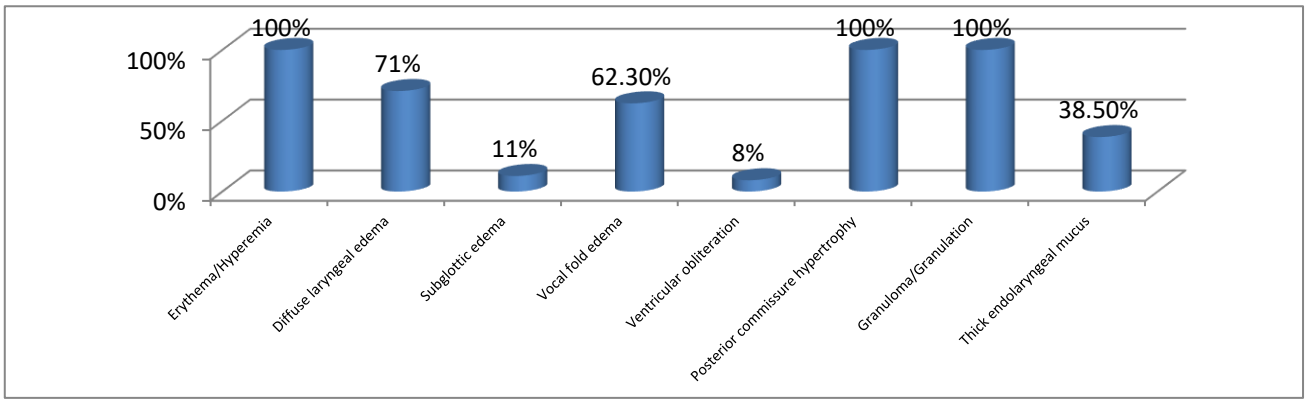

Figure 2: Endoscopic findings among patients with LPRD.

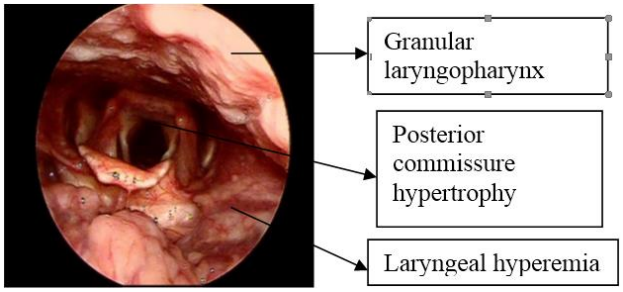

Figure 3: LPRD.

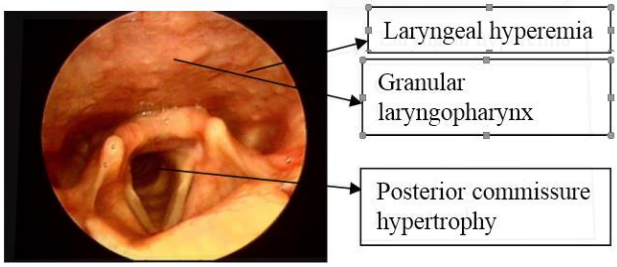

Figure 4: GERD.

Foreign body/sticky sensation in throat was the foremost presenting complaint found in 68.5% of the study population, followed by excessive throat mucus (61.5%) and constant throat clearing (49%). Hoarseness of voice was seen in 7.5% 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. 71% of the cases had diffuse laryngeal oedema and thick endolaryngeal mucus ('positive string sign') was noted in 38.5% cases. Subglottic edema and ventricular obliteration were rare findings, found only in 11% and 8% cases respectively.

The study patients were randomly divided into two groups- one treated with esmoprazole 40 mg capsules and alginate syrup and the other with esmoprazole capsules, alginate syrup and magnesium glycinate (250 mg) supplement.

Both the groups showed appreciable improvement in their mean RSI and RFS score at 1 month and 3 months follow-up. In both the groups the p value was calculated to be <0.05 and was found to be statistically significant.

DISCUSSION

The effects of the symptoms of LPRD and GERD are believed to be secondary to the irritative effects of gastric refluxate on the sensitive pharyngeal and esophageal mucosa.[11] The harmful agents in the refluxate are primarily acid and activated pepsin.

The optimal treatment of LPRD is neither standardized nor validated.[12] LPRD is a multifactorial disease, whose symptoms are nonspecific. LPR appears to be a different clinical variation of GERD.

It has been estimated that 10 to 50% of patients with laryngeal complaints have a GER-related underlying cause.[13]

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.[14]

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.[15]

Another study says that one of the strategies to increase PPI efficacy is to use magnesium formulations such as in esomeprazole, omeprazole or pantoprazole.[16]

Whether magnesium based PPIs or magnesium based antacids are more effective than magnesium supplements alone need to be evaluated.

Hypomagnesemia has been reported in adult patients taking PPIs for at least 3 months, but most cases occurred after a year of treatment.[17,18] The cause for hypomagnesemia is attributed to PPIs aggravating the TRPM6/TRPM7 genes that may lead to decreased magnesium intestinal absorption.[19]

So this further warrants the concomitant supplementation of Mg along with long term PPI usage in LPRD.

No studies have been conducted yet to establish whether Mg has a role in the management of LPRD.

Moreover there is no clinical evidence of a definitive role of Mg deficiency causing LPRD.

From the results of our study, we see that LPRD is predominantly a disease in females. In both of the sexes, middle-aged persons (30-50) are most often affected. The severity of disease in different age groups, as obtained from mean RFS score, seems to be similar in male and female and it is more in middle aged patients in both the groups. However, the symptom scores were much higher in females than males in respective age groups.

Foreign body sensation in the throat was the most common complaint and among the endoscopic signs granular laryngopharynx, laryngeal erythema, and posterior commissure hypertrophy were found in all the cases.

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 a 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

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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REFERENCES

1. Sataloff RT. Gastroesophageal reflux related chronic laryngitis. Commentary. Arch Otolaryngol Head Neck Surg. 2010;136(9):914-5.

2. Lynch KL. Gastroesophageal Reflux Disease (GERD) in Merck Manual Professional Version. 2019. Available at: https://www.msdmanuals .com/en-in/professional/gastrointestinal-disorders/ esophageal-and-swallowing-disorders/gastroesopha geal-reflux-disease-gerd. Assessed on 24 September 2021.
3. Simic PJ. Acid Reflux (GERD). E-medicine health. 2019. Available at: https://www.emedicinehealth. com/acid_reflux_disease_gerd/article_em.htm. Accessed on 24 September 2021.
4. American Gastroenterological Association website. Understanding heartburn and reflux disease. 2020. Available at: https://patient.gastro.org/gastroeso phageal-reflux-disease-gerd/. Accessed on 24 September 2021.
5. Allgrove J. Physiology of calcium, phosphate and magnesium. Endocr Dev. 2009;16:8-31.
6. Quamme GA. Recent developments in intestinal magnesium absorption. Curr Opin Gastroenterol. 2008;24:230-5.
7. Shils ME. Experimental human magnesium depletion. Medicine (Baltimore). 1969;48:61-85.
8. Hess MW, Hoenderop JG, Bindels RJ, Drenth JP. Systematic review: hypomagnesaemia induced by proton pump inhibition. Aliment Pharmacol Ther. 2012;36:405-13.
9. Mackay JD, Bladon PT. Hypomagnesaemia due to proton-pump inhibitor therapy: clinical case series. QJM. 2010;103:387-95.
10. Institute of Medicine & Food and Nutrition Board. Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride. Washington, DC: National Academies Press. 1997.
11. Bough I, Sataloff R, Castell D, Hills J, Gideon R, Spiegel J. Gastroesophageal reflux laryngitis resistant to omeprazole therapy. J Voice. 1995;9:205-11.
12. Hogan W, Shaker R. Medical treatment of supraesophageal complications of gastroesophageal reflux disease. Am J Med. 2001;111(8A):197-201.
13. Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope. 1991;101(4):1-78.
14. Potter JD, Robertson SP, Johnson JD. Magnesium and the regulation of muscle contraction. Fed Proc. 1981;40(12):2653-6.
15. Remes-Troche JM, Sobrino-Cossío S. Efficacy, safety, and tolerability of pantoprazole magnesium in the treatment of reflux symptoms in patients with gastroesophageal reflux disease (GERD). Clin Drug Investig. 2014;34(2):83-93.
16. Hein J. Comparison of the efficacy and safety of pantoprazole magnesium and pantoprazole sodium in the treatment of gastro- oesophageal reflux disease: a randomized, double-blind, con- trolled, multicentre trial. Clin Drug Investig. 2011;31(9):655-64.
17. Chen J, Yuan YC, Leontiadis GI, Howden CW. Recent safety concerns with proton pump inhibitors. J Clin Gastroenterol. 2012;46(2):93-114.
18. Ito T, Jensen RT. Association of long-term proton pump inhibitor therapy with bone fractures and effects on absorption of calcium, vitamin B12, iron, and magnesium. Curr Gastroenterol Rep. 2010;12(6):448-57.
19. Srinutta T, Chewcharat A, Takkavatakarn K, Praditpornsilpa K, Eiam Ong S, et al. Proton pump inhibitors and hypomagnesemia: A meta-analysis of observational studies. Medicine (Baltimore). 2019;98:e17788.
20. Nagahama K, Nishio H, Yamato M, Takeuchi K. Orally administered L-arginine and glycine are highly effective against acid reflux esophagitis in rats. Med Sci Monit. 2012;18(1):9-15.
21. Dai Q, Cantwell MM, Murray LJ, Dietary magnesium, calcium: magnesium ratio and risk of reflux oesophagitis, Barrett's oesophagus and oesophageal adenocarcinoma: a population-based case-control study. Br J Nutr. 2016;115(2):342-50.

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