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Medicine

STUDY OF SERUM MAGNESIUM IN ACUTE MYOCARDIAL INFARCTION

G. Bala Sreenivas — Assistant professor, Department of General Medicine, Government Medical College, Mahabubnagar, Telangana

Nishant Tummalasugur* — Associate professor, Department of General Medicine, Government Medical College, Mahabubnagar, Telangana *Corresponding Author

ABSTRACT

INTRODUCTION: Acute myocardial infarction (AMI) is the most important consequence of coronary artery disease(CAD) and Magnesium has been implicated in the pathogenesis and complications of AMI.

AIM: To study the relation between the change of serum magnesium levels during AMI and association of magnesium levels with the complications of AMI.

METHODOLOGY: The present study was a prospective, case control study involving 50 patients with AMI and 10 healthy controls, admitted in department of medicine SVS medical college, Mahabubnagar during the period of August 2015- July 2017, fulfilling the inclusion and exclusion criteria.

RESULTS: Of the 50 patients 37(74%) were males 23(46%) were female patients. Majority of the patients were above 40 years of age(n=42, %=84%). Smoking (62%) was the most common risk factor andanterior wall MI(38%) was the most common presentation. There was significant association between AMI and hypomagnesemia and also the complications arising out of AMI and hypomagnesemia.

CONCLUSION: In the present study there was statistically significant association of hypomagnesemia with AMI and its complications.

KEYWORDS : Acute myocardial infarction, magnesium levels, Hypomagnesemia, arrhythmias

INTRODUCTION

Acute myocardial infarction is the most important consequence of coronary artery disease and it can lead to complications such as ventricular arrhythmia and congestive heart failure. Some of the major risk factors that contribute to AMI are hypertension, dyslipidemia, diabetes, smoking, alcoholism, obesity, stress, increasing age and lack of exercise[1] Magnesium is an essential micronutrient for human beings and plays an important role in normal myocardial physiology. It's a cofactor in more than 300 enzymes system of the body in human cell. Its possible site of action includes vascular smooth muscle, platelets, and myocardial cells[2]. Magnesium is a trace mineral involved in several hundred chemical reactions in the body, including carbohydrate utilization, ATP metabolism, muscle contraction, transmembrane transport and the synthesis of fat, protein, and nucleic acids. It has a lot of therapeutic potential. It is less clear whether it is useful in patients with congestive heart failure or acute myocardial infarction.Magnesium depletion can induce hyperlipidemia and subsequently atherogenic deposits in coronary arteries leading to atherosclerosis.

Normal magnesium level fall between 1.7 and 2.2 meq/L. Usually, a serum level <1.7 meq/L is taken as reference. Hypomagnesemia is an electrolyte disturbance in which there is low level of magnesium in blood. Hypomagnesemia may result from a number of conditions including inadequate intake of magnesium, chronic diarrhea, malabsorption, chronic stress, alcoholism, and medication such as diuretic[3].

Magnesium is of major importance in the treatment of arrhythmia and coronary artery disease. Patients with coronary heart disease (CHD) suffer from magnesium deficiency. Oral combination therapy with magnesium and potassium improves endothelial function in these patients and reduce platelet dependent thrombosis. Within the myocardial cell, low magnesium concentration is associated with membrane destabilization, while high magnesium concentration are membrane stabilizing and therefore antiarrhythmic. Magnesium is a potent vasodilator and plays an important role in muscle contraction[4]. CHD features among the indications for oral magnesium therapy. It could be shown that magnesium improves exercise duration and general well being in these patients. Individuals treated with intravenous magnesium post-infarction were at significant lower risk of dying from ischemic heart disease-related complications[5].The present study is undertaken to observe thechanges in magnesium levels during AMI and to find the prognostic value of serum magnesium levels in reference to the complications. This will enlighten the use of magnesium infusion tominimize the complications after myocardial infarction.

AIM OF THE STUDY

To know whether there is any change in the serum magnesium level in patient's with acute phase of myocardial infarction.Changes in the serum magnesium level, and its relation with the occurrence of complications of acute myocardial infarction and to compare the patients with altered serum magnesium levels with normal serum magnesium levels in A.M.I.

MATERIALS AND METHODS

SOURCE OF DATA: 50 patients with acute myocardial infarction admitted in department of medicine SVS medical college, Mahabubnagar during the period of August 2015- July 2017 are taken for the study, considering the inclusion and exclusion criteria. Age and sex matched 10 healthy volunteers without any symptoms and signs of IHD were taken as controls.

Inclusion Criteria: Patients diagnosed with acute myocardial infarction based on WHO criteria including, typical history, typical ECG changes of acute myocardial infarction, elevated cardiac enzymes

Exclusion Criteria: Patients with history of alcoholism, cirrhosis, carcinoma, chronic diarrhoea, vomiting, pregnancy, leprosy, rheumatoid arthritis, renal failure, patients on diuretic therapy, patients on magnesium containing compounds like laxatives, antacids, patients who were treated elsewhere and patients presenting more than 24 hours after episode.

Study design :case-control study
Duration of the study: August2015- July 2017

50 acute myocardial infarction cases and 10 healthy controls were included in the study.

Serum magnesium is estimated within first 24 hours of chest pain. Serum magnesium estimated by Colorimetric method using calmagite.

Statistical method: Observations are tabulated on a sheet using Microsoft excel, represented using appropriate charts and graphs. Statistical analysis carried out with SPSS software version 16.0. Data was summarised by mean+/- standard deviation for continuous data and percentages for categorical data. The association between variables was done by chisquare test/ fisher's exact test for categorical data. All "p" values <0.05 were considered statistically significant.

RESULTS

A total of 50 patients with acute MI and 10 healthy controls were included in the study.

As shown in Table 1 there were 37(74%) male and 13(26%) patients with a male to female ratio of 2.1:1.

Table 1. Sex distribution of patients with acute MI		
Gender	No. of patients	% of patients
Male	37	74%
Female	13	26%
Total	50	100%

Age distribution of patients is depicted in Table 2.

Table 2. Age distribution of patients with acute MI			
Si. No.	**Age group in years**	**No. of patients**	**% of patients**
1	≤40	8	16%
2	41-50	13	26%
3	51-60	15	30%
4	61-70	14	28%

As shown in the Table 3 smoking (62%) was the most common risk factor followed by diabetes(52%), hypertension(48%), dyslipidemia (44%) and alcohol consumption(40%) respectively

Table 3. Distribution of patients according to risk factors			
Sl. No	**Risk factor**	**No. of patients**	**% of patients**
1	Hypertension	24	48%
2	Diabetes	26	52%
3	Smoking	31	62%
4	Alcohol	20	40%
5	Dyslipidemia	22	44%

In the present study anterior wall MI(38%) was the most common presentation followed by inferior wall MI(30%), anterolateral MI(16%), anteroseptal MI(14%) and RVMI(2%).

Table 4. Distribution of patients according to site of infarction			
Sl. No	**Site of infarction**	**No. of patients**	**% of patients**
1	Anterior wall	19	38%
2	Inferior wall	15	30%
3	Anterosepatal	7	14%
4	Anterolateral	8	16%
5	RVMI	1	2%

Of the 50 patients with acute MI, 16(32%) patients had hypomagnesemia, whereas the serum magnesium levels were normal in all the controls suggesting significant association of hypomagnesemia with AMI (p value was 0.049)

Table 5. Number of cases & controls with Hypomagnesemia & Normomagnesemia			
Sl. No.		**Cases(No. and %)**	**Controls(No. and %)**
1	Normomagnesemia	34(68%)	10(100%)
2	Hypomagnesemia	16(32%)	0(0%)

Of the 34 patients with normomagnesemia 2 patients had arrhythmias, none had heart failure or heart blocks, whereas in patients with hypomagnesemia 6 patients had arrhythmias, 3 patients had heart failure and 3 patients had heart blocks.

Table 6. Association of magnesium levels with cardiac complications & death			
Sl. No	**Complications**	**Normomagnesemia (n=34,%= 68%)**	**Hypomagnesemia (n=16, %=32%)**
1	Arrhythmias	2	6
2	Heart failure	0	3
3	Heart blocks	0	3
5	Total	2	12

There was significant association of hypomagnesemia with arrhythmias (p value is 0.009), heart failure(p value is 0.029) and heart block(p value 0.029) in cases of AMI.There was significant association between the total number of cardiac complications with hypomagnesemia(p value is < 0.05).

There are more number of deaths in AMI patients with hypomagnesemia(3 out of 16 patients) than in patients of AMI with normal serum magnesium levels(1 out of 34 patients). There was no statistically significant association of hypomagnesemia with death in cases of AMI as p value was 0.091.

DISCUSSION

Magnesium has been known to have an influence in the causation of AMI and also its sequelae like arrhythmias. It plays a major role in the pathogenesis of other cardiovascular diseases as well. Mg ions are found to be essential for the maintenance of the normal functional integrity of the myocardium[6].Several investigations have shown that the serum magnesium level is low in the first 24 hours following AMI and later on rose gradually to attain the normal level in about three weeks time[7].

The reported prevalence of altered serum Mg concentrations among patients with AMI is highly variable from 0% to almost 50% of normal value[8]. Low serum Mg level was observed in the present study in first 24 h (1.22± 0.29 m.eq/L) in all cases, as compared to the normal healthy control(2.1± 0.13 m.eq/L). Similar results have been obtained by studies conducted by Giesecke D et al[9],Kafka H et al[10],Bordia A et al[11].Serum Mg levels decrease to a nadir before the peak of the creatine kinase enzyme activity, i.e., within 24 h and they start normalising thereafter. This fall can be explained by a shift of Mg from extracellular to intracellular compartment, which appears to occur by increased uptake of magnesium into adipocytes following catecholamine induced lipolysis and formation of intracellular magnesium "soap" with free fatty acids[12].

The results of our study shows that there is remarkable decrease in extracellular Mg concentration during AMI and this may be due to the fact that during infarction, the ATP production is minimized. As a result, Mg is not utilized for the production of ATP and the intracellular free Mg concentrations rise rapidly and as a consequence, the influx of calcium into the myocardium is lowered. Thus Mg acts as calcium antagonist. Effects of Mg deficiency on the heart are also complicated by intracellular potassium depletion and hypokalemia[13].

AMI is a severe stressor and also accounts for the alteration of Mg in the myocardium. Due to stress, the beta-adrenergic receptors of adrenal gland gets stimulated and the catecholamines are released. Catecholamines decrease concentration due to a shift of Mg into cells as a result of stimulation of beta-adrenergic receptors[13-19]. High catecholamines may be one of the contributing factors for the hypomagnesemic state during infarction.

Earlier, it was observed that patients with AMI are magnesium deficient and this deficiency increases during the acute phase of infarction. But later it was observed that the Mg infusion in patients with suspected AMI could prolong survival. The Mg ion has multiple effects on the myocardium; among them are antiplatelet, antiarrythmic and coronary vasodilator effects. However, its efficacy for prolonging post AMI survival is probably due to its ability to preserve left ventricular function by reducing calcium mediated ischemic damage[13].The most important protective effect of Mg during MI is the restriction of the cellular loss of magnesium-adenosine tri phosphate, the essential substrate for many cellular reactions[15,19].

A comparative data of present study with other studies.

Table 7.Showing hypomagnesemia in AMI in different studies

Sl. No.	Study	Total No. Of Patients studied	No. of Hypo-magnesemic Patients	Percentage of Hypo-magnesemic Patients
1	LakshmanLalet al[20]	40		80%
2	MBKChoudhury et al[21]	32		86 %
3.	John E. Madias et al[22]	517	132	25.9%
4.	Dyckneret. al.[8]	342	147	46%
5.	SB.AgarwaLet al[23].	31	4	12%
6.	A.K. Dayal et. Al.	21	5	23.84%
7.	Ryzenet.al.[24]	104	8	7.7%
8.	Present study	50	16	32%

Table 8.Comparision of serum magnesim levels

Sl. No	Study	cases	Controls	Mean magnesium level (cases)	Mean magnesium level(controls)
11	Lakshman Laletal[20]	40	40	1.01±0.94mg/dl	2.20±2.23mg/dl
2	Chakraborty Pketal[25]	50	50	1.71±0.17mg/dl	2.16±0.25 mg/dl
3	Madias et al[22]	517		1.48±0.15mg/dl	
4	Govindmohan et al[26]	53	30	1.412 ± 0.132 mg/dl	2.514±0.16 mg/dl

5	Abraham et al[27]	65		1.70 mg/dl	
6	Sachdev et al	30		1.83±0.087mg/dl	2.44±0.162mg/dl
5	Present study	50	10	1.22±0.29m.eq/L	2.1±0.13m.eq/L

It is observed that in studies conducted by Govindmohan et al, Chakraborty PKetal, LakshmanLal et al ,Madias et al the mean value of serum magnesium is less in patients with AMI compared with serum magnesium levels in controls. In the present study also the mean value of serum magnesium is less in patients with AMI compared with serum magnesium levels in controls.

Magnesium is also known for its role in the electrical stability and energy balance of cardiomyocytes[28].Low serum magnesium has been associated with accelerated atherosclerosis[30].QT prolongation is a well-established risk factor for sudden cardiac disease[30],and serum magnesium was shown to influence the QT interval in a clinical setting[31].

Mild hypomagnesemia is a common electrolyte abnormality[33], particularly in the elderly who have increased magnesium loss due to diuretic therapy or interstitial renal disease. Magnesium regulates several cardiac channels including the calcium channel and outward potassium current through the delayed rectifier[33].Lowering the cytosolic magnesium concentration in magnesium depletion will markedly increase these outward currents, shortening the action potential, and increasing susceptibility to arrhythmia. A relationship has also been found between the plasma magnesium concentration and ventricular arrhythmia occurring in the second or 3rd week after myocardial infarction.

Magnesium ion has recently been considered as a principle cardiovascular cation. It has many critically significant roles in the maintenance of normal homeostasis of the body. It plays a major role in cardiac homeostasis. Magnesium is essential ATP activation necessary for the maintenance of the sodium-potassium pump. Magnesium deficiency has been attributed to the causation of arrhythmias in AMI patients.

Table 9.Comparision of present study with study by A. Akilaet al[7]

	A. Akila et al	Present study
No. Of cases	50	50
Males	42	37
Females	8	13
Male:female ratio	5.25:1	2.84:1
Maximum incidence of AMI	4th&5th Decades	5th&6th Decades
Risk factors		
Smoking	35	31
Hypertension	15	24
Diabetes	18	26
Anterior wall MI	21	19
Inferior wall MI	17	15
Antero septal	9	7
Antero lateral	3	8
Arrhythmias	25	8
Mortality	7	4
Mean serum Mg level on day 1in total cases	1.86±0.39 mg/dl	1.784 ± 0.44 m.eq/L
Mean serum Mg level in cases without complications	2.08±0.41 mg/dl	2± 0.28 m.eq/L
Mean serum Mg level in cases with complications	1.65±0.26 mg/dl	1.22± 0.29 m.eq/L

Dyckner T et al[8], among 905 admissions, found 342 patients with acute myocardial infarction, 563 with other diagnoses. Acute myocardial infarction group had markedly reduced serum magnesium levels compared to the reference group. The occurance of life threatening ventricular premature beats, ventricular tachycardia or ventricular fibrillation on admission was found to be high in patients with acute myocardial infarction with reduced serum magnesium level. Uncontrolled studies suggest that the administration of intravenous magnesium at this time can reduce the frequency of potentially fatal ventricular arrhythmia[27].

In study conducted by Ceremuzynski L, et al[17] the mean plasma magnesium concentration was 1.83 mg/dl (0.76 mmol/L) in patients with no abnormal rhythm, 1.68 mg/dl (0.7 mmol/L) in those with multifocal ventricular premature complexes and 1.5 mg/dl (0.65 mmol/L) in those with unsustained ventricular tachycardia[34]. 13 patients with complex arrhythmia and hypomagnesemia received IV magnesium over 24 h, a normal rhythm was restored in ten.

Table 10.Comparision of present study with study byGovind Mohan et al[26]

Cases	Govind Mohan et al	Present study
Total number of AMI cases	53	50
Total number of cases without complications	11	36
Total number of cases with complications	42	14
Total number of cases with arrhythmias	28	8
Total number of cases with conduction defect	4	3
Total number of cases with heart failure	10	3
Complications resulting in death	6	4
Serum magnesium (mean ± SE) in total cases	1.382 ± 0.21 mgllOO ml	1.784 ± 0.44 m.eq/L
Serum magnesium, (mean ± SE) in cases with complications	1.267±O.19 mgllOO ml	1.22± 0.29 m.eq/L
Serum magnesium (mean ± SE) in cases without complications	1.412 ± 0.13 mgllOO ml	2± 0.28 m.eq/L

Ceremuzynskiet al[35] selected 48 patients with acute myocardial infarction of duration over 24 hours and infused magnesium or placebo. The occurance of ventricular tachycardia (3 or more subsequent premature ventricular beats with a rate more than 120/ min) was significantly decreased ($p<0.001$), but the occurance of other ventricular arrhythmias was unaffected.

Table 11. Mean serum Mg level in total cases and in cases with arrhythmias

Study	Mean serum Mg level on day 1 in total cases	Mean serum Mg level in cases with arrhythmias
A. Akila et al[7]	1.86±0.39 mg/dl	1.65±0.26 mg/dl
Govindmohan et al[26]	1.38± 0.21mgldl	1.16± 0.21 mg/L
Ceremuzynski L et al[35]	1.83 mg/dl	1.5 mg/dl
Present study	2± 0.28 m.eq/L	1.35± 0.32 m.eq/L

There is a significant difference in the magnesium level in patient with arrhythmias and without arrhythmias.

Raismusenet al[29] selected 273 patients with diagnosis of acute myocardial infarction and subjected them to IV administration of magnesium or placebo. A significant reduction in the occurance of ventricular arrhythmia in the magnesium group was noticed when compared to placebo group ($p<0.05$). Shecter et al subjected 103 patients diagnosed of having acute myocardial infarction to magnesium infusion or placebo for 48 hours. A significant fall in mortality rate ($p<0.01$) was found. The occurance of tachyarrhythmias in need of treatment (10/50) has been very low in the magnesium group when compared to the placebo group (24/53). Smith et al randomly administered 24 hours continuous magnesium sulphate infusion or placebo in 400 patients with the suspicion AMI. Out of which, 200 patients were diagnosed of having acute myocardial infarction. There is no significant variation in the mortality rate or the occurance of ventricular dysrhythmia in need of treatment among the magnesium and placebo groups.

Felstedtet al[36] randomly subjected 298 patients with the suspicion of acute myocardial infarction to magnesium infusion or placebo for 24 hours. Myocardial infarction was confirmed in 162 patients. During 245 days period, no variation was noted in the occurance of tachyarrhythmias. Increase in the occurance of bradyarrhythmias was noted among patients infused with magnesium. Singh et al subjected 264 patients with suspicion of acute myocardial infarction to potassium, magnesium, 2% glucose or 10% glucose infusion. 228 patients were confirmed to have myocardial infarction.There was no

difference in the mortality rate and ventricular tachycardia or fibrillation between the two groups.

Morton et al[37] assigned 76 patients to get either magnesium infusion 0.38 mmol/l per kg every 12th hourly or placebo for the first 36 hours of hospital stay. No difference was noticed in the occurance of ventricular tachycardia among the two study groups.

Rasmussen et al[29] came to similar conclusions where the complications in patients who received magnesium therapy was linked with a fall in the number of arrhythmias which needed treatment during the first week in hospital. Magnesium therapy inhibits the post-infarctional hypomagnesemia. Iseriet al[38] in their study treated multifocal atrial tachycardias successfully with parenteral magnesium and potassium. Magnesium administered together with potassium, stabilizes the ionic balance of the cells and thus prevents spontaneous ectopics.

LezekCeremuzynskiet al[17] proved that life threatening arrhythmias in AMI are prevented by I.V. magnesium sulfate. This was in agreement with the findings of Rasmussen et al, and Smith et al, Schechter et al encourages implementation of magnesium treatment into clinical practice.

Isinget al[39] performed the following study. Seven 24 hours electrocardiograph (ECG) recordings and blood samples were taken within 3 weeks in 42 patients. Ca++, K+, and Mg++ concentrations in serum, and K+ and Mg++ in the erythrocytes, were determined by atomic absorption spectroscopy. One half of the patients were infused with 81 mmol/day as MgSO4 for 3 days. In patients who exhibited intense electrolytic alterations 10-20 days after AMI, there was a significantly higher rate in the frequency of couplets and/or tachycardia in the 2-20 days period after AMI. In patients infused with MgSO4, the fluctuation in serum electrolytes and the rate of arrhythmias were significantly reduced.

Magnesium treatment may reduce the incidence of ventricular fibrillation, ventricular tachycardia, severe arrhythmia needing treatment , but it may increase the incidence of profound hypotension, bradycardia, and flushing[40]. Magnesium probably functions as an inorganic calcium channel blocker and there are several plausible mechanisms for a beneficial effect in acute myocardial infarction (Woods 1991).Research on animals and humans has shown that magnesium is a peripheral (Mroczek 1977) and coronary vasodilator (Vigorito 1991). It can increase the threshold for depolarization of cardiac myocytes, thereby reducing the likelihood of cardiac arrhythmia caused by injury currents near ischemic or infracted tissue (Haverkamp 1988; Tzivoni 1990). Magnesium decreases reperfusion injury by preventing or lessening mitochondrial calcium overload in ischemic myocardial cells during the first few minutes of reperfusion (Ferrari 1986) (namely, the restoration of blood flow to an organ or tissue) and preserving intracellular Adenosine Triphosphate (ATP) and creatine phosphate reserves (Borchgrevink 1989), and inhibits platelet function, perhaps indirectly by release of prostacyclin (Watson 1986). Thus, magnesium-infusion started early after the onset of myocardial ischemia might limit infarct size, prevent serious arrhythmias, and reduce mortality. Time is critical in management of AMI. If thrombolytic treatment is not given, spontaneous reperfusion occurs in at least a third of patients during the first 12-24 hours after AMI (Woods 1995). The benefits from supplemental magnesium administration may be lost when there is a delay of more than 15-45 minutes after the onset of reperfusion (Antman 1995b). Careful laboratory studies, conducted since the Fourth International Study of Infarct Survival (ISIS-4) findings, have continued to explore the role of magnesium in reducing myocardial damage around the time of reperfusion, and have demonstrated its critical nature, with any benefit lost if treatment is delayed (Christensen 1995; Herzog 1995; Ravn 1999).

The American Heart Association 1992 guidelines for cardiopulmonary resuscitation and emergency cardiac care now include a recommendation that magnesium sulfate be added for the management of torsade de pointes, severe hypomagnesemia, or refractory ventricular fibrillation[41]. Intravenous magnesium is now regarded as the treatment of choice even when hypomagnesemia is not present. Torsade de pointes is a unique ventricular tachycardia most commonly precipitated by drugs that prolong QT interval (e.g., Quinidine), electrolyte imbalance (hypokalemia and hypomagnesemia) or a slow heart rate and/or shortening the QT interval. Two large prospective epidemiologic studies have examined the relationship between serum magnesium concentration and the subsequent development of CHD[42].Both suggest that low serum magnesium is a risk factor for CHD

Some limitations of the present study must be acknowledged. Although the present study and many otherstudies have indicated a trend towards disturbedmagnesium homeostasis in acute myocardial infarction,particularly in cases of pump failure, seriousarrhythmias and mortality, the data seems to be inconclusive because of smaller number of patients in each study. A much larger sample size would be needed to have necessary power for a more robust death/myocardial infarction endpoint. Secondly, the sample was from a single medical centre, so results may not be representative of the general population.

Strengths of the present study are the blood sample required for estimation of serum magnesium is collected from the patient at the same time when the blood is collected for the other basic investigations so that inconvenience of repeated sampling of blood to the patient is avoided. The test of estimation of serum magnesium is available at our institute so that sample need not be sent outside and the test is provided at low cost.

CONCLUSIONS

The present study comprised of estimation of Serum Magnesium concentration in 50 acute myocardial infarction patients on admission by Calorimetric method using calmagite. The percentage of hypomagnesimic acute myocardial infarction patients in present study is 32% which is statistically significant. No difference was observed in serum magnesium level in patients with different site of infarction. Cardiac arrhythmias were developed in 6 (38%) hypomagensimic patients and 2 (6%) normomagnesmic patients. This is statistically significant. Statistically not much difference was noticed in mortality between the hypomagnesmic 3(18%) and normomagnesimic patients 1 (3%) . Prophylactic administration of the intravenous magnesium sulphate may be considered in all cases of Acute Myocardial infarction as an adjuvant to thrombolytic therapy and in patients not suitable for thrombolysis to prevent cardiac arrhythmias & reduce short term mortality irrespective of serum magnesium levels as it is safe and cheap.

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