



Review Article

Magnesium poisoning with analytical aspects and its management

A K Jaiswal^{1,*}, Rajesh Kumar², Kiran Bisht³, Deepak Kumar Sharma⁴,
Madhuri Gupta⁵, Atul Basnal⁶

¹Dept. of Forensic Medicine and Toxicology, All India Institute of Medical Sciences, New Delhi, India

²Dept. of Forensic Medicine and Toxicology, Army College of Medical Sciences, New Delhi, India

³Amity Institute of Forensic Sciences, Amity University, Noida, Uttar Pradesh, India

⁴Quality Council of India (Board NABL), Haryana, Gurugram, India

⁵Dept. of Pharmacology, All India Institute of Medical Sciences, New Delhi, India

⁶Laboratory Oncology Unit, Dr. BRAIRCH, All India Institute of Medical Sciences, New Delhi, India



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ABSTRACT

Magnesium is an alkaline earth metal represented as Mg and has atomic number 12 and atomic mass 24. It is one of the most abundant metal found in the atmosphere of the earth and sea water. Magnesium acts as cofactor to various enzymes in the biological system and is very essential part of diet, several medications and health supplements. High concentration of magnesium and its compound in the blood serum results into toxicity and hypermagnesemia. Such condition is generally common in people with renal defects, hypothyroidism or accidental exposure to huge amount of magnesium and its salts. Magnesium poisoning can cause severe health issues including depression of CNS, neuromuscular and cardiovascular manifestation, with other symptoms including vomiting, nausea, paralysis etc. This paper discusses the general features, techniques of analysis, clinical diagnosis, symptoms and treatments related to the magnesium poisoning.

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1. Introduction

Magnesium is a greyish white alkaline earth metal, represented by symbol Mg. It ranks eighth in the series of most abundant element found in earth's crust and is third most abundant element found in sea water.¹ Naturally occurring magnesium generally occurs in combined forms with other compounds and exists in +2 oxidation state, whereas the free elemental state of the metal can also be produced artificially which is comparatively more reactive. Magnesium is one of the key elements found in living cells and is known to act as cofactor for more than 300 enzymes. Several biological processes such as glycolysis, oxidative phosphorylation, phosphate transfer reactions, ATPase activity etc. requires magnesium as a direct or indirect factor. Magnesium also has a very important role in

maintaining nucleotides during RNA and DNA synthesis.²

Exposure of human beings to magnesium is very common and obvious. It is naturally present in various fruits, vegetables, nuts, dairy, sea food etc. It is also consumed in several health supplements and medicines such as laxatives and antacid. Processes such as mining, production of magnesium alloys is also a source of human exposure to magnesium. Several experimental studies suggest that the blood level of magnesium more than 2.6mg/dl leads to hypermagnesemia, which have toxic effects on the body and lead to severe health problems. There is a need to understand the probable exposure of magnesium in order to take preventive measures. Also, proper techniques of analysis and management is required in order to avoid further damage.

* Corresponding author.

E-mail address: ashokjaiswal72@gmail.com (A. K. Jaiswal).

2. Sources of Magnesium

Magnesium being an essential element of living cells and very abundant in earth's crust, make its occurrence very common in nature. Some of the sources of magnesium has been listed and discussed below.

1. Magnesium is found in many foods such as green leafy vegetables, legumes such as kidney beans, soy products.
2. Nuts such as cashew, peanuts and almonds and grains are also a good source of magnesium.
3. Magnesium is present in sea water.
4. It is present in earth crust as magnesium ores such as magnesite, dolomite and carnallite.
5. It is also present in mantle of earth.
6. Industries deals with magnesium alloys in order to make various parts of automobiles and aircraft.
7. It is also present in several household appliances.
8. Several compounds of magnesium such as magnesium hydroxide, sulphate and chloride are used in several medicines and agents for laxative and antacids.
9. It is also is a part of magnesium supplements.
10. It is used in blasting compositions, incendiaries, pyrotechnics and signal flares.

3. Exposure of Magnesium

1. Intake of high dosage of magnesium supplements or medicines which contain magnesium as one of the components.
2. Taking high amount of magnesium rich diet can also cause hypermagnesemia.
3. Occupational exposure to magnesium and its compounds is very common in industries related to metallurgy, electronic industry, manufacturing or processing of the magnesium and its compounds.
4. Use of magnesium in agriculture industries, fertilizer, construction material, pulp and paper industry results in their direct release to atmosphere.³
5. Being a part of various blasting compositions, blasting flares and pyrotechnics it is released to the atmosphere.
6. Oxides of magnesium is also released into atmosphere naturally as mineral periclase.⁴

4. Pharmacokinetics of Magnesium

4.1. Absorption

Magnesium and its compounds when taken orally get dissociated into magnesium cations (Mg^{2+}) due to acidic pH of the stomach. Nearly 15% of the Mg^{2+} are absorbed in the small intestine, by solvent drag mechanism and intercellular diffusion. Absorption of these cations is also dependent on the type of food and its ability to form complex. Several studies in human suggest that the absorption of magnesium is also dependent on the type

of magnesium compound and availability of other factors. Magnesium chloride, citrate and lactate are known to get absorbed more rapidly as compared to magnesium hydroxides and oxides due to their solubilities.^{5,6} Various studies, also suggests role of vitamin D is very important in absorption of magnesium. Absorption of the magnesium in intestine is dependent upon the magnesium concentration of the body and not on the amount ingested. In case of intravenous administration, the effect is observed immediately and last for about 30-60 min.

4.2. Distribution

Human body contain approximately 26 g of magnesium, out of which nearly 60% is found in bones, followed by 20% in skeletal muscles, 19% soft tissues, and nearly 1% in extracellular fluid. Kidney has a key role to play in maintaining plasma magnesium levels. The serum magnesium level is regulated via renal magnesium reabsorption.⁷ Most of the absorbed magnesium is stored in bone.

4.3. Excretion

Excretion by urine is the main method of elimination of magnesium from body, which accounts for 80-90% of Mg^{2+} ion excretion. Some hydroxides of magnesium and unabsorbed magnesium ions are directly eliminated in feces.⁸

5. Mechanism of Toxicity

Compound of magnesium such as magnesium sulphate act as a depressant of CNS and respiratory system. Mild dosage cause flushing, sweating and vasodilation, whereas high dosage results into blockage of neuromuscular transmission and hypotension.

6. Onset and Duration of Action

The appearance of symptoms may be within few days to few weeks depending upon the compound magnesium and dose of uptake. In case of acute poisoning symptoms may appear within hours, however in chronic poisoning the appearance of symptoms may take several months or years.

7. Fatal Dose/ Fatal Period

Several studies suggest that oral fatal dose of magnesium for human ranges from 0.5 to 5 g/kg for a healthy adult. The symptoms may vary from mild to severe depending upon the age, sex, health condition and various internal as well as external factors.⁹

8. Normal and Reference Value

Normal and toxic level of magnesium are discussed in Table 1.

Table 1: Showing normal and toxic levels of magnesium.

Matrixes	Normal level	Toxic level
Blood	1.7-2.2 mg/dl	More than 2.6 mg/dl
Serum	2.2-2.7 mg/dl	More than 7.0 mg/dl
Urine	3.0-4.3 mg/dl	More than 5.0 mg/dl

9. Systemic Effects on Body

Poisonous effect of magnesium is very uncommon because kidneys are efficient in eliminating excess magnesium from the body. Hypermagnesemia is usually found in patients with undergoing health issues or accidental ingestion of large amount of sea water. Some common reasons for hypermagnesemia include intake of large amount of magnesium salts or drugs with impaired renal function and undergoing dialysis. Studies suggests that the rectal administration of the magnesium medication are also a common cause for magnesium poisoning. Patients with Addison's disease and hypothyroidism are also reported with slightly high levels of magnesium in the plasma. Some of the effects of the hypermagnesemia has been discussed below.¹⁰

9.1. Neuromuscular manifestation

Several evidences suggest that the serum levels of calcium higher than 2mmol/L, results into neuromuscular blockage and vasodilation. Higher concentration of magnesium ions results into inhibition of presynaptic acetylcholine release from neuromuscular and sympathetic junction. Prolong effects include sleepiness and loss of tendon reflexes.¹¹

9.2. Cardiovascular manifestation

Hypotension is the commonly observed symptom in case of hypermagnesemia. Initial symptoms show reduction in supine and erect blood pressure. Studies show that with increase in the blood magnesium concentration other conditions such as asystole, blockage of heart, paradoxical bradycardia can be observed.

9.3. Hypocalcaemia

With increased concentration of the magnesium in blood serum the levels of the calcium decreases. Decrease in the levels of calcium in turn lead to further deficiencies and a series of symptoms.

9.4. Miscellaneous

Other common effects of increased magnesium concentration include nausea, vomiting, dilation of pupils, facial flushing, paralysis and coma.

10. Analytical Tests for Magnesium Poisoning

10.1. Qualitative analysis

10.1.1. Sodium hydrogen phosphate test

1. It is detected by usual group analysis with sodium hydrogen phosphate.
2. White ppt is obtained with sodium hydrogen phosphate.

10.1.2. Cobalt nitrate test

1. A drop of test solution is mixed with cobalt nitrate on charcoal.
2. Rosy pink incrustation confirms the presence of magnesium.

10.1.3. Triazine dye test

1. Drop of solution containing magnesium is taken in spot plate
2. Above solution is acidified with HCl
3. Few drops of titan yellow solution is added to it
4. Few drops of NaOH is added to the mixture and mixed well
5. Red flocculent precipitate is appeared which confirm the presence of magnesium

10.1.4. Caustic soda test

1. A drop of test solution is taken in a test tube.
2. Titan yellow reagent and a drop of 0.1N caustic soda solution are added to it.
3. Orange or red color is obtained, which confirms the presence of magnesium.

10.2. Qualitative analysis

10.2.1. Titration with EDTA

Magnesium ion reacts with electron pair donors compounds in order to form coordination compound or complex ion called chelated, which can be used for quantitative analysis. EDTA is commonly used for the process of chelation and analysis. For titration of Mg^{2+} the solution is firstly buffered at pH 10 and the end point is determined by addition of Eriochrome black T which results into formation of a coloured chelate with Mg. The colour is again changed when the Mg^{2+} is released in order to form complex with EDTA.

10.2.2. Scanometric method

This technique is based on the procedure of scanning a solution which contain pink-coloured complex produced by

combination of Titan yellow and the magnesium ion. This is a highly sensitive method and can be used for wide variety of sample.¹²

10.2.3. Atomic absorption spectrometry (AAS)

It is a very conventional technique used for analysis of trace metals in different samples. Solution containing sample is aspirated as aerosols into flame. The gaseous atoms of the molecule absorb electromagnetic radiations in order to produce measurable signals. These signals are then amplified and detected using detectors.¹³

10.2.4. Inductively coupled plasma mass spectrometry (ICPMS)

It is commonly used method for ultra-trace analysis of metals. Here, the sample is atomized and small polyatomic ions are created which are further detected as compared to AAS this technique is more accurate and has great speed and sensitivity.

10.2.5. Spark source atomic emission spectrometry (SPAES)

This method does not require dissolution of the sample and best used by conductive samples. An electric spark is passed into the sample, which results into excitation of the metal atoms present in the sample. The energy released then can be detected by various detectors.

10.2.6. X-ray fluorescence spectrometry (XRF)

This technique measures absorption, emission, fluorescence, as well as diffraction and scattering of the given sample. It is a non-destructive technique which relies on bombarding sample with high energy X-rays, which results into ionization of electrons of innermost shell.

11. Clinical appearances/ Symptoms in Magnesium Poisoning

High amount of magnesium in serum due to magnesium rich diet is very uncommon. This condition is generally observed in people with intake of high magnesium supplement or having health issues such as kidney failure. Inhalation fumes of compounds containing magnesium can also lead to certain specific symptoms.

11.1. In case of acute toxicity

1. Lethargy.
2. Nausea.
3. Vomiting.
4. Facial flushing.
5. Stomach cramps.
6. Depressed reflexes.

11.2. In case of chronic toxicity

1. Respiratory paralysis.
2. Hypotension.
3. Circulatory collapse.
4. Heart block.
5. Asystole.
6. Hypocalcaemia.

12. Diagnostic Investigation

Following diagnostic investigations are very useful in case of magnesium poisoning.

1. Recording medical history of the patient is necessary in order to have correct diagnosis.
2. Diagnosis such as arterial blood, CBC, X ray of chest, pulmonary function test can be carried out in order to get clear idea about the exposure.¹⁴
3. Elevated levels of magnesium in urine, plasma and serum.

13. Management/ Treatment

All types of exposures to magnesium in levels higher than accepted should be taken seriously and treated according to the severity of the symptoms.

13.1. Observation at home

Ingestion or inhalation of small amount of compound with mild symptoms can be treated at home. Keeping patient away from the further exposure. In case of dermal exposure and irritation in eyes, multiple washing with water or saline is usually carried out.

13.2. Hospital management

Patient with normal kidney function (glomerular filtration rate (GFR) over 60 ml/min) and mild asymptomatic hypermagnesemia require no treatment. But higher magnesium levels should be taken seriously and treated according to the severity of the symptoms.

13.3. Decreasing absorption

1. After acute exposure of magnesium either ingestion or inhalation, one should immediately remove the patient from further exposure.
2. External exposure and irritation in eyes require frequent washing and irrigation with water or saline.
3. Decontamination done by gastric emptying with a nasogastric tube for large recent ingestions. Activated charcoal is not effective in case of magnesium toxicity. Do not administer a cathartic.

In more severe cases, close monitoring of the ECG, blood pressure, and neuromuscular function and early treatment

are necessary:

13.4. Supportive measures

1. Maintain an open airway and assist ventilation if necessary.
2. Replace fluid and electrolyte losses caused by excessive catharsis.
3. Treat hypotension with intravenous fluids and dopamine.

13.5. Chelation therapy

1. In severely poisoned patients the presence of acute renal failure often limits the potential for antidotes.
2. There is no specific drugs and antidotes for hypermagnesemia. However, administration of intravenous 10% calcium gluconate or chloride solution (10 ml iv repeatable over 5 minutes) can serve as an antidote. It alleviates respiratory depression, hypotension, and arrhythmias.

13.6. Enhanced elimination

1. Hemodialysis rapidly removes magnesium and is the only route of elimination in anuric patients.
2. Hemoperfusion and repeat-dose charcoal are not effective.
3. Forced diuresis using intravenous furosemide and normal saline enhance Mg elimination.

14. Conclusion

Magnesium and its compounds are one the abundantly found compounds in nature and human body. It has a important role to play in the functioning of various enzymes and processes. Use of magnesium in various industries, food supplements, and medication is very common which makes human susceptible to overdose and poisoning. There is a need to understand the underlying symptoms, diagnostic features and related treatment regarding the same. Any symptom mild or severe in patients, must not be ignored and should rush for immediate medical help for further treatment.

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16. Conflict of Interest

None.

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Author biography

A K Jaiswal Chemist / Scientist

Rajesh Kumar Assistant Professor

Kiran Bisht Student

Madhuri Gupta Scientist

Atul Basnal Student

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