MAGNESIUM


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Abstract:-
Magnesium biomedical research is presently both very exciting and very frustrating. It is interesting because there is chance that many people obtain their good health by enhancing their magnesium consumption. This interest is influenced by the present and recent past existence of journals entirely dedicated to magnesium research. On the other side, magnesium research leads to the occurrence of frustration for 2 reasons, one funding for nutrition related magnesium research has not been a high priority among potential sources of research support. Two, in various areas of magnesium biomedical research, conclusions are very difficult to draw due to seemingly contradictory results. This chapter deals with overview of function, overview of metabolism, nutritional status assessment, bioavailability from foods and supplements and parenteral pharmacological uses.

Introduction:-
Magnesium is treated as the second most abundant intracellular cation. It is responsible for the activity of various enzymes along with phosphotransferases. Bone consists of 50% of the bodys magnesium, a very little proportion of the bodys content is the ECF. Dietary intake of magnesium is generally about 1.2 mmol (300 mg) daily. Magnesium is available in cereals, green vegetables and meat.

Significant amounts are seen in biliary and gastric secretions. Factors concerned with the regulation of magnesium absorption have not been deformed, but may be linked to active transport across the intestinal mucosa with the help of a process involving vitamin D. Renal conservation of magnesium is atleast partly regulated by PTH as well as aldosterone. If the dietary consumption is reduced, renal conservation mechanisms are generally so excellent that depletion happens in a slow manner. Plasma (generally) is generally maintained within narrow limits, which indicates close homeostatic control. Significant alterations in the bodys cintent can happen with little or no change detectable in serum (magnesium). In this aspect, magnesium is very much like potassium. The serum (magnesium) may be normal even though a state of intracellular depletion persists.
Literature Survey:-
Magnesium Influences a multitude of physiological processes. The basis for these effects can be classified into many categories. One category is that magnesium is required as a cofactor for a large number of enzyme catalysed reactions, particularly reactions that need ATP for energy. These ATP requiring enzymes incorporate those that add phosphate to other enzymes, phosphorylation and the development of cell signalling molecule cyclic adenosine monophosphate (cAMP). Both these functions control many processes within cells. Another broad category of magnesium biochemical function is intracellular free magnesium ions behaving as a physiological modulator.

These modulations add, competing with calcium for gaining entry into cells via cell membrane channel passage. Normally, mineral competitions are considered from a negative perspective. That is, one mineral competes another, particularly for intestinal absorption, which can produce a deficiency. In contrast a competition between calcium and magnesium for cell membrane channels appears to retain many cellular processes in balance. This balancing act may also happen outside cells where magnesium plays a role in antagonizing calcium promotion of blood clotting. Besides influencing calcium function, magnesium also regulates potassium function, even though effects are quite different. One function of magnesium on potassium is to obstruct channels where potassium can leave cells. This assists justify the unequal allotment of intracellular and extra cellular potassium supporting the former. Na, K ATPase enzyme is helpful in pumping sodium out of cell’s and potassium in. There may be other ways that magnesium influences potassium distribution. These links between magnesium and potassium are seen in severe magnesium deficiency, where there are body potassium depletion and low serum potassium readings. The influence of intracellular magnesium concentration on cellular processes seems to be far reaching, involving affect’s on the synthesis of membrane phospholipids and lipid second messengers. These synthesis patterns are altered by low magnesium intake in a manner that can create profound disturbances on cell function, particularly in cardiac cells. Magnesium also balances a very few structures by binding to phosphate groups. Examples involve binding to phospholipids in cell membranes and to the phosphates in nucleic acids.

Magnesium shows indirect antioxidant actions, which are likely unpaired by the biochemical functions already mentioned. Even though magnesium has not been traditionally appeared as an antioxidant magnesium deficient animals exhibit signs of pro oxidant state. These signs include: above normal serum values for molecules linked to a pro inflammatory state, more sensitivity of lipoproteins to oxidation, more molecules for lipid peroxidase, low plasma values for radical scavenging capacity, functions for antioxidant enzymes, high magnitude of neurogenic oxidative responses in vivo and for myocardial tolerance to oxidant stress. Along with magnesium deficiency in cultured cells can enhance production of free radicals and the radical precursor hydrogen peroxide. The perfect biochemical mechanisms essential for each magnesium indirect antioxidant actions are difficult to identify because there are many possibilities. Among these is the capability of magnesium to influence the stability and lipid composition of cell membrane which in turn may effect cell tendencies to produce certain radicals. Another possibility is that since magnesium is required for control of so many processes, some of these processes likely regulate production of pro oxidant as well as antioxidant molecules. A lot of this regulation
may be influenced by the pro-inflammatory molecule substance P, which attains high level in magnesium deficient rats. The magnesium actions just debated only involve about a third of the body’s magnesium. This statement is prepared because about two third of the body’s magnesium is observed in bone. Magnesium influences the bone health via effects that occur outside the bone. For example, magnesium influences the secretion of parathyroid hormone. And insulin like growth factor, both of which influence bone metabolism. The effects of magnesium deficiency on parathyroid hormone are unusual. As a deficiency enhances serum, PTH levels can rise or fall at different times, but during the rise there can be very low receptor reactivity to the hormone.

**Overview of metabolism:** Magnesium absorption happens by both a saturable carrier mediated process and simple diffusion. Absorption does not appear to be controlled in the way that happens for minerals such as calcium. There is some evidence that vitamin D status influences magnesium absorption, but in most circumstances magnesium absorption appears to occur mainly independent of vitamin D hormone influence. In addition an enhancement in magnesium absorption because of vitamin D hormones may be largely balanced by enhanced urinary excretion. The major control of body magnesium content is via regulation of kidney magnesium reabsorption. This process is responsible to serum magnesium which is responsive to magnesium intake. Whatever it may be, kidney reabsorption of magnesium can also be influenced by other factors, namely certain drugs and hormonal changes. Originally many situations that cause severe magnesium deficiency, intricate heavy renal loss of magnesium. As mentioned earlier, about two third of the body’s magnesium is absorbed in the bone. Part of this magnesium is in equilibrium with the plasma. Extracellular magnesium accounts for only 1% of the total body magnesium. In the serum over half the magnesium is ionized, While a 3rd is bound to protein, especially albumin and the rest is bound to the low molecular weight anions.

**Nutritional Status Assessment:**
The most common means of measuring magnesium status in serum is serum total magnesium. Serum is given more importance over plasma because of the possible magnesium contamination and interferences with some assays because of the presence of the anti coagulant in the collection tube. Serum magnesium is completely affected by dietary magnesium as well as short term changes in renal magnesium losses. Whatever it may be, serum magnesium values do not always reflect intracellular magnesium content or total body magnesium content. Generally, factors, namely fluctuations in albumin or pH can influence serum magnesium. Serum magnesium is the starting point for any evaluation of magnesium status and values below 0.7 mm usually mean that substantial magnesium depletion has taken place. Note that this is not a tremendously low value relative to the normal range which is 0.70 to 1.05 mM. This reflects that has magnesium stores drop homeostatic mechanisms plays a role against big changes in serum values. Muscle biopsy magnesium contents behave as suitable way to estimate magnesium status since over a 4th of the body’s magnesium is typically observed in muscle. Nuclear magnetic resonance (NMR) Spectroscopy may eventually be used. Regularly as a non invasive means of determining muscle ionized magnesium. This basic method already exists, but has not yet been widely applied as a magnesium status assessment Tool. Total erythrocyte magnesium give response to dietary magnesium interventions, but values do not always correlate with other tissue tools of magnesium. Genetics may show a substantial influence. Also
anything affects Erythrocytes cell Age distribution can affect magnesium values. Mononuclear blood cells (MNC) total magnesium contents appeared to reflect magnesium status In some but not all circumstances, especially in a very few subjects, MNC magnesium correlates with muscle magnesium in contract MNC magnesium values are are reported as normal for a group of subjects with severe magnesium depletion. In another experimental study, mononuclear cell magnesium is not a good marker of magnesium status in a short term magnesium Depletion in rats. In human magnesium supplementation studies mononuclear cell magnesium is enhanced in some studies. In contract values are not enhanced in some other supplementation studies, even though pre supplementation magnesium status may have already been excellent in these studies. Thus the usefulness of MNC magnesium for status evaluation is still Debatabe compared to total blood cell magnesium contents erythrocyte ionised magnesium Seems to be be a very good indicator of magnesium status, even though there is some oscillation in erythrocyte ionised magnesium content as well as cells Circulate. It may be small enough to still use this approach for magnesium status estimation. The most straight way to count erythrocyte ionised magnesium is by an NMR technique. The fluorescent approach needs navigation around a number of procedural as well as interpretation sitfalls. The zero point titration approach has compared favourably with the NMR measures in 3 studies, particularly for relative results. Serum ionised magnesium is usually performed with the help of a magnesium specific electrode. Even though the quality of such electrodes may not be constant. There is another method to the electrode approach for assuming serum ionised magnesium.

This alternative approach Utilises Ultra Filtration followed by a total magnesium reading in the low Molecular weight fraction. Unfortunately, there can be a lot of technical pitfalls in this methodology. Namely the magnesium partitioning during ultra filtration being affected by pH changes. Urinary total magnesium is also utilized for estimating magnesium status, particularly following acute parenteral magnesium load, a type of magnesium tolerance test. For the measurements without the acute load, the applicability to status assessment can be rationalised by the fact that nearly all absorbed magnesium is eventually eliminated in the urine. So urinary elimination of magnesium in healthy subjects is directly proportional to dietary intake as well as magnesium stores. More urinary magnesium takes place if there is heavy renal losses of magnesium. Therefore you more urinary magnesium values can explain about either good or bad magnesium Status. Whatever it may be, a combination of high urinary magnesium with low serum magnesium behaves as an indication of magnesium reduction because of heavy renal losses. In summary, serum magnesium is the most used magnesium assessment method, even though it shows a very few diagnostic limitations. Several other methods may be more useful in some conditions. Even though technical and practical considerations can Influence their use.

**Bio availability from Foods and Supplements:**
There is not a lot of data on magnesium absorption from various foods and diets in humans, even though a very few experimental studies are available. Balance studies have set the percent absorption at anywhere from about 20% upto about 70% whatever it may be, This would confide in the amount of magnesium being consumed with low percent absorptions. At higher acute intakes Whatever it may be, an absorption of about 40 to 50% Is frequently viewed as normal, particularly for children and young adults with western diets dependent on some balance studies. For
a high magnesium mineral diet the percent absorption on an empty stomach is about 46% while the percent absorption jumps to over 52% after consumption with a meal. All these percentages have to be interpreted especially with care, since values can vary with technique used, the subjects studied and the amount of magnesium administered. Whatever it may be this percent absorptions exhibit that An absorption of magnesium is far better than minerals like iron, and that magnesium from a number of sources show somewhat similar absorptions. There is some work on food factors that affect magnesium absorption.

Some carbohydrates Namely, fructose and fermentable carbohydrate polymers can enhance magnesium absorption. Dietary fibre, which reduces absorption of some minerals, has demonstrated combined results for magnesium. Where there is reduction, it does not seem to be as much As for some other minerals. Magnesium citrate Is also treated well absorbed complex. As mentioned earlier in some study and absorption of Magnesium citrate 4 to 5 times as well as magnesium oxide. Magnesium taurate consist of some theoretical appeal, because magnesium and taurine have been considered to utilise complementary roles in counter acting a very few health problems. Whatever it may be, to this authors knowledge, no published human studies compare magnesium taurine or other types of magnesium supplements. There is an animal study of magnesium acetyl taurinate where this complex reduces Autogenic seizures in magnesium deficient mice. This effect is not completely duplicated by magnesium chloride and vitamin B6. There is also a rat study of magnesium, acetyl taurinate compared to other magnesium complexes. In this case, magnesium acetyl taurinate is more effective compared to a variety of magnesium Complexes In preventing symptoms occurred by the combination of ionic acid along with magnesium deficiency.

This is one of the several complexes where a particular magnesium complex may exhibit an advantage for a specialised bioactivity. A few others are mentioned in this and other sections. Magnesium pidolate may exhibit another example where one magnesium complex exhibit better specialised bioactivity compare to other magnesium complexes. In rats, Even though Magnesium deficiency induced aggressive behaviour is inhibited by a number of magnesium salts. (Aspartate, chloride, gluconate, lactate, and pidolate). Magnesium pidolate is treated as the best At some subcategory measures in another experimental work which examined some reactions to activity altering drugs magnesium as pidolate but not as asparate or lactate generated a neuro sedative effect.

Magnumides diglycinate chelate has demonstrated more absorption properties compare to magnesium oxide in a subgroup of subjects Who have undergone ileal resection. Ileal resection makes people inclined to magnesium deficiency, but oral magnesium treatment becomes problematic because of the sensitivity to the Laxative effects of magnesium complexes. A crossover study was conducted in this population utilising stable isotope methodology.

**Current research on supplement use.**

Parenteral pharmacological uses:

Parenteral magnesium has been proposed as needful for a number of uses that are not intended mainly to rectify magnesium deficiency. Examples include treatment and prevention of eclampsia, as well As for treatment of Acute myocardial infarction.
Over Hypomagnesaemia
(Low serum magnesium) An essentially low serum magnesium generally mentions magnesium deficiency because of heavy renal losses. Examples of conditions that can create magnesium deficiency are as follows.

- Chronic alcoholism
- Chronic diarrhoea
- Certain drugs particularly some diuretics, certain antibiotics and selected cancer chemotherapy drugs namely cisplatin
- Gitelman syndrome
- Parathyroid disease
- Uncontrolled diabetes (through body magnesium redistribution can also be a factor)
- Very low calorie intakes (including self imposed conditions such as anorexia nervosa and so called protein sporing fasts).

Examples of causes of Low magnesium absorption are gastrointestinal problems, namely Malabsorption abnormalities, as well as excessive Vomition and diarrhoea. In cases of substantial hypomagnesemia, oral magnesium supplements can often be useful, even though in severe cases parenteral administration can be justified. It can also be essential to cure the Root cause of the problem. If possible. A primarily clue to the cause can be measure of urinary magnesium to compare a case of excessive losses, especially from poor absorption.

Blood Pressure:
For example, magnesium effects on sodium, potassium pump on calcium ion flow can influence vascular tone, Reactivity as well as dilatation of blood vessels. Blood pressure could also be influenced by the magnesium antioxidant actions named in the function selection, since oxidant stress is responsible for causing hypertension. In addition magnesium influences secretion of hormones, which can show impact on blood pressure. In light of these possible functions links of magnesium to blood pressure, it is not pressure surprising that in animals magnesium deficiency can enhance hypertension. In addition, there are some links between parameters of magnesium status assessment and blood pressure. Even though the results do not yield a totally clear cut relationships, still a good number of human epidemiological Studies. Demonstrate correlations between magnesium consumption and blood pressure. High magnesium diets are typically more in other minerals, and phytochemicals can influence blood pressure. Unfortunately, studies of magnesium supplementation and blood pressure did not show consistent results.

The major problem is that many experimental works have a small sample size for a blood pressure study. Blood pressure studies needs a good number of subjects because the major end point is not very strong and is influenced by various factors including emotional ones. Another reason for the variable results could be that magnesium consumption may influence blood pressure only under a combination of certain conditions. Such a circumstance combination could be as follows:

- Subjects originally show at least a marginal magnesium deficiency
- The deficiency is rectified by the given dose of the given magnesium complex
- The subjects primarily have high blood pressure but it is not so far advanced that, physical changes do not allow magnesium to build an impact. The high blood pressure is due to A particular process that responds to magnesium.
One opinion is that the particular process involves the renin angiotensin aldosterone system. Another opinion established on a study comparing Responders and non responders is that depletion is intra erythrocyte Sodium is a discriminating factor. In an experimental work where Responders and non responders are compared and discrepancies can be found for commencing plasma renin activities. In another experimental work, discrepancies can be found predicted on the depletion in intra erythrocyte sodium, for example magnesium aspirate supplementation decreases blood pressure in a study where there is no predictive value for commencing magnesium status or dietary intake. Whatever it may be dietary intake does not essentially predict Status if some types of hypertensive subjects have more magnesium needs. If magnesium can influence blood pressure, how much of a change can be predicted? In some experimental works, the change has been small, but in some cases the systolic change has been in double digits.

Serum Lipids in Non Diabetic Subjects.
In some animal experimental works, moderately high magnesium consumption influences serum or Tissue lipid consumptions in a manner that would be treated beneficial, especially in humans. This effect does not essentially involve obstruction of a magnesium deficiency. One mechanism could be magnesium attaching to lipids and Bile salts In the GI tract and decreasing their absorption. There could be different actions of magnesium on serum lipids that does involve rectification of a marginal magnesium deficiency. Along these lines, in a few experimental works, serum or platelet ionized magnesium values exhibit inverse correlations with certain serum lipid values.

There are 2 studies by overlapping authors that look at the response of serum lipids to enhanced magnesium consumption. In this experimental works which involve about 400 subjects. Magnesium consumption is enhanced from about 400 milligram per day to about 1000 milligram by dietary intervention. The enhanced consumption leads to 10% reduction in serum cholesterol, LDL cholesterol as well as triglycerides. Unfortunately it is very difficult to confirm whether these effects are due to magnesium alone, Other dietary factors or the combination of magnesium plus other dietary factors also. In a final study, 1000 milligrams magnesium oxide supplementation of Hyperlipidemic subjects originally enhances serum cholesterol slightly to due to an enhancement in LDL cholesterol values. Return to pre treatment levels, particularly after a washout. In summary, there is not yet conclusive Proof That high doses of magnesium consistently give rise to beneficial effects on serum lipids, even though this is a possibility. If this is present, it may not always need rectification of marginal magnesium deficiency.

Prevention of Cardiac Vascular Disease in Non Diabetic Subjects:
The possible link of magnesium to serum lipids and blood pressure exhibits risk of cardiovascular diseases. In addition, magnesium could influence this risk with the help its Antioxidant as well as anti inflammatory properties. For example, magnesium deficient rats consist of lipoproteins with high susceptibility to atherosclerosis related oxidation. Magnesium also shows its effect on cardiac muscle integrity in part. With the help of regularity effects on antioxidant enzymes and cardiac phospholipid composition.
Moreover, magnesium limitation of calcium movements can influence heartbeat, vascular spasm trends, platelet aggregation, vasodilatation and other cardiovascular relevant processes. There is also an idea, even though still controversial that magnesium is a part of pre ischemic conditioning process that improves later heart recovery from ischemic stress. A number of epidemiological experimental works have identified correlations between magnesium consumption or blood magnesium status indicators and risk of very few types of cardiovascular disease along with stroke as well as ischemic heart disease. In subjects with dilated cardiomyopathy, magnesium does not enhance left ventricular ejection fraction nor prognosis compared to Placebo. One experimental work of magnesium supplementation in subjects with cardiovascular disease originally gives negative results.

The study is performed with survivors of an acute myocardial infarction. By one statistical analysis, though not other, cardiac events are more in the magnesium group compared to placebo group. Whatever it may be the magnesium supplement is the hydroxide from form which has mentioned earlier may not always be a good choice as a magnesium supplement because of antacid effects only. In conclusion, for subjects who exhibit cardiovascular disease, magnesium supplementation provides many benefits in severe experimental works. Some physicians may think that there already enough proof to try a modest to dose of magnesium in cardiac rehabilitation patients. Other physicians may be more cautious because of the possible drawback in one experimental work.

**Diabetes** For example, a number of studies report low serum magnesium values in many. Even though not all subjects with type 1 or type 2 diabetes. The causes of low serum magnesium are more renal magnesium loss plus some magnesium dispersion away from the blood into certain tissues. Another relationship between diabetes and magnesium is that erythrocyte ionized magnesium even though not resolved in all that many diabetic subjects tends to exhibit low values. This can occur even in subjects with normal serum magnesium levels. Similarly, low serum ionized magnesium can be seen in type diabetic adults and children even with normal mean serum total magnesium values. There is also a notification of low muscle magnesium contents in type one diabetic subjects. Lastly, a series of experiments in diabetic subjects exhibit inverse correlation between Serum magnesium and measures regarding primary or secondary symptoms of diabetes.

**References:**
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