

## Correlation of Serum Magnesium, Ascorbic Acid and C – Reactive Protein Levels in cases of Uncontrolled Type -2 Diabetes Mellitus.

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**Abstract :** The study was conducted on 100 subjects of age upto 30-70 yrs were taken and divided into cases & controls, each containing 50 pts . FBS, S. Mg, vit. C & S. CRP levels were measured in all patients. In cases of type 2 DM (n=50), the serum Mg levels ranged from 0.79-2.25 mg/dl with a Mean $\pm$ SD of 1.756 $\pm$ 0.330 mg/dl. Serum Magnesium level showed highly significant negative correlation with serum sugar levels (t=5.8120; p<0.001), while in the similar group ascorbic acid levels ranged from 0.30-0.62mg/dl with a Mean  $\pm$ S.D. of 0.341 $\pm$ 0.120 mg/dl with a statistically highly significant negative correlation with FBS (t=9.733; p<0.001), and the serum C reactive protein levels in the case group ranged from <6-96 mg/dl with a mean  $\pm$ S.D of 23.06 $\pm$ 15.20 mg/l. S. CRP values also showed statistically significant positive correlation with FBS. (t=4.067; p<0.001). **Conclusion:** The S. Mg & Vit C level were inversely correlated with levels of FBS & duration of diabetes while S. CRP level correlated directly to duration of diabetes & FBS.

### INTRODUCTION

Type 2 Diabetes mellitus accounts over 80% of cases of diabetes and his slow onset, heterogenous disorder resulting from interaction between environmental factors and polygenic inheritance<sup>1</sup>.

Diabetes mellitus is the most common pathological state in which secondary magnesium (Mg) deficiency occurs. Magnesium is known to be related to the carbohydrate and fat metabolism<sup>2</sup>. Magnesium is essential in the glycolic cycle that converts sugar to ATP (Adenosine triphosphate) bioenergy. It helps to stabilize ATP, nucleic acid metabolism, acts as a co-factor in the glucose transporting mechanism and various enzymes in carbohydrate oxidation<sup>3</sup>. Magnesium may also play a role in the release and action of insulin<sup>4</sup>.

In diabetes, plasma magnesium is more often decreased than red blood cell magnesium. Plasma magnesium levels are correlated mainly with the severity of the diabetic state, glucose disposal and endogenous insulin secretion. Various mechanisms are involved in the induction of Mg depletion in diabetes mellitus, i.e. insulin and epinephrine secretion, modifications of the vitamin D metabolism, decrease in vitamin B6 and taurine levels, increase of vitamin B5, C and glutathione turnover as well as, treatment with high levels of insulin and biguanides.

Hyperglycemia causes oxidative stress, which not only increases non enzymatic glycosylation & oxidation of proteins involved in the pathogenesis of the complications of diabetes; these adversely affect leukocyte function thereby reducing the cellular ascorbate levels (Vit. C). Hyperglycemia increases urinary losses of ascorbate. Compared to apparently healthy people, diabetics appear to consume less vitamin C<sup>5</sup>. This may explain why diabetic patients have low levels of ascorbic acid. Low levels of ascorbic acid make the diabetic patient more susceptible to wound infections, delayed healing, endothelial dysfunction and tenosynovial disease.

CRP may have indirect influence on insulin resistance and secretion through altered innate immune response due to heightened systemic inflammation<sup>6,7</sup>. Elevated IL-6 and C- reactive proteins are associated

with hyperglycemia, insulin resistance and overt type-2 diabetes mellitus. Elevated CRP also stimulates endothelial production of E-selectin, ICAM-1 and VCAM-1 (important mediators of impaired vascular reactivity), reduced insulin delivery and increased peripheral insulin resistance<sup>8</sup>. TNF may also mediate insulin resistance indirectly by increasing free fatty oxidation, stimulation of insulin counter regulatory hormones or cytokines e.g. IL-6 and CRP or by direct inhibitory effects on glucose transporter protein, GLUT-4, insulin receptor substrates, or glucose stimulated insulin release by pancreatic beta cells.

The aim of the present study was to estimate serum magnesium, plasma ascorbic acid level and serum C-reactive protein levels in uncontrolled type 2 diabetic patients and to compare them with normal healthy individuals and to correlate them with the duration of the disease.

### MATERIALS AND METHODS

The present study was a case/control study, comprising of total 100 subjects. 50 patients in the age group 30-70 years, 50 normal healthy persons, age and sex matched from the same population served as control. The subjects were divided into 3 groups according to their age; group 1 (30-45) years; group 2 (46-60 years) and group 3 (>60 years). The patients suffering from hypothyroidism, renal failure, hepatic dysfunction, CVA, CHF, those on statins, hormones and oral contraceptives were excluded from the study.

The patients were kept on overnight fast i.e. approximately on 12 hours of fasting. 10 ml of venous blood was taken in disposable syringe under aseptic conditions by vein puncture in antecubital vein & sent for S.Mg, CRP & FBS in simple syringe while Vit C in EDTA tube. The plasma glucose was estimated by GOD/POD method. Serum Mg levels were estimated by calorimetric kit method using xylidyl blue described by Bohuan C (1962)<sup>9</sup>. Ascorbic acid was estimated quantitatively by titration with 2,6 dichlorophenol indophenols and CRP was estimated by Biolatex CRP direct kit method<sup>10</sup>.

### RESULTS

#### Laboratory parameters in control & study groups

In this study the serum Mg levels in normal individuals (n=50) ranged

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from 1.88-2.75 mg/dl with a Mean±SD of 2.264±0.278 mg/dl. In cases of type 2 DM (n=50), the serum Mg levels ranged from 0.79-2.25 mg/dl with a Mean±SD of 1.756±0.330 mg/dl. The difference of serum Mg level between the two i.e. the control and the patient group was statistically highly significant with the patient group having lower levels as compared to the control group.<sup>11,12</sup> (t=5.8120;p<0.001).(Table 1)

In the present study in normal subjects (n=50) the plasma ascorbic acid levels ranged from with a mean±SD of 1.18±0.409 mg/dl. In cases of patients with type 2 DM (n=50), the ascorbic acid levels ranged from 0.30-0.62mg/dl with a Mean ±S.D. of 0.341±0.120 mg/dl and this difference was statistically highly significant (t=9.733;p<0.001),with the patient group having significantly lower levels than the control group.<sup>13</sup> (Table 1)

The serum C reactive protein levels in control subjects(n=50) ranged from <6-24 mg/dl with a mean±SD of 10.71±6.187 mg/dl. In patients of type 2 DM (n=50), the serum C reactive protein levels ranged from <6-96 mg/dl with a mean ±S.D of 23.06±15.20 mg/l. The difference of C reactive protein between the two i.e. controls and the patient group was statistically highly significant, with the patient group having higher levels than the control group.(t=4.067;p<0.001)<sup>14</sup>. (Table 1)

As shown in figure-1 mean serum CRP was increased in all the studied cases as compared to controls (p<0.05), but the rise in serum CRP was maximum in age group of 40-60 years. Similarly value of mean serum ascorbic acid was found to be low in all the cases as compared to controls(p<0.05), but maximum reduction was found in the age group of 40-60 years. Whereas value of mean serum magnesium level was less but not much difference in cases as compared to controls, but the reduction was maximum in 30-40 years age group.

**Laboratory parameters & duration of diabetes**

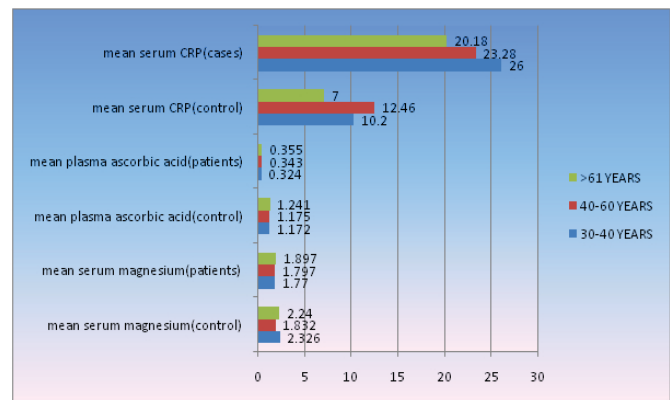
Table 2 shows that serum Mg level was 1.52 – 2.25 mg/dl with mean of 1.875 ± 0.22 mg/dl in patients with diabetes for 1-3 yrs while those with duration of >3-5 yrs had serum Mg level 1.54 -1.87 mg/dl with mean of 1.77 ± 0.126 mg/dl and those with duration of 5-7 yrs had serum Mg level of 0.79 – 2.20 mg/dl with mean of 1.684 ± 0.43 mg/dl. These values in patients of diabetes with >7 yrs duration were low and in range of 0.79 – 2.20mg/dl but this difference was statistically insignificant.

**Table 1:** Showing comparison of serum Mg, Vitamine C and CRP levels in both cases and control groups

	Subjects	No	Serum Mg levels(mg%)		Plasma Ascorbic acid levels(mg%)		Serum CRP levels(mg%)	
			Range	Mean±S.D	Range	Mean±S.D	Range	Mean±S.D
1	Normal (control)	50	1.88-2.75	2.264±0.278	0.42-1.50	1.18±0.409	<6-24	10.71±6.187
2	Patients of T2DM	50	0.79-2.25	1.756±0.330	0.20-0.62	0.341±0.120	<6-96	23.06±15.20

**Table 2:** Showing variation of serum Mg, Vitamin C and CRP levels with duration of disease

S. No	Duration of disease (yrs)	No	Serum Mg levels(mg%)		Plasma Ascorbic acid levels(mg%)		Serum CRP level(mg%)	
			Range	Mean±S.D	Range	Mean±S.D	Range	Mean±S.D
A	1-3	27	1.52-2.25	1.875±0.222	0.20-0.62	0.372±0.132	<6-48	17±14.21
B	>3-5	06	1.54-1.87	1.77±0.126	0.23-0.56	0.366±1.426	<12-48	20±14.53
C	>5-7	07	0.79-2.20	1.684±0.434	0.24-0.35	0.28±0.042	6-96	26.85±41.74
d	>7years	10	0.79-2.20	1.526±0.442	0.21-0.42	0.269±0.08646	6-96	33.6±27.26



**Figure1:** Showing Mean Variations in the levels of Serum Mg, Vitamin C and CRP in both cases and controls

In our study serum ascorbic acid level was 0.20-0.62 mg/dl with mean of 0.372±0.132 mg/dl in patients with diabetes for 1-3 yrs while those with duration of >3-5 yrs had serum Mg level 0.23-0.56 mg/dl with mean of 0.366±1.426 mg/dl and those with duration of >5-7 yrs have serum Mg level of 0.24-0.35 mg/dl with mean of 0.28±0.042 mg/dl. These values in patients of diabetes with >7 yrs duration were low and in the range of 0.21-0.42 mg/dl. But this difference was statistically insignificant.

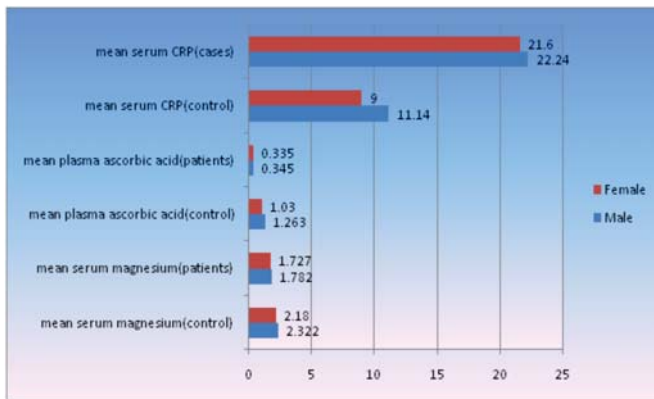
In our study serum CRP level was <6-48 mg/dl with mean of 17±14.21mg/dl in patients with diabetes for 1-3 yrs while those with duration of >3-5 yrs had serum Mg level <12-48 mg/dl with mean of 20±14.53 mg/dl and those with duration of 5-7 yrs had serum Mg level of 6-96 mg/dl with mean of 26.85±41.74 mg/dl. These values in patients of diabetes with >7 yrs duration were further low and in the range of 6-96mg/dl. But this difference was statistically insignificant.

**Correlation of laboratory parameters & fasting blood glucose levels**

Figure-2 Shows comparison of mean serum magnesium, serum ascorbic acid & serum CRP values in diabetic males and females versus controls. The difference was found to be more in females as compared to males.

Table-3 Shows that as values of fasting blood sugar increases, the

values of mean serum magnesium and mean plasma ascorbic acid values were found to be decreasing while value of serum CRP was increasing ( $p < 0.05$ ).



**Figure 2:** Showing Mean levels of Serum Mg, Vitamin C and CRP levels in males and females of both cases and controls

**Table 3:** Showing variation of Serum Mg, Vitamin C and CRP levels in cases with fasting blood glucose level

GROUP NO.	SERUM LEVELS	NO.OF INDIVIDUALS	FASTING PLASMA GLUCOSE LEVELS(mg%)	
			RANGE	MEAN±SD
SERUM MAGNESIUM				
A	<1.8	28	110-420	201±87.45
B	1.8-2.0	12	105-162	135.16±16.95
C	>2.0	10	76-165	113.9±23.225
PLASMA ASCORBIC ACID				
A	0.20-0.34	30	104-420	194.46±85.49
B	0.35-0.50	12	104-250	134.16±38.180
C	≥0.51	8	76-162	118.875±28.180
SERUM C-REACTIVE PROTEIN				
A	<0.6-4.8	28	<150	121.26
B	<0.6-4.8	15	150-250	187.93
C	1.2-9.6	7	>251	322.42

## DISCUSSION

Diabetes mellitus is a widespread disease, currently the most common endocrine disorder around the world<sup>15</sup>. Hypomagnesemia is frequently seen in patients of DM.<sup>16,17</sup> Hypomagnesaemia may be defined as a serum magnesium concentration  $< 1.8$ mg/dl or  $> 2$ SD below the mean of the general population<sup>18,19</sup>. It has been reported to occur in 13.5 to 47.7 % of nonhospitalized diabetic patients as compared to nondiabetic patients having prevalence of 2.5 to 15% among<sup>18,19</sup>. The cause of diabetes associated hypomagnesaemia is not exactly known with certainty but the possible mechanisms are (1) increased loss of Mg in urine due to the osmotic action of glycosuria and (2) depression of the net tubular reabsorption of Mg due to hyperglycemia per se<sup>20</sup>. Possible causes of hypomagnesaemia in patients with Type 2 diabetes include decreased intake, esophageal dysfunction, diabetic gastroparesis, enhanced gastrointestinal loss, diarrhea as a result of autonomic dysfunction, enhanced renal Mg loss, increased filtered load, glomerular hyperfiltration, osmotic diuresis (glycosuria), volume expansion as a result of excessive volume replacement, metabolic acidosis (diabetic ketoacidosis), hypoalbuminemia, microalbuminuria and overt proteinuria, reduced renal reabsorption. endocrinologic dysfunction: insulin deficiency or resistance, electrolyte abnormalities: phosphate and potassium depletion with the use of diuretics.

Mg can retard or prevent the induction of insulin resistance and diabetes mellitus. It acts as a co-factor in glucose transporting

mechanisms of the cells and also plays an important role in glucose metabolism by acting as a critical co-factor for the activities of various enzymes involved in glucose oxidation. The ability of insulin once bound to the receptor to activate tyrosine kinases is reduced in hypomagnesemia. As a result, reduced peripheral glucose uptake and oxidation often occur in subjects with hypomagnesemia<sup>21</sup>. Hypomagnesemia induced complications include retinopathy, nephropathy, foot ulcers, dyslipidemia and neurological abnormalities<sup>22</sup>.

Ascorbic acid (vitamin C) is a water soluble vitamin needed for the growth and repair of tissues in all parts of the body. Vitamin C is one of many antioxidants<sup>23</sup>. Low levels of ascorbic acid have been associated with a variety of conditions including hypertension, gallbladder disease, stroke, some cancers, and atherosclerosis. People with diabetes have high levels of free radicals and low level of antioxidants, including vitamin C. Most studies have found that diabetics have at least 30 % lower circulating ascorbic acid levels than normal although it may be due to their lower intake, increased urinary excretion of the vitamin and defective transport across cell membranes, along with increased oxidation of ascorbic acid to dehydroascorbic acid (DHAA)<sup>24</sup>.

There is some evidence that vitamin C supplementation may reduce the nonenzymatic glycosylation of proteins<sup>25</sup>. Finally, ascorbic acid may lower sorbitol levels in red blood cells independent of changes in diabetic control,<sup>26</sup> which is associated with development of diabetic complications including cataracts, retinopathy and neuropathy.

The mechanisms by which chronic inflammation can evoke type 2 diabetes are not clear. Adipose tissues can synthesize and release the main pro-inflammatory cytokines; TNF- $\alpha$ , IL-1 and IL-6. Pro inflammatory cytokines and phase reactants are involved in multiple metabolic pathways relevant to insulin resistance, including insulin regulation, reactive oxygen species, lipoprotein lipase action and adipocyte function<sup>27</sup>.

CRP activates complement, binds to Fc receptors and acts as an opsonin for various pathogens. CRP is a marker of low grade inflammation and may have indirect influence on insulin resistance and insulin secretion through altered innate immune response due to heightened systemic inflammation. Circulating value of CRP reflects ongoing inflammation and/or tissue damage much more accurately than do other laboratory parameters of the acute-phase response, such as plasma viscosity and the erythrocyte sedimentation rate. It shows no diurnal variation and is not affected by eating. It is a useful non specific biochemical marker of inflammation, measurement of which contributes importantly to (a) monitoring of response to treatment of inflammation and infection and (b) detection of intercurrent infection in immunocompromised individuals. In NHANES III survey, both glycemia and insulin resistance correlated with markers of inflammation, demonstrating a link between the dysmetabolism of DM and poor vascular outcomes. CRP is a hallmark of metabolic syndrome<sup>28</sup>. Insulin Resistance Study (IRAS), showed that CRP was positively correlated with the body mass index, waist circumference, blood pressure, triglyceride, cholesterol, low density lipoprotein cholesterol, plasma glucose and fasting insulin and inversely related to high density lipoprotein cholesterol an insulin sensitive index.<sup>29</sup>

## CONCLUSION

In the present study the serum magnesium levels in patients of type-2 DM (n=50) were significantly low and ranged from 0.79-2.25 mg/

dl with a Mean  $\pm$  S.D. of  $1.756 \pm 0.3302$  mg/dl. Similar results were also found in a study by Chambers EC et al 2006<sup>30</sup>. The serum Mg levels had inverse relation with the duration of the disease. Thus the chronicity of type-2 diabetes mellitus worsens the serum magnesium status and thereby enhances the potential for the development and progression of diabetic complications. Serum Mg shows negative correlation with the fasting blood glucose levels, thus indicating that magnesium affects the disposal of glucose loads from the blood.

In patients of type-2 DM, the plasma ascorbic acid levels were significantly lower than normal individuals and ranged from 0.20-0.62 mg /dl with a Mean  $\pm$  S.D. of  $0.341 \pm 0.120$  mg /dl. Similar results were also observed in a study by Gruia V et al. in 2008<sup>31</sup>. Plasma ascorbic acids levels were found to be inversely related to the duration of the disease and the blood glucose levels thus making these individuals more susceptible to diabetic complications.

The serum C-reactive protein levels in patients of type 2 DM were statistically high than normal individuals and ranged from <6-96 mg/ dl with mean  $\pm$  S.D of  $23.06 \pm 15.20$  mg. Similar results were also found in a study done by King DE et al<sup>32</sup>. Serum C –reactive protein levels were found to be related directly to the duration of the disease and the blood glucose levels.

## REFERENCES

- Ostenson CG. The pathophysiology of type 2 diabetes mellitus. An overview. *Acta Physiol Scand* 2001;171:241-7.
- Garfinkel D. Role of magnesium in metabolism. *Magnesium* 1988; 7: 249 - 61.
- Mooradian A , Failla M, Hoogwerf B, Maryniuk M, Wylie rosett J. Selected vitamins and minerals in diabetes. *Diabetes Care*. 1994; 17: 464-79.
- Schoeder HA, Balassa JJ, tipton IA. Abnormal trace metals in . *Jl Chron Dis*. 1962; 15: 941-64.
- Singh RB. Dietary intake and plasma levels of antioxidant vitamins in health and disease: a hospital based case – control study. *J Nutr Environ Med*. 1995; 5: 235 - 42.
- Pick Up JC , Crook M. Is type 2 diabetes mellitus disease of the innate immune system? *Diabetologia*. 1998; 41: 1241-8.
- Pick up JC, Mattock MB, Chusney GD, Burt D. NIDDM as a disease of the innate immune system: association of acute phase reaction and interleukin - with the metabolic syndrome X *Diabetologia*. 1997; 40: 1286 - 91.
- Gabay C, Kushner I. Acute Phase protein and other systemic responses to inflammation. *N Engl J Med*. 1999; 340: 448-54.
- Bohoun C. Estimation of serum magnesium levels. *Clin Acta*. 1962; 7: 811-7.
- Hayasni H, Longrippo G. ACRP latex test for the qualitative and semi-quantitative protein in human serum sample. *H Ford Hosp. Med J*. 1972; 20: 91-2.
- Ma J, Folsom AR, Melnick SL, ekfeldt JH, Sharret AR. Association of serum and dietary Mg with cardiovascular disease, hypertension, diabetes mellitus, insulin and carotid artery wall thickness. The ARIC study. *Atherosclerosis Risk in communities Study. J Clin Epidemiol*. 1995; 48: 927-40.
- Monika KW, Michael BZ, Giatgen. A, Richard FH. Low plasma magnesium in type 2 diabetes. *Swiss Med Wkly* 2003; 133: 289-92.
- Som S. Ascorbic acid metabolism in diabetes mellitus. *Metabolism*. 1981; 30(6): 572-7.
- Rodriguez Moran M, Guerrero Romero F. Increased levels of CRP in non controlled diabetic subjects. *J Diabetes Complications*. 1999; 13: 211-5.
- Powers AC. Diabetes mellitus. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL (eds): *Harrison's Principles of Internal Medicine*, 16 th ed. New York ; Mc Graw Hills. 2004; 2: 2125-80.
- Tossello L. Hypomagnesaemia and diabetes mellitus : a review of clinical implication . *Arch Intern Med* 1996; 156: 1143-8.
- Sheehan JPM. Magnesium deficiency and diabetes mellitus. *Magn Trace Elem* 1991; 10: 215-9.
- Pham PC, Pham PM, Pham PA, Pham SV, Pham HV, Miller JM et al. Lower serum Mg levels are associated with more rapid decline in patients with diabetes mellitus 2. *Clin Nephrol* 2005; 63: 429-36.
- McNair P, Christensen MS, Christiansen C, Madsbad S, Trans LJ. Renal hypomagnesaemia in human diabetes mellitus: Its relation to glucose homeostasis. *Eur J Clin. Invest* 1982; 12: 81-5
- Walzi MK, Zimmerman MB, Spinas GA, Hurrell RF . Low plasma magnesium in type 2 diabetes. *Swiss Med Wkly* 2003; 133: 289-92
- Suarez A. Decreased insulin sensitivity in skeletal muscle of hypomagnesaemia rats. *Diabetologia*. 1993; 36(Suppl 1): A82
- Sales CR, de Fatima Campos Pedrosa L: Magnesium and diabetes mellitus: Their relation. *Clin Nutr* 2006; 25: 554-62.
- Frei B. On the role of vitamin C and other antioxidants in atherogenesis and vascular dysfunction. *Proc Soc Exp Biol Med*. 1999; 222 (3): 196 - 204.
- Vinson JA, Howard TB 3. Inhibition of protein glycation and advanced glycation end products by ascorbic acid and other vitamins and nutrients. *J Nutr Biochem* 7; 1996(20): 659-63.
- Pecaro RE, Chen MS. Ascorbic acid metabolism in diabetes mellitus. *Ann NY Acad. Sci*, 1987; 498: 248-58.
- Cunningham JJ. Vitamin C; an aldolase reductase inhibitor that normalizes erythrocyte sorbitol in insulin dependent diabetes mellitus's. *Am Coll Nutr*. 1994; 13 (4): 344 - 50.
- Freeman DJ, Noorie J, Caslake MJ, Gaw A, Ford I, Lowe Gd et al. C-reactive protein is an independent predictor of risk for the development of diabetes in the west of Scotland Coronary prevention Study. *Diabetes*. 2002; 51: 1596-600.
- Danesh C. reactive protein reassessed. *New England Journal of Medicine*. 2004; 350(14): 1450-2.
- Devraj S, Jialal LA. A novel marker of cardiovascular risk. C-reactive protein . *The American Journal of Cardiology*. 2003; 91(2): 200-2.
- Chambers EC, Heshka S, Gallagher D, Wang J, Pi-Sunyer X, Pierson RN. Serum Magnesium and Type-2 Diabetes in African Americans and Hispanics: A New York Cohort. *Journal of the American College of Nutrition*. 2006; 25(6): 509-513.
- Gruia V, Arsene-Nipulescu A, Maria M, Mireia N, Gradinaru D, Manuel By. Correlations Between Some Plasmatic Redox Parameters In Diabetic Patients. *FARMACIA* 2008; vol LXI6: 692-698.
- King DE, Mainous AG, Buchanan TA, Pearson WS. C-Reactive Protein and Glycemic Control in Adults With Diabetes. *Diabetes care*. 2003; vol 26: 1535.

## DRUG PROFILE

### Fosfomycin

Fosfomycin trometamol is a synthetic, broad-spectrum, bactericidal antibiotic against gram-positive, gram-negative aerobic microorganisms blocking the condensation of uridine diphosphate-N acetylglucosamine with p-enolpyruvate. **Pharmacokinetics:** Fosfomycin is rapidly absorbed following oral administration; oral bioavailability is 37%. Fosfomycin is not bound by plasma proteins; and is distributed to kidneys, bladder wall, prostate and seminal vesicles. The drug is excreted unchanged in both urine and feces. Approximately 38% of a 3g dose of Fosfomycin is recovered from urine and 18% is recovered from feces. Urine Fosfomycin concentration was attained within 6-8 hours, following oral administration. **Indications:** Fosfomycin trometamol is indicated only for the treatment of uncomplicated urinary tract infections (acute cystitis) in women due to susceptible strains of *Escherichia coli* and *Enterococcus faecalis*; drug is not indicated for treatment of pyelonephritis or perinephric abscess. **Dosage and Administration:** The recommended dose for women 18 years of age and older for uncomplicated urinary tract infection (acute cystitis) is one sachet of 3gm in 100ml of water; it can be taken with or without food. **Precautions:** Repeated daily doses of Fosfomycin do not improve the clinical success or microbiological eradication rates compared to single-dose therapy. Dosage adjustment is not necessary in renal and hepatic impairment. **Undesirable Effects:** In clinical trials, the most frequently reported adverse events were diarrhea, headache, vaginitis, nausea, rhinitis, back pain, dysmenorrhea, pharyngitis, dizziness, abdominal pain, pain, dyspepsia, asthenia and rash.

### Check-list

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