Effect of Thiazide and Loop Diuretics on Serum Magnesium and other Electrolytes in Cardiac Patients

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Abstract:
Diuretics are agents that promote diuresis and are widely used for various indications like hypertension, edema of cardiac, renal failure or liver cirrhosis, acute pulmonary edema. Despite its key role, diuretics have serious side effects like volume depletion and electrolyte disorders, with greater relevance in ageing population. Thiazide and loop diuretics have shown to cause alterations in serum magnesium and other electrolyte levels resulting in fatal complications like ventricular arrhythmias, coronary artery vasospasm or sudden death. This severely affects the quality of life of the patient especially those with cardiac illness. By this review we aim at reinforcing the importance of magnesium supplementation and the importance of including serum magnesium among the frequently monitored parameters, in the cardiac department.

Keywords: thiazide diuretics, loop diuretics, electrolytes, hypomagnesemia, arrhythmia

I. INTRODUCTION:

Diuretics are agents that cause production of urine by promoting excretion of salt and water from the kidneys. Diuretic are classified into loop diuretics, thiazide diuretics, potassium sparing diuretics, carbonic anhydrase inhibitors and osmotic diuretics. Diuretics are widely used for indications like hypertension, edema of cardiac, renal failure or liver cirrhosis, acute pulmonary edema. The mechanism of action of each class of diuretic is specific, based on the site of their action. Loop diuretics prevent reabsorption of sodium and chloride ions in the loop of Henle by exerting their diuretic action on Na (+)-K (+)-2Cl (-) cotransporter in the thick ascending limb. This class includes furosemide, bumetanide, and torsemide. Thiazide diuretics inhibits sodium reabsorption by inhibiting the Na (+)-Cl (-) cotransporter in the distal convoluted tubule. This class includes chlorothiazide, chlorthalidone, hydrochlorothiazide, indapamide, metolazone. Diuretics have shown to influence serum electrolyte levels causing alterations in sodium, potassium, magnesium, calcium and other markers like uric acid. Magnesium is the second most abundant intracellular cation after potassium. It plays a key role in a variety of enzymatic reactions, energy- equiring metabolic processes and anaerobic phosphorylation, protein and DNA synthesis as well as in transmembrane transport mechanisms. Normal range 0.7-1 mmol/L (1.5-2 mEq/L); 1.7-2.4 mg/dL

Hypomagnesemia and depletion of intracellular stores, especially in cardiac muscle, have been responsible for a variety of cardiovascular and other functional abnormalities. These may include various arrhythmias, such as atrial fibrillation and torsade de pointes, impairment of cardiac contractility and vasoconstriction. Sodium is equally important for heart function and is needed for voltage gated sodium channels in the outer membranes of cardiac cells. It is important for initiating the action potential and triggering contractions of cardiac muscle fibres. Normal range: 135-145 mEq/L

Potassium is an electrolyte which is crucial to heart function and plays a key role in skeletal and smooth muscle contraction as well as conduction of electric impulses in the body. It also has a role in regulating blood pressure. Its deficiency (hypokalemia) can cause weakness as cellular processes are affected. Normal range- 3.5 – 5.0mmol/L

Calcium ions play an important role in activating muscle contractile process. An excess of calcium ions cause spastic contractions whereas its deficiency causes cardiac flaccidity. Normal range: 8.5-10.2mg/dL

Uric acid is a product of the metabolic breakdown of purine nucleotides, and is a normal component of urine. High blood concentration of uric acid can lead to gout and are associated with other medical conditions including diabetes and kidney stone. Epidemiological studies have confirmed the strong relationship of gout and hyperuricemia with hypertension and diabetes. Normal range-2.4 – 6.0 mg/dL (female) and 3.4-7.0 mg/dL (males)

II. REVIEW OF LITERATURE:

S.P. Chinchilla, et al., (2015), conducted a study on ‘Serum Magnesium Levels in Patients in Relation To Diuretic Treatment’. A prospective, recruitment, transversal design, case-
control study was conducted in 602 patients (53% male, median age 73 years) to evaluate the serum Magnesium levels in patients with Pyrophosphate Arthritis (PPA) and controls (279), as well as the impact of treatment with diuretics and administered doses on serum magnesium. Serum magnesium levels were obtained, as well as data regarding use of diuretics, type and doses at the time of analysis. The result was found that patients on diuretic therapy had a lower serum magnesium level than patients without them. The rate of hypomagnesemia was higher in patients on diuretics (22.6% v/s 5.0%). Thus, serum magnesium levels are associated to high-dose thiazide use.

N Cohen, et al., (2003); conducted a study on ‘Serum Magnesium Aberrations in Furosemide(Frusemide) treated patients in Congestive Heart Failure: Pathophysiological Correlates and Prognostic Evaluation’. An observational study was conducted in a tertiary reference center with 404 consecutive patients admitted with congestive heart failure as one of the diagnosis and previously treated with furosemide for at least 3 months. Hypomagnesemia was found in 50 patients and it emerged as being significantly associated with shorter survival.

Spyridon Arampatzis, et al., (2013); conducted a study on ‘Impact of Diuretic therapy-associated Electrolyte Disorders present on admission to Emergency Department: a Cross-Sectional Analysis’. A Cross-sectional analysis was conducted using patients presenting to the emergency room (ER) of the Inselspital, University Hospital, Bern, Switzerland. Data on diuretic medication, baseline characteristics and laboratory data including electrolytes and renal function parameters were obtained. A multivariate logistic regression model was performed to assess the impact of factors on electrolyte disorders and patient outcome. It was found that among patients on diuretic therapy, 4% had hyponatremia and 12% hypernatremia, 11% showed hypokalemia and 4% hyperkalemia. Loop diuretics were an independent risk factor for hypernatremia and hypokalemia, while thiazide diuretics were associated with the presence of hyponatremia and hypokalemia.

Rodenburg, et al., (2014); conducted a study on ‘Thiazides and the Risk of Hypokalemia in the General Population’. A population-based cohort study was conducted to assess the risk of thiazide-induced hypokalemia in men and women in the general population, using Cox proportional-hazard regression analysis over a 10-year period with thiazide use as a time-varying exposure. During the follow-up, 507 cases of hypokalemia occurred in 13328 patients. Thiazide use was associated with an 11 times higher risk of hypokalemia than no use. The risk of thiazide-induced hypokalemia is high, and more than twice as high in men as in women.

Ariel J. Reyes, et al., (2005); conducted a study on ‘The increase in Serum Uric Acid concentration caused by Diuretics might be beneficial in Heart failure’. A randomized, placebo-controlled and double blinded study was conducted to assess the effects of add-on treatment with diuretic on morbidity and mortality, in asymptomatic patients with major cardiac dysfunction and at high risk of developing cardiac failure. Minimal doses of diuretics like hydrochlorothiazide 12.5 mg, chlorothalidone 12.5 – 25mg and bendrofluazide 12.5mg once daily was used in the study and the effects were studied. The results showed that increase in serum uric acid caused by diuretics was apparent at low doses and showed a dose dependent fashion. Antihypertensive treatments with dosages of diuretics that is substantially lower than those used in the past, increase serum uric acid concentration. Indeed serum uric acid may be more susceptible to change by diuretics than even serum potassium.

III. CONCLUSION:

Diuretics remain a major component of drug therapy in both hypertension and heart failure. There have been several studies showing diuretic induced electrolyte abnormalities. Abnormalities like hypomagnesaemia, hyponatremia, hypokalemia can occur with both loop and thiazide diuretics. The risk is related to duration of action as well as potency of the diuretic. Hyperuricaemia and metabolic alkalosis are also risks that can occur at higher doses of diuretic therapy. Electrolyte disturbance can result in fatal complications like ventricular arrhythmias, coronary artery vasospasm or sudden death. This review aims at comparing the extent of hypomagnesemia when treated with thiazide and loop diuretics, and hence its effect on the quality of life. By this review we aim at reinforcing the importance of magnesium supplementation and the importance of including serum magnesium among the frequently monitored parameters, in the cardiac department.

IV. REFERENCES:


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