The Effect Of Magnesium Deficiency On Blood Pressure Control In Hypertensive Patients With Diabetes Mellitus

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A. Study Purpose and Rational

The goal of this study is (1) to document whether magnesium deficiency exists in sufficient numbers in the diabetic hypertensive population being sampled. Goal number (2) is to determine whether magnesium supplementation can enhance blood pressure control in patients with hypomagnesemia.

Magnesium is the fourth most abundant cation in the human body. It is predominantly an intracellular cation. Experimental, epidemiological and clinical studies over the past several years suggest that magnesium is actively involved in the maintenance of normal cardiovascular function. [ ] Patients with diabetes mellitus have been shown to be at increased risk of magnesium depletion.[ ]

Often this hypomagnesemia is due to increased urinary excretion of magnesium. However, it can also be secondary to decreased intestinal absorption, reduction in bone magnesium levels and effects of hormones and exogenous drugs.C I In some past studies magnesium deficiency has been linked to hypertension.[ ]

B. Description of study design and statistical analysis

After giving informed consent patients will be scheduled for a standard physical exam and history. Height and weight of each patient will be recorded. A list of all medications being taken by the patient will be documented. During this initial visit a fasting serum chemistry 7, fasting renin level, serum magnesium level, and a glycosylated hemoglobin will be drawn. A twentyfour hour urine for creatinine and protein will be collected. This *will be* used to assess creatinine clearance. Also a baseline echocardiogram will be obtained. The study will be divided into parts. In part one after the initial visit the subjects will be asked to return in two weeks to have their blood pressure checked. This will involve having the patient lying in a supine position for ten minutes prior to having the measurement taken. Five minutes later a repeat measurement will *be* taken in a supine position. All subsequent blood pressure measurements will be carried out in the above manner and recorded in the same arm. All patients will be instructed not to smoke cigarettes or drink alcoholic beverages within thirty minutes before their scheduled visits. Two weeks later all subjects will be asked to return for a blood pressure check and repeat chemistry 7, glycosylated hemoglobin, and serum magnesium. This will end part one of the study.

Part two of the study will include all patients with documented serum hypomagnesemia (serum Mg<)and an average systolic blood pressure greater than or equal to 150mmHg (see sect. G- subjects and methods for greater detail). This group of subjects will be randomly assigned to placebo vs. magnesium chloride supplementation group. The,subjects will be blinded to which group *they* have been assigned. At this visit they will receive instructions to take the tablet once a day preferably after a meal. Each patient will have their blood pressure checked at this time. In one week both groups will return for repeat labs (chemistry 7, fasting renin level, serum magnesium) and blood pressure check. Two weeks later the subjects will return for repeat blood pressure check and a final set of labs(serum magnesium, glycosylated hemoglobin). At this point all would have completed three weeks of placebo or magnesium chloride supplements. All subjects will be asked to return one week later for an exit interview and final blood pressure check. The purpose of this interview is to provide a sense of closure for the subjects, thank them for their participation and gain more general information. Specifically, a multiple choice questionnaire will be administered to determine side effects if any,compliance and whether or not subjects knew which tablet they had received.

a. Statistical Analysis

The subjects will be randomized with a fixed randomization scheme with an allocation ratio and block size. The Moses-Oakfard assignment algorithm will be used.

b. Statistical Analysis and Power

This study proposes to establish whether exogenous magnesium supplementation can produce a 15-mm 14g reduction in systolic blood pressure after one month of therapy in a single group of diet-controlled diabetics with stage H hypertension. A dependent T-test will be used to test the null hypothesis that exogenous magnesium fails to reduce systolic blood pressure within subjects. A power analysis, assuming a 5% type I error rate and a paired T-test with 30 subjects, showed 80% power to detect a 0.66-standard deviation effect size when within-subject measures have a correlation of 0.40. The literature indicates that standard deviation of the month-to-month systolic blood pressure changes of similar subjects to be approximately 20-mm Hg. Thus this study will have 80% power to detect a 12-mm Hg therapeutic efficacy for magnesium.

C. Description of Study Procedures

The only procedure involved WO-Ald be veniplAncture done in a routine manner. Normally blood sampling would not be done on such a frequent basis but this will pose no harm to the patients involved in the study. After the initial physical exam and history, each visit should take approximately twenty minutes. The anticipated duration of each subjects participation will be spread over two months.

D. Study Drugs

The drug in question is magnesium chloride(MgC12). It is a commonly prescribed mineral salt which can also be found in over, the Counter mineral supplements. The dose in this Study will be 384mg once a day orally. This a dose prescribed in common practice. Common side effects include diarrhea and dyspepsia. Often taking the supplements with food can alleviate these side effects.

E. Medical Devices

None will be used in this study.

F. Study Questionnaires

Patient questionnaire will consist Of Multiple choice questions to identify side effects and subjects knowledge of the contents of the tablets ingested. It will also assess compliance with the supplement/placebo.

G. Description of Study Subjects and Method of Recruitment

Potential subjects will be recruited by their private medical doctors. A memorandum will be sent to rill AIM clinic doctors briefly describing the study and asking that they identify any patients eighteen years and older with type I or II diabetes mellitUS and hypertension (systolic greater than or equal to 150mmHg) for enrollment in the study. The address and phone number of potential subjects will be obtained from the clinic doctors. Verbal consent would have been obtained from the patient by their clinic doctors. The potential subjects will be contacted by phone or mail and an appointment setup. During this in person visit the potential Subject will be briefed on the study and written consent will be obtained.

Exclusion criteria will be diabetes less than six months, hypertension less than six months, renal failure on dialysis, creatinine clearance< 80ml/min, daily use of prednisone within the last two months(asthmatics on brief tapers, i.e. one week will not be excluded). Patients with documented congestive

heartnfailure or use of cyclosporine/cisplatin will also be excluded. Patients on carbenicillin, diuretics, frequent ethanol ingestion may be included but ingestion *of* the above will be documented.

H. Confidentiality of Study Data

I. Location of Study

J. Risks and Benefits

The anticipated potenti.al benefit of participating in the study would be lower systolic blood pressure. The only risk involved would be hypermagnesemia in those patients receiving MgCL2 supplements. However patients at greatest risk for this (renal failure, renal insufficiency, congestive heart failure) will be excluded from the Study. The remaining patients will have their serum magnesium levels checked regularly thus this risk will be minimal and read4ly identified. Patients with normal renal function excrete excess magnesium in the urine.

K. Alternative Studies

L. Compensation and Costs to Subjects

The only cost to the patient will be travel expense and possible missed hours from work. The possibility *of* monetary compensation for the this will have to be further thought Out.

M. Minors and Research Subjects

No minors will participate in this study

N. Radiation or radioactive substances

None of the above will be used in this study

O. References

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