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Changes of Total Content of Serum Magnesium in Elderly Chinese Women with Osteoporosis

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ABSTRACT

Objective: To explore whether the serum levels of magnesium (Mg) and calcium (Ca) differ between osteoporotic and nonosteoporotic elderly Chinese women.

Methods: Using WHO classification criteria based on bone mineral density (BMD), general healthy Chinese women older than 65 yr were classified as osteoporosis (OP), osteopenia, and normal group according to the T-score of the femur neck. Then their physical characteristics, serum levels of magnesium (sMg), calcium (sCa), and other biochemical measurements were analyzed.

Results: Altogether, 324 subjects were included in the final analysis with 77 in OP, 137 in osteopenia, 110 in normal group. The level of sMg in women with OP is significantly higher (0.91±0.11 mmol/L) than both the osteopenia (0.88 ± 0.09 mmol/L) and the normal (0.87±0.08 mmol/L) even after being adjusted for both age and body mass index (BMI), which might result from potentially low levels of sCa. sMg inversely related to sCa in subjects with OP (r=–0.240, p=0.038), whereas the total levels of sCa and sMg kept relatively steady.

Conclusion: High content of sMg and potentially low content of sCa could be a feature of the serum profile of elderly Chinese women with OP, the clinical significance of which needs further elucidation. Supplementation of Mg for elderly Chinese women with OP did not appear to be necessary.

Index Entries: Osteoporosis; elderly Chinese women; serum magnesium; serum calcium.

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INTRODUCTION

Postmenopausal osteoporosis of elderly women, induced presumably by both loss of estrogen and advancing age, develops as a consequence of an imbalance of mineral metabolism in bone, while the body contents of mineral elements, such as calcium (Ca), phosphorus (P), and magnesium (Mg), are finely regulated through storage in the bone, excretion from kidney, and absorption in the intestine, among which bone exerts one of its functions to maintain Ca homeostasis by remodeling.

Serum Ca (sCa), the main source of bone mineralization, may be potentially insufficient in postmenopausal osteoporosis, because supplementation of this element can successfully prevent bone loss and reduce vertebral fracture, and, accordingly, this regime has become the basic therapy for osteoporosis *(1,2).*

Less research, however, focused on the role of Mg, another essential element for bone mineralization, to bone health, even a possible role of Mg in therapy for osteoporosis was suggested as early as in 1960 *(3).* Later, studies found dietary intake of Mg reduced and serum Mg (sMg) decreased in postmenopausal women with osteoporosis *(4,5).* In addition, supplementation of Mg appeared to be able to prevent fractures and result in increased bone mineral density (BMD) *(6).*

To our knowledge, head to head reports are sparse regarding to the serum change of Mg and its relationship with Ca in elderly women with osteoporosis, especially in the oriental population. The present study was therefore designed to explore whether the serum magnesium and calcium profiles differ between osteoporotic and nonosteoporotic elderly Chinese women.

SUBJECTS AND METHODS

Subject

Participants for this cross-sectional analysis were recruited from a community-based population in Beijing, P. R. China, by the way of local media, poster, and health lecture between September 2002 and March 2003. To be eligible for participation, women had to be Chinese residents in Beijing and over 65 yr of age, to be ambulatory without hip replacement, and to be in good general health. Furthermore, patients were excluded if they met any of the following criteria: (1) estimated creatinine clearance rate less than 30.0 mL/min, (2) uncontrolled or severe diabetes, (3) diseases such as thyroid diseases, rheumatoid arthritis, etc., or recently concomitant medication such as glucocorticoids, estrogens, SERM, bisphosphonates, etc., known to affect bone metabolism except calcium supplementation, and (4) hypercalcemia (defined as calcium level more than

2.78 mmol/L) or high sGOT/sGPT/sALP (two times higher than upper normal limitation).

The Peking Medical College Union Hospital Ethics Committee approved the study procedure and written informed consent was obtained from each participant prior to screening.

Methods

Data Collection and Anthropometric Measurements

On appointed attendance at the menopausal outpatient clinic located at Peking Union Medical College Hospital (PUMCH), participants were requested to complete a self-made questionnaire that includes a general medical and social history, reproductive history, and menopause time. Anthropometric measurements were made of height, body weight, and blood pressure. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m^2).

Bone Mineral Density (BMD) Measurements

BMD at the left femur region was assessed with posteroanterior projection, using standard techniques from dual-energy X-ray absorptiometry (Lunar Prodigy scanner, Lunar, Madison, WI) after the questionnaire was completed. All BMD measurements were done by the same technician and the variation coefficient for consecutive determinations of image in our laboratory was less than 1.0% at the femur region. BMD value, recorded in grams per square centimeter, was then expressed as T-scores based on local reference that was specifically established for the Chinese population. All spinal scans were reviewed for evidence of prevalent vertebral fractures when a patient had a femoral neck BMD T-score less than or equal to –1.5 but more than –2.5.

Biochemical Measurements

Overnight fasting blood and urine samples were obtained between 0800 and 0930 in the morning from all subjects at the same day before the questionnaire was completed. Blood samples were centrifuged and the serum was stored at –20°C until analyzed. Biochemical measurements were done of blood glucose, serum glutamic oxaloacetic transaminase (sGOT), glutamic-pyruvic transaminase (sGPT), serum creatinine (sCr), blood urea nitrogen (BUN), calcium (sCa), phosphate (sP), magnesium (sMg), potassium, sodium, total protein (sTp), albumin, total alkaline phosphatase (tALP). A hematological study was done for excluding abnormal states of hemoglobin and white blood cell (WBC) and urine from abnormal states of renal function. Biochemical parameters were measured in serum using a BM/Hitachi 717 (Au 400 automated analyzer system, Olympus Japan).

Statistical Analysis

Initial data management used Foxpro 6.0 program to create a data file for each data set; the final data analysis was performed using SAS 6.12 (SAS Institute, Cary, NC) on a Windows computer. We used the WHO classification ranges based on BMD T-score to classify subjects as normal group (T-score ≥ -1), osteopenic group ($-1 >$ T-score > -2.5), or osteoporotic group (T-score ≤ -2.5). If a previous spinal fracture was affirmed, patients in osteopenic group were reclassified into osteoporotic group. However, analysis of the data excluding the women with identified spinal fracture did not affect the significance of the results.

Continuous variables were expressed as mean±SD; those in a category were expressed as a frequency (percentage). The normal distribution of variables was confirmed by calculating skew and kurtosis before applying standard tests. One-way analysis of variance (ANOVA) was applied when comparing differences of groups with a post-hoc test using Tukey's method. Covariate analysis and partial correlation, adjusted for confounding variables (such as age, BMI), were used to determine the difference contents of sMg between groups. A minimum p value of <0.05 was the necessary condition for statistical significance.

RESULTS

General Population Profile

Initially, 344 women over 65 yr of age were invited for screening in this study; 83 were diagnosed as osteoporosis, including 16 with a previous vertebral fracture. Later, 4 were excluded due to low creatinine clearance and 2 with hypercalcemia. In 149 participants located in osteopenic group, 12 were excluded because of low creatinine clearance rate; 112 were identified as normal bone mass group, 2 of which were excluded due to hypercalcemia. Ultimately, 324 were included in the final analysis. There was significant difference in age, height, weight, BMI among three groups; yet, prevalence of other diseases was comparable (Table 1).

Biochemical and BMD Measurements

Values of all biochemical indicators measured were in the normal range, but the sMg level in OP group (0.91±0.11 mmol/L) was significantly higher than in the osteopenia (0.88±0.09 mmol/L) and normal (0.87±0.08 mmol/L) groups (p=0.02). In addition, the level of the product of calcium and phosphorus was lower in OP group but did not reach statistical significance (p=0.06). Interestingly, the total serum level of both Ca and Mg, the two bivalent cations, is very similar among three groups (Table 2).

Tables 1
Number and Physical Characteristics of Three Groups
Categorized by BMD Measurements

GROUP	Osteoporosis A (n=77)	Osteopenia B (137)	Normal BMD C (110)	P
Age (years)	72.10±3.95*^	70.31±3.59*	69.15±3.30	<0.01
low-75	61(79.22)	125(91.24)	101(91.82)	<0.01
75-high	16(20.78)	12(8.76)	9(8.18)	
Age at menopause (years)	48.17±3.96*	48.50±4.63	49.56±3.63	0.05
Years since menopause	23.94±5.93*^	21.81±6.07*	19.58±4.72	<0.01
Height (m)	152.69±5.49*^	155.16±4.54	156.14±5.25	<0.01
Weight (kg)	57.34±8.64*^	60.34±8.60*	66.05±10.96	<0.01
BMI (Kg/m^2)	24.57±3.27*	25.05±3.36*	27.10±4.26	<0.01
Low-<28	67(87.01)	117(85.40)	64(58.18)	<0.01
28-high	10(12.99)	20(14.60)	46(41.82)	
Hypertension	36(46.75)	60(43.80)	57(51.82)	0.45
Coronary heart disease	15(19.48)	34(24.82)	18(16.36)	0.25
Diabetes Mellitus	6(7.79)	12(8.76)	15(13.64)	0.33
Hyperlipemia	8(10.39)	21(15.33)	12(10.91)	0.46
Calcium supplementation	36(46.75)	50(36.50)	44(40.00)	0.34
BMD				
Neck (g/cm^2)	0.596±0.046*^	0.679±0.035*	0.817±0.059	0.00
Neck (T score)	-2.64±0.39*^	-1.95±0.32*	-0.79±0.49	0.00

* indicates A or B vs C: $p<0.05$
^ A vs B: $p<0.05$

Covariate Analysis

Covariate analysis, in which sMg value was taken as the dependent variable, revealed a significant relationship between sMg and sCa. When age and BMI were taken into account as covariates, the model still showed statistical significance among each group (F=3.80, p=0.024), but not age (F=0.26, p=0.612) or BMI (F=2.19, p=0.140).

When sCa level was also considered, the difference of sMg was not significant among groups (F=2.09, p=0.126), age (F=0.23, p=0.636), and BMI

Table 2
Comparison of Chemical Measurement's Among Groups

	Osteoporosis A (n =77)	Osteopenia B (n=137)	Normal BMD C (n=110)	P值
tALP (u/L)	77.61±18.87	74.11±16.97	72.21±21.47	0.16
sGPT (u/L)	19.60±10.12	19.09±8.31	20.79±11.76	0.41
sGOT (u/L)	24.00±8.60	23.47±5.73	23.35±7.37	0.81
Total protein (g/L)	78.38±5.65	77.83±4.56	78.08±4.94	0.74
Albumin (g/L)	44.32±2.60	44.86±2.21	44.91±2.24	0.18
Albumin/globins	1.33±0.21	1.38±0.19	1.38±0.21	0.15
BUN (mmol/L)	5.94±1.42	5.89±1.42	5.91±1.50	0.97
Creatinine (mg/dL)	1.11±0.14	1.13±0.14	1.15±0.16	0.12
Calcium (mmol/L)	2.45±0.10	2.46±0.10	2.48±0.09	0.17
Phosphorus (mmol/L)	1.27±0.14	1.28±0.14	1.30±0.14	0.17
Ca*P	3.10±0.36	3.16±0.36	3.23±0.38	0.06
Sodium (mmol/L)	143.87±2.26	144.09±2.44	143.67±2.40	0.40
Potassium (mmol/L)	4.31±0.29	4.36±0.40	4.38±0.31	0.41
Magnesium (mmol/L)	0.91±0.11*^	0.88±0.09	0.87±0.08	0.02
Ca+Mg (mmol/L)	3.36±0.13	3.34±0.12	3.35±0.12	0.70
Ca/Mg	2.73±0.37*	2.84±0.32	2.86±0.29	0.03

* indicates A vs C: $p<0.05$
^ indicates A vs B: $p<0.05$

($F=2.29$, $p=0.131$), while sCa showed significance ($F=8.23$, $p=0.004$). Therefore, the high level of sMg in the OP group seemed to be dependent on the low level of sCa.

Correlation Studies Between sMg and Other Ions in Serum (Table 3)

In the overall group, correlation studies revealed a significant negative correlation between sMg and sCa ($r=-0.166$, $p=0.003$), and when stratifying by group, only correlation between sMg and sCa in patients with osteoporosis was statistically significant ($r=-0.240$, $p=0.038$).

Table 3
Correlation Studies of Magnesium and Other Ions in Serum
(adjusted by Age and BMI)

	Osteoporosis		Osteopenia		Normal bone mass		Total	
	r	P	r	P	r	P	r	P
Ca	**-0.240**	**0.038**	-0.152	0.079	-0.103	0.289	**-0.166**	**0.003**
Phosphorus	-0.035	0.765	-0.090	0.299	-0.193	**0.045**	-0.101	0.069
Ca*P	-0.113	0.333	-0.141	0.103	-0.209	**0.030**	**-0.150**	**0.007**
Potassium	0.205	0.078	0.078	0.370	0.133	0.171	**0.111**	**0.046**
Sodium	0.085	0.467	0.075	0.385	0.176	0.068	**0.120**	**0.031**

DISCUSSION

Our study found that, first, serum content of Mg of elderly Chinese women with osteoporosis, diagnosed by low femur neck BMD, was statistically higher than that of women without OP, which might be the compensatory reaction to a low level of serum calcium as suggested from covariate analysis. Second, total content of both calcium and Mg remains relatively steady in the elder female population and sMg is inversely related to sCa in the subset with osteoporosis. These initial findings could yield some insights into development of senile osteoporosis and might have implications in the treatment of elderly Chinese women with OP.

The result of high sMg in patients with OP is markedly inconsistent with previous studies, where low or normal levels of magnesium in women with OP *(3,5)* were generally reported. The exact mechanism of difference needs further elucidation, besides the age of our subjects, elderly, and the race, oriental. Also, a different location of diagnosis and different serum calcium load may account for another part of this discrepancy.

High sMg in Chinese elderly women with OP, possibly resulting from both elevated level of parathyroid hormone (PTH) of elderly people and the vegetarian-preferred life style in the Chinese population, does contribute some benefits to bone strength. It has been verified by animal experiment that Mg depletion adversely affects bone health *(7,8),* whereas inadequacy of Mg is common in the occidental diet *(9).* Whether or not this contributes to the mechanism of high prevalence OP in Chinese postmenopausal women but with low hip fracture rate *(10,11)* perhaps merits some examination.

PTH plays a key role in calcium metabolism and development of senile OP. It is well known that bone function controls Ca homeostasis through bone remodeling. So when PTH rises after 60 yr of age *(12,13),* assumed to be induced by a decreased ability of calcium absorption and renal retention for Ca, bone loss could occur to maintain serum Ca level. PTH may simultaneously mobilize Mg into circulation as a surrogate for Ca because half of the total Mg was stored in bone tissue, but total sCa and sMg remained steady. Under PTH regulation, Mg, synergizing as well as antagonizing Ca, exerts its multiple physiological functions including coordinating Ca absorption and full use.

The limitation of this study design makes it unable to define how the change of Mg participates in the occurrence and development of postmenopausal osteoporosis. In addition, the high prevalence of hypertension, which can lead to high magnesium for unknown reasons *(14),* and two fifths of participants with Ca supplementation, would bias the real extent of relationship between sCa and sMg. A clinical study about the change of sMg in the context of Ca supplementation is being undertaken in a cohort of elderly Chinese women with osteoporosis.

In summary, high levels of serum Mg and potentially low levels of Ca could characterize the serum profile of elderly Chinese women with osteoporosis, which might be different from early postmenopausal osteoporosis. It would be more useful to use a combination of both sCa and sMg to determine the status of serum electrolytes in patients with OP. Our results highlighted Ca supplementation but did not support Mg supplementation as one of clinical strategies to treat OP in elderly Chinese women. Further research on the change of sMg after Ca supplementation will better elucidate the significance of high magnesium in elderly Chinese women with OP.

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