Original Article
http://mjiri.iums.ac.ir

Medical Journal of the Islamic Republic of Iran (MJIRI)
Iran University of Medical Sciences

The relationship between sodium intake and some bone minerals and osteoporosis risk assessment instrument in postmenopausal women

Mohammadreza Vafa*[1], Sepideh Soltani[2], Farid Zayeri[3], Mahtab Niroomand[4]
Azadeh Najarzadeh[5]

Received: 11 March 2015 Accepted: 17 November 2015 Published: 28 May 2016

Abstract

Background: The results of the studies on the effects of sodium on bone metabolism have been inconsistent. There is no definitive answer to the question of whether sodium restriction can be associated with a lower incidence of osteoporosis. What reinforces the necessity of designing this study is the lack of findings with the approach of examining the effects of sodium on bone in our country.

Methods: This was a cross-sectional study conducted on 185 retired female teachers aged 45 to 70. Sodium intake was evaluated using two methods: A 24-hour recall and a 12-hour urine sample. To assess bone health, ORAI index was calculated for each individual. Urinary calcium, phosphorus, potassium and serum vitamin D and PTH were measured as laboratory variables. To compare the general characteristics of the participants across tertiles of urinary sodium, the analysis of variance (ANOVA) was used for quantitative variables and the Chi-square test for categorical variables.

Results: Phosphorous, calcium and potassium urinary excretion rate increased with the increase in urinary sodium ($p<0.05$). However, the changes in serum vitamin D, and PTH levels across tertiles of urinary sodium were not significant. Changes in urinary sodium levels were not significant ($p=0.933$) in ORAI groups (sorted by rating). The relationship between urinary calcium and sodium was apparent in low calcium intake ($r=0.415$, $p<0.001$), but not in higher calcium intake ($r=0.144$, $p=0.177$).

Conclusion: Although urinary calcium and potassium increased with the increase in sodium intake, no relationship was found between sodium and ORAI.

Keywords: Urinary Sodium; Urinary Calcium; ORAI; Bone Health.

Cite this article as: Vafa M, Soltani S, Zayeri F, Niroomand M, Najarzadeh A. The relationship between sodium intake and some bone miner-als and osteoporosis risk assessment instrument in postmeno-pausal women. *Med J Islam Repub Iran* 2016 (28 May). Vol. 30:377.

Introduction

In the past two decades, Middle Eastern and North African countries encountered nutritional transitions (1). One of the most important aspects of changes in dietary pattern is the excessive consumption of high- salt foods (1). The growing prevalence of non-communicable diseases such as cardiovascular diseases, hypertension and stroke are associated with high sodium intakes (2,3). The adequate intake of salt for older adults is set at 3.3 g for men and 3 g for women (4). The average consumption of salt in the world is more than 5.8 g/day (5). Thus, the average salt intake is much greater than the acceptable levels to keep the body healthy. The current recommendation to reduce salt intake to 6 g/day is primarily based on the evidence that refers to the role of salt in the preva-

[1]. (**Corresponding author**) (PhD, Professor of Nutritional Sciences, Department of Nutrition, School of Public Health, Iran University of Medical Sciences, Tehran, Iran. rezavafa@yahoo.com
[2]. Department of Community Nutrition, School of Nutrition Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran. s.soltani@iums.ac.ir
[3]. PhD, Associate Professor of Biostatistics, Departments of Biostatistics, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. fzayeri@yahoo.com
[4]. Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. mahtabniroomand@yahoo.com
[5]. Department of Nutrition, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. azadnajarzadeh@ssu.ac.ir

lence of hypertension and cardiovascular diseases (2). Although high salt intake can affect bone metabolism, this association makes no mention of a criterion for determining the levels of salt intake (6).

Osteoporosis is the most common metabolic bone disease. According to WHO criteria, osteoporosis is defined as bone mineral density decreased to≤2.5 standard deviations from the mean bone mineral density in healthy young population (7). Genetics, nutritional, hormonal, life style and environmental factors contribute to the etiology of osteoporosis. Among these factors, dietary intake can be an important factor not only for prevention, but also for controlling the progression of this complication (8). The results of the studies on the effects of sodium on bone metabolism have been inconsistent (9-11). There is no definitive answer to the question of whether restriction in sodium intake can be associated with a lower incidence of osteoporosis (9,10). Based on our research, limited studies have directly reported the negative effects of sodium on bone mineral density (9,11). The results of these studies conducted on postmenopausal women have shown that the increased urinary sodium exacerbates the bone metabolism (9,11). Documents on this topic have indicated an increase in urinary calcium of about 1.1 mmol (44mg) per 100mmol (2300mg) of sodium excretion (12). Studies have suggested that the calcitriol (1, 25- dihydroxy vitamin D) concentration increases and leads to a possible increase in intestinal calcium absorption to compensate for the loss of calcium in response to high sodium intake (13). Some evidence has shown that this compensatory process is observed only in young women (14). The ability of calcium absorption is decreased in postmenopausal women due to the attenuation of vitamin D synthesis (14).

The most reliable method to measure bone mineral density is dual-energy X-ray absorptiometry (DXA) (15). Although the U.S. Preventive Services Task Force Guidelines considers using this method to screen bone density in all women aged 65 years or older, there is no recommendation for women in the two initial decades of menopause (15). In line with the findings of epidemiological studies to determine the risk factors of osteoporosis, certain criteria were developed to assess the incidence risk of these complications. Osteoporosis Risk Assessment Instrument (ORAI) is one of the most common of these criteria used for postmenopausal women at higher risk of osteoporosis in many countries (12,16). Age, weight and estrogen therapy are the components of this risk assessment tool (16). The purpose of this study was to investigate the association between urinary sodium and ORAI and other bone minerals in postmenopausal women.

Methods

Study Design

One hundred eighty-five female teachers aged 45 to 70 years participated in this cross-sectional study. The sample size was estimated based on the Iranian average sodium intake reported in a previous study (17). The Institutional Review Board of Tehran University of Medical Sciences approved the research protocol and the informed consent form before participants were approached to take part in the research and prior to any data collection. Recruitment and exclusion criteria were detailed in the calling form. Eligibility criteria were one year or more without menstruation, absence of medical conditions such as polycystic ovarian syndrome, hyperthyroidism, rheumatoid arthritis, osteoarthritis, renal damage and kidney stone. Exclusion criteria were taking vitamin and mineral supplementations within the past six months, and using diuretics and medications known to affect bone metabolism. In addition, a briefing session was held to introduce the objectives of the study and relevant risk factors for osteoporosis. The participants were asked to enter their personal information in the questionnaire, if they decided to participate in the study.

Among the 300 women who met the eligibility criteria, 185 were randomly selected, and their general information was collected. Two 24-hour recalls (one week day and one weekend day) were applied to estimate nutrient and energy intake. We used Nutritionist IV software (N-squared Computing, San Bruno, CA) to analyze dietary intake.

ORAI Index

Three components of ORAI are weight, age and estrogen usage. The scoring system to calculate ORAI index is as follows: Weight (+9 points for less than 60 kg, +3 points for a body weight between 60 and 70kg, and 0 point for weights above 70 kg); age (+15 points for ages 75 years or older, +9 points for ages between 65 and 74 years; +5 points for ages between 55 and 64; 0 point for 45 and 54); estrogen usage (+2 points for non-current usage of estrogen) (16). The threshold score for ORAI reported that scores less than 9 indicate a low risk of low BMD, and scores equal to or greater than 9 indicate a high risk of low BMD (16).

Serum and Urinary Biochemical Samples

Sodium, potassium, calcium and phosphorous excretions were assessed based on a 12-hour urine sample. The samples were identified only by code numbers. Before the test, 10 ml chloridric acid 6N was added to the urine sample to prevent the formation of phosphate and calcium oxalate deposits, which interfere with the test results. All samples were diluted 1:9 with distilled water; therefore, the results were multiplied by 10. The Ion Selective Electrode method on the Kodak Ektachem 750 XRC analyzer was used for the biochemical analysis of urine sodium and potassium. The CVs (coefficients of variation) were as follows: Sodium 0.4%, and potassium 1.3%. Urinary calcium and phosphorus excretions were analyzed using an automatic analysator Biotecnica- 3000 plus (Tripod, Rome, Italy). Serum PTH concentration was measured with an immunoradiometric assay (Nichols Institute, San Juan Capistrano, CA, USA). The intra and inter-assay CV were 1.2% and 7.8%, respectively. Serum 1, 25-dihydroxy vitamin D was measured by radioimmunoassay after column chromatography (Diasorin, Stillwater, MN, USA). The intra-assay coefficient of variation ranged from 3.2% to 8.6% (depending on 1, 25 D3 level).

Statistical Analysis

Data were analyzed using SPSS software (version 18 for Windows, 2007, SPSS, Inc, Chicago, IL). The assumption of normality was evaluated by Kolmogorov-Smirnov test. To compare the general characteristics of the participants across tertiles of urinary sodium, the analysis of variance (ANOVA) was used for quantitative variables and the Chi-square test for categorical variables. All other variables were quantitative except for the ORAI and tertiles of urinary sodium. In addition, the Pearson's correlation test was used to examine the relationship between dietary and urinary calcium and sodium. $P<0.05$ was considered statistically significant.

Results

General characteristics of the participants and changes in laboratory parameters across tertiles of urinary sodium are shown in Table 1. The first tertile of urinary sodium was less than 87.442mEq/L, the second tertile was between 87.442 and 145.441mEq/L, and the third tertile was more than 145.441mEq/L. The mean ages at menarche and menopause were 13.97 (1.47) and 48.49 (5.45) years, respectively. The mean of sodium, calcium and potassium intake did not change across the tertile groups with respect to the tertile groups of 12-hour urine sodium excretion. An increase in urinary excretion rate of calcium and potassium was observed in parallel with an increase in urinary sodium ($p=0.003$ and $p<0.001$, respectively). Urine phosphorus levels also showed an increasing trend with the increased urinary

Table 1. Baseline Characteristics, Serum and Urinary Biochemical Profiles of Patients Stratified according to Tertiles of 12-h Urinary Sodium Excretion

	All		Urinary Sodium						p*
			1 (< 87.442 mEq/L)		2 (87.442 – 145.441 mEq/L)		3 (>145.441 mEq/L)		
	185		61		63		61		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (yr)	56.01	4.99	55.49	4.15	56.08	5.83	56.08	5.83	0.561
Weight (kg)	72.60	13.01	72.45	12.84	71.70	12.02		14.25	0.700
Menarche (yr)	13.97	1.47	14.11	1.52	13.81	1.53	13.98	1.37	0.513
Menopause(yr)	48.49	5.45	48.87	4.01	48.67	4.50	47.92	7.31	0.594
Calcium (mg)	744.27	235.25	779.16	265.517	723.94	206.08	730.38	231.24	0.365
Sodium (mg)	3566.92	925.61	3605.31	984.91	3513.65	887.02	3583.56	916.27	0.848
Potassium (mg)	2511.29	693.55	2613.16	692.62	2428.44	611.36	2494.98	768.84	.327
Serum									
$1,25(OH)_2D_3$ (ng/ml)	30.93	1.86	35.48	1.94	30.90	1.96	27.54	1.94	0.112
PTH (mg/mL)	23.98	1.91	26.00	1.89	21.13	2.04	25.11	1.77	0.167
Urine									
Calcium (mg/dl)	5.88	1.51	5.01**	1.51	5.75 **	1.44	6.91	1.51	0.002
Phosphorous (mg/dl)	50.11	1.58	44.66 ♯	1.65	50.11♯	1.47	54.95	1.54	0.045
Potassium (mEq/L)	35.70	2.18	33.11	2.81	66.06 ǂ	1.65	70.79 ǂ	1.54	0.006
ORAI (%)									0.935
<9 point	60.52		32.10		33.94		33.96		
≥9 point	39.53		34.21		34.27		31.52		
Usage of estrogen (%)	2.7		8.2		0		8.2		0.653

* Using ANOVA and Post Hoc (Tukey HSD) for quantitative variables and chi square for Qualitative variables
** Significantly different compared to the third tertile (p<0.021)
♯ Significantly different compared to the third tertile (p<0.042)
ǂ significantly different compared to the first tertile (p<0.034)

sodium (p=0.042). The changes in serum vitamin D, and PTH levels across tertiles of urinary sodium were not significant (p>0.05). Seventy-three (39.53%) of the 185 participants were at a high risk of low BMD based on the ORAI score equal to or greater the 9 point. In the group with an ORAI score of less than 9, there were approximately equal numbers of participants in each of the tertiles of urinary sodium. A similar frequency distribution was observed in the group with greater than 9 points of ORAI index. No significant interaction was detected in the ORAI score across tertiles of urinary sodium in either less and greater than 9 ORAI index groups.

The effect of calcium intake on the association between urinary calcium and sodium is shown in Table 2. The mean calcium intake of participants was 774.24 (235.25) mg/day. The relationship between urinary calcium and sodium was apparent in women with low calcium intake (r = 0.415, p<0.001), but not in women with higher calcium intake (r=0.144, p=0.177).

Table 3 displays the association between urinary sodium and calcium. The linear regression modeling approach resulted in the following equation:

Urinary calcium= (urinary sodium×0.001) + 0.066

Based on the crude model, sodium excretion can explain approximately 10 % of the variance of urinary calcium. A significant correlation was still observed between urinary calcium and sodium after adjusting for calcium sodium and potassium intake,

Table 2. Correlations between Urinary Sodium and Calcium Excretion based on Calcium Intake

	Correlation Coefficient (R)*	
	Urinary sodium (mEq/L)	p
Urinary Calcium (mg/dl)		
All Participants	0.255	<0.001
Calcium Intake below the Mean†	0.451	<0.001
Calcium Intake above the Mean†	0.144	0.117

*Data are presented as Pearson Correlation Coefficients (R).
†Mean calcium intake are 744.27 mg/d.

Table 3. Linear Regression Coefficient in the Association between Urinary Sodium and Calcium Excretion

	Urinary Calcium			
	β	SE	R^2	p
Urinary Sodium				
Crude	0.001	0.0001	0.098	<0.001
Adjusted*	0.001	0.0001	0.168	<0.001

*Adjusted for Calcium, Sodium, Potassium and Phosphorous Intake, Weight, PTH and Vitamin D

serum vitamin D and PTH and weight.

Discussion

The major findings of this study suggested that urinary excretion rate of calcium, potassium and phosphorus increased in parallel with increased urinary sodium. However, vitamin D levels and serum PTH and ORAI did not show any association with urinary sodium.

Although the gold standard tool to measure sodium intake is the 24-hour urine (5), this method is expensive, uncomfortable and difficult when it comes to collection of population samples (5). Overnight urine sample is easily obtained. On the other hand, several studies have reported a good correlation between overnight sodium and 24-hour urine collections (18). Thus, in this study, an overnight urine sample was used to estimate sodium intake.

Urinary Sodium and Calcium Excretion

In this study, a significantly increasing trend was found in the levels of urinary calcium with increased urinary sodium. Urinary sodium positively correlated with urinary calcium (r=0.290, p=0.01). High dietary sodium intake has generally been found to affect calcium metabolism adversely. Ho et al. reported that in China's adult population, high sodium intake is the main factor in the excretion of calcium (19). Harrington suggested an association between increased levels of sodium intake and urine calcium loss in postmenopausal women (20). Teucher et al. showed that urinary excretion of calcium is more significant during high-salt diet (11.2g/d) compared to low-salt diet (3.9g/d) (21).

It seems that the link between sodium and calcium results from their interactions in the kidney (22). Typically, more than 99% of sodium and 95% of calcium were reabsorbed in the renal tubules (22). Changes in urinary calcium, in parallel with raised urinary sodium, were attributed to the existence of linked re-absorption pathways for both ions in the convoluted portion of the proximal tubule and thick ascending loop of Henle (23). Therefore, the fractional absorption of calcium is decreased in parallel with increased sodium reabsorption in the kidney.

The relationship between urinary calcium and sodium is affected by calcium intake. In our participants, urinary sodium and calcium excretion were associated at lower levels of calcium intake, but not at higher levels. These findings are similar to the reports of Carbone and Nordin who suggested that the hypercalciuric effect of sodium was observed in low Ca intake (10,24). In line with previous studies, Bedford and Barr found that in premenopausal women, a relationship exists between urinary sodium and calcium with calcium intakes of less than 506mg per 1000 calories, but not in high intakes (25). This suggests that in low calcium intake, the interrelated transportation pathway in renal tubular is the reason for intensifying the relationship between urinary sodium and calcium (23). Independent sodium reabsorption mechanism was noticed in high calcium intake. Therefore, the linked reabsorption pathway of sodium and calcium has disappeared in high calcium intake (23).

Response rate for Na –induced calciuria was extracted using regression equation. In our study, it was shown that for each 100 mmol (2,300mg) increase in urinary sodium, calcium excretion would increase by 1.43 mmol (57.2mg). The Na induced-calciuria has been reported to range from 0.48 to 2.3 mmol in loading studies (26)

and from 1.0 to 3.0mmol in epidemiological surveys (27). Therefore, the calciuric effect of sodium in our study was in the range reported in this field.

Urinary Sodium and Serum PTH, Vitamin D and Phosphorous Excretion

Although our results showed that urinary excretion of phosphorous was significantly higher in participants in the second and third tertile of urinary sodium, the plasma PTH level was not associated with urinary sodium. In line with this study, Natri et al. reported that reducing sodium intake neither caused changes in plasma PTH nor was associated with urinary phosphorous excretion (28). On the contrary, it was found that sodium intake led to significant changes in serum PTH concentration, but no difference was found in urinary phosphorous (21). Ilich and Carbone reported that sodium had no effect on hemostats of PTH (29,30). In support of the findings of previous studies, Nakamura demonstrated that serum PTH was in the normal range in spite of relatively high average of sodium intake (31). He suggested that the adequate vitamin D levels compensated for Na- induced hypercalciuria, so it may not increase the PTH levels (31). In this study, the average level of vitamin D was around 30 ng/ ml, which is in the normal range. In addition, Zemelet al. reported that sodium infusion leads to increased PTH within the first 15 minutes (32). The half-life of intact PTH is 4 minutes (32). Therefore, it seems that measuring PTH in the fasting state was the reason for lack of correlation between sodium and PTH in our study.

Sodium induced acidosis is associated with the weak function of Na Pi2a carrier and leads to a decreased reabsorption of phosphorus, and exacerbates its urinary excretion (33).

In this study, changes in urinary sodium did not relate to vitamin D levels. Breslau demonstrated that in premenopausal women, Na induced hypercalciuria led to an increase in 1, 25-dihydroxy vitamin D. However, in postmenopausal women, no changes were observed in vitamin D in response to high sodium intake (14). Failure to find an association between sodium and vitamin D has also been reported by Massey and Harrington (34,35). As suggested by Breslau, it seems that no change in vitamin D in response to sodium intake is linked to age and estrogen status (14).

Urinary Sodium and Potassium excretion

Our study revealed that excess urinary sodium was associated with increased urinary potassium excretion. This finding is supported by Castenmiller who found that potassium excretion significantly increased in response to high-sodium diet (178 mmol/d) compared to low-sodium diet (22 mmol/d) (36). A similar finding was reported by Harrington who recorded potassium excretion of 70.6 and 66.9 mmol/d in response to two levels of sodium intake of 180 and 65mmol/d, respectively (20). Ginty et al. confirmed a positive association between sodium and potassium excretion (37). The possible link between sodium and potassium excretion can be explained by increased extracellular fluid volume in response to sodium intake (33). An increase in the concentration of extracellular fluid potassium results in potassium secretion in distal tubule and cortical collecting duct in the kidney (33). Therefore, the high sodium intake can induce potassium excretion.

Urinary Sodium and ORAI

ORAI index is not associated with urinary sodium (Table 1). In this study, ORAI index has been used as a tool to assess the status of bone health. There is a great deal of scientific evidence supporting this index in identifying a person with low bone mineral density in high-risk populations including postmenopausal women (38-40, 16). Estrogen and body weight have been introduced as the main reasons for low bone density (15). These factors were used to calculate ORAI, so this index is one of the best pre-screening measures for low

bone density.

To our knowledge, this study was the first document that has independently used ORAI tool to identify low bone density. Hence, no documents have applied this index directly to determine bone health. Therefore, to discuss the relationship between sodium and bone health, we invoked documents in which DXA was regarded as the reference method for bone density. In line with our findings, Dawson et al. reported that bone density would not be affected by sodium in women's 118 mmol/day, and in men's 156mmol/day sodium intake (26). Reid indicated that receiving sodium of about 2430 mg/d for two years did not change bone density in the 122 women participating in his study (41). Carbone et al. also supported these results in a study (24). Devin study, in contrast to the previous report, showed that after adjusting for confounders' variables such as weight, calcium intake and physical activity, a negative correlation was found between increased sodium intake and hip bone density in postmenopausal women (9). Devin suggested that a reduction in urinary sodium from 3,450 mg per day (equivalent to 8/8g salt) to 1,725mg per day (equivalent to 4/4g salt) has a similar effect on bone density to an increase in calcium intake of 891 mg/d(9). However, the results from this study revealed that no change occurred in bone density with sodium intake of less than 92mmol/d (9).

In a two-year study, Bedford and Barr confirmed that sodium intake (estimated based on 24-hour urine samples) was inversely associated with BMD at the total hip in young women who had an average calcium intake of less than 506 mg per 1,000 calories (25). In a three-year prospective study, Ilich noticed that 3,000 mg/d sodium intake could not affect bone density in women with high calcium intake. In the study, forearm and spine BMD increased in 96% of the participants with an increase in sodium intake. He suggested that mild increased levels of PTH in response to Na- induced calciuria led to decreased fecal Ca loss by preserving endogenous Ca and increased renal Ca reabsorption (29). Intermittent administration of PTH stimulates the production of preosteoblasts and maturation of lining osteoblasts (29). Controversy exists among evidences assessing whether high sodium intake exacerbates bone resorption.There are a controversy results in the relationship between sodium and bone mineral density. Some reasons for this include the lack of accurate estimation of sodium intake, supplementation with calcium and vitamin D, and effects of other nutrients on bone health.

This study had some limitations. The cross-sectional nature of this study did not allow us to show the causal relationship between sodium and indicators of bone health. The small sample size did not allow for detecting the weak associations across the variables. Moreover, it seems that using only one random urine sample cannot accurately estimate the day-to-day variation in sodium intake. Because the use of high doses of sodium supplements is not acceptable in ethical considerations, the design of cohort studies for groups at risk for osteoporosis (postmenopausal women), can express the real effect of sodium intake on bone mineral density. The use of spot urine samples can cover day-to-day variation in sodium intake and can be an exact estimation.

Conclusion

Overall, this study reported a direct association between urinary sodium and urinary calcium, potassium and phosphorus. However, no relationship was found between vitamin D, PTH levels in serum and ORAI on the one hand and urinary sodium on the other.

Acknowledgements

This study was supported by a grant from Tehran University of Medical Sciences, Tehran, Iran. We are truly grateful to those who participated in this study.

References

1. Atinmo T , Mirmiran P , Oyewole O E , Belahsen R, Serra-Majem L. Breaking the poverty/malnutrition cycle in Africa and the Middle East. Nutr Rev 2009;67 Suppl 1:40-46.
2. Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK, et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). Br Med J 2007;334:885-888.
3. Xie J, Sasaki S, Joossens J, Kesteloot H. The relationship between urinary cations obtained from the INTERSALT study and cerebrovascular mortality. J Hum Hypertens 1992;6:17-21.
4. Krause MV, Mahan LK, Escott-Stump S, Raymond Janice L. Krause's food & the nutrition care process. 13th ed. Elsevier Health Sciences 2012.
5. Paul E, Ian B. Background document prepared for the Forum and Technical meeting on Reducing Salt Intake in Populations. In sodium intake around the world. Paris 2006 5-7th October.
6. Greeley A. A pinch of controversy shakes up dietary salt. 1997; (http://www.FDA.gov/fdac/features/1997/797_salt.html, ed).
7. WHO study group. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis; WHO, Geneva 1994.
8. Kitchin B, Morgan S. Nutritional considerations in osteoporosis. Curr Opin Rheumatol 2003;15:476-80.
9. Devine A, Criddle R, Dick IM, Prince RL. Alongitudinal study of the effect of sodium and calcium intakes on regional bone density in postmenopausal women. Am J Clin Nutr 1995;62: 740-745.
10. Nordin B, Need A, Morris H, Horowitz M. The nature and significance of the relationship between urinary sodium and urinary calcium in women. J Nutr 1993;123:1615-1622.
11. Nordin BEC, Polley KJ. Metabolic consequences of the menopause: a cross-sectional, longitudinal and intervention study on 557 normal postmenopausal women. Calcif Tissue Int 1987; 41:Sl-S59.
12. Consensus Conference from the national institutes of health. osteoporosis prevention, and therapy. J Am Med Assoc 2001;285:785-95.
13. Breslau NA, McGuire JL, Zerwekh JE, Pak CY. The role of dietary sodium on renal excretion and intestinal absorption of calcium and on vitamin D metabolism. J ClinEndocrinolMetab 1982;55: 369-373.
14. Breslau NA, Sakhaee K, Pak CY. Impaired adaptation to salt-induced urinary calcium losses in postmenopausal osteoporosis. Trans Assoc Am Phys 1985;98:107-115.
15. US. Preventive Services Task Force.Screening for osteoporosis in postmenopausal women recommendations and rationale .Ann Intern Med 2002;137: 526-528.
16. Cadarette S, Jaglal S, Kreiger N, McIsaac W, Darlington G, Tu J. Development and validation of the osteoporosis risk assessment instrument to facilitate selection of women for bone densitometry. Can Med Assoc J 2000;162:1289-1294.
17. Azizi F, Rahmani M, Allahverdian S, Hedayati M. Effects of salted food consumption on urinary iodine and thyroid function tests in two provinces in the Islamic Republic of Iran. EastMedi health journal 2001;7:115-20.
18. Mill JG, da Silva ABT, Baldo MP, Molina MCB, Rodrigues SL. Correlation between sodium and potassium excretion in 24- and 12-h urine samples. Braz J Med Biol Res 2012;45:799-805.
19. Ho S, Chen YM, Woo JL, Leung SS, Lam TH, Janus ED. Sodium is the leading dietary factor associated with urinary calcium excretion in Hong Kong Chinese adults. Osteoporos Int 2001;12: 723–731.
20. Harrington M, Bennett T, Jakobsen J, Ovesen L, Brot Ch, Flynn A, et al. The effect of a high-protein, high-sodium diet on calcium and bone metabolism in postmenopausal women and its interaction with vitamin D receptor genotype. Br J Nutr 2004;91:41-51.
21. Teucher B, Dainty JR, Spinks CA, Majsak-Newman G, Berry DJ, Hoogewerff JA, et al. Sodium and bone health: impact of moderately high and low salt intakes on calcium metabolism in postmenopausal women. J Bone Miner Res : the official journal of the American Society for Bone and Mineral Research 2008;23:1477-1485.
22. Shortt C, Flynn A. Sodium-calcium inter-relationships with specific reference to osteoporosis. Nutr Res Rev 1999;3:101-115.
23. Suki WN. Calcium transport in the nephron. Am J Physiol 1979;273:111-116.
24. Carbone L, Bush AJ, Barrow KD, Kang AH. The relationship of sodium intake to calcium and sodium excretion and bone mineral density of the hip in postmenopausal African-American and Caucasian women. J Bone Miner Metab 2003;21: 415-420.
25. Bedford JL, Barr SI. Higher Urinary Sodium, a Proxy for Intake, Is Associated with Increased Calcium Excretion and Lower Hip Bone Density in Healthy Young Women with Lower Calcium Intakes. Nutrients 2011;3:951-961.
26. Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. Sodium excretion influences calcium homeostasis in elderly men and women. J Nutr 1996;126:107-112.
27. Zarkadas M, Gougeon-Reyburn R, Marliss EB, Block E, Alton-Mackey M. Sodium chloride supplementation and urinary calcium excretion in postmenopausal women. Am J Clin Nutr 1989;50: 1088-1094.

28. Natri AM, Karkkainen M, Ruusunen M, Puolanne E, Lamberg- Allardt C. A 7-week reduction in salt intake does not contribute to markers of bone metabolism in young healthy subjects. Eur J Clin Nutr 2005;59:311-317.

29. Ilich Jasminka Z, Brownbill Rhonda A, Coster Daniel C. Higher habitual sodium intake is not detrimental for bones in older women with adequate calcium intake. Eur J Appl Physiol 2010; 109:745-755.

30. Carbone D, Barrow D, Bush J, Boatright MD, Michelson Jean A, Pitts Kathleen A, et al. Effects of a low sodium diet on bone metabolism. J Bone Miner Metab 2005;23:506-513.

31. Nakamura K, Hori Y, Nashimoto M, Okuda Yoko, Miyazaki H, Kasai Y, et al. Dietary Calcium, Sodium, Phosphorus, and Protein and Bone Metabolism in Elderly Japanese Women: A Pilot Study Using the Duplicate Portion Sampling Method. Nutrition 2004;20:340-345.

32. Zemel MB, Gualdoni SM, Walsh MF, Komanicky P, Standley P, Johnson D, et al. Sodium excretion and plasma renin activity in normotensive black adults as affected by dietary calcium and sodium. J Hypertens 1986;4:366-371.

33. Guyton J, Hall E. Textbook of Medical Physiology: Enhanced E-book. Elsevier Health Sciences 2001

34. Harrington M, Bennett T, Jakobsen j, Ovesen Lars, Brot Ch, Flynn A, et al et al. Effect of a high-protein, high-salt diet on calcium and bone metabolism in postmenopausal women stratified by hormone replacement therapy use. Eu J Clin Nutr 2004;58:1436-1439.

35. Massey LK. Effect of dietary salt intake on circadian calcium metabolism, bone turnover, and calcium oxalate kidney stone risk in postmenopausal women. Nutr Res 2005;25:891-903.

36. Castenmiller JJM, Mensink RP, Van der Heijden L, Kouwenhoven T, Hautvast JGAJ, deLeeuw PW. The effect of dietary sodium on urinary calcium and potassium excretion in normotensive men with different calcium intakes. Am J Clin Nutr 1985;41:52-60.

37. Ginty F, Flynn A, Cashman KD. The effect of dietary sodium intake on biochemical markers of bone metabolism in young women. Br J Nutr 1998;79:343-350.

38. Cadarette S, Jaglal S, Murray T. Evaluation of decision rules for referring women for bone densitometry by dual-energy x-ray absorptiometry. J Am Med Assoc 2001;286:57-63.

39. Alvah R, Cass MD, Angela J, Shepherd MD, Carol A, Carlson, BA. Osteoporosis Risk Assessment and Ethnicity: Validation and Comparison of 2 Clinical Risk Stratification Instruments. J Gen Intrn Med 2006;21:630-635.

40. Cook RB, Collins D, Tucker J, Zioupos P. Comparison of questionnaire and quantitative ultrasound techniques as screening tools for DXA. Osteoporos Int 2005;16:1565-1575.

41. Reid IR, Ames RW, Evans MC, Sharpe SJ, Gamble GD. Determinants of the rate of bone loss in normal postmenopausal women. J Clin Endocrinol Met 1994;79:950-954.