EVALUATION OF RISK FACTORS IN MALE PATIENTS WITH OSTEOPOROTIC HIP FRACTURES

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ABSTRACT

To evaluate the association of risk factors, Homocysteine(HCY) and Bone mineral density(BMD) in male patients with osteoporotic hip fractures. The data regarding the risk factors such as increasing age, history of smoking, alcohol consumption, physical inactivity, excessive consumption of coffee was collected by using a questionnaire. Plasma HCY levels were measured by using a kit from Bayer health care LLC, USA. The assay principle is competitive immunoassay using direct chemiluminiscence technology. BMD was measured by using ultrasound technique in both patients and control groups. A significant increase in HCY levels in association with the risk factors was found in patients with osteoporotic hip fractures when compared to control group. The present investigation also revealed an accelerated bone loss as indicated by the decreased BMD in patient groups as the age advances with other risk factors like smoking, alcoholism, physical inactivity and excessive intake of coffee, when compared to control groups. The present study clearly establishes the effect of increased HCY levels and other risk factors in lowering BMD which results in the incidence of osteoporotic hip fractures.

KEY WORDS: Bone mineral density (BMD), Homocysteine(HCY),

Introduction

Osteoporosis is one of the most common causes of hip fractures in older population, as it results in the decreased bone density, affecting the overall strength of bones[1]. The term hip fracture refers to cervical and intertrochanteric fractures of femur[2]. In common use, it also refers to hip fracture following minor trauma. Fractures of hip are occurring with increasing frequency as the longevity of the population has increased. In fact, hip fractures account for more than 70% of all fracture surgeries in patients above 70 years of age[3]. The

number of hip fractures expected to rise significantly during the next 25 years as a result of increase in the older population especially in Africa, Asia and Latin America[4]. India seems to have the highest prevalence of osteoporosis[5]. Osteoporotic fractures occur more commonly in Indian males than females and usually occur 10-20 years earlier in Indian men and women compared to Caucasians in the west[6]. In order to prevent the incidence of osteoporotic hip fractures, it is necessary to evaluate the role of risk factors like low physical activity, smoking, alcohol consumption and coffee intake which may cause these fractures. According to a study done in Philadelphia USA, previous physical activity was found to be one of the important determinants of risk of hip fracture in men[7]. Similar observation regarding the incidence of hip fracture among men and its inverse association with baseline physical activity was reported in Finland[8]. The involvement of the risk factors has been revealed by a study from Sweden[9]. Apart from these factors, the recent studies have implicated plasma HCY levels as a risk factor for osteoporotic hip fracture[10]. However, the knowledge of these risk factors for hip fracture in Asian population is very much limited.

Estimation of plasma HCY levels, measurement of BMD and evaluation of these risk factors will be of immense use in planning preventive strategies for hip fracture. However not much information is available about them in India. In view of the above and since hip fracture is becoming an important health priority this study has been planned with following objectives.

Objectives

Evaluation of the risk factors such as smoking, alcohol consumption, excessive coffee intake and physical inactivity and their association with homocysteine and BMD in male patients with osteoporotic hip fracture.

Materials and Methods

This study was conducted in the Departments of Biochemistry and Orthopedies, MMC & RI, Mysore. The study was approved by institutional ethical committee and informed consent was taken from patients and controls before the study. A case control study design was used to evaluate the association between the risk factors and osteoporotic hip fracture. Cross sectional observational study was done among the cases to evaluate the association of risk factors with HCY and BMD.

Definition and selection of Cases: Hip fracture sustained after minor trauma confirmed by X-ray hip fracture which includes cervical and intertrochanteric fracture of femur. Male patients in the age group of 50 years and above admitted for hip fracture for the second time, and old cases of hip fractures re-admitted or referred from some other hospital. Control subjects were selected in the age group 50 years and above without hip fracture. Previous history of hip fracture, known cases of diabetic, hypertension, chronic inflammatory diseases and Thyroid diseases constituted the exclusion criteria.

Sample size: Based on the 30% prevalence of low physical activity in the general population and an expected odds ratio of 2, with level of significance at 0.05 and a power of 80% a minimum sample size of 100 was used in each group with a total of 200[11]. Six (6) subjects out of 100 controls were excluded due to non acceptance to give blood samples for analysis. Written consent was obtained from the patients and control subjects. Using the pre tested questionnaire, data was obtained from the patients and control subjects.

Measurement of risk factors

Smoking: Anyone who smokes cigarette, cigar, beedi on a regular basis (daily) was considered as smoker. Smoker was classified as current smokers and past smokers. Information on duration of smoking and the number smoked per day was obtained from the current smoker. Information on duration of smoking and how long since stopped was obtained from past smoker.

Alcohol Use: Anyone who takes alcohol on regular basis was considered as alcohol consumer. Among alcohol consumers, information about number of years of drinking alcohol and average number of drinks in a week was recorded.

Coffee intake: Information was obtained if the patient takes coffee on regular basis and if so, number of cups consumed in a day was recorded.

Physical inactivity: Level of physical activity was assessed by physical activity questionnaire developed a St.John's Medical College Bangalore[12]. It is calculated by 24 hours energy expenditure by BMR[13].

Blood samples were collected from patients and control subjects using EDTA vacutainers and centrifuged. Plasma was separated and frozen immediately at-20 C. The

samples were thawed and the plasma HCY concentration were measured using a kit from Bayer health care, LLC, USA. The assay principle is competitive immunoassay using direct chemiluminiscence technology. The values were expressed in terms of µmol per litre.

BMD was measured using a technique involving ultrasound of the heel bone and results were expressed as T-Score, which is number of standard deviations by which the patient BMD differs from the mean peak BMD for young normal subjects of the same gender.

Statistical Analysis

Data entry was done in Microsoft excel, Statistical analysis was done using SPSS statistical software. Mean and standard deviation were calculated for Age , Homocysteine and BMD.Odds Ratios were calculated for each risk factor by Univariate analysis and 95%CI and p value was found. Student t test was used to find out association of Homocysteine and BMD values with risk factors, correlation between HCY and BMD was done by regression analysis.

	Cases(100)		**Controls(94)**	
Mean Age +SD (yrs)	66.86±5.6		64.36±10.42	
	Number	Percentage	Number	Percentage

Results

Table -1 shows Mean age, Homocysteine levels and BMD values among patients of osteoporotic hip fractures and controls. The mean age of the cases was 66.86+/- 5.6 years. Further these Patients recorded significant increase in HCY levels along with decreased BMD when compare to control subjects.

Table-1.Mean age and Risk factors of Osteoporotic Hip fractures in cases and controls.

Smokers	28	28%	8	8.5%
Alcoholics	28	28%	10	10%
Coffee consumers	88	88%	80	85%
Physical Inactivity	52	52%	44	46.8%

Table- 2 reveals the risk factors studied in patients. Out of all the risk factors studied (smoking, alcohol consumption , excessive coffee intake , and physical inactivity) The percentage of coffee consumers was highest constituting about 88% followed by physical inactivity. Table-3 demonstrates the odds ratio calculated for each risk factors by univariate analysis. Which credits the number of times these patients are susceptible for hip fracture with respect to each risk factors. Smokers showed highest odds ratio of 4.18 followed by alcohol consumers which was 3.26.

Table-2 .Odd's ratio calculated for each Risk Factors by Univariate Analysis

Risk factors	Odd's Ratio
Smokers	4.18
Alcoholics	3.26
Coffee consumers	1.28
Physical Inactivity	1.23

Table-3. Association of Homocysteine values with risk factors.

Risk Factors	Homocysteine(Mean+SD)	t-Value	p-Value
Smokers Non –Smokers	29.50 +8.14 24.12+6.3	2.332	0.0245*
Alcoholics Non-Alcoholics	27.6+6.2 23.3+5.25	2.472	0.0170*
Coffee consumers No Coffee Consumption	26.59+7.13 18.83+2.36	2.617	0.0122*
Physical Inactivity Physically active	26.33+8.24 24.87+6.23	0.675	0.5031

*Significant $p<0.05$

According to table-4 significant association of HCY values are seen with smokers alcoholic and coffee consumers among cases, which showed statistically significant increase

Risk Factors	BMD(Mean+SD)	p-value
Smokers	-4.169 +1.339	0.067
Non –Smokers	-3.375+0.55	
Alcoholics	-4.008+1.261	0.0734
Non-Alcoholics	-3.45+0.72	
Coffee consumers	-3.69+0.94	0.0165*
No Coffee Consumption	-3.016+0.29	
Physical Inactivity	-3.61+0.94	0.9249
Physically active	-3.59+0.90	

in HCY values compared to non smokers, non alcohol and coffee consumers among the cases respective. Where as increase in HCY values was not statistically significant in cases with physical inactivity. Table-5 shows association bone mineral density (BMD) values with risk factors. Statistically significant reduction in BMD was observed in cases who were coffee consumers. All though reduced BMD values were also observed in smokers alcohol consumers and physical inactivity , the values were not statistically significant. Table-6 shows significant negative correlation between HCY and BMD values($p<0.0001$) Which is also depicted in Figure -1.

Table-4.Association of BMD(Bone Mineral Density)values with Risk factors

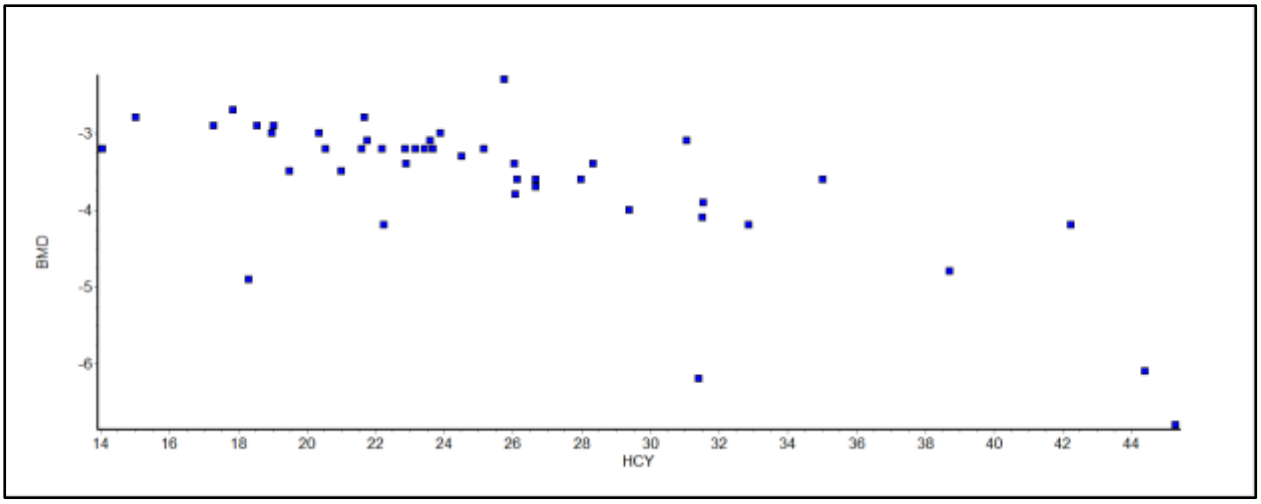
*Significant $p<0.05$

Table-5.Correlation between Homocysteine and BMD(Bone Mineral Density)values

Homocysteine	BMD	r-value	p-value
		-0.7155	<0.0001*

*Significant

Figure-1.Showing the significant Correlation between Homocysteine and BMD(Bone Mineral Density)values.



Discussion

The incidence of osteoporotic hip fractures increases with the advancing age, due to decrease in BMD, the causes for the same are not completely elucidated .Inadequate nutrition in aged individuals will result in under nourishment, especially with regards to vitamins and minerals. The deficiency of these accessory food factors will lead to decrease in bone strength or BMD as revealed in the present study. This effect of age in lowering the BMD or increasing the osteoporosis is compounded by the risk factors like smoking, alcohol, excessive coffee consumption and physical inactivity. In the present study, a highly significant increase in plasma HCY levels was seen in patients with osteoporotic hip fractures when compared to control group. Increased HCY levels stimulate osteoclast activity, suggesting a mechanistic role of HCY on bone resorption leading to increased collagen breakdown and interferes with collagen cross linking ,thus impairing the bone strength, which leads to decrease in the density of bone[14]. The increased HCY levels found in patients indulging in smoking may be due to high nicotine levels which influence the methylation reactions[15].

Odds Ratio as shown in table -3 indicates that smokers and Alcohol consumers are more susceptible for osteoporotic hip fractures when compared with other risk factors.

Smoking and coffee are known to decrease BMD and increase the incidence of osteoporotic hip fractures because of their effect on calcium metabolism. Further these two risk factors will increase the production of free radicals which ensues in bone resorption. The pharmacologically active compound nicotine, present in tobacco, also decreases the osteoblastic activity[16].

The present study has shown significantly increased levels of homocysteine in smokers, alcohol and increased coffee consumers among cases .Increased levels of Homocysteine causes an acute phase induction of Pyridoxal Phosphatase activity associated with increased production of IL-6.This would result in stimulation of the activity of Vitamin B6 levels and reducing cystathionine beta synthase activity [14,17]. Increased HCY levels in patients consuming alcohol may be due to vitamin depletion. This increased HCY levels stimulate osteoclastic activity thus impairing the bone strength leading to decreased BMD and consequent osteoporotic hip fractures. Further Alcohol is also shown to increase the parathormone (PTH) and reduce the concentration of Vitamin D metabolites required for efficient Calcium absorption. This results in suppression of bone mineralization by osteoblasts[18].

The high HCY levels found in patients with physical inactivity or sedentary lifestyle may be due to lack of exercise .These patients also recorded significant decrease in BMD .Exercise is known to increase muscle strength and Bone Density. Since the patients with physical inactivity are devoid of exercise they are more prone to hip fractures as indicated by high HCY levels and decreased BMD[19].

Conclusions

To prevent the incidence of hip fractures in aged individuals proper protective measures for these risk factors are essential. Further research work involving other biochemical bone markers and genetic markers are needed to fully understand the biochemical and pathophysiologic mechanisms that result in greater bone loss.

References

1. Cooper C, Campion G,Melton 3rd LJ.1992 Hip fractures in the elderly:a world wide projection. *Osteoporos int 2:285-289*

2. Craig S.Bartlett III, Robert L Buly and David L Helfet. Intertrochanteric and subtrochanteric fractures of the proximal femur In clinical Orthopedics edited by *Edward V Craig. I edition 1999*

3. Penning D. Principles of fracture management in elderly patients in:Newman Rj.Ed.Orthogeriatrics: Comprehensive orthopaedic care for the elderly patient. *Oxford: Butterworth-Heinemann.1992:420-435.*

4. WHO.Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. *WHO Tech Rep Ser 1998-843.*

5. Gupta A.Osteoporosis in India-Nutritional hypothesis *Natl Med J India. 1996:9:268-74.*

6. Deepika R Sharma, Shalini Rao. Osteoporosis Epidemiology review and panacea osteoporosis evaluation sudy. *J Indian Med Assoc Vol 98 No 10.Oct 2000.658*

7. Grisso JA, Kelsey O'Brien LA, Miles CG, Sidney S,Masilin G,La Pann K, Moritz D, Peters B. Risk factors for hip fracture in men. Hip fracture study group.*Am J Epidemiol.1997 May 1;145(9):786-93*

8.Kujala UM, Kapiro J, Kannus P, Sarnas, Koskenvuo M.Physical activity and Osteoporotic hip fracture in Men.*Arch Intern Med 2000 Mar 13;160(5):705-708*

9. Baron JA, Farahmand BY, Weiderpass E, Michaëlsson K, Alberts A, Persson I, Ljunghall *S.Arch Intern Med. 2001 Apr 9*;161(7):983-8.

10. Robert R, McLean, Paul F Jacques, Jacob Selhub, Katherine L Tucker, Elizabeth J.Samelson et al.Homocysteine as a predicition factor for hip fracture in older persons. *N Engl J Med 2004;351-1027-1030.*

11. SK.Lwanga and S.Lemeshow. Sample size determination in health studies. *A practical Mannual WHO 1991.p51.*

12. Bharathi AV, Sandhya N, Vaz M.The development and characteristics of a physical activity questionnaire for epidemiological studies in urban middle class Indians. *Indian J Med.Res 2000 March; 111:95-102*

13. Ainsworth BE.Compendium of physical activities: Classification of energy costs of human physical activities. *Med.Sci Sports Exers 1993:25.71-82*

14. Meera S, M.Sukharaja, B.G.Sagar, N.Kantharaj Homocysteine and its association with osteoporotic hip fractures. *J Biomedicine, Volume 30 No 3-2010*

15. Godin C and Crooks P.In vivo depletion of S-adenosyl-L-homocysteine and S-adenosy1-L methionine in guinea-pig lung after chronic S(-)nicotine administration. *Toxicology Letters, 1986;31:23-29.*

16. Walker LM, Preston MR, Magnay JL, Thomas PB, El Haj AJ 2001 Nicotinic regulation of c-fos and osteopontin expression in human derived osteoblast cells and human trabecular bone organ culture. *Bone 28:603-608*

17. McCarty MF, Increased homocysteine associated with smoking, chronic inflammation and aging may reflect acute phase induction of phosphatase activity. *Medical Hypothesis, 2000;55:289-93.*

18. Laitinen K, Valimaki M.Alcohol and Bone Calcif Tissue *Int 1991;49:S70-S73.*

19. Gregg EW, Pereira MA, Caspersen CJ(2000)Physical activity, falls and fractures among older adults: A review of epidemiological evidence. *J Am Geriatr Soc 48:883*.