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Osteoporosis in males and its association with tobacco; smokers and chewers

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Abstract
Background: In men, osteoporosis is not a disease of over 50 anymore. Younger men are now being reported with bone injuries, illnesses and perioperative complications including delayed fracture-healing. Tobacco use has been found to have negative effects on the musculoskeletal system leading to decrease in bone mineral density. This study was aimed to determine the effects of tobacco, cigarette and chewable on bone mineral density.
Methods: Free orthopedic camps in different towns of Karachi during 2014 were set up where married males gathered to participate in this cross-sectional study. A total of 987 males, ±45 years old, tobacco users (smokers or chewable, since±15 years), were recruited, after an informed signed consent. Bone mineral density, using random sampling technique by heel scan device was checked and subjects' information regarding diets, habits, medical & surgical history was obtained through interviewer-administered questionnaire.
Results: The 668 subjects (mean age 44.4±9.8 years), habitual chewable tobacco users had mean bone mineral density (0.31±0.04) significantly (3.66 times) lower (p=0.004) compared to smokers (0.33±0.03g/cm2) and non tobacco users (CI-1.754, 8.437). Osteoporosis was detected in 20% of chewable tobacco users compared to 12% in smokers and 3.8% in non tobacco users. Highest frequency of osteoporosis was displayed by chewers of betel quid (18%) and gutka (17%) compared to Naswar (14%), areca nut(12%) and smokers(12.3%).
Conclusion: Chewable tobacco is a very strong risk (OR 3.66 times) factor for lowering bone mineral density, which leads subsequently to osteoporosis in men compared to non tobacco users.

Keywords: Male osteoporosis, Hip Fractures, smokeless tobacco, BMD

1. Introduction
Osteoporosis, defined as an asymptomatic systemic bone disease is characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture [(1)]. In men, osteoporosis is a significantly increasingly health problem just as it is for women. In 2002, men with osteoporosis and low total bone mass were more than 14 million. This figure, according to National Osteoporosis Foundation's Report published in 2002, is expected to increase to more than 17 million in 2010 and possibly more than 20 million in 2020[(2)]. Men are estimated to lose bone mineral density (BMD) at a rate of up to 1% per year with advancing age [(3,4,5)]. In the absence of an identifiable etiology, male osteoporosis is referred to as 'idiopathic osteoporosis' in men aged 30-70 years and as 'age-related osteoporosis' in older men[(6)]. Among the toxic substances involved in the etiology of osteoporosis, tobacco plays a major role[(7)] and it is considered as potentially modifiable risk factor. Experiments on rats show that smoke exposure whether it is direct or passive is associated with increased bone turnover and inhibit bone formation and increase bone resorption.[(8)] Of all osteoporotic fractures, hip fractures contribute to the greatest morbidity and mortality, and constitutes almost 30% of all hip fractures that occur in men[(9)]. In 50% of osteoporotic men, an underlying cause can be identified secondary to osteoporosis. The popularity of chewable tobacco in Pakistan with the strong inclination of children toward it warrants urgent action. These products are used under the misconception that nicotine in this form is harmless, whereas, absorption through oral mucosa is faster and more nicotine in lesser time is dumped into bloodstream compared to cigarettes leading to faster addictive inclination [(10)]. The objective of this study was to find out the effects of chewable tobacco on bone mineral density and osteoporosis comparing it with cigarette smokers and non tobacco users.

Materials and Methods

This cross -sectional study was conducted in Ziauddin University Karachi from February to November 2014 with prior approval from Ziauddin University ethics review committee. A total of 987 males, ±45 years old, cigarette smoker or chewable tobacco users since ±15 years, who agreed to participate were recruited in the study after an informed signed consent. Information on demographics, educational status, occupation, lifestyle, dietary and chewable habits, surgical and medical history was obtained by an interviewer-administered questionnaire. Excluded were those men who had chronic disease (asthma or diabetes etc.) or were on drugs altering the equilibrium of bone such as calcium plus vitamin supplements.

The bone mineral density through Single x-ray absorptiometry (SXA), being inexpensive and an effective way of establishing the risk of fracture in future, was done on right foot heel of all 987 subjects. For maximum exposure, the patient placed his right foot on the moulded support plate. The BMD was recorded and expressed in grams per square centimeter (g/cm2).

Statistical Analyses was done by entering the data on SPSS ver: 20. All qualitative variables are presented as percentages and frequencies. All quantitative variables are presented as mean and standard deviation. A P-value less than 0.05 were considered significant.

Results

A total of 987 subjects which included 668 subjects with tobacco exposure (211 cigarette smokers and 457 chewable users) and 319 without tobacco exposure were finalized. Participant characteristics of the subjects are shown in Table 1.

Among the 211 cigarette smokers majority were smoking since last ±15 years and were consuming more than ±1 packet per day and 457 chewable tobacco users majority were consuming it since ±10 years.

When education was seen with the frequency of osteoporosis it observed that the prevalence was seen higher in those who had attained matric or intermediate graduation (p-value 0.01). (Table1). When prevalence of osteoporosis was stratified by the type of chewable tobacco it was seen that while only 14% of participants consumed gutka. 17% of its consumers displayed osteoporosis. (Table 2).

Table 1: relationship of education, health status and habit with osteoporosis.

Prevalence of Osteoporosis with tobacco use, education and health status			
	N=987	**Osteoporosis**	**p-value**
Education			
Matriculation	587	49	0.001
Intermediate	267	43	
Higher	133	21	
Health			
Not good	442	84	0.0001
Good	382	26	
Excellent	163	3	
Habit			
Smoker	211	26	0.0001
Smokless tobacco	457	75	
No habit	319	12	

Table 2: BMD and Osteoporosis in subjects with different habits (chewable tobacco and smoking) comparing it with controls.

Subjects n= 987	**Chewable tobacco users [(n= 668 (67.7%)]**				**Smokers**	**Non tobacco users**
	Gutka	**Naswar**	**Areca nut**	**Paan**		
	138 (14%)	199 (30%)	50 (7.5%)	281 (42%)	211(11.3%)	319 (32%)
BMD	±2.0	±2.0	±1.5	±1.5	± 2.0	±1.3
Osteoporosis(134)	23 (17%)	28 (14%)	6 (12%)	51 (18%)	26(12.3%)	12(3.8%)

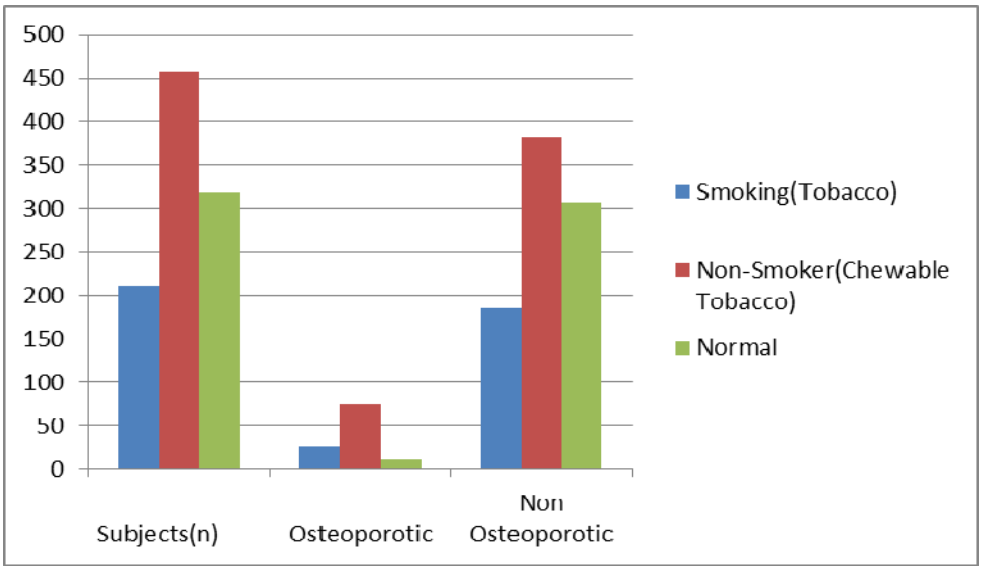

Fig 1: Comparison of osteoporosis between smokers, chewable tobacco users and controls

Figure one shows high frequency of osteoporosis among chewable tobacco users compared to non users or smokers. Smokers were found to be 3.45 (CI-1.493-8.695) times more prone to osteoporosis compared to controls.

Discussion

This study demonstrates a strong association of tobacco, chewed or smoked with osteoporosis. Smokers were found to be 3.45 (CI-1.493-8.695) times more prone to develop osteoporosis at an early age compared to controls. It has been have found that BMD is decreased in smokers as from our data out of total number n=211 of cigarette smokers, n=26 (12%) were osteoporotic. Majority of them were smoking since last ±5 years and were consuming more than ±10 cigarettes per day. Many studies have provided evidence that smoking affects the balance of the naturally occurring processes of bone resorption and bone formation, resulting in low BMD.[11][12] Exposure to smokeless tobacco extracts reportedly inhibits osteoblast metabolism. [13]

Smokers are weak, have poorer balance and impaired neuromuscular performance, which results in increased risk of falls[14]. This is most likely due to its potential impact on cellular differentiation and compromised microcirculation both required for fracture repair, subsequently bone healing is decreased[15,16]. Smoking also decreases the secretion of parathyroid hormone which leads to reduction in calcium absorption hence increasing the risk of osteoporosis[17] Smoking reduces the level of Vitamin D[18], increases free radicals and oxidative stress which affects bone resorption[19].

Compared to smokers, chewable tobacco users were found to be at higher risk (3.66 times) of osteoporosis. This study highlights for the first time the difference in incidence of osteoporosis between smokers and chewable tobacco users in Pakistan. Out of 987 subjects , 457 were addicted to chewable tobacco [Gutka, Niswar, Paan (Betel Quid) and Areca Nut (chalia)].The odds ratio calculated between chewable tobacco users and controls for osteoporosis was found out to be 3.66 (CI-1.754, 8.437) compared to 3.45 (CI-1.493-8.695) in smokers. Several epidemiological studies have established a link between chewable tobacco use and tobacco smoke but none of them recognized any association of these with Osteoporosis in males [20]. In this study osteoporosis was detected in 75(16%) among these chewers compared to 26(12%) in non tobacco users. A study conducted in Maras City, Turkey on 120 male subjects (60 smokeless powder users, 60 smokers) found that smokeless powder users had lower BMD compared to smoker males.[21] Another study in the US demonstrated smokeless tobacco or snuff use as a risk for osteoporosis.[22] Other studies have also established that tobacco & smokeless tobacco is the cause of low bone mineral density and thus may increase the risk for osteoporosis[23].

Osteoblast viability affected in paan chewers

Although betel quid is considered as the fourth most psychoactive substance worldwide [24] in this study it was found the most popular amongst the study population and the highest cause of osteoporosis. According to our data 281(29%) were in the habit of paan/betel quid chewing, out of which 51 (18%) were found osteoporotic. Majority of them were eating paan/betel quid since last ±7 years and were consuming more than ±4 packets per day. Betel quid is mostly sold by venders and the ingredients and chemical composition of all varies accordingly. The effect of factors related to betel quid chewing are complex. Several *in vitro* studies have suggested that areca nut extracts inhibit immune reactions [25], affect osteoblast viability. Possible effects of ripe areca nut extracts is on viability and gene expression of alkaline phosphatase (ALP), receptor activator of nuclear factor-kappaB ligand (RANKL) and osteoprotegerin (OPG) in human osteoblasts[26].

Naswar dipping and decreased bone mineralization

Naswar dipping was the second [154 (24.4%)] most common form of smokeless tobacco addiction among low socioeconomic areas of Karachi as a single form of chewable tobacco[27]. According to report published in 2006 tobacco is grown in KPK approximately on 30800 hectares. There is demand for two types of tobacco varieties flue-cured Virginia (FCV) tobacco and White Patta (WP) tobacco. According to local dealers WP, contains more nicotine and used 80 percent in Naswar manufacture as compare FCV. According to our data 199(20%) were in the habit of Naswar dipping. Out of total number 28(14%) were found osteoporotic. Majority of them were with naswar habit since last ±10 years and were consuming more than ±1 packet per day. Naswar contains various types of substances, among which nicotine is addictive[28]. Exposure to nicotine has been associated with low bone mineral content[29] It induces oxidative stress that leads to bone loss [30,31]. As a sign of oxidative stress, organs or tissues produce and overexpress inflammatory mediators such as IL-1 and IL-6 etc. Since IL-1 is one of the bone-resorbing cytokines.

Circulating testosterone levels are deceased by Gutka

In this study gutka was third highest addiction (40.3%) compared to other tobacco formulation. A total of 138(14%) subjects were found in the habit of gutka chewing. Out of them 23(17%) were found osteoporotic. Majority of them were eating gutka since last ±5 years and were consuming more than ±1 packet per day. Since its formulation in 1975, gutka has been the most popular among masses, mostly due to its frequent availability and a very low-price. Gutka, contains a mixture of tobacco, areca nut, slaked lime and a number of spices . It produces a variety of adverse morphological and metabolic changes including reduced body weight gain, and decrease in circulating testosterone levels[32]. Testosterone has a direct effect on osteoblast function. Dihydrotestosterone (DHT) increases the proliferation of osteoblast, and induces osteoblast differentiation. Testosterone also increases the lifespan of both osteoblasts and osteoclasts by affecting apoptosis [33].

Areca nut alters gene expression

Areca nut mixed with aniseed formulations were marketed earlier as mouth fresheners. Now areca nut packets also contain a pinch of tobacco and unfortunately is one of the major addictive products among masses especially children of lower socioeconomic group. Areca nut ranked forth 50 (7.5%) in popularity among the chewable tobacco preparations [21] in our study group and also showed the lowest 6 (12%) incidence of osteoporosis. May be this was because of low quantity of tobacco in it. Majority of subjects were eating areca nut since last ±10 years and were consuming more than ±3packets/day. Usually habit of chewing areca nut starts early in their younger age due to peer pressure.[34] The possible effects of ripe areca nut extracts (rANE) is on viability and gene expression of alkaline phosphatase (ALP), receptor activator of nuclear factor-kappaB ligand (RANKL) and osteoprotegerin (OPG) in human osteoblasts[26].

Conclusion

Chewable tobacco is a very strong risk factor for lowering bone mineral density which subsequently leads to osteoporosis. Lowering an individual's risk for osteoporosis and fracture must focus not only on treatment but also on

modification of risk factors.

References

1. Khosla S, Amin S, Orwoll E. Osteoporosis in men. Endocr Rev 2008;29:441-64
2. Khosla S. Update in male osteoporosis. J Clin Endocrinol Metab 2010;95:3-10
3. Hannan MT, Felson DT, Dawson-Hughes B, Tucker KL, Cupples LA, Wilson PWF, Kiel DP2000 Risk factors for longitudinal bone loss in elderly men and women: the Framingham osteoporosis study. J Bone Miner Res 15:710–20 [PubMed]
4. Jones G, Nguyen T, Sambrook P, Kelly PJ, Eisman JA 1994 Progressive loss of bone in the femoral neck in elderly people: longitudinal findings from the Dubbo osteoporosis epidemiology study. BMJ 309:691–95 [PMC free article] [PubMed].
5. National Osteoporosis Foundation. *Clinician's Guide to Prevention and Treatment of Osteoporosis.* Washington, DC: National Osteoporosis Foundation; 2002.
6. Gielen E, Vanderschueren D, Callewaert F, Boonen S. Osteoporosis in men. *Best Pract Res Clin Endocrinol Metab. 2011 Apr; 25(2):321-35.*
7. Moinuddin MM, Jameson KA, Syddall HE, Sayer AA, Martin HJ, Robinson S, Cooper C, Dennison EM. Cigarette Smoking, Birthweight and Osteoporosis in Adulthood: Results from the Hertfordshire Cohort Study. Open Rheumatol J 2008; 2: 33-37.
8. Shu-guang Gao,[#1] Kang-hua Li,[#1,3] Mai Xu,[1] Wei Jiang,[1] Hong Shen,[2] Wei Luo,[1] Wen-shuo Xu,[1] Jian Tian,[1] andGuang-hua Lei[1,3] Bone turnover in passive smoking female rat: relationships to change in bone mineral density BMC Musculoskelet Disord. 2011; 12: 131. Published online 2011 Jun 11. doi: 10.1186/1471-2474-12-131
9. Johnell O, Kanis JA 2006 An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int 17:1726–33 [PubMed]
10. Baig S, Zil-a-Rubab. Trends Leading to Oral Cancer. Pak J of Med Dent 2013, Vol. 2 (01): 46-49
11. Szulc P, Garnero P, Claustrat B, Marchand F, Duboeuf F, Delmas PD. Increased bone resorption in moderate smokers with low body weight: the Minos study. J Clin Endocrinol Metab 2002; 87(2):666–74.
12. Vogel JM, Davis JW, Nomura A, Wasnich RD, Ross PD. The effects of smoking on bone mass and the rates of bone loss among elderly Japanese-American men. J Bone Miner Res 1997; 12(9):1495 –01.
13. J.S. Henderson,R.B. Johnson Department of Periodontics, University of Mississippi Medical Center, Jackson, MS 39216-4505, U.S.A The effects of smokeless tobacco extract on bone nodule formation and mineralization by chick osteoblasts in vitro. Arch Oral Biol 1995; 40 : 615-21 [PubMed]
14. Nelson HD, Nevitt MC, Scott JC, Stone KL, Cummings SR. Smoking, alcohol, and neuromuscular and physical function of older women.
15. Vestergaard P, Mosekilde L. Fracture risk associated with smoking: a meta-analysis. J Intern Med 2003; 254(6):572–83.
16. Haverstock BD, Mandracchia VJ. Cigarette smoking and bone healing: implications in foot and ankle surgery.J Foot Ankle Surg 1998; 37(1):69 –74.
17. Kapoor D, Jones TH. Smoking and hormones in health and endocrine disorders. Eur J Endocrinol 2005; 152(4):491– 99
18. Brot C, Jorgensen NR, Sorensen OH. The influence of smoking on vitamin D status and calcium metabolism.Eur J Clin Nutr 1999; 53(12):920–26.
19. Duthie GG, Arthur JR, James WP. Effects of smoking and vitamin E on blood antioxidant status. Am J Clin Nutr 1991; 53(4 Suppl):1061S–1063S.
20. Ayo-Yusuf OA, Olutola BG. Epidemiological association between osteoporosis and combined smoking and use of snuff among South African women Nigerian Journal of Clinical Practice • Mar-Apr 2014 Vol 17 Issue.
21. Bakan B, Sucaklı MH, Özkan F, Bilal O, Sütçü IA. İmam University Faculty Comparison of Bone Mineral Density Levels in Maraş Powder (Smokeless Tobacco) Users and Smokers in Healthy Men DO I: 10.4274/tod.32032 Türk Osteoporoz Dergisi 2013;19: 12-6.
22. Quandt SA, Spangler JG, Case LD, Bell RA, Belflower AE. Smokeless tobacco use accelerates age-related loss of bone mineral density among older women in a multi-ethnic rural community. J Cross Cult Gerontol 2005;20:109-25.
23. Benson BW, Shulman JD. Inclusion of tobacco exposure as a predictive factor for decreased bone mineral content. Nicotine Tob Res 2005;7:719-24.
24. Gupta PC, Ray CS: Epidemiology of betel quid usage. Ann Acad Med Singapore 2004, 33(4 Suppl):31-36.
25. Hung SL, Lee YY, Liu TY, Peng JL, Cheng YY, Chen YT: Modulation of phagocytosis, chemotaxis, and adhesion of neutrophils by areca nut extracts. *J Periodontol* 2006, 77(4):579-585.
26. Ling LJ, Ho FC, Chen YT, Holborow DW, Liu TY, Hung SL: Areca nut extracts modulated expression of alkaline phosphatase and receptor activator of nuclear factor kappaB ligand in osteoblasts. *J Clin Periodontol* 2005, 32(4):353-359.
27. Editorial, Taxing Tobacco, *Published in Dawn, June 2nd, 2014.* 29.Tomar SL. Is use of smokeless tobacco a risk factor for cigarette smoking? The U.S experience. Nicotine Tob Res 2003;5:545e53.
28. Benson BW, Shulman JD. Inclusion of tobacco exposure as a predictive factor for decreased bone mineral content.Nicotine Tob Res 2005; 7: 719-24.
29. Banfi G, Iorio EL, Corsi MM. Oxidative stress, free radicals and bone remodeling. Clin Chem Lab Med 2008; 46: 1550-5.
30. Swami S, Suryakar AN, Katkam RV, Kumbar KM.Absorption of nicotine induces oxidative stress among bidi workers. Indian J Public Health 2006; 50: 231-5.
31. Daniel N. Willis,[1] Mary A. Popovech,[1] Francesca Gany,[2] Carol Hoffman,[1] Jason L. Blum,[1] and Judith T. Zelikoff[1,*] Toxicity of Gutkha, a Smokeless Tobacco Product Gone Global: Is There More to the Toxicity than Nicotine Int J Environ Res Public Health. 2014 Jan; 11(1): 919–33.
32. Annie W.C. Kung Androgen and bone mass in men Asian J Androl 2003 Jun; 5: 148-54
33. Qureshi A, Dawani N and Shaikh AK. Areca nut consumption patterns among primary school children of Karachi Journal of the Dow University of Health Sciences Karachi 2013, Vol. 7 (1): 25-9