Vit D Status and Osteoporosis in Tobacco Consuming Men in Rural Region Surrounding Wardha City, Maharashtra, Central Part of India

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Abstract

Background: Awareness towards tobacco consumption has increased and it is well accepted too but will it help to cease the consumption. With widespread menace of tobacco consumption in developing country like India, not much data of study is available currently about tobacco consumption and osteoporosis around the rural region of Wardha a central part of India.

Aim: Vit D status and osteoporosis in tobacco consumers and non consumers.

Objective: To asses influence of tobacco consumption on Sr. Vit D, Sr. ionized Ca, Sr. Phosphate, Sr. parathyroid hormones the biochemical markers of bone turnover and Bone mineral density in a cohort of 214 healthy men in rural area surrounding Wardha region of Maharashtra.

Design: A cross sectional study

Subjects: 214 healthy men aged around 30-50 years with no disease history were included in the study.

Results: Tobacco consumers had significantly reduced levels of Sr 25 OH Vit D (P<0.02), PTH (P<0.001). There was no significant difference in Sr ionized Calcium between tobacco consumers and Non tobacco consumers. We got negative effect of tobacco consumption on Sr Osteocalcin (P<0.01).

Conclusion: Calcium and Vit D metabolism is significantly deranged by habit of tobacco consumption and cannot be explained by life style factors. Vitamin D- PTH system depression among tobacco consumers represent a other mechanism for the deleterious effects of tobacco consumption on the bones and contribute to reported risk of osteoporosis among tobacco consumers.

Sponsorship: Intra mural Grant from DMIMS(DU)

Keywords: Tobacco consumers, 25- Hydroxy Vitamin D, Parathyroid Hormone, Osteocalcin, Bone Mineral Density.

Introduction

Tobacco chewing, smoking and other means of consuming tobacco are rampant in rural parts throughout India. Two third of worlds smokers live in only ten countries. 40% live in India and China alone. India counts for 10% of total tobacco consumers¹,²,³.
Vit D is an essential molecule for the development of bone and growth. Tobacco smoking is in most studies found to be associated with a low bone mass and an increased risk of osteoporotic fracture\(^3\). An increased bone loss has been registered in smokers\(^4\). The lifestyle habits are more causative factors among smokers compared to non-smokers poor nutrition, less physical activity and more intoxication all of which play a role. Smoking tobacco also has direct toxic effect on bone cells is also a possibility\(^5\). Hormonal metabolism of pituitary, thyroid and glucocorticoids may also be affected by smoking\(^6\).\(^8\). Metabolites of Vit D and Parathyroid hormone are important in bone and calcium metabolism. Few studies have done investigation on effect of smoking on 25OH Vit D and PTH.\(^9\).\(^15\).

This cross sectional study was undertaken to investigate the impact of tobacco smoking and chewing on bone metabolism and compare the circulating levels of Serum calcium and Serum Vit D metabolism of healthy 214 rural men who are in the age group of 30 to 50 years.

Aim: Vit D status and osteoporosis in tobacco consumers.

Objectives:
1. To measure the serum levels of ionic calcium, Phosphate and alkaline phosphatase for screening.
2. To measure the height, weight and BMI
3. To measure the Serum level of total Vit D
4. To measure the Serum level of Para Thyroid Hormone
5. To measure the Serum level of Osteocalcin
6. To measure the Bone mineral Density

Materials and Method

Study Design: A cross sectional study

Study Setting: Department of Biochemistry, JNMC Wardha, under DMIMS DU

Duration of study: 1 Year

Subjects: On the basis of previous pilot study on prevalence of tobacco consumption in rural area around Wardha city 214 subjects were selected by 19 cluster sampling method total 15 different villages around Wardha city.

Materials and Method

Inclusion Criteria: Men in the age group of only 30-50 years were selected. Healthy men who do not having any disease or disorder or on any treatment specially hormones were included in study. Only men around the Wardha from rural area were only included in the study. Females were not included in the study because we wanted to exclude the study of menopause and disorders related to menopause like hormonal and osteoporotic effects.

Exclusion Criteria: Men with no age match are excluded. Men with any disease or disorder excluded.

Biochemical screening was done before inclusion that ensured that all subjects had Sr levels of Ca, PO4 and alkaline phosphatase within normal range.

Sample Size: 214

Sampling Method: By cluster sampling method. It was a cross sectional study, results on pilot study of prevalence of tobacco use in rural region of Wardha was taken into consideration for sample size calculation. 214 men were selected by 10 cluster sampling method from 9 different villages around the Wardha city. The study was carried out during January 2019 to December 2019,

Observation and Results

Of the total tobacco consumers 47 were found to be bidi smokers. They were smoking more than 10 bidis per day, 41 were consuming raw tobacco with calcium carbonate more than 7 times per day, 13 were consuming Gutka/khainy more than 7 occasions per day, none was found using snuff. The age span of the study was kept between 30-50 years and age factor was not counted for any observations. All tobacco consumers those were selected, they have a habit of consuming tobacco at least continuous for 3 years in past. Non tobacco consumers who have left the habit of smoking at least for the past 3 years were also included.

The baseline parameters for inclusion in the study and differences between tobacco consumers and non tobacco consumers are depicted in Table No. 1.
<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Parameters</th>
<th>Non tobacco consumers (n=112) Mean ± SD</th>
<th>Tobacco consumers (n=101) Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age (Yeats)</td>
<td>44±2.9</td>
<td>43±2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>BMI (Kg/m²)</td>
<td>26.63± 4.12</td>
<td>26.76 ±5.72</td>
<td>NS</td>
</tr>
<tr>
<td>3</td>
<td>Ionic Calcium (mmol/l)</td>
<td>1.16 ±0.10</td>
<td>1.14± 0.09</td>
<td>NS</td>
</tr>
<tr>
<td>4</td>
<td>Sr. Phosphate (mg/dl)</td>
<td>3.54 ± 0.60</td>
<td>3.76 ± 0.61</td>
<td>NS</td>
</tr>
<tr>
<td>5</td>
<td>Sr. Alkaline Phosphatase (IU/L)</td>
<td>341.48 ± 106.29</td>
<td>387.26 ± 125.84</td>
<td>&lt;0.006</td>
</tr>
</tbody>
</table>

BMI was just similar for the two groups. No significant difference was observed. No significant differences were found in Sr ionized calcium amongst two groups. Increased Sr phosphate level amongst tobacco consumers was noted. There was significant difference observed between levels of Alkaline phosphatase amongst two groups.

<table>
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<tr>
<th>Sr.No</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vit D (ng/ml)</td>
<td>19.51 ± 8.58</td>
<td>16.22 ± 6.23</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2</td>
<td>PTH (pmol/l)</td>
<td>1.73 ± 1.96</td>
<td>1.281 ± 2.72</td>
<td>&lt;0.039</td>
</tr>
<tr>
<td>3</td>
<td>Osteocalcin (ng/l)</td>
<td>15.27 ± 3.7</td>
<td>13.20 ± 3.3</td>
<td>0.1</td>
</tr>
<tr>
<td>4</td>
<td>BMD spine (g/cm²)</td>
<td>1.039 ± 0.13</td>
<td>1.004 ± 0.14</td>
<td>0.05</td>
</tr>
<tr>
<td>5</td>
<td>BMD Total hip (g/cm²)</td>
<td>0.994 ± 0.11</td>
<td>0.816 ± 0.11</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Hypovitaminosis D means Serum levels of 25(OH)D below 20ng/ml was seen in 22.7% of the tobacco consumers and 15.2% in Non tobacco consumers. No linear relationship was observed between number of bouts of tobacco consumption and Total Sr Vit D or PTH.

A non significant decrease of mean serum total Vit D levels was observed when tobacco consumers were classified as Bidi smokers, Raw tobacco chewers and Gutka/Khainy chewers. Low levels of Vit D and PTH in tobacco consumers the mechanism for which could not be explained properly. Many toxic chemicals are present in tobacco and tobacco smoke which must be causing the lower values of Vit D and PTH.

Serum total vit D was not correlated with serum PTH in tobacco consumers. PTH and Serum total vit D were negatively related to each others in Non Tobacco consumers (P<0.04).

Results showed there was positive correlation between BMI and PTH (P<0.001) in both the groups. Body weight was lower in tobacco consumers as compared to non tobacco consumers.

Tobacco consumption was still anindependent predictor of PTH in multiple regression analysis (p<0.005).

Tobacco consumers showed lower levels of Osteocalcin than non tobacco consumers.Osteocalcin and Total Vit D were highly correlated but multiple regression analysis showed smoking was still an independent predictor of Osteocalcin (P<0.01).

To assess the influence of possible confounding factor like alcohol intake on parameters like PTH and total Vit D, we did multiple regression analysis with BMI and smoking. Alcohol consumption was not significant predictor of PTH and Vit D. Smoking was positively correlated with Vit D and with BMI negatively.
Tobacco consumers had decreased age adjusted BMD when compared to non tobacco consumers all the time. Relationship of Total Vit D and Bone density among tobacco consumers and non tobacco consumers was seen. There was inverse relationship between Sr Vit D and bone density. It was of not much significance for the hip bone in non tobacco consumers.

**Discussion**

As per data of NFHS-III, in India 55.8% male and 10.8% female of the age group of 12-60 years were tobacco consumers in different forms. of the males 32.7% were reported to be smokers and 36.5% were tobacco chewers, while in females it was 1.4% and 8.4% respectively[2]. In India tobacco consumption is widespread; it is also prevalent in the central part of India Maharashtra. Our study region and population was not unusual and was suitable for our present study to see the effects of tobacco consumption. In our study population of cohort of normal men, there was significant negative association between tobacco consumption, total Vit D and PTH. William B. Ogunkolade et al also found that there is negative correlation of Vit D and PTH with betel nut and also tobacco consumption in the form of chewing tobacco in their cross sectional study of British Bangladeshi subjects [17]. A similar study got the results of 10% lower values of 25(OH)Vit D and PTH in smokers in the control group mean difference was 2.8ng/ml. results correlate well with our study [11].

In one of the Swedish study also it was reported lower values of PTH in young women smokers[12]. In another Swedish study also reported lower levels of PTH in a population based study of men and women aged 25 ± 64 years [13]. Another study carried out by Scragg et al 1995 observed no association between smoking and serum 25 (OH) D over elder English women. However these studies of negative findings were consisting of small number of subjects. Lower levels of PTH found in tobacco consumers can’t be explained on the differences in ionized calcium or Serum phosphate. We think that the lower levels of PTH are due to corresponding decrease of total vit D levels. In rural set up there was no such noticeable difference among tobacco consumers and non tobacco consumers but confounding factor like alcohol intake. Tobacco consumers can have difference with non tobacco consumers that means tobacco consumption and tobacco non consumption in intake of caffeine, intake of calcium and vitamin D, Exercise and alcohol intake, which also acts as confounding factors and shows association between smoking and vit D and PTH levels[18]. Our study could establish that alcohol consumption by tobacco consumers aggraves the condition and shown lowered levels of VitD. Further more it was observed that tobacco consumption was still associated significantly with serum levels of total vit D and PTH.

Establishment of mechanism by which tobacco consumption lowers the PTH and VitD could not be explained properly. Tobacco itself and its smoke contains various toxic compounds like tars and nicotine. Also contains various heavy metals like nitrosamines, hydroxyquinones, cadmium, thiocynates and others[20,21,22]. Intracellular calcium is increased by hydroxyquinone and it also affects the liver [23]. There may be altered metabolism of Vit D as tobacco consumers have more hepatic degradation of estrogen [24]. The lower values of PTH in tobacco consumers may be due to lower secretion or more degradation of estrogen. We didn’t get correlation between lower PTH who has half life of few minutes and,25(OH)2 D who has half life of few hours. Other studies also failed to detect such correlation[25]. There might be an impaired 1-alpha hydroxylation of the tobacco consumers. Accumulation of cadmium in kidney may also cause the lower levels of 25(OH)2 [26,27]. Low levels of serum calcium may be due to the reduced serum 1,25(OH)2 D[28]. Calcium levels in serum are unchanged may be due to the hormones acting for maintaining serum calcium in normal values. Though levels of PTH and 1,25(OH)2 D are low the plasma level of calcium remains unchanged this could be due to decreased uptake of calcium in bone. In our study we observed low levels of Sr. Osteocalcin in tobacco consumers. Low Osteocalcin levels in tobacco consumers shows decreased osteoblastic activity[29,30]. In our study there was no significant difference for the Sr. Alkaline phosphatase activity/. There was no difference in serum alkaline phosphatase activity in tobacco consumers and non tobacco consumers. A recent study demonstrated the male smokers have lowered parameters such as PTH, Vit Dstatistically significant over non smokers. Our study suggests that tobacco consumption compared to normal males has an inhibitory effect on bone formation. Sensitive bone markers and studies on RNAs also suggest the toxic content of tobacco effect on bone formation. In our study we got decrease in Bone Mineral Density in tobacco consumers compared to non tobacco consumers. Association between Bone Mineral Density and circulating concentrations of 25(OH) D has been demonstrated in number of studies. Non tobacco
consumers may compensate for such as low calcium intake leading to decreased bone mineralization but this compensation is not as much effective in tobacco consumers.

**Conclusion**

Our study concludes that tobacco consumption decreases total vitamin D and PTH. Tobacco consumers have decrease in serum levels of vit D and decrease in PTH levels. These differences were not explained only by other confounding factors like low socio economic status and intake of alcohol. Lower levels found couldn’t be explained with proper mechanism involved. But it is explained only on the basis of observations obtained. The important finding in study was suboptimal levels of Vit D i.e. serum levels of Vit D below 15 ng/ml was 50% higher in tobacco consumers. The trend was higher in age group of 40-50 years. Though the difference found is small and though the size of sample is not large enough the findings are clinically important to correlate among tobacco consumers for the decreased bone mass and for treatment of fractures and osteoporosis.

**Ethical Clearance:** Taken from institutional ethics committee.

**Source of Funding:** Self.

**Conflict of Interest:** Nil.

**References**

2. Krall & Dawson-Hughes. Effect of calcium and vitamin d supplementation on bone density In men and women 65 years of age or older. The New England Journal of Medicine, 1997; 337 (10); 670-76.
4. Su-jin Ket al. Impact of smoking on thyroid gland: dose-related effect of urinary cotinine levels on thyroid function and thyroid autoimmunity. Scientific Reports. 2019; 9:
11. Landin-Wihelmsen K et al. Serum intact parathyroid hormone in a random population sample of men and women:relationship to anthropometry, life-style factors, blood pressure, and vitamin D. Calcif. Tissue Int. 1995; 56, 104 ± 108.
18. Hoffmann D, Hoffmann I. The changing cigarette,