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Original Article

The investigation of effects of proton pump inhibitors (PPI) using on maxillary bone mineral density

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Abstract

Aim: Proton pump inhibitors (PPI) have been widely used throughout the world. The effects of the PPIs on bone mineral density (BMD) is important for oral surgeons. The aim of this study was evaluate alterations in bone mineral density in patients using PPI.
Material and Methods: A total of 92 patients were enrolled in the study and were separated into 4 groups (24 in control group, 22 in Lansoprazole group, 24 in Pantoprazole group and 22 in Esomeprazole group). Hounsfield Unit scores were measuredseparately of the incisor, canine, premolar, molar and tubule regions in the jaws with computed tomography. The measurement area in the dental regions was defined as an area of 2mm2 at least 2mm from the apex of the teeth. All data were collected and statistically analysed.
Results: There was no significant difference between the groups in respect of mean age. There were no significant differences between the control and the study groups. Also no significant difference was found among the study groups.
Conclusion: These data revealed that there were no correlations between decreased maxillary bone mineral density and proton pump inhibitor use. Further studies with more extensive samples should take into consideration drug doses and the period of use.

Keywords: Bone Mineral Density; Hounsfield Unit; Proton Pump Inhibitor.

INTRODUCTION

Proton pump inhibitors (PPI) have been used throughout the world for more than 30 years (1). PPIs are used in many conditions, such as functional dyspepsia, gastro-oesophageal reflux disease, peptic ulcer (stomach-duodenum) and to prevent or treat the side-effects of non-steroid anti-inflammatory drugs and aspirin, for the eradication of Helicobacter pylori (Hp), to treat upper gastro-intestinal system bleeding associated with erosive gastoduodenitis and acid-peptic diseases, as prophylaxis and treatment for stress ulcers, in Zollinger-Ellison syndrome, laryngeopharyngeal reflux disease and to reduce iron absorption in hemochromatosis (1). These drugs are used by millions of people each day and as a safe drug group, can be bought without a prescription in many countries, including the USA. Just as for all drugs that are widely used in the general population, the side-effects of PPI have become a topic of interest.

As PPI reduce calcium absorption in the duodenum, reports have been published that they could impair the fracture repair mechanism, reduce bone mineral density and increase the risk of bone fractures (2-8).

In Oral and Maxillofacial Surgery Clinics, all conditions that could affect bone health must be taken into consideration as previously investigated Behcet's Disease and Familial Mediterranean Fever (FMF) by Asutay F et al (9) and Atalay Y et al (10). Bone volume and quality is known to play an important role in bone augmentations, surgical interventions and the application of dental implants (11-13). Therefore, bone mineral density must be considered in the success of all surgical interventions to the maxilla and mandible.

The aim of this study was to evaluate the effect on bone mineral density of PPIs, which are widely used in Turkey and throughout the world, and to discuss these potential effects on dentoalveolar surgical interventions.

MATERIAL and METHODS

Patients

Approval for the study was granted by the Ethics Committee of Bezmialem Foundation University Medical Faculty (decision no: 71306642-050.01.04). All procedures were

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applied in compliance with the principles of the Helsinki Declaration.

The data used were collected from the records of patients treated in the Medical and Dental Faculties of Afyon Kocatepe University. A total of 92 patients were included, comprising a control group of 24 healthy patients (12 males, 12 females) who were non-smokers and had no systemic disorder, and 22 patients (12 males, 10 females) using Lansoprazol for at least 6 months, 24 patients (12 male, 12 female) using Pantoprazol, and 22 patients (12 males 10 females) using Esomeprazol. Patients receiving any therapy (radiotherapy, chemotherapy) or taking any other drugs (steroids etc) that could affect bone mineral density were excluded from the study.

All the patients had been taking PPI for at least 6 months for various reasons. Evaluation was made with Hounsfield Unit (HU) measurements taken on computed tomography (CT) images. No additional tests were requested for the patients included in the study.

Bone Mineral Density Measurements

Measurements were taken separately of the incisor, canine, premolar, molar and tubule regions in the jaws on CT images. The measurement area in the dental regions was defined as an area of 2mm^2 at least ^{2}mm from the apex of the teeth (Figure 1).

Statistical Analysis

Statistical analyses of the study data were made using IBM SPSS vn 22 statistics software. Conformity of the data to normal distribution was assessed with the Shapiro Wilk test. Descriptive statistics were stated as mean± standard deviation for continuous variables showing normal distribution and as median (minimum-maximum) values for those not showing normal distribution. In the comparison of more than 2 independent groups of continuous variables with normal distribution, the One-Way ANOVA test was applied, and for the comparison of more than 2 independent groups of continuous variables not showing normal distribution, the Kruskal Wallis test was used. The level of statistical significance was defined as α=0.05.

RESULTS

No significant difference was determined between the groups in respect of mean age (Table 1). According to the results obtained from the measurements, no statistically significant difference was determined in respect of bone mineral density values between the control group and the patient groups using PPIs (Table 2). No statistically significant difference was determined between the patient groups using different PPI drugs (Table 2).

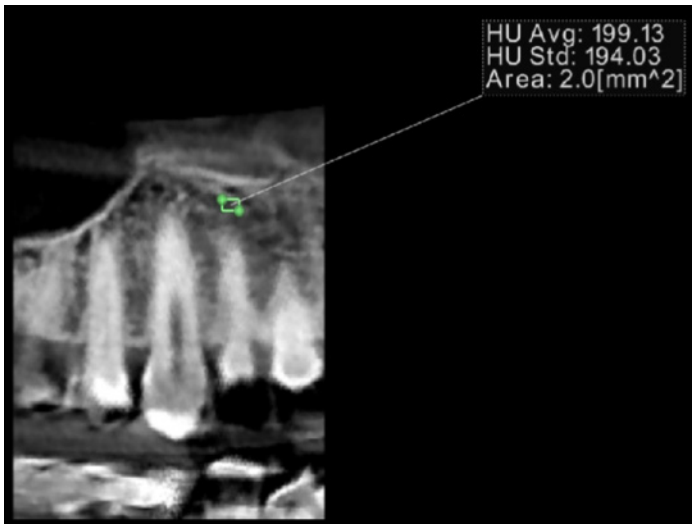

Figure 1. Hounsfield unit scores were obtained from the apexes of incisors (central and lateral), the apex of canine tooth, the apex of premolars, the apex of molars, and the region of tuber maxilla. These regions of measurements are shown on the figure as ^{2} mm^2 area.
Abbreviations: HU, Hounsfield units; SD, standard deviation

Table 1. Mean age values of all groups

Group 1 (Control)	Group 2	Group 3	Group 4
42.3±5.6	47.7±7.2	44.8±6.4	45.65±6.9

Table 2. Bone mineral density values obtained by cone-beam computerized tomography

Regions	Group 1	Group 2	Group 3	Group 4	P*
Incisor [Median (Min:Max)]	193.50 (69:447)	171.50 (44:538)	156 (30:402)	163.50 (72:286)	0.871
Canine (Mean.±St.D.)	219.95±97.952	223.77±96.389	261.55±86,373	252.77±99.850	0.378
Premolar [Medyan (Min:Max)]	195.50 (55:432)	214.50 (1:502)	241.50 (73:559)	224 (63:403)	0.727
Molar (Mean.±St.D.)	236.95±122.761	192.91± 122.795	203.41 ± 98,926	180.36± 110.916	0.401
Tuberositas Maxilla [Median (Min:Max)]	58.50 (6:182)	45.50 (17:182)	21.50 (2:110)	36.50 (4:83)	0.058

DISCUSSION

The aim of this study was to investigate the effect of the use of PPI on any potential bone mineral density (BMD) changes and to discuss the effects of these potential changes on dentoalveolar surgical procedures.

PPI is one of the most widely used drugs throughout the world and can be purchased without a prescription in some countries. As it is deemed to be safe, it is suitable for long-term use and thus, the effects of long-term use on bone metabolism have become an area of interest (1). Gray et al (14) reported that long-term PPI use had no

significant effect on BMD. However, Targownik et al (15) stated that the risk of osteoporotic bone fracture was significantly increased with long-term use of more than 5 years. Similarly, Yang YX et al (16) and Freedberg DE et al reported that long-term PPI use increased the risk of fractures. Studies such as these have claimed that that long-term use of PPIs could lead to changes in bone metabolism. Therefore, this has attracted the interest of all physicians performing bone surgery.

Esfahanizadeh et al (18) reported that in cases of osteopenia and osteoporosis, there is a significant relationship between skeletal and jaw bone densities and this affects both the mandible and the maxilla. This demonstrated that the jaw bones could be affected by a potential change in BMD and a relationship may be established between measurements made of the jawbones and skeletal BMD. In the current study, evaluation was made from measurements taken from the maxilla.

BMD has been an important subject in maxillofacial surgery for many years. Following the understanding that BMD is one of the most important factors affecting the success of dental implants, there started to be greater interest in the diseases, treatments and drugs affected positively and negatively by this condition (13). Pommer et al (19) and Türkyilmaz et al (13) reported a significant relationship between bone quality and implant stability. In the study by Pommer et al (19), BMD was stated to be the most important factor affecting primary stability in the application of dental implants in a maxillary sinus region with limited bone volume.

In an experimental animal model by Al Subaie et al (20), the use of systemic PPI was reported to have a negative effect on bone healing and implant osteo-integration. Malizos et al (21) and Devescovi et al (22) reported that PPI caused a negative effect on bone through the reduced expression of BMP-2 and BMP-4. However, Giannoudis et al (23), Yu et al (24) and Fraser et al (8) stated that this situation originated from reduced calcium absorption. In a study of the use of PPI for at least 6 months, Özdil K et al (25), reported that bone density was significantly reduced. Amoake AO et al (26) reported that there was no relationship between low bone density and PPI use in patients aged >65 years, and this was independent of the duration of drug use. When literature is examined in general, it can be concluded that there is no consensus related to the effect of PPIs on fracture risk, independently of the duration of use. The differences in results can be considered to be due to the differences in sample sizes and measurement techniques.

CT is an indispensable technique for detailed examination of the head and neck region, just as it is for the whole body. Being able to make real measurements on CT allows the interpretation of bone quality examination (13,27,28). However, detailed imaging makes it difficult to achieve standardization of the slices on which the measurements are to be made. In the current study, it was aimed to reduce the margin of error and provide more reliable mean values by taking the measurements from different regions of the maxilla.

Limitations of this study could be considered to be that no evaluation was made in respect of gender, there was no information about the drug doses and the sample was limited in number. There is a need for further studies including these data.

According to the analysis of the results obtained from the measurements made on the CT images of patients using PPI for at least 6 months, no significant relationship was determined between the use of PPI and changes in maxillary bone mineral density. Furthermore, for clearer understanding of the potential effect of this on the success of maxillary surgical procedures, there is a need for further studies of more extensive samples, taking into consideration drug doses and the period of use.

Competing interests: The authors declare that they have no competing interest.
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