SHORT COMMUNICATION

The Increase of Serum Osteocalcin (BGP) after Tooth Extraction Required for Orthodontic Treatment

Kiyokazu Kaida, Ayao Hirashita, Tadayoshi Fukui, Satoshi Nagasaka and Yosuke Kuwahara

*Department of Orthodontics, Tsurumi University, School of Dental Medicine
2-1-3, Tsurumi, Tsurumi-ku, Yokohama 230-8501, Japan*

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Introduction

Bone Gla-protein (BGP, osteocalcin) is the most abundant non-collagenous bone matrix protein synthesized by osteoblasts. The serum BGP level is considered to reflect overall osteoblastic activity. In particular, Price *et al.*¹⁾ reported that the increase of serum BGP level was generally observed in patients with diseases characterized by prominent bone turnover. Serum BGP levels in adult humans without bone diseases and renal disturbances are known to be relatively stable^{1,2)}. However, the number of reports on whether the local increase of bone turnover in such adults affected the level of serum BGP is small^{3,4)}. Research on whether the extraction of teeth in orthodontic therapy in humans affects serum BGP or not is especially scarce⁵⁾. The purpose of this study is to elucidate the changes of serum BGP before and after permanent tooth extraction required for orthodontic therapy.

Materials and Methods

1. Materials

The sample population consisted of twenty-six adult females aged 18 y 9 m to 29 y 6 m ($22 \text{ y } 6 \text{ m} \pm 3 \text{ y } 1 \text{ m}$) undergoing tooth extraction for orthodontic treatment in the orthodontic clinic of Tsurumi University, School of Dental Medicine. None of the subjects was

suffering from any evident disease or receiving any medication that might affect bone or mineral metabolism. All of the subjects gave their informed consent for examination of the biological parameters in their serum. Extracted teeth for orthodontic needs were two premolars in five patients, four premolars in fourteen patients, four premolars and third molars in four patients and other teeth in three patients (Table 1).

2. Biochemical measurements

Standard methods were used for sampling venous blood (5–6 ml), at 10 : 00 a.m.–12 : 00 p.m. before commencement of orthodontic treatment, and 2–4 weeks after tooth extraction before setting the edgewise appliance in fasting subjects for determination of serum components. After these samples were allowed to clot for 30 minutes, sera were separated by a clinical centrifuge (3,000 rpm, 10 minutes), and were stored frozen for the following analysis. Serum osteocalcin was measured using a commercial radioimmunoassay (“YAMASA” RIA kit, Chiba, Japan). Details are given elsewhere⁶⁾. Intra- and inter-assay coefficients were 1.3–4.8% and 5.5–5.7%, respectively. The other components were determined by EDTA-Titration for serum calcium (Ca), by photometry for serum alkaline phosphatase (Alk-p), serum inorganic phosphorus (IP), and serum urea-nitrogen (Urea-N), and by protein hand refractometer for total serum protein (Total-P).

Table 1 Extraction site

Case No.	1	2	3	4	5	6	7	8	9	
Extraction sites	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{8}{8}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{5}{5}$	
Before treatment	26y1m	21y2m	20y1m	22y8m	19y4m	19y6m	25y8m	20y5m	19y4m	
After extraction	26y2m	21y3m	20y1m	23y1m	19y6m	19y7m	25y10m	20y8m	19y5m	
10	11	12	13	14	15	16	17	18	19	20
$\frac{4}{4}$	$\frac{8}{8}$	$\frac{5}{8}$	$\frac{5}{4}$	$\frac{4}{5}$	$\frac{4}{5}$	$\frac{4}{5}$	$\frac{8}{4}$	$\frac{8}{5}$	$\frac{4}{3}$	$\frac{4}{5}$
$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{8}{8}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{4}$	$\frac{4}{5}$	$\frac{5}{5}$
19y3m	19y9m	23y2m	25y1m	26y2m	23y11m	20y1m	19y11m	25y6m	27y9m	21y2m
19y4m	20y5m	23y5m	25y4m	26y7m	24y4m	21y0m	20y4m	25y8m	27y11m	21y6m
21	22	23	24	25	26					
$\frac{5}{5}$	$\frac{4}{4}$	$\frac{4}{8}$	$\frac{8}{8}$	$\frac{5}{4}$	$\frac{5}{5}$					
20y11m	20y8m	24y0m	29y6m	25y10m	23y2m					
21y3m	21y1m	24y2m	29y8m	26y0m	23y5m					

The data were examined statistically by Wilcoxon signed rank test. Linear regression analysis was conducted to examine the correlations between serum BGP and other components such as serum Alk-p, serum Ca, serum IP, Urea-N and Total-P in each group.

Results

The results are shown in Figs. 1 and 2. There was no significant difference in the serum BGP level between the healthy adult humans examined with the YAMASA kit (8.59 ± 2.55 ng/ml⁶⁾) and our patients before treatment examined in the same manner (8.93 ± 3.01 ng/ml). Moreover, the level for each of the other serum components was in the range of the adult standard (serum Alk-p, 6.73 ± 1.73 KAU, standard level 3–10 KAU ; serum CA, 9.49 ± 0.37 mg/dl, standard level, 9–11 mg/dl ; serum Inorg-P, 4.02 ± 0.85 mg/dl, standard level, 3.5–5.0 mg/dl ; serum Urea-N, 13.32 ± 2.55 mg/dl, standard level, 8–18 mg/dl ; Total-P, 7.25 ± 0.38 g/dl, standard level, 6.5–8.0 mg/dl). Compared with serum BGP level before and after tooth extraction in each case, it increased after tooth extraction in 20 of the 26 patients (76.9%), and it decreased in the remaining 6 patients (23.1%). A significant increase in the serum

BGP level (10.46 ± 3.34 ng/ml : Tied P-Value = 0.0018, $p < 0.01$) was seen after tooth extraction, compared to its level before treatment.

The decreased amount was relatively large in Cases 6, 11, 15 and 19. The extracted teeth in those cases were four premolars in Cases 6 and 15, four premolars and two third molars in Case 11 and four premolars and one canine in Case 19. The differences in the number of extracted teeth as well as in the extraction site had no influence on the serum BGP. There were no significant differences between before and after tooth extraction in other serum components. Furthermore, there was no significant correlation between the amount of serum Alk-p and that of serum BGP.

Discussion

Serum calcium (Ca), serum inorganic phosphorus (IP) and serum alkaline phosphatase (Alk-p) play important roles in the metabolism of bone remodeling. In particular, serum Alk-p has been, and still is, the most frequently used biochemical marker for metabolic bone diseases. However, Price *et al.*¹⁾, described that serum BGP was superior to serum Alk-p as a marker for bone metabolism, though the correlation between serum bone Gla-protein (BGP, osteocalcin) and serum Alk-p is often recognized in bone diseases.

Fig. 1 Change of serum BGP in each case.

Fig. 2 Level of serum components before and after tooth extraction.

One of the reasons is that BGP is found peculiarly in bone tissue, and Alk-p not peculiarly in bone tissue. In this investigation, the levels of serum BGP and other components clearly indicated that the subjects were healthy and free from any disease and were not receiving any medication that might affect bone or mineral metabolism during any experimental stage. Garcia-Carrasco *et al.*²⁾ reported that the serum BGP level was significantly correlated with trabecular bone volume, osteoid surfaces, osteoblastic surfaces and the bone formation rate in adults without any bone dis-

ease. Obrant *et al.*³⁾ observed that serum BGP increased one to two months after major bone fracture, possibly as a manifestation of bone repair.

There are some reports on the healing process of tooth extraction wounds in healthy human beings⁵⁾. The findings are that bone healing and osteogenesis begin 7–9 days after extraction and continue for about 5 weeks. The reason why we sampled blood 2–4 weeks after tooth extraction in this study is that the serum BGP level is considered to reflect overall osteoblastic activity⁸⁾. Therefore, the present results, indicating a significant elevation of serum BGP level after tooth extraction, suggest that the local increase of bone turnover taking place after tooth extraction could increase serum BGP.

On the other hand, a correlation between Alk-p and BGP has been found in hypoparathyroidism, acromegaly, and postmenopausal osteoporosis. However, it is also reported that absence of a correlation may sometimes occur between these two⁹⁾. In the present study, there was also no significant correlation between the amount of serum Alk-p and that of serum BGP. The reasons for this absence of correlation are not clear, but one of them is that BGP and Alk-p might represent different aspects of osteoblastic function⁹⁾.

We are presently examining the levels of serum BGP and other serum components on different stages from the start of orthodontic treatment up to the end of the treatment. This additional research is expected to bring us further explanation of whether the serum BGP might be affected by local bone remodeling derived from orthodontic tooth movement.

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