The Bone Turnover Markers in Healthy Thai Adults as the Standard Values

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The present study of the bone markers in the healthy Thai females and males enrolled 588 females and 53 males with age range from 25 to 42 years. The potential modification of variations was controlled. The bone resorptive markers, betaCTx, of females and males were 0.3 ± 0.169, 0.412 ± 0.191 ng/ml respectively. The bone formation markers, PINP, of females and males were 44.5 ± 19.92, 58.1 ± 37.7 ng/ml respectively. These markers could be recognized as the standard values for comparison.

***Keywords**: NMID osteocalcin, betaCTx (βCTx), betacrosslap, PINP, Bone turnover markers*

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As the researches on the normal values of bone markers are controversial, the present study showed the suitable values for referencing especially in Thailand. The selection of standard population is rather complicated due to the variations of bone markers. In this research, the young adult females and males, age range from 25 to 42 years were chosen for finding the standard values with the following reasons:

1) This age is the peak of the bone mass with a little fluctuated bone texture.

2) The physical and mental conditions of young people are healthy, *i.e.* having active hormones and no underlying diseases.

3) The active bone activities are decreased at these ages and also this peroid is manifested by closing of epiphysis.

4) The bone remodeling is active and manifests a coupling effect.

The present study showed that the relationship of bone cells was a failure called uncoupling effect if the value of betaCTx below 0.3 ng/ml. Whenever the value of betaCTx was more than 0.3 ng/ml, the coupling effect would occur (Fig. 1).

Material and Method

The subjects enrolled in this investigation were 641 young volunteers in the healthy conditions. They were 588 females and 53 males with age range between 25 to 42 years.

The reagents were not available at the same period. So, the female group was classified into 3 groups for the investigation of betaCTx, NMID osteocalcin and PINP separately in the meantime 53 male volunteers were checked up (Table 1).

Every case was aspirated 8 ml of the fasting venous blood between 8:00-9:00 am. The blood samples were centrifuged for plasma. The plasmas were investigated for bone markers and the screening for general profiles: blood sugar, renal and liver profiles and lipid profiles which the unhealthy blood was in the exclude criterion.

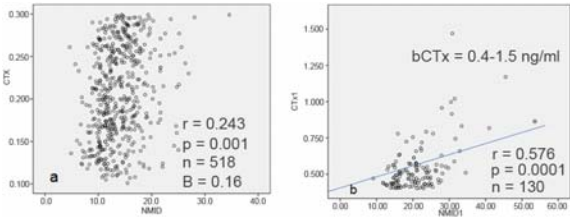

Fig. 1 The correlation of NMID Osteocalcin and bCTx happened if the value of βCTx was 0.1-0.3 ng/ml (Fig. a), r =0.243 meanwhile the linear correlation between NMID osteocalcin and βCTx, r= 0.576 (Fig. b) occurred when the value of βCTx was between 0.4 to 1.5 ng/ml. On the other hand, there was no correlation (r = 0.035) when βCTx was below 0.1 ng/ml[1]

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The Betacrosslap, βCTx, was specifically achieved by using monoclonal antibody that recognized an octapeptide on the C-terminal (telopeptide) of the collagen type 1, a potential specific marker of bone resorption[2].

The NMID osteocalcin was done by the method of immunoassay using the Elecsys NMID osteocalcin assay (Roche®) by two monoclonal antibodies specifically direct against epitopes on NMID fragment including intact fragment.

The PINP was detected by the Elecsys total PINP test (Roche®) analyzing all forms of PINP, i.e. intact and broken forms.

The data were statistically calculated by SPSS.

All the volunteers have no underlying diseases, no alcoholic and smoking habits, no bone medication or any kinds of medicine, *e.g.* anticonvulsive drugs or hormonal therapy which will disturb the bone metabolism. The included criteria were regular menstruation, aged between 25-42 years with normal daily activities.

Results

The final results of both females and males were shown in Table 2 and 3 respectively.

The males' bone turnover markers were outnumbered the females. This result was corresponded to Tsai's report[3].

Table 1. The numbers of female and male volunteers were examined for the bone markers

	Female	Male
Betacrosslap, betaCTx	356	53
NIMID osteocalcin	123	53
PINP	109	53

Table 2. Female bone marker values

	mean	SD	CV
Betacrosslap, betaCTx	0.31	0.169	1.8
NMID osteocalcin	16.46	7.69	2.14
PINP	44.5	19.92	2.23

Table 3. Male bone marker values

	mean	SD	CV
Betacrosslap, betaCTx	0.412	0.191	2.14
NMID osteocalcin	19.65	9.1	2.15
PINP	58.1	37.7	1.54

Discussion

The finding of the normal values is a hard task because of the difficulty of the population selection. The subjects must be representatives of the normal values whose young people belong to. They are in the growth period while the menopausal elderly are the group of insufficiency, aging and physiologic changes that cannot be the normal values. As a result, the young adult females and males are focused to be the target of the present study. They are in proper conditions: physiologic stability, and stability of bone growth. This population is selected as the normal group after the elimination of the interfered factors such as screening of the underlying diseases, eradication of the risk factors for osteoporosis, *i.e.* smoking habit, alcoholic drinking, caffeine intakes, and all kinds of bone medication.

The second study[4] of bone markers in the normal, young adults was confirmed. The results showed the value of beta βCTx or betacrosslap in females and males which were 0.3 ± 0.14 and 0.5 ± 0.09 ng/ml respectively. The findings were similar but the number of study was small: 24 and28 respectively. The coefficients of variations (CV) were 2.14 and 5.55 which were rather outnumbered these series: 1.8 and 2.14 respectively (Table 2 and 3).

The benefits of normal values are helpful not only for making a decision of the treatment if a patient has higher values than the young adults but also for monitoring the antiresorptive therapy which the values should be decreased within 3-6 months at 30-50 per cent[5]. The combination application of bone turnover and bone mineral density measurement can predict the risks of fracture[6,7]. The bone markers reflect bone metastasis especially bCTx and PINP[8].

The application needs skilled selections because the bone markers have potential modification of variations, *i.e.* diurnal, age, fasting blood.

The present study was performed by control status of the samples obtained at 8.00-9.00 for fasting blood in the condition of no previous medication. The samples were separated by gender. The volunteers were suitably included according to the criterion. The comparison should be conducted in the same situation of the control. The referent values are useful and helpful for application of bone markers in clinical practice.

Potential conflicts of interest

None.

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การศึกษาค่าปกติของโบนมาร์เกอร์ในคนไทย

ณรงค์ บุณยะรัตเวช

รายงานการหาค่าปกติของโบนมาร์เกอร์ชนิดสร้างกระดูก ได้แก่ พีหนึ่งเอ็นพี และเอ็นมิท ออสติโอคัลซิน และชนิดสลายกระดูก ได้แก่ ซีทีเอกซ์ ในกลุ่มอาสาสมัคร ชาย หญิง จำนวน 641 รายแบ่งเป็นชาย 53 รายและหญิง 588 ราย อายุระหว่าง อายุ 25-42 ปี ทุกคนได้รับการตรวจร่างกายว่าปกติ ไม่มีโรคแทรกใดๆ และได้รับการตรวจเลือดหลังอดอาหารหลังเที่ยงคืนในเวลาตรงกันคือ 8.00-9.00 น. แล้วนำไปหา ค่า บี-ซีทีเอกซ์ เอ็นมิท ออสติโอคัลซิน และพีหนึ่งเอ็นพี สำหรับกลุ่มสตรี ที่ได้รับการตรวจแต่ละรายการของโบนมาร์เกอร์ไม่เท่ากันเนื่องจากน้ำยาที่ใช้ยังมีไม่ครบ แต่ในชายได้รับการตรวจพร้อมกันหมดทุกรายการ ค่าโบนมาร์เกอร์ในชายจะสูงกว่าสตรี (ในตารางที่ 2 และ 3) ค่าที่ได้มีประโยชน์พอสรุปกว้างๆ คือ นำไปใช้เปรียบเทียบกับกลุ่มประชากรอื่นๆ ว่าแตกต่างกับค่าปกติเพียงใด เพื่อสะดวกในการวางแผนรักษาเพื่อการเฝ้าติดตามดูผลของยาห้ามการสลายกระดูก และเพื่อการพยากรณ์การเสี่ยงของกระดูกที่จะหักในอนาคต