Study of Validity of Pyridinoline and Correlation of Pyridinoline and Beta Crosslap in Postmenopausal Women

Narong Bunyaratavej MD*,
Shutipen Buranasinsup PhD**

** Department of Orthopaedic Surgery, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*
*** Department of Pre-clinic and Applied Animal Science, Faculty of Veterinary Science, Mahidol University, Nakornpathom, Thailand*

This research studied the validity and correlation of β-CTx (Betacrosslap) and Pyridinoline (PYD) in 71 cases of postmenopausal Thai women who attended at the osteoporosis clinic. The validity consisted of sensitivity, specificity and accuracy of PYD. They were 53.44, 84.6 and 59.15 % respectively. So, the validity of pyridinoline test was rather poor and the correlation between betacrosslap and pyridinoline was weak (r = 0.123, p = 0.0001) which was not significant in practice.

In conclusion, the pyridinoline test was not proper for bone resorption even pyridinoline was abundant in bone.

Keywords: *Pyridinoline (PYD), BetacrossLap, betaCTx, Validity*

J Med Assoc Thai 2011; 94 (Suppl. 5): S76-S78
Full text. e-Journal: *http://www.mat.or.th/journal*

The degradation products of the type1 collagen which are main constituents of bone matrix have shown a promise as biomarkers of the bone resorption especially at the C-telopeptide. At present, the popular method is immunoassay which highly specific monoclonal antibodies recognize the different domains of C-terminal telopeptide regions of the alpha 1 collagen. Additionally, all current assays are based on the CrossLaps antibodies which reflect the epitope consisting of 8 amino acids sequence, EKAHD-β-GGR octapeptide where the aspartate (D) residue is beta isomerized. So, the bond between aspatrate and glycine is strong and is hardly digested by any enzymes. The epitope or octapeptide is most stable and also is a site for the crosslink binding. The β-CrossLaps is an antibody that is specific for the EKAHD-β-GGR which there is lesser than 0.2 %[1] cross reactivity with non-isomerized 8 aminoacids.

This method is popular for detecting the bone resorption at the C-terminal named βCTx or betaCrossLap. However, many studies[1] showed that the correlation between betaCTx and alphaCTx was strong (r = 0.76-0.982).

There are 2 types of pyridium cross-links: pyridinoline (PYD) and deoxypyridinoline (DPD).This cross-links are used as bone resorption marker indices involving collagen type1 telopeptide. Both pyridium cross-links are found in bone but the deoxypyridinoline is common in the mineralized collagen and now known to be present in the cardiovascular tissue, intramuscular collagen and some ligaments. These findings have little recognized the DPD as a bone-specific marker due to the other pool size in other tissues. The pyridium cross-links are essentially absent in skin. The PYD is considered as a cross-link marker for bone.

The PYD cross-link is the development of amino acid in the crosslink texture[2] rather than the βCTx which is a specific amino acid sequences at the C-telopeptide, close to the cross-link site[3]

Material and Method

The present study aimed to find:

1. The correlation between β-CTx and PYD.
2. The evaluation of validity of PYD.

The procedure was conducted as follows:

Correspondence to:
Bunyaratavej N, Department of Orthopaedic Surgery, Siriraj Hospital, Mahidol University,Bangkok 10700, Thailand.
Phone: 0-2419-4545
E-mail: todrnarong@yahoo.com

Seventy-one female cases were involved in this study. The routine of 4 ml of fasting blood was checked and centrifuged for serum separation and then kept in -20□C. This process was done in order to study the normal values of β-CTx and Pyridinoline for comparison with the results of the present study[4]. The value of β-CTx was used as the standard criteria for detecting the bone resorption. As the reagent of pyridinoline is an enzyme immunoassay for quantitation of pyridinoline crosslinks in serum, Microvue™ serum PYD EIA kit was used. The reagent of β-CTx is immunoassay for bone resorption, so BetacrossLap Roche Diagnostic™ was recommended. Every case was checked by the two reagents for β-CTx and pyridinoline at the same time and conditions.

All data were compared with the normal values of bone markers and also calculated the sensitivity, specificity and accuracy.

Results

The data were calculated and analyzed by SPSS and compared with the normal data from the young adult females who were checked by betacrosslap (β-CTx) and pyridinoline, PYD, (Table 1).

The correlation between the beta crosslap (β-CTx) and pyridinoline showed no correlation, r = 0.123 p = 0.0001 (Fig. 1). The statistical data were calculated as shown in Table 2.

All data (n = 71) were calculated and put into four by four table for sensitivity (TP) and specificity (TN).

TP or true positive means the number of case who showed bone resorption when the betacrosslap as standard was applied = 31.

FP or false positive means the number of case who were absent of bone resorption but the result showed bone resorption = 2.

FN or false negative means the number of case who had bone resorption but the result could not detect = 27.

TN or true negative means the number of case without bone resorption and compatible with the negative result = 11.

Calculation of validity[5]

Sensitivity = TP/(TP + FN) = 31/58X100 = 53.44%.

Specificity = TN/ (FP+TN) = 11/(2 + 11)X100 = 84.6%.

Accuracy = (TP + TN)/71X100 = 92.5%.

The validity of pyridinoline is summarized in Table 3.

Table 1. The normal values of bone markers in young adult females[4]

	Mean ng/ml	SD
Betacrosslap (β-CTx)	0.30	0.14
Pyridinoline (PYD)	0.78	0.18

Discussion

In clinical practice, it is considered that the correlation of bone markers is necessity because

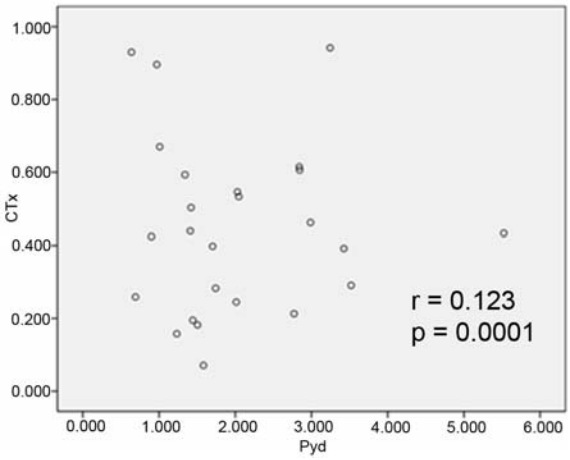

Fig. 1 The correlation (r) between the betacrosslap and pyridinoline showed weak correlation (r = 0.123, p = 0.0001)

Table 2. The statistical results of bone markers: BetacrossLap and Pyridinoline from 71 cases

	Minimum	Maximum	Mean	SD	CV	r
BetacrossLap (CTx)	0.034	0.942	0.3436	0.227	0.656	
Pyridinoline (PYD)	0.42	5.52	1.81	0.941	0.519	
Linear correlation (r)						0.123

CV= Coefficient of variation, unit of bone markers = ng/ml

Table 3. The results of validity: accuracy, sensitivity and specificity of the reagent of pyridinoline (PYD)

	Percent
Sensitivity	53.44
Specificity	84.6
Accuracy	59.15

physicians can estimate the result of other items of bone markers if the current values have been known. The correlation between β-CTx and PYD is weak (r = 0.123).

When the sensitivity (TP) of PYD is 53.44 %, this means the chance of positive result in a group of bone resorption is reliable only 53.44 % that is low sensitivity.

When the specificity (TN) of PYD is 84.6%, this implies the chance of negative result in the normal subjects equals to 0.846 or 84.6 %.

The accuracy of PYD is not suitable for checking the bone resorption when its value is 59.15%

Summary

The PYD is not proper for checking the bone resorption when the accuracy is 59.15%. The Betacrosslap is still recognized as the detection of bone resorption.

Potential conflicts of interest

None.

References

1. Leary ET. C-telopeptides. In: Eastell R, Baumann M, Hoyle NR, Wieczorek L, editors. Bone markers: biochemical and clinical perspectives. London: Martin Dunize; 2001: 39-48.
2. Eyre DR, Paz MA, Gallop PM. Cross-linking in collagen and elastin. Annu Rev Biochem 1984; 53: 717-48.
3. Robin SP. Pyridium cross-links as bone resorption markers. In: Eastell R, Baumann M, Hoyle NR, Wieczorek L, editors. Bone markers: biochemical and clinical perspectives. London: Martin Dunize; 2001: 49-55.
4. Buranasinsup S, Jangsangthong A, Bunyaratavej N. Preliminery report: correlation between the circulating bone biomarkers and vitamin D in the healthy Thai people. J Med Assoc Thai. In Press 2011
5. Vanitbancha K. Understand the statistic in journal. In: Bunyaratavej N, editor. Bone forum 2011. Bangkok: Concept Medicus; 2011: 72-108.

การศึกษาความสัมพันธ์ระหว่าง ไพลิดิโนลีนกับบีตาคลอสแลบ และความเที่ยงตรงของไพลิดิโนลีนในกลุ่มสตรีวัยหมดประจำเดือน

ณรงค์ บุณยะรัตเวช, ชุติเพ็ญ บูรณะสินทรัพย์

ในการศึกษาโบนมาร์เกอร์ของหญิงไทยวัยหมดประจำเดือน 71 ราย โดยหาค่าความสัมพันธ์ระหว่างไพลิดิโนลีน กับ บีตาคลอสแลบ พบว่ามีความสัมพันธ์เชิงเส้นตรงน้อย (r = 0.0123) และการหาความเที่ยงตรง (validity) ของไพลิดิโนลีน มีค่าเฉพาะเจาะจง (specificity) ดี เท่ากับ ร้อยละ 84.6 คือโอกาสที่ผลการตรวจจะเป็นลบหรือไม่มีการสลายกระดูกเกินปกติในคนปกติเป็น 0.846 หรือ ร้อยละ 84.6 แต่ความไว (sensitivity) ค่อนข้างต่ำมีค่าเท่ากับร้อยละ 53.44 หมายความว่าโอกาสที่ผลถูกต้องหรือบวกในกลุ่มคนที่มีการสลายกระดูกมีเพียง 0.5344 หรือร้อยละ 53.44 นอกจากนี้พบว่าประสิทธิภาพ (accuracy) ของน้ำยามีเพียง ร้อยละ 59.15 ดังนั้นการใช้การตรวจไพลิดิโนลีนเพื่อดูการสลายกระดูกยังไม่สมควร