

Rubert M¹, Martínez-Calatrava MJ², de la Piedra C¹

¹ Bioquímica Investigación

² Laboratorio de Patología Osteoarticular

Instituto de Investigación Sanitaria - Fundación Jiménez Díaz - Madrid

Normal values of the aminoterminal propeptide of type I collagen (PINP) and the isomer beta I collagen carboxyterminal telopeptide (β -CTX) in serum of healthy premenopausal women of the Community of Madrid

Correspondence: Concepción de la Piedra - Laboratorio de Bioquímica - Fundación Jiménez Díaz - Avda. Reyes Católicos, 2 - 28040 Madrid (Spain)

e-mail: cpiedra@fjd.es

Date of receipt: 17/10/2013

Date of acceptance: 21/01/2014

Summary

Introduction: In the laboratory it is sometimes difficult to find the normality intervals of the population itself, there being a tendency to give the normality value specified by the manufacturer of the reagent. The aim of this work was to calculate the normality values for aminoterminal propeptide of type I collagen (PINP) and for the beta isomer of carboxy-terminal telopeptide of type I collagen (β -CTX) in the blood of a group of premenopausal women from the autonomous Community of Madrid.

Materials and methods: The study was carried out in 50 healthy premenopausal women between 27 and 40 years of age (mean \pm standard deviation of 34 ± 3 years, working in a hospital and a pharmaceutical laboratory in Madrid).

Blood levels of PINP and β -CTX were determined using the technique of electrochemiluminescence (Elecsys, Roche).

Results: Normal values of 36.2 ± 12.9 ng/ml (range 10.4 to 62) for PINP and 0.306 ± 0.121 ng/ml (range of 0.064 to 0.548) for β -CTX were obtained.

Conclusions: Although the population sample used was small and localised, we consider that these values may be used as the normality interval for Spanish women.

Key words: *normality interval, PINP, β -CTX.*

Introduction

The use of markers for bone remodeling in clinical practice raises the necessity of having appropriate and reliable normal values with which the patient data may be compared. The aim of this work was to calculate the normality values for aminoterminal propeptide of type I collagen (PINP) and for the isomer beta carboxy-terminal telopeptide of type I collagen (β -CTX) in the serum of healthy premenopausal women of the Community of Madrid (Spain).

Materials and methods

The study was carried out in 50 healthy premenopausal women of between 27 and 40 years of age, with the mean \pm standard deviation of 34 ± 3 years, staff of the Jiménez Díaz Foundation Hospital and the offices of a pharmaceutical laboratory in Madrid. All the subjects completed a short questionnaire to discount bone metabolism diseases, hypothyroidism or hyperthyroidism or diabetes, as well as taking a haemogram and basic biochemistry which included thyroid hormones. None of the subjects were taking oral contraceptives. The blood was taken in fasting, at between 8 and 10 in the morning. The blood was centrifuged and the serum separated and immediately frozen aliquots were stored at -80°C for the analysis of bone markers.

The PINP in the serum was determined by the electrochemiluminescence technique using the Elecsys (Roche) automatic method. The sensitivity of the method is 0.01 ng/ml and the inter- and intra-analysis variation coefficients are $<1.8\%$ and $<4.3\%$ respectively.

The β -CTX in serum was also determined through electrochemiluminescence using the same Elecsys (Roche) method. The sensitivity of the method is 5 ng/ml and the inter- and intra-analysis variation coefficients were $<2.1\%$ and $<2.4\%$ respectively.

Results

Values (mean \pm SD) of 36.2 ± 12.9 ng/ml (range: 23.3-49.1) were obtained for PINP and 0.306 ± 0.121 ng/ml (range: 0.185-0.427) for β -CTX Table 1). Figure 1 shows the values of the quartiles corresponding to each marker.

Discussion

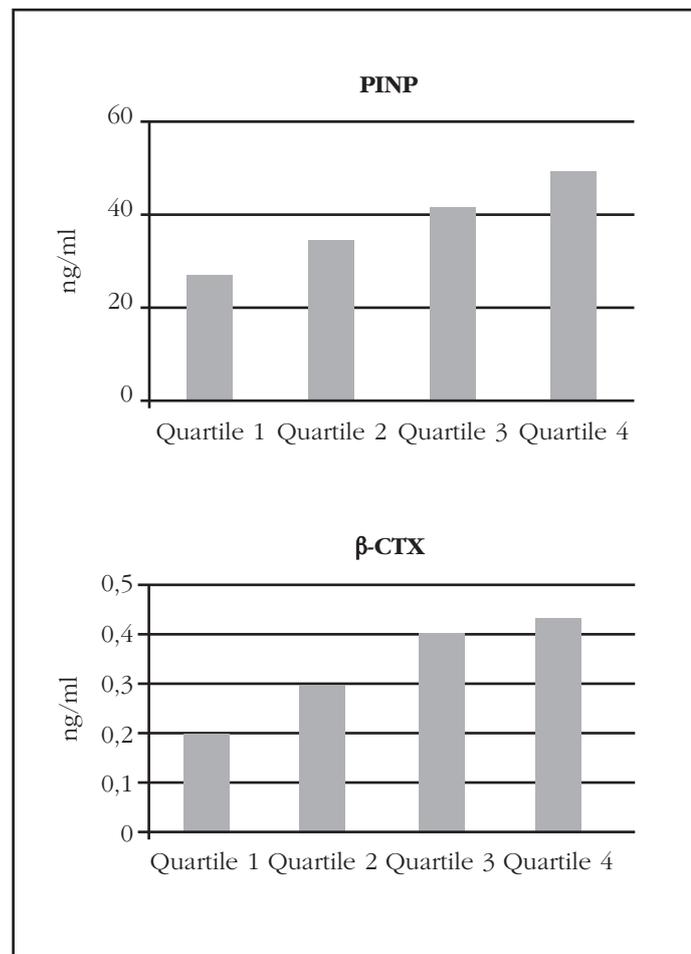
Following the criteria of other researchers such as Richard Eastell, we consider that the normality range for markers for remodelled bone should be that of healthy premenopausal women of between 30 and 45 years of age, who have already re-

Table 1. Normal values of PINP and β -CTX in a group of healthy premenopausal women (n=50) of the Community of Madrid

	PINP (ng/ml)	β -CTX (ng/ml)
Mean \pm SD	36.2 \pm 12.9	0.306 \pm 0.121
Range values	23.3–49.1	0.185–0.427
Normal range (Mean \pm 2 SD)	10.4-62	0.064–0.548

SD: standard deviation.

Figure 1. Average values for the quartiles corresponding to aminoterminal propeptide of type I collagen (PINP), and to the isomer beta carboxy-terminal telopeptide of type I collagen (β -CTX) in the serum of healthy premenopausal women of the Community of Madrid



ached their peak of bone mass, since although bone remodelling activity increases postmenopause, the aim of antiosteoporotic treatments is to return the patients' remodelling activity to premenopausal levels, and preferably to its first quartile¹.

Due to the small differences which may be seen in different geographic areas, it appeared interesting to us to compare the values obtained in our work with earlier studies carried out in Spanish women.

Thus, the values of PINP we obtained are similar to those found by Álvarez et al.²: average value 33.8 ng/ml in the control group of healthy postmenopausal women, although using a different method (radioimmunoanalysis – RIA of Orion Diagnostica). Using the same technique, Peris et al.³ reported values of PINP in serum of 30±11 ng/ml in a group of healthy premenopausal women. As can be seen, the values found using RIA are slightly lower than those obtained by electrochemiluminescence in our work: 36.2±12.9 ng/ml.

As was expected, the values found in a group of healthy postmenopausal women are higher than those for premenopausal women, since bone remodelling accelerates in the postmenopausal state. Thus, Martínez et al.⁴ reported average values of 47.7±19.9 ng/ml in a group of 1,080 healthy postmenopausal women, and Schoppen et al.⁵ found average values of 40.9±12.6 ng/ml in a Group of 18 women who were also healthy and postmenopausal.

With respect to levels of β -CTX, our values are similar to those found by Kanterewicz et al.⁶ in a population of 34 premenopausal women: 0.305±0.150 ng/ml, obtained using the same method used in our study (Elecys, Roche). Martínez et al.⁴, in the aforementioned work found levels (0.387±0.197 ng/ml) higher than ours in a group of 1,080 healthy postmenopausal women, and it was the same case with values obtained by

Schoppen et al.⁵: 0.47±0.14 ng/ml in the group of 18 healthy postmenopausal women.

Conclusions

Given the similarity to those found by other authors in our country, we consider that the values of PINP and β -CTX (36.2±12.9 ng/ml and 0.306±0.121 ng/ml, respectively) obtained in this work may be safely used as normality values for these markers for bone remodelling in Spanish women.

Bibliography

1. Eastell R, Barton J, Hannon RA, Chines A, Garnero P, Delmas PD. Relationship in early changes in bone resorption to the reduction in fracture risk with risendronate. *J Bone Miner Res* 2003;18:1051-6.
2. Álvarez L, Ricos C, Peris P, Guañabens N, Monegal A, Pons F, et al. Components of biological variation of biochemical markers of bone turnover in Paget's bone disease. *Bone* 2000;26:571-6.
3. Peris P, Álvarez L, Monegal A, Guañabens N, Durán M, Pons F, et al. Biochemical markers of bone turnover after surgical menopause and hormone replacement therapy. *Bone* 1999;25:349-53.
4. Martínez J, Olmos JM, Hernández JL, Pinedo G, Llorca J, Obregón E, et al. Bone turnover markers in Spanish postmenopausal women: the Camargo cohort study. *Clin Chim Acta* 2009;409:70-4.
5. Schoppen S, Pérez-Granados AM, Carbajal A, de la Piedra C, Pilar Vaquero M. Bone remodelling is not affected by consumption of a sodium-rich carbonated mineral water in healthy postmenopausal women. *Br J Nutr* 2005;93:339-44.
6. Kanterewicz E, Peris P, Puigoriol E, Yáñez A, Rosique P, del Rio L. FRODOS Research Group. Distribution of serum CTX in a population-based study of postmenopausal women taking into account different anti-osteoporotic therapies (the FRODOS Cohort). *J Bone Miner Metab* 2013;31:231-9.