Dr. Ganesan G Ram
Associate Professor of
Orthopaedics, Sri Ramachandra
Medical College, Tamil Nadu,
India

Dr. PV Vijayaraghavan
Professor of Orthopaedics,
Sri Ramachandra Medical
College, Tamil Nadu, India

Can a urine test predict osteoporotic fracture?

Dr. Ganesan G Ram and Dr. PV Vijayaraghavan

Abstract
Objective: The aim of this study is to find out whether urinary telopeptide measurement can diagnose osteoporosis.
Materials and Method: The study was conducted among patients who come to Sri Ramachandra hospital as inpatient or out patient during the period October 2015 to October 2017. Institutional ethics committee approval was obtained prior to the study. The inclusion criteria for the study were women aged 65 or older, Women age > 60 with risk factors, Younger postmenopausal women with one or more risk factors, (other than being female), Men aged 70 or older and Men > 50 with risk factors and any person having fresh fragility fracture. The patients with confirmed osteopenia/osteoporosis based on DEXA scan forms the case group and age and gender matched control without osteopenia/osteoporosis forms the control group. The results from DEXA scan were taken as gold standard against urinary n telopeptide.
Results: Fifty persons had DEXA normal and became control while twenty osteopenic and forty osteoporotic persons formed the case group. We had 47 persons in cases group (Osteoporotic) having fractures and seven from control group having fracture. The mean value of urinary n telopeptide in cases and control were 182.5 and 49.8 respectively.
Conclusion: Urinary n telopeptide is a dynamic measurement of what is actually happening in bone at any given time. Hence simple urine test - Urinary n telopeptide can be used to diagnose osteoporosis.

Keywords: osteoporosis, DEXA scan, fracture, telopeptide, and osteopenia

Introduction

Osteoporosis is a systemic disease of the skeleton characterized by low bone mass and microarchitecture deterioration of bone tissue leading to bone fragility and susceptibility to fractures [1]. As osteoporosis is asymptomatic early screening and detection helps in a great way in prevention of fractures [2]. At present Common technologies used to examine bone density are plain-film radiographs, quantitative computed tomography, dual-photon absorptiometry, and, more recently, ultrasonography and dual-energy x-ray absorptiometry (DXA). DXA is considered as gold standard now in diagnosing osteoporosis. The aim of this study is to find out whether urinary n telopeptide measurement can diagnose osteoporosis.

Materials and Methods

The study was conducted among patients who come to Sri Ramachandra hospital as inpatient or out patient during the period October 2015 to October 2017. Institutional ethics committee approval was obtained prior to the study. The inclusion criteria for the study were women aged 65 or older, Women age > 60 with risk factors, Younger postmenopausal women with one or more risk factors, (other than being female), Men aged 70 or older and Men > 50 with risk factors and any person having fresh fragility fracture[3]. The risk factors were Low body weight; (BMI < 20), Family history of osteoporosis, Personal history of fragility fracture and/or fracture as an adult, History of fragility fracture in a first-degree relative, Long-term use of glucocorticoids, Current tobacco smoking, Alcohol in amounts > 2-3 drinks per day, Estrogen deficiency at an early age (<45yrs) Low calcium intake (lifelong) and/or Vitamin D deficiency, sedentary lifestyle Testosterone/estrogen depletion in men [4, 5]. The exclusion criteria were any pathological fracture, History of any illness affecting bone metabolism like renal failure, hepatic failure, active malignancy, hyperthyroidism or hyper parathyroidism.

Correspondence
Dr. Ganesan G Ram
Orthopaedics Department,
Sri Ramachandra Medical
College, Porur. Chennai,
Tamil Nadu, India

Person who were willing for the study and comes under inclusion criteria underwent DEXA scan, urinary N telopeptide and blood bone mineral profile tests. DEXA scan was done using GE healthcare Lunar prodigy advance machines. Urinary n telopeptide test was done by ELISA technique. Urine should be collected in an appropriate collection device with a tight fitting lid preferably a second void of the morning (spot) urine specimen or a 24-hour urine specimen. Specimens with visible whole blood contamination or visible hemolysis may interfere with the assay and was discarded. Collection of a new specimen was done in those persons. Sample was Stored refrigerated (2-8 °C) for up to 72 hours or at room temperature for up to 24 hours. Urinary n telopeptide (ELISA) kit utilizes micro wells as the solid phase onto which Ntx has been adsorbed. Ntx in the specimen competes with the solid phase Ntx for binding sites of a monoclonal antibody labeled with horseradish peroxidase. The amount of antibody bound to the solid phase is therefore inversely proportional to the amount of Ntx in the specimen. Quantitation of the Ntx concentration in the specimen is determined spectrophotometrically and calculated from a standard calibration curve. Assay values are corrected for urinary dilution by urinary creatinine analysis and expressed in nanomoles bone collagen equivalents per liter (nM BCE) per millimole creatinine per liter (mM creatinine).

The patients with confirmed osteopenia/osteoporosis based on DEXA scan forms the case group and age and gender matched control without osteopenia/osteoporosis forms the control group. The sample size was calculated to be atleast 43 in each group. The results from DEXA scan were taken as gold standard against urinary n telopeptide. The results obtained was statistically analysed and their normal distribution, the mean, the range and the standard deviation were calculated. The mean values are compared by probability values according to the independent sample test. The 'p' value of <0.05 will be considered statistically significant.

Results

We had totally 110 persons participated in the study. Fifty persons had DEXA normal and became control while twenty osteopenic and forty osteoporotic persons formed the case group as per table 1. From table 2 we had 47 persons in cases group (Osteoporotic) having fractures and seven from control group having fracture.

Table 1: DEXA scan results.

			Groups		Total
			Cases	Controls	
Dexa Scan	Normal	Count	0	50	50
		%	0.0%	100.0%	45.5%
	Osteopenia	Count	20	0	20
		%	33.3%	0.0%	18.2%
	Osteoporosis	Count	40	0	40
		%	66.7%	0.0%	36.4%
Total		Count	60	50	110
		%	100.0%	100.0%	100.0%

Table 2: Fracture patients in both group

			Groups		Total
			Cases	Controls	
Associated with Fracture	No	Count	12	44	56
		%	21.7%	88.0%	51.8%
	Yes	Count	47	7	54
		%	78.3%	12.0%	48.2%
Total		Count	60	50	110
		%	100.0%	100.0%	100.0%

Table 3: Group statistics

Ntx Value	N	Mean	Std. Dev	Std. Error Mean
Cases	60	182.540	159.9683	20.6518
Controls	50	49.839	31.3343	4.4313

Table 4: Independent sample test.

		Levene's test for equality of variances		t-test for Equality of Means						95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference		Lower	Upper
Ntx Value	Equal variances assumed	29.0	.000	5.77	108	.000	132.70	22.99		87.114	178.287
	Equal variances not assumed			6.28	64.3	.0005	132.70	21.12		90.509	174.891

Discussion

DEXA scan have an important role in the evaluation of patients at risk of osteoporosis and currently the gold standard for its diagnosing [6, 7]. Wherever there is radiation there is a chance of danger of cancer related to that. Any accidental exposure of radiation can cause drastic implication. Most of the expense associated with the use of DXA is in the cost of the instrument itself, which is likely to be in excess of $100,000. The possible factors that may alter the results in DEXA were different machines, different location of the same machine, different technician, different people, different positioning, artifacts: this applies to anything seen in the scanners field of vision. This can occur due to digesting calcium pills (often seen in the stomach or intestines on the scan), back arthritis, vertebroplasty as well as with zippers on dresses.

Immunoassays for biochemical markers of bone resorption were emerging that appear to be sufficiently specific and convenient for clinical use [8]. The need for them arises because, as the impact of osteoporosis on the aging population increases and better tools to aid in risk prediction and prevention of osteoporosis was mandatory. Some of the bone biomarkers were total alkaline phosphatase, Tartrate resistant acid phosphatase, c terminal telopeptide of collagen type 1, osteocalcin, Hydroxyproline, Pirydinolin, Urinary n telopeptide etc. The telopeptide were from type I collagens, which form 90% of organic bone matrix and were cross-linked at N and C terminal ends of molecule. In the process of resorption amino and carboxyl terminal fragments of collagen were released. The Ctx is immediately fragmented while Ntx fragments enters the circulation and filtered by kidney, which is the stable degradation end product of bone metabolism [9].

The mean value of urinary n telopeptide in cases and control were 182.5 and 49.8 respectively. Similarly the number of

fractures in the cases group was high compare to the control group. The group statistics from table 3 and independent sample test as per table 4 clearly implies that urinary n telopeptide is statistically significant in diagnosing osteoporosis and fracture. Urinary n telopeptide assessment is being cheaper than DEXA. The cost of single region DEXA scan is around 2500 rupees while urinary n telopeptide Elisa kit is around 1500 only. If urinary n telopeptide test were done more frequently and more in number the kit can be purchased in a much cheaper rate.

Conclusion

Bone density as measured by DEXA provides a static snapshot of bones and does not distinguish if bone loss is ongoing or not. But urinary n telopeptide is a dynamic measurement of what is actually happening in bone at any given time. Hence a simple urine test- Urinary n telopeptide can be used to diagnose osteoporosis.

References

1. Anonymous. Consensus development conference: Prophylaxis and treatment of osteoporosis. Am J Med. 1990; 90:107-10.
2. National Osteoporosis Foundation. What is Osteoporosis and what causes it? https://www.nof.org/patients/what-is-osteoporosis/. Accessed, 2017.
3. Pietri M, Lucarini S. The orthopaedic treatment of fragility fractures. Clinical Cases in Mineral and Bone Metabolism. 2007; 4(2):108-116.
4. Khan AA, Hodsman AB, Papaioannou A, Kendler D, Brown JP, Olszynski WP. Management of osteoporosis in men: an update and case example. CMAJ. 2007; 176:345-8.
5. Shepherd AJ, Cass AR, Ray L. Determining risk of vertebral osteoporosis in men: validation of the male osteoporosis risk estimation score. J Am Board Fam Med. 2010; 23:186-94.
6. Kanis JA, Gluer CC. for the Committee of Scientific Advisors, International Osteoporosis Foundation. An update on the diagnosis and assessment of osteoporosis with densitometry. Osteoporos Int. 2000; 11:192-202.
7. Punda M, Grazio S. Bone densitometry--the gold standard for diagnosis of osteoporosis. Reumatizam. 2014; 61(2):70-4.
8. Kleerekoper M, Edelson GW. Biochemical studies in the evaluation and management of osteoporosis: current status and future prospects. Endocr Pract. 1996; 2:13-9.
9. Jayaram N, Bijoor AR, Rajagopalan N, Venkatesh T. The value of serum and urinary n-Telopeptide in the diagnosis of osteoporosis. Indian J Orthop. 2002; 36:9.