

Incidence of secondary hyperparathyroidism among postmenopausal women with end-stage knee osteoarthritis

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ABSTRACT

Purpose. To evaluate the incidence of secondary hyperparathyroidism (SH) among postmenopausal women with end-stage knee osteoarthritis scheduled for total knee replacement (TKR).

Methods. 283 Caucasian postmenopausal women aged 49 to 81 (mean, 70) years with end-stage idiopathic knee osteoarthritis were scheduled to undergo primary TKR. They had been menopausal for 7 to 31 (mean, 19) years. Their preoperative serum levels of intact parathyroid hormone (I-PTH), calcium, phosphorus, creatinine, and the clearance of creatinine were evaluated.

Results. 100 patients had abnormally elevated serum I-PTH. The overall incidence of SH was 35%. Serum levels of calcium and phosphorus were elevated in 33 and 12 patients, respectively. The serum level of I-PTH correlated positively with patient age ($r=0.158$, $p=0.008$) and serum creatinine level ($r=0.138$, $p=0.021$) and negatively with clearance of creatinine ($r=-0.169$, $p=0.004$).

Conclusion. SH is common among elderly

postmenopausal women and may affect bone healing and implant fixation. Preoperative screening/evaluation of the serum PTH level in postmenopausal women scheduled for TKR is recommended.

Key words: arthroplasty, replacement, knee; hyperparathyroidism, secondary; osteoarthritis; parathyroid hormone

INTRODUCTION

Parathyroid hormone (PTH) is an important regulator of bone metabolism and calcium homeostasis.^{1,2} Continuously elevated levels activate osteoclasts with unknown negative impacts; its intermittent administration induces osteoblast activity and may enhance early fixation of implants with the bone growing on the surface.³⁻⁵

Secondary hyperparathyroidism (SH) manifests as a result of decreased calcium intake, impaired intestinal absorption of calcium due to ageing or disease, vitamin-D deficiency, impaired renal function with diminished 1 α -hydroxylase enzyme availability, or parathyroid gland resistance to

1,25(OH)₂D-facilitated inhibition of PTH secretion.^{6,7} It is a 'silent epidemic'^{6,8,9} among postmenopausal women—the most common group undergoing total knee replacement (TKR). Nonetheless, preoperatively the PTH level is usually not evaluated. We assessed the incidence of SH in postmenopausal women with end-stage knee osteoarthritis scheduled for TKR.

MATERIALS AND METHODS

This study was approved by the scientific research board of our institution. Informed consent was obtained from all patients. Between November 2004 and March 2007, 283 Caucasian postmenopausal women aged 49 to 81 (mean, 70) years with end-stage idiopathic knee osteoarthritis were scheduled to undergo primary TKR. They had been menopausal for 7 to 31 (mean, 19) years. Those with any known endocrine disorder, rheumatoid, or other secondary arthritis were excluded, as were those with end-stage renal disease or failure, because distinguishing primary from secondary hyperparathyroidism in patients with renal disease was difficult.⁵ No patient had had any fracture or orthopaedic surgery in the previous 24 months. Patients with osteopenia or osteoporosis were not excluded, regardless of the receipt of treatment.

Patients were fasting for at least 12 hours before blood sampling one day before the TKR. The serum levels of intact PTH (I-PTH), calcium, phosphorus, creatinine, and the clearance of creatinine were determined.

Data were not normally distributed among groups and therefore the Kolmogorov-Smirnov test was used. Groups were compared using 2-tailed tests. The alpha level was set at 0.05. The correlations between the serum I-PTH level and patient age, serum creatinine level, or clearance of creatinine were determined using the Spearman rank correlation. The independent impacts of weight, patient age, serum creatinine level, and clearance of creatinine on serum I-PTH level were assessed using multiple regression analysis. The extent of the variance of the serum I-

PTH levels was also calculated.

RESULTS

100 patients had abnormally elevated serum I-PTH levels. Two of them were unaware of their occult primary hyperparathyroidism (caused by parathyroid adenomas) and therefore excluded from further analysis. The overall incidence of SH was 35% (98/281 patients). Serum calcium levels were elevated in 33 and low in 4 patients. Serum phosphorus levels were elevated in 12 and low in 6 patients.

The serum I-PTH level correlated positively with patient age ($r=0.158$, $p=0.008$) and serum creatinine level ($r=0.138$, $p=0.021$) and negatively with the clearance of creatinine ($r=-0.169$, $p=0.004$). In multiple regression analysis, 7.3% of the variance in serum I-PTH values ($R^2=0.073$, $p<0.001$) was significant; serum creatinine level was the largest contributor (standardised beta=0.275, $p=0.08$) [Table].

DISCUSSION

Intermittent administration of PTH enhances bone formation by increasing osteoblast numbers and activity, by postponing their apoptosis, and by restricting mineralisation activity.¹⁰ It increases bone density and the contact of regenerating bone with the implant in a dose- and time-dependent manner, thus enabling early fixation.^{4,11} It increases bone strength and incorporation of cemented and uncemented titanium implants,^{12,13} and stimulates implant anchorage in both normal and low-density trabecular bone.¹⁴

Continuous administration of PTH decreases bone mass by activating osteoclasts.³ Bone resorption offsets bone deposition.¹⁵ The negative impact on the synthesis of type-I collagen and bone formation may predispose to a non-satisfactory result.¹⁰ The risk of prosthetic loosening is determined during the first postoperative month^{10,16}; bone loss is most obvious (as high as 54 to 57%) in the first 6 months post TKR.¹⁷

Table
Multiple regression analysis

Variable	Non-standardised coefficients		Standardised coefficients	t	p value
	B	SE	Beta		
Age	0.832	0.468	0.148	1.78	0.076
Weight	-0.230	0.412	-0.040	-0.56	0.576
Creatinine	38.652	14.555	0.275	2.65	0.008
Clearance of creatinine	0.157	0.253	0.083	0.618	0.537

Not only does SH contribute to increased bone loss and skeletal fragility, it also leads to neuromuscular impairment. This increases the risk of falls and periprosthetic fractures in patients with SH undergoing TKR,⁶ as most TKRs were performed regardless of the serum PTH level or bone mineral density (BMD).

This study had limitations. First, the BMD of our patients should have been evaluated using dual-energy X-ray absorptiometry, as those with SH might be liable to osteopenia or osteoporosis.⁶ Second, the Vitamin D status of our patients should have been evaluated, as Vitamin D deficiency may lead to SH, increased bone turnover, bone loss, and even osteomalacia.^{7,9} Third, the follow-up period should have been longer in order to detect any early prosthetic loosening in patients with SH. SH is responsible for the development of irreversible bone

loss.⁷ We therefore aimed to detect and deal with the actual causes of SH in each patient.

SH is common among elderly postmenopausal women,^{6,8,9} and to some extent due to reduced renal functional reserve as people age. Regardless of the actual cause of SH (insufficient daily calcium intake, impaired intestinal absorption of calcium due to ageing or disease, vitamin-D deficiency, prolonged immobilisation or problematic mobilisation, or a combination of all or some of these factors),⁵⁻⁹ bone healing and implant fixation may be affected in such patients. Further (especially multi-centre) studies are needed.¹⁸ Preoperative screening/evaluation of the serum PTH level in postmenopausal women scheduled for TKR is recommended. Patients with SH undergoing TKR should be monitored more closely as they may be at higher risk of periprosthetic fracture and prosthetic loosening.

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