

# Low dose estrogen replacement therapy in early postmenopausal women effect on urinary magnesium and calcium: creatinine ratios

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**Summary:** The purpose of this study was to investigate whether treatment for prevention of osteoporosis by means of postmenopausal hormone replacement therapy (HRP) and daily exercise, had any effect on ratios of urinary calcium:creatinine (Ca:Cre) and magnesium:creatinine (Mg:Cre). A group of 33 early postmenopausal women (menopause onset 12-18 months previously), mean age 49.12 years, were treated during 6 months with low doses of transdermal estrogen (Estraderm TTS 25µg, Ciba-Geigy) opposed by oral progestogen (Duphaston 10 mg, 10 days every month), and daily exercise (walking for 1 hour). Despite HRT's statistically significant lowering effect on Ca:Cre and Mg:Cre ratios, these returned to pretreatment levels 6 months after withdrawal from HRT. The mechanism by which HRT affects magnesuria and calciuria is discussed.

**Key words:** Menopause; Estrogen replacement therapy; Magnesuria; Calciuria.

## INTRODUCTION

A sedentary life style, lack of exercise, dietary problems and hormonal deprivation in postmenopausal women are the

main factors to affect bone resorption and osteoporosis. Hormone replacement therapy (HRT) is the generally accepted treatment.

This study investigated whether HRT in low doses combined with regular daily exercise, could prevent osteoporosis when administered at an early postmenopausal stage. As indicators we used the ratios of urinary calcium: creatinine (Ca:Cre) and magnesium: creatinine (Mg:Cre).

## MATERIALS AND METHODS

Thirty-three healthy women aged 45-52 years (mean age  $49.12 \pm 2.06$  years), with natural mean menopause of 12 to 18 months (mean  $15.09 \pm 2.66$  months), were randomly selected. All were nonsmokers, from mid-high socioeco-

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nomic class, and participated in our study after giving their verbal consent.

Fear of osteoporosis, a subject widely discussed in the media, and not symptoms of postmenopausal syndrome, was the main reason for the women visiting our outpatient clinic.

After confirming the subjects' postmenopausal status by findings of serum FSH higher than 40 I.U./l, and excluding any contraindication for HRT, with the patients acting as their own controls, biochemical tests were conducted before administering HRT. Urinary Ca:Cr and Mg:Cr ratios were assessed in a 24-hour urine collection.

Normal ranges at our laboratory are, for urinary Mg 3.5-6.0 mmol/l, for calcium 100-300 mg/24 hours, and for Cr 1000-2000 mg/24 hr.

After 6 months of HRT and after an interval of 6 more months without treatment, the same analyses were repeated. The study extended over 3 years but individual follow-up lasted 1 year. Methods were described in detail in a recent paper (1).

Treatment for the prevention of osteoporosis consisted of administering twice-weekly doses of Estraderm TTS 25 (a transdermal system from Ciba-Geigy, releasing 25µg estradiol in 24 hours) for 3 weeks, opposed for the last 10 days by daily doses of Duphaston 10 mg (Duphar, Holland), subsequent treatment was given after an interval of one week. The subjects were also instructed to exercise regularly, by walking about 1 hour daily, and doing some aerobic exercises.

Statistical analysis was performed by the Student's t test.

## RESULTS

The treatment was well tolerated. During the 6 months of treatment there was a decrease in urinary Mg:Cr ratio, from  $0.0042 \pm 0.0016$  to  $0.0036 \pm 0.0015$ , which is statistically significant ( $p < 0.01$ ). The Ca:Cr ratio decreased from a mean of  $0.171 \pm 0.061$  to  $0.147 \pm 0.065$ , also statistically significant ( $p < 0.01$ ), (Table 1). Ratios returned to pretreatment level 6 months after completion of treatment.

## COMMENT

Women lose approximately 15% of their bone mass during their first postmenopausal years. This bone loss is associated with a rise in plasma and urinary Ca (2, 3). It is generally believed that the rise in urinary Ca after menopause is secondary to an increased bone resorption, attributed to estrogen deficiency (4).

An alternative explanation is that the rise in bone resorption is secondary to a rise in urine Ca, due to the effect of estrogen deficiency on tubular resorption of Ca (5). This theory is supported by the presence of estrogen receptors in the kidneys (6). According to Nordin *et al.* (5), there is a leak of Ca during menopause which significantly contributes to bone resorption.

Table 1. - Urinary Mg:Cre and Ca:Cre ratios before and at cessation of estrogen replacement therapy (mean  $\pm$  SD).

No. of Subjects	Age yrs	Months after Menopause	Before	at Cessation of Treatment
33	49.12 $\pm$ 2.06	15.09 $\pm$ 2.66		
Mg:Cre			0.0042 $\pm$ 0.0016	0.0036 $\pm$ 0.0015 $p < 0.01$ Df = 32 T = 3.026
Ca:Cre			0.171 $\pm$ 0.061	0.147 $\pm$ 0.065 $p < 0.01$ Df = 32 T = 3.126

More than 300 enzymatic reactions are Mg-dependent<sup>(7)</sup>. Lindsay *et al.*<sup>(8)</sup> found that serum and urinary Mg levels are significantly higher in postmenopausal women, but are reduced by HRT. These authors observed that changes in Mg status are similar to the changes in Ca metabolism. Higher urinary Mg levels are related to increase in bone remodelling and loss of bone mass. A reduction in serum and urinary Mg after HRT supports this argument.

Our findings coincide with Prince *et al.*<sup>(9)</sup>, showing that a combination of HRT and daily exercise may prevent bone loss.

In all the 33 relatively young, postmenopausal participants of our study the urinary Mg:Cr and Ca:Cr ratios were within normal range before treatment, and returned to normal range 6 months after its cessation; with hormonal treatment the ratios were lowered, thus suggesting decreased bone resorption.

Our results are promising. However, the follow-up of a large group of women over a longer period of time is warranted.

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