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Osteoporosis and genetic influence: a three-generation study

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Summary: We have studied 27 triads of mother, daughter and grandmother for possible genetic influence on distal and proximal forearm bone density, measured by single photon absorptiometry.

We found a significant correlation of bone density at the proximal forearm between the mothers and grandmothers ($r = 0.499$, $P < 0.01$). There was also a weak correlation between proximal forearm bone densities of mothers and daughters ($r = 0.327$, $P < 0.1$).

Significant correlations were found between the three generations for grip strength, pedometry, height and triceps skinfold thickness. There was also significant correlation between mother and grandmother for alcohol intake. There was no correlation for contraceptive pill use, smoking, dietary calcium intake, body weight or body mass index.

The study concludes that, although there are similarities in bone mineral content between the three generations, genetic factors cannot be conclusively proven to be the major determinant of bone density. Lifestyle and environmental factors may have a bearing on achieving the peak bone mass and subsequent development of osteoporosis.

Introduction

The risk of osteoporosis is determined by multiple factors.[1] Genetic influence is considered to be one of the major factors determining peak bone mass, which, together with subsequent bone loss, defines the degree of osteoporosis. Osteoporosis is determined by the peak bone mass achieved and the subsequent bone loss.

The importance of genetic influence on bone mineral content has been suggested previously. Black women have higher bone mineral content compared to white women[2] and females of African origin have a lower prevalence of osteoporosis.[3] Further evidence comes from studies of bone density in monozygotic and dizygotic twins[4–6] and relatives of patients suffering with osteoporosis.[7] However, data are scarce regarding bone mineral content across generations in the healthy population and lifestyle similarities have not always been considered.

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Methods and sample

We performed a cross-sectional study of bone density across three female generations in a community setting. We looked at lifestyle factors that could have a bearing on bone density. To our knowledge no study has been performed that has addressed the issue of correlation of bone density across three generations in the healthy population.

We had recruited 560 premenopausal women for a study of bone density in a mixed social class group general practice in Beaconsfield, Buckinghamshire.[8] The subjects had been identified from the age and sex register, and acceptance rate was 70%.

We contacted all the subjects in the earlier study ($n = 560$) by a standard letter inviting them to join this three-generation study of bone density. Entry criteria were that they had a daughter (above 17 years) and mother, both in good health and willing to join the study. Exclusions were subjects in poor health, on hormone replacement therapy, systemic steroids or having pathology that could affect bone density.

We recruited 27 sets of mother, daughter and grandmother for this study. All the subjects were of Caucasian origin and in good health. None of the daughters was pregnant or lactating.

The study involved one visit to the surgery where the subject was interviewed by a research nurse. History regarding contraceptive pills, parity and breast feeding, alcohol intake in units per week (unit = 10G alcohol) and smoking was noted. The weekly intake of calcium from dairy products was estimated by a dietary recall questionnaire.

Height was recorded using a stadiometer, weight by a beam balance and triceps skinfold thickness by Harpenden callipers. Grip strength was measured in the non-dominant arm using a semi-inflated bag connected to an anaeroid barometer. Activity was measured using a pedometer attached at hip level and worn for 24 hours.

Bone density was measured in the non-dominant forearm using single photon absorptiometry. The ND 110B bone scanner with a ^{125}I source has a coefficient of variation of 1-2% for the six measurements at the proximal and four at the distal wrist. Measurements were corrected for soft tissue effect and total bone width.

The study extended over a period of one year and was ethically approved.

Results

The mean ages were: mothers 49.7 (± 3.6), daughters 23.9 (± 4.1) and grandmothers 76.9 (± 6.7). The average values of forearm bone density in mother, daughter and grandmother groups are shown in Table I.

There was no significant correlation between age and proximal or distal bone density within any of the groups. The only significant correlation (Pearson product-moment correlation coefficient) of density between generations was for proximal bone density between mother and grandmother ($r = 0.475$, $P < 0.05$) though a borderline correlation for proximal bone density was also found for the mother and daughter ($r = 0.327$, $P < 0.1$).

We examined data for pedometry, grip strength, triceps skinfold thickness, calcium intake, alcohol, smoking, contraceptive pill use, parity and breast feeding but these showed no significant correlations with bone density.

Between the generations the only significant correlations were between mothers and daughters for triceps skinfold thickness ($r = 0.381$, $P < 0.05$), pedometry ($r = 0.654$, $P < 0.001$), height ($r = 0.386$, $P < 0.05$) and grip strength ($r = 0.384$, $P < 0.05$). In addition there was a borderline correlation for grip strength between grandmother and daughter ($r = 0.361$, $P < 0.1$). Correlation was also found between mother and grandmother for alcohol consumption ($r = 0.406$, $P < 0.05$) and height ($r = 0.717$, $P < 0.01$). Lifestyle variables in the three generations are shown in Table II.

Age showed negative correlations with the grandmothers' grip strength ($r = -0.444$, $P < 0.05$), grandmothers' triceps skinfold thickness ($r = -0.342$, $P < 0.1$) and mothers' pedometry ($r = -0.422$, $P < 0.05$). Multiple regression analysis was carried out to determine whether inclusion of any of these variables could improve the fits for bone density between generations. None were found to give any significant improvement.

Discussion

Our study shows similarities in bone density of grandmothers, mothers and daughters, supporting the concept of genetic factors having effects on bone density.[2-8]

Although our results support the possibility of genetic influence on bone density, nonetheless environmental and lifestyle factors such as physical activity, obesity, smoking, alcohol, parity, breast feeding and the use of contraceptive pills can also influence bone mineral density.

We found significant intergenerational correlation for some of the variables (grip strength, pedometry height and obesity). Indeed these cor-

Table I Age and bone mineral contents (BMC) in mother, daughter and grandmother groups

	Mothers (n = 27)	*Daughters* (n = 27)	*Grandmothers* (n = 27)
Mean age (years)	49.7 (±3.6)	23.9 (±4.1)	76.9 (±6.7)
Age range (years)	45-57	17-31	67-92
Proximal BMC (g/cm)	1.43 (±0.18)	1.41 (±0.16)	1.02 (±0.23)
Distal BMC (g/cm)	1.10 (±0.15)	1.07 (±0.14)	0.08 (±0.20)

Table II Lifestyle variables in the three generations

	Mothers (n = 27)	*Daughters* (n = 27)	*Grandmothers* (n = 27)
Weight (kg)	65.5 (± 10.3)	62.3 (± 10.1)	64.7 (± 19.4)
Body mass index	24.7 (± 4.1)	22.9 (± 2.4)	26.7 (± 6.8)
Alcohol (units/week)	6.5 (± 5.2)	4.2 (± 3.8)	3.0 (± 4.1)
Contraceptive pill use	48%	59%	4%
Smoking	26%	7%	26%

relations were higher than those for bone density. It is possible despite our failure to find significant correlation in multivariate analysis that the correlations for bone density could be explained by similarities in lifestyle, which reflect parental influence rather than the genetic influence.[9,10] Our data do not allow us to distinguish between the effects of nature and nurture.

Although other work has pointed to the significance of a family history of osteoporosis, this effect may be due to lifestyle similarities rather than the genetic factor.

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