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The effect of altered feeding times on bone collagen turnover and the skeletal circadian rhythm.

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Studies of nutrition in relation to skeletal health tend to emphasise average daily dietary composition. However, the timing of nutrient intake may be of physiological relevance. Bone resorption exhibits a marked circadian rhythm with a peak occurring during the night. The mechanisms underlying this rhythm are uncertain. It has been suggested that this circadian rhythm might relate to nutrient intake. The aim of the present study was to examine whether the circadian rhythm of bone resorption is reversed if the feeding pattern is shifted by 12 h.

Ten healthy volunteers (4 males and 6 females, mean age 30 years (range 21–41 years), mean BMI 26 kg/m^2 (range 22–35 kg/m^2)) participated in a two-way cross-over study. Volunteers were studied on two occasions in a randomised order. On one occasion volunteers were given standardised meals at 06.00 hours, 22.00 hours and on the following day at 03.00 hours (snack) and 06.00 hours. On another occasion volunteers were given identical standardised meals at normal 'daytime' feeding times, given at 18.00 hours and on the following day at 10.00 hours, 15.00 hours (snack) and 18.00 hours The 24-hour energy content of the meals was equivalent on both occasions (calculated as approximately 115% of UK Estimated Average Requirements, adjusted for gender). The daily food composition was calculated to be 15% protein, 55% carbohydrate, and 30% fat +/−3% and the participants had free access to mineral water throughout the study. No other foods or drinks were consumed in between these times until the end of the study. On each occasion serum and urine samples were collected three-hourly for 24 hours. We assessed the effect of altered feeding times on the following skeletal variables: serum C-telopeptide of type I collagen (sβCTX) and urinary N-telopeptide of type I collagen (uNTX), both markers of bone resorption and on parathyroid hormone (PTH).

There was a significant circadian rhythm for both control days (peak 03.00–06.00 hours; nadir 12.00–15.00 hours) (cosinor[1], $P<0.001$) and nocturnal feeding (peak 18.00–21.00 hours; nadir 00.00–03.00 hours) (cosinor[1], $P=0.0039$). The mean amplitude was similar for sβCTX and uNTX (103 and 98% for the control group respectively and 58 and 49% for the altered feeding time group respectively). There was also a significant difference in circadian rhythm between the two groups (cosinor[1], $P<0.001$). The effect of feeding on the circadian rhythm of bone resorption was independent of circadian variation in serum PTH concentration.

We conclude that bone resorption exhibits a marked circadian rhythm. A 12 h phase shift in feeding times results in reversal of the circadian rhythm of bone resorption in healthy individuals, suggesting that feeding does influence the circadian rhythm of bone resorption. However an attenuated nocturnal rise in bone resorption with reversed feeding suggests that factors other than feeding may also determine the rhythm. The timing of nutrient intake may be of relevance to skeletal health.

[1] Cosinor analysis is a statistical method used to analyse circadian rhythms. The best fitting model in each individual is characterised by a mean (M), amplitude (A) (the distance from the mean to the peak) and the phase angle (time) of the peak (ϕ). A zero amplitude test assesses whether the amplitude is significantly different from zero (that is, the probability that the data is better described by a cosine curve than by a straight line), which tells us whether the circadian rhythm of each bone markers for each protocol were significant. Also Hotteling's unpaired two-sample test evaluates whether there was any significant differences in the circadian rhythm between the two protocols.