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URINARY HYDROXYPROLINE EXCRETION IN OSTEOMALACIA

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Ever since Westall (1955) first noticed the presence of hydroxyproline in the urine of normal persons, urinary hydroxyproline excretion in normal individuals and its significance in different diseases has been a subject of extensive investigations. It has been shown to vary with age and sex. It is increased in several disorders of bone metabolism such as hyperparathyroidism, hyperthyroidism, acromegaly, Cushing syndrome, metastatic bone disease etc. (Bonadonna et al. 1966, Dull & Henneman 1963, Laitinen et al. 1966, Lee & Lloyd 1964). In osteomalacia (Klein & Curtiss 1964, Kowalessar et al. 1964) there have been stray reports of increased excretion of hydroxyproline in urine. The purpose of this study was to establish whether there was any significant difference in the urinary hydroxyproline excretion in osteomalacia as compared with suitable controls.

MATERIAL AND METHODS

Proven cases of osteomalacia were selected for this study, the diagnosis being established by standard biochemical, radiological and histological criteria. They were kept on meat and collagen free diet for three days. Apart from routine haematological, urine and stool examinations, their serum calcium, phosphorus and alkaline phosphatase estimations were done and their urine was collected. Urine from suitable healthy age and sex matched controls was similarly collected. In all, 31 controls and 38 patients with osteomalacia were studied. Urinary hydroxyproline was estimated by the method of Prockop & Udenfriend (1960). Urinary creatinine estimation was also done in a few cases.

RESULTS

Total hydroxyproline excretion in 24 hours was studied in 30 controls and 28 patients (Table 1).

Table 1. Total urinary hydroxyproline excretion in urine per 24 hours in controls and osteomalacia.

	Min.	Max.	Mean	S.D.	S.E.
Control	9.81	112.50	32.97	21.93	4.0038
Osteomalacia	39.00	410.00	121.2857	87.113	16.462

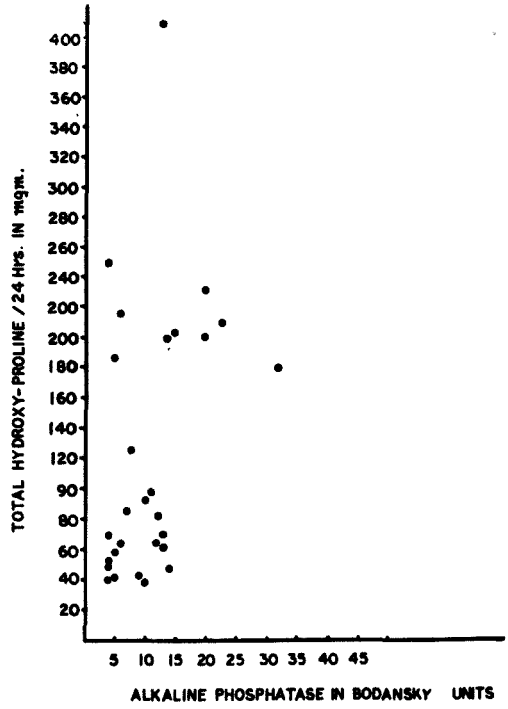

Figure 1. Showing the correlation between serum alkaline phosphatase and total hydroxyproline excretion in urine in mg/24 h ($r = .3808$; $P < .05$).

The total hydroxyline excretion in 24 hours was significantly higher in osteomalacia than in controls ($t = 20.0918$; $P<.001$). Further, the total hydroxyproline excretion was found to correlate well with the serum alkaline phosphatase values in these patients (Figure 1).

In order to avoid pitfalls of 24-hour urine collection, the hydroxyproline/creatinine ratio was calculated in 28 controls and 31 osteomalacia patients (Table 2).

Table 2. Hydroxyproline/creatinine ratio in urine of controls and osteomalacia.

	Min.	Max.	Mean	S.D.	S.E.
Control	.0171	.1057	.0488	.0259	.0049
Osteomalacia	.0400	.0600	.2100	.1510	.0271

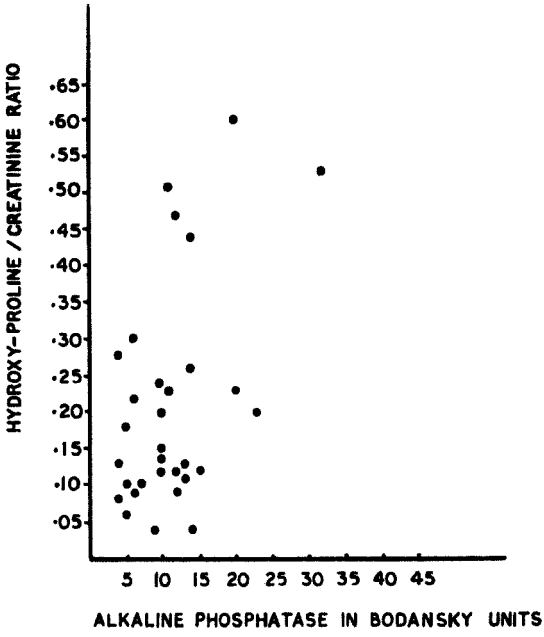

Figure 2. Showing the correlation between serum alkaline phosphatase and hydroxyproline/creatinine ratio ($r = .4922$; $P < .01$).

The difference between the two groups was statistically significant ($t = 3.9035$; $P<.001$). The hydroxyproline/creatinine ratio in these patients was found to correlate well with the serum alkaline phosphatase values (Figure 2).

DISCUSSION

Urinary hydroxyproline excretion in healthy adults on meat and collagen free diet is fairly constant, though it may vary quite a bit from one individual to another. The urinary hydroxyproline is derived mainly from body collagen in such healthy persons. The relationship between

urinary hydroxyproline excretion and bone collagen metabolism has been fairly well established. Dull & Henneman (1963) are of the opinion that the measurement of urinary hydroxyproline excretion may provide a rapid and useful index to the metabolic activity of bone matrix in various diseases. Clinical studies have shown it to be high in diseases where bone matrix is metabolically more active.

In the present study the total urinary hydroxyproline excretion in 24 hours shows a wide scatter in the control series, the maximum being as high as 112.50 mg. However, the mean value is 32.97 mg, which compares well with other published series. Both the 24-hour urinary hydroxyproline excretion as well as the hydroxyproline/creatinine ratio were significantly higher in osteomalacia as compared to the control group. This indicates that the bone matrix in osteomalacia is metabolically more active. Whether this rise is due to increased bone resorption, as held by many authors (Benoit et al. 1963, Bonadonna et al. 1966, Smith & Nordin 1964) or to increased bone formation, as suggested by some (Klein et al. 1966) is difficult to say. The correlation between the total hydroxyproline excretion as well as the hydroxyproline/creatinine ratio with the serum alkaline phosphatase in the present study suggests that urinary hydroxyproline excretion reflects bone formation.

SUMMARY

1. Total hydroxyproline excretion in urine per 24 hours was studied in 28 patients suffering from osteomalacia and 30 controls. It was significantly higher in osteomalacic patients.

2. Hydroxyproline/creatinine ratio was calculated in 28 controls and 31 osteomalacic patients. This was also significantly higher in the latter.

3. Both total hydroxyproline excretion per 24 hours and hydroxyproline/creatinine ratio correlated well with the serum alkaline phosphatase values in osteomalacic patients.

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