

CHRONIC HYPOPHOSPHATEMIA IN THE RENAL HOMOGRAFT RECIPIENT

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ABSTRACT

Tubular dysfunctions of renal homograft cases have been reported from several aspects (1). However, chronic hypophosphatemia of the kidney transplant recipient is a relatively new topic (4). It is encountered frequently and is considered to be very important in differential diagnosis of persistent hyperparathyroidism.

We studied this chronic hypophosphatemia in our intrafamilial renal homograft recipients.

SUBJECTS AND METHOD

Since June, 1972, 109 renal homografts have been transplanted at our two facilities (98 cases from living-related donors and 11 cases from cadaveric donors).

For this series 32 living-related cases were selected who had a minimum follow-up period of longer than one year, stable and good kidney functions (serum creatinine levels below 2.0 mg/dl) and were on regular diet without taking any phosphate-binding antiacids.

The patients were divided into three groups according to their serum phosphate levels (serum and urine phosphate levels were measured by SMA-phosphomolybdate with reduction method).

Group I (hypophosphatemic, serum phosphate below 2.5 mg/dl): 9 cases.

Group II (intermediate, serum phosphate around 3.0 mg/dl): 18 cases.

Group III (normal, serum phosphate between 3.2 mg/dl and 4.4 mg/dl): 10 cases.

The following items were compared in the above three groups: serum calcium levels measured by SMA-OCPC method, tubular resorption of phosphate (% T.R.P.) (3), phosphate excretion index (P.E.I.) (6), twenty-four hour urinary excretion of β_2 -microglobulin (5), serum parathyroid hormone (P.T.H.) (7), and serum $1\alpha\text{-}25(\text{OH})_2\text{D}_3$ (2).

RESULTS

Although the serum calcium levels were compared in these groups, they all were within the normal ranges (between 8.5 mg/dl and 10.5 mg/dl) and showed no significant differences.

The % T.R.P. level displayed remarkable differences in the three groups, and P.E.I.

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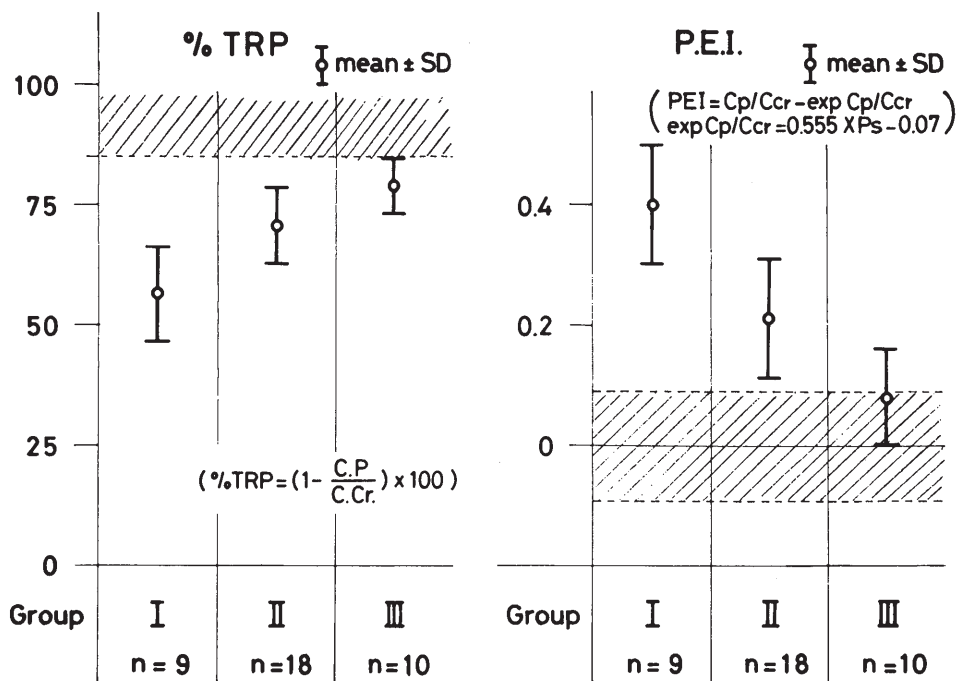


Fig. 1 The shaded areas show the normal ranges.

revealed further differences from the normal values in Group III (Fig. 1).

The results of twenty-four hour urinary excretion of β_2 -microglobulin which is increased in patients with impaired proximal tubular function were shown in Fig. 2. Each dot in the figure indicates the average of more than three values for each patient. Group I showed high values. Group III was close to the normal range and Group II exhibited intermediate values.

In order to rule out involvement of the parathyroid gland and an impaired Vitamin D metabolism, the serum P.T.H. and serum $1\alpha\text{-}25(\text{OH})_2\text{D}_3$, which is the most potent substance of the Vitamin D metabolites, were measured (Figs. 3 and 4). Each dot indicates the average of the two values for each patient. Most cases in each group evidenced a normal P.T.H. level, although each group had sporadic cases with a high P.T.H. value. As for serum $1\alpha\text{-}25(\text{OH})_2\text{D}_3$, all patients of Group I had higher than normal levels (43.3 ± 4.5 pg/ml). Both Group II and Group III patients also displayed at least normal levels of $1\alpha\text{-}25(\text{OH})_2\text{D}_3$.

It is thus concluded from these results that chronic hypophosphatemia in renal homograft recipients is due to the proximal tubular dysfunction of the transplanted kidney which is independent from involvement of the parathyroid gland or inadequate levels of active Vitamin D metabolites.

DISCUSSION

Our interest in chronic hypophosphatemia of renal homograft recipients dates back to 1978 when we transplanted a renal homograft into two uremic patients both of whom had definite

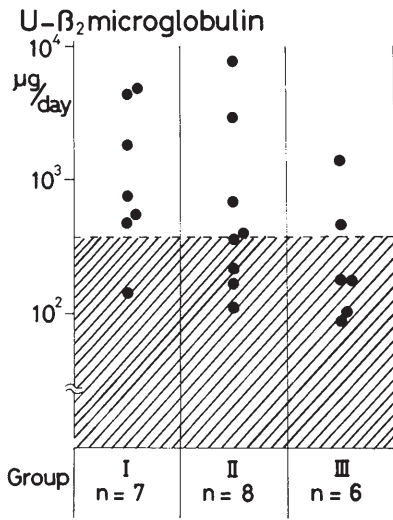


Fig. 2 The shaded area shows normal values.

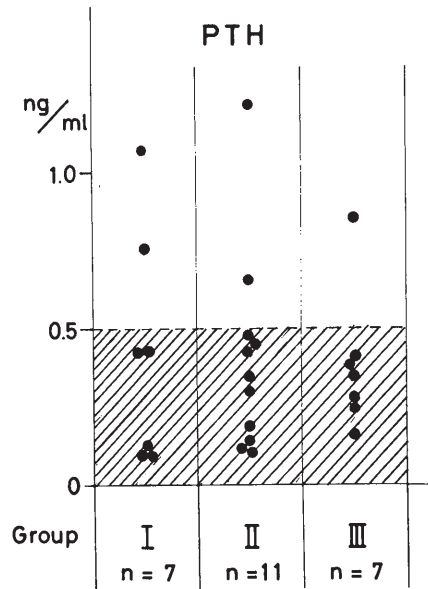


Fig. 3 The shaded area represents normal range.

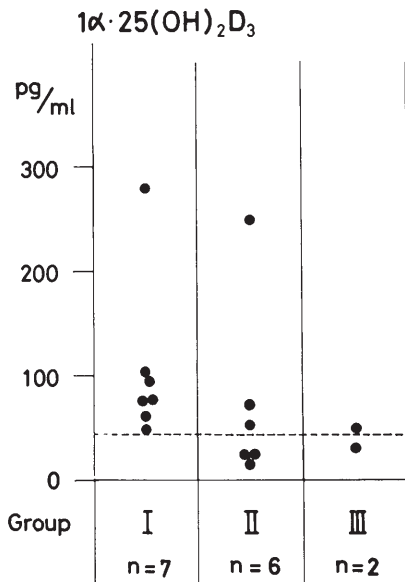


Fig. 4 The dotted line shows normal value.

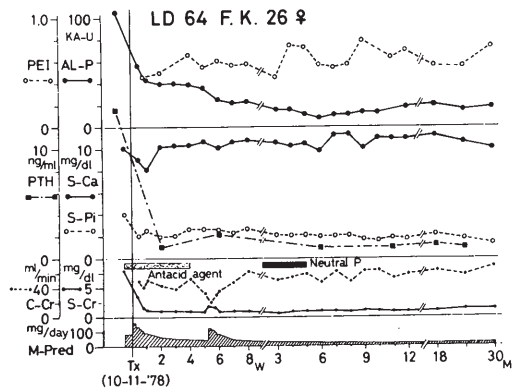


Fig. 5 Post kidney transplant course of LD 64.
 C-Cr : Creatinine clearance
 S-Cr : Serum creatinine
 M-Pred : Methyl-prednisolone (Immuno-suppressive drug)

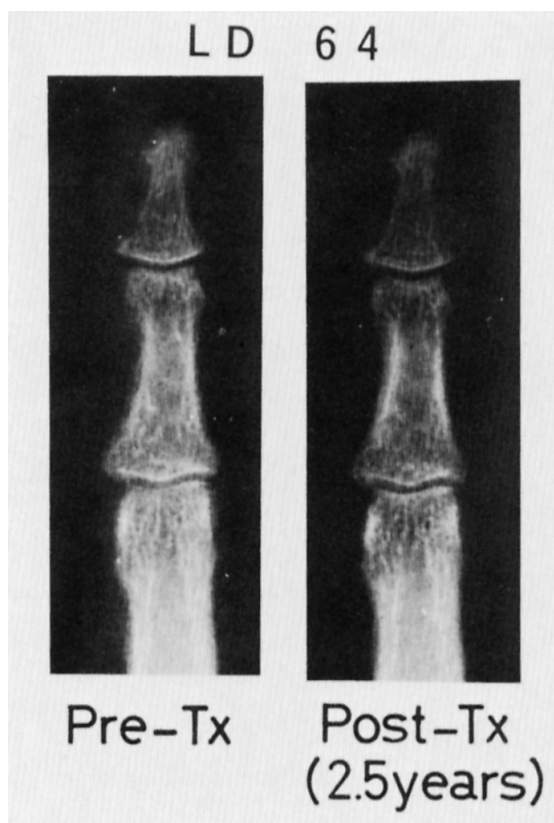


Fig. 6 Roentgenographies of patient's index finger before the transplant and 2.5 years after the transplant.

renal osteodystrophies due to secondary hyperparathyroidism. One of them has shown universal improvement of all the parameters of hyperparathyroidism, including serum alkaline phosphatase, serum parathyroid hormone, phosphate excretion index, and roentgenographic osteodystrophies.

Another case had one rejection episode which was treated successfully and then developed persistent hypophosphatemia associated with high phosphate excretion index (P.E.I.). Such hypophosphatemia was resistant to oral administration of a neutral phosphate substance, but other parameters of the hyperparathyroidism, namely, serum alkaline phosphatase (AL-P), parathyroid hormone (P.T.H.), and skeletal roentgenographies, showed remarkable improvements (Figs. 5 and 6). This patient also had adequate levels of $1\alpha\cdot 25(\text{OH})_2\text{D}_3$ (41.7 pg/ml and 57.8 pg/ml).

These experiences have made us investigate chronic hypophosphatemia in our transplant patients. We have learned that frequent chronic hypophosphatemia in renal homograft recipients is due to an intrinsic proximal tubular defect without involvement of the parathyroid gland and Vitamin D metabolism. Moreover, neither the phosphate excretion index nor the tubular resorption phosphate is a reliable parameter in the follow-up study of persistent hyperparathyroidism in renal homograft recipients.

SUMMARY

The cause of chronic hypophosphatemia in renal homograft recipients was investigated in 32 recipients from living-related donors not on oral phosphate-binding antiacid who had a stable and good graft function with a minimum follow-up of longer than a year. They were divided into three groups (hypophosphatemic, borderline, and normal) according to the serum phosphate levels.

Serum calcium, tubular resorption of phosphate, phosphate excretion index, twenty-four hour urinary excretions of β_2 -microglobulin, serum parathyroid hormone and $1\alpha\cdot 25(\text{OH})_2\text{D}_3$ were measured and compared in the three groups. From these data it was concluded that chronic hypophosphatemia in renal homograft recipients is due to intrinsic proximal tubular dysfunction independent of the parathyroid gland or Vitamin D metabolism involvement. This should be remembered in the follow-up studies of post-transplant hyperparathyroidism.

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