Age-Dependent Phosphate Homeostasis Is Regulated by a Circulating Factor

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Key Words

Phosphate · PHEX gene · Development

Abstract

To evaluate the age-dependent phosphate homeostasis, we studied the serum inorganic phosphate (P_i) concentration in 78 recipients, aged 5–25 years, a year after renal transplantation (RT). The significant age-dependent decline of the serum P_i concentration was observed in recipients ($p < 0.0001$) as well as in normal children. Our study revealed that a circulating factor may play a central role in the age-dependent change of phosphate regulation in human.

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Introduction

During development the serum inorganic phosphate (P_i) concentration is maintained at a higher level than during adult life to meet the needs of the growing organisms. This is seen because tubular P_i reabsorption in the kidney decreases with aging [1]. Although the age-dependence was also observed at the level of NPT2 (the type II

sodium-phosphate cotransporter) protein expression [2], its molecular mechanism remains to be clarified. With the aim of evaluating the age-dependent phosphate homeostasis, we studied the recipients' serum P_i concentration a year after renal transplantation (RT).

Patients and Methods

78 patients, aged 5–25 years, who received living-related RT were enrolled in this study and their serum P_i concentrations were examined a year after RT. They had not been administered vitamin D and phosphate-binding antacids and their graft function at a year after RT was stable. Total ischemia time, warm ischemia time, the frequency of acute rejection, the dosage of steroids and nephrotoxicity by ciclosporin or tacrolimus were not different in any age group. All of the donors were either the recipients' father or mother who were in their twenties to their forties, and their serum P_i level before RT were within normal range (0.81–1.45 mmol/l).

Results

As figure 1 shows, based on Kruskal-Wallis test we observed that the serum P_i concentration at a year after RT decline significantly in correlation with their age ($p < 0.0001$).

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Fig. 1. Relationship between serum phosphate level and recipients' age. Mean $\pm$ SE serum phosphate level in recipients at a year after RT decline age-dependently in Kruskal-Wallis test ($p < 0.0001$).

Discussion

The age-dependent decline of recipients' serum P_i concentration in this study is similar to that of normal children. That is, when adult kidney is transplanted to children, age-dependent phosphate balance is maintained.

A previous study showed that the phosphate regulation in the newborn and infant period is related to change in expression of NPT2 accompanied with nephrogenesis [2]. Moreover, it has been suggested that an age-dependent decline in the PHEX (phosphate-regulating gene with homologies to endopeptidases on the X chromosome) gene may underlie a similar decrease in NPT2 mRNA and protein expression [3]. These studies indicate that the expression of NPT2 through a circulating factor, which might be regulated by PHEX gene, could be associated with age-dependent change of tubular P_i reabsorption in mammalian animals [4]. Our study reveals that it's not the aging of kidney but a circulating factor that may play a central role in the age-dependent change of phosphate regulation in human.

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