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Albumin-normalized serum zinc: a clinically useful parameter for detecting taste impairment in patients undergoing dialysis

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ABSTRACT

Patients with renal failure often experience decreased serum zinc that remains uncorrected after dialysis. A complication of this depletion is taste impairment, which can detrimentally influence diet and nutrition. However, because more than half of all serum zinc is bound to albumin, we hypothesized that normalizing serum zinc to albumin levels may be associated with taste impairment. A total of 65 patients undergoing dialysis but not receiving supplementary zinc and 120 control patients not undergoing dialysis (60 malnourished patients and 60 healthy controls) were tested for their receptiveness to saltiness using various salt concentrations. Patients' total protein and albumin levels were measured, and linear regressions were extrapolated between serum zinc levels and total protein or albumin. Patients undergoing dialysis had significantly lower levels of total serum zinc compared with control patients. However, uncorrected zinc levels were not correlated with taste impairment. Normalizing zinc levels against total protein or albumin resulted in extrapolated equations that revealed a significant correlation with taste impairment. Our data suggest a statistical correlation between zinc and albumin in both healthy subjects and patients undergoing maintenance hemodialysis, or protein-energy malnutrition without hemodialysis, allowing for a quantitative measure for taste impairment.

1. Introduction

Patients with end-stage renal failure often experience severe trace-metal deficiency that cannot be corrected by dialysis [1,2]. In these cases, the diseased kidney has a diminished capacity not only to remove organic solutes from the body but also to monitor subtle changes in the concentration of inorganic compounds that may cause functional or biochemical disturbances [3,4].

Excessive accumulation or depletion of trace elements may have significant clinical implications including increased risk for cancer, cardiovascular disease, immune deficiency, anemia, renal function impairment, and bone disease [5–10]. Because the healthy body is capable of maintaining homeostasis, most individuals are rarely affected by an occasional decrease in these elements. However, accurate quantification of these elements is critical to maintaining the health of patients with underlying chronic diseases because these patients are more

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sensitive to the potential trace-element imbalances that accompany many disorders. Specifically, these patients' abnormal metabolism of macrominerals and trace elements may influence secondary effects and outcomes.

To improve the health and survival of patients with chronic kidney disease and end-stage renal disease, the National Kidney Foundation's, Kidney Disease Outcomes Quality Initiative established reference ranges for calcium, phosphate, and parathyroid hormone serum levels [11]. However, less emphasis has been directed to the presence of other trace metals in patients with chronic and end-stage renal disease.

Zinc is an essential trace element for numerous biological processes including immune function, cell differentiation, and cell replication [12,13]. Although the prevalence of trace metal deficiencies varies in patients on hemodialysis with end-stage renal failure, the rate of hypozincemia in this patient population has been found to be approximately 40% [14]. As with other trace elements, the role of zinc in maintaining necessary biological processes has not been fully elucidated and, as a result, is not part of the standard of care for patients with kidney diseases.

Reports have revealed that serum zinc concentration decreases in patients with renal failure [15,16]. However, these data have not been entirely consistent across studies [5], which may be caused by the body's varied interactions between serum albumin and zinc. Of the total circulating zinc, 32% is tightly bound to a macroglobulin and is not readily lost during dialysis, and so it may be confined within the liver. Of the remaining 68% of circulating zinc, 66% is found to be bound to albumin and 2% is bound to amino acids [17–19]. Thus, of the total circulating zinc, only a small fraction is thought to be chemically active [17,20].

Kidney Disease Outcomes Quality Initiative guidelines recommend that calcium be corrected by albumin in patients with kidney disease, but neglect to provide similar suggestions about other trace elements, especially zinc. One important feature of serum zinc depletion is that it can lead to taste impairment and, ultimately, to reduced caloric intake and malnourishment, which could be possibly caused by zincs' ability to act as a cofactor for metalloenzymes [19,21–26]. Previous research has shown that patients undergoing dialysis have taste impairment and that supplementation with zinc sulfate can improve taste dysfunction [21–24]. However, Ng et al [27] found no abnormality in the taste threshold in patients with chronic renal failure. Furthermore, Henkin et al [28,29] have suggested that zinc sulfate is equal to a placebo in the treatment of taste and smell dysfunction. These differing results demonstrate that serum zinc alone may not be sufficient to determine taste impairment. To reassess this potential relationship, we sought to develop an equation to effectively calculate the relationship between serum zinc levels and taste impairment.

We hypothesized that albumin-normalized serum zinc would improve the correlation between taste impairment. To test this hypothesis, we measured serum zinc, protein, and albumin levels in various patients on and off dialysis, as well as respective controls. These patients were then tested on their salt-taste sensation. These results were then mathematically extrapolated into an equation that could normalize zinc with serum albumin to see whether a correlation existed, providing a clinically useful relationship.

2. Methods and materials

2.1. Subjects

Ethical approval for this study was obtained from the ethics committee of Kawashima Hospital, and each participant and/or his/her legal guardian provided written, informed consent. We enrolled a total of 185 patients who were admitted to Kawashima Hospital in Tokushima, Japan. Patients were divided into 2 groups (Table). The first group consisted of 65 patients (age range, 35-81 years; mean ± SD age, 61.9 ± 12.91 years; sex, 28 men and 37 women) who underwent maintenance hemodialysis at our hospital. The second group consisted of 60 patients who were diagnosed as having protein-energy malnutrition but did not undergo hemodialysis (age range, 38-76 years; mean ± SD age, 63.2 ± 10.94 years; sex, 24 men and 36 women) and 60 healthy control subjects (age range, 19-63 years; mean ± SD age, 25.7 ± 9.89 years; sex, 12 men and 48 women). Malnourished and healthy patients were combined in the control group because patients undergoing hemodialysis could range from healthy to malnourished.

Patients undergoing hemodialysis were dialyzed 3 times a week for 3.5 to 5 hours per session; dialysis duration averaged 11.69 ± 7.53 years. Blood flow rate for patients undergoing hemodialysis was 200 to 250 mL/min, with a dialysate flow rate set at double each patient's blood flow rate (eg, approximately 400 to 500 mL/min).

Most enrolled patients on hemodialysis fasted before blood draws, and all malnourished and control patients fasted. Blood samples were obtained from both fasting and nonfasting patients at baseline and were immediately tested for total plasma albumin, zinc, and copper (dialysis patients' baseline albumin 3.67 ± 0.284 g/dL and total protein 7.7 ± 8.38 g/dL; malnourished patients' baseline albumin 2.36 ± 0.453 g/dL and total protein 6.17 ± 7.66 g/dL; healthy controls' baseline albumin 4.54 ± 0.645 g/dL and total protein 8.53 ± 8.22 g/dL). Samples were tested in accordance with standard methodology: bromocresol green (albumin), atomic absorption spectrophotometry (zinc), and colorimetry (copper).

Table – Baseline chemistry values of subjects

	Controls (n = 120)	Hemodialysis [a] (n = 65)
Sex		
Male	58%	43%
Female	42%	57%
Sodium (mEq/L)	142	140
Blood urea nitrogen (mg/dL)	13.4	17.4
Creatinine (mg/dL)	0.82	3.98[b]
Zinc (μg/dL)	76.4	59.7 [b]
Albumin (g/dL)	3.5	3.7
Total protein (g/dL)	7.4	7.7

Results are given as means and categorical values as percentages.
[a] Hemodialysis values are from patients immediately after hemodialysis.
[b] Significant differences were only observed in creatinine and zinc.