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Brief Report

Intensification of Anemia by Secondary Hyperparathyroidism in Hemodialysis Patients

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Abstract

The excessive amounts of parathyroid hormone in secondary hyperparathyroidism (SHPTH) is suggested to interfere with normal erythropoiesis. In SHPTH, during chronic renal failure, due to the impairment of erythropoietin synthesis, this effect is more pronounced. In the present study the role of secondary hyperparathyroidism in the severity of anemia was evaluated in hemodialysis patients (n=36; 16 females and 20 males) with the end-stage renal failure. CBC, Hgb, Hct, calcium, phosphorus, alkaline phosphatase, intact parathyroid hormone (iPTH), serum iron, total iron binding capacity, transferin saturation, ferritin as well as dialysis adequacy were measured. Partial correlation test was performed for analysis of the data making adjustments for age, duration of hemodialysis and ferritin levels. The mean±SD for iPTH, Hgb and Hct were 439.4 ± 433 pg/ml, 9 ± 1.9 and 28.8 ± 6.3 respectively. The mean duration of hemodialysis for the patients was 25.1 ± 24 months. A reverse correlation was found between iPTH and Hct and Hgb as well as between alkaline phosphatase and Hgb and Hct (0<0.05). It was shown that severity of hyperparathyroidism correlated with severe of anemia. It is concluded that secondary hyperparathyroidism per se can intensify anemia in hemodialysis patients. A more efficient control of hyperphosphatemia and parathormone hypersecretion is thus needed to achieve a better management of anemia in hemodialysis patients.

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Keywords • Anemia • hyperparathyroidism, secondary • erythropoietin

Introduction

Anemia is commonly one of the leading causes of increased cardiovascular morbidity and mortality in patients with chronic renal failure (CRF). In this study we evaluated the role of secondary hyperparathyroidism in severity of anemia in hemodialysis patients. The present investigation is performed on 36 patients (16 females and 20 males of whom 23 were over 40 years old), with end stage renal failure and undergoing regular hemodialysis. Serum calcium, phosphorus, alkakine phosphatase (ALP), Hgb, Hct, urea reduction rate and serum iron, total iron binding capacity, ferritin, transferin as well as intact PTH (iPTH) were measured. None of the patients received ACE-inhibitors, NSAIDS and none had external blood loss or ADPKD. At the end of each dialysis session all the patients

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Table 1: Minimum, maximum and mean±SD of some of the data

Vabiable	Unit	Minimum	Maximum	Mean±SD
Hemoglobin	mg/dl	6	14.5	9 ± 1.9
Hematocrit	%	20	52	28.8 ± 6.3
Ferritin	ng/ml	94	1000	183 ± 4.2
Transferrin Saturation	%	22	100	45.5 ± 18
Urea Reduction Rate	%	49	77	59.5 ± 6.1
Phosphate	mg/dl	3	12	6.6 ± 2.3
Intact Parathyroid Hormone (iPTH)	pg/ml	25	2234	439.4 ± 433.6
Alkakine Phosphatase (ALP)	Iu/L	100	1280	385 ± 227
Calcium x Phosphate	---	30	95	54 ± 16

received an intravenous dose of Eprex 2000U. Descriptive data stratified as mean±SD and partial correlation test was used for adjustment of age, ferritin levels and duration of hemodialysis. The mean duration of hemodialysis was 25.1±24 months. The number of hemodialysis sessions were 3, 2 and once per week for 58, 39, and 3 percent of patients respectively. The mean±SD, minimum and maximum values of our data are presented in Table 1. We found a reverse correlation (Fig. 1) between serum iPTH and Hgb (r=-0.302, p=0.044) and between ALP and Hgb (r=-0.343, p=0.025) as shown in Fig.2. Also a reverse correlation between iPTH and Hct (r=-0.428) and between ALP and Hct (r=-0.309) were observed ($p<0.05$).

The reverse correlation found between iPTH and Hct and Hgb as well as between ALP and Hct and Hgb levels, signify secondary hyperparathyroidism(SHPTH) in hemodialysis patients. These, among other factors, contribute to the severity of anemia in these patients. Trovato, et al[1] in their studies on 45 hemodialysis patients showed a reverse correlation between high degree of anemia and hyperparathyroidism and also a higher requirement of patients with elevated iPTH for recombinant human erythropoietin (r-HuEpo). Neves et al.[2] studying a total of 86 elderly patients with hyperparathyroidism showed that they had lower Hct and Hgb levels compared to younger patients on a similar dose of erythropoietin (Epo). Other studies have shown beneficial effect of parathyroidectomy (PTX) on anemia in hemodialysis patients undergoing treatment for SHPTH.[3,4] Yasunga et al, showed a significant increase of hemoglobin level from three months after PTX, that was associated with a consistent increase in reticulocyte count[5]. Also Fugita et al, reporting on 13 parathyroidectomized hemodialysis patients found a 10% increase in RBC mass after PTX[6]. Moreover, in the

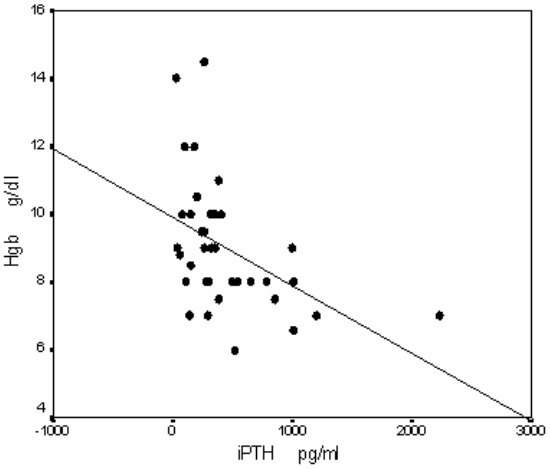

Figure 1: Reverse correlation of iPTH with Hgb (r=-0.520, p=0.001)

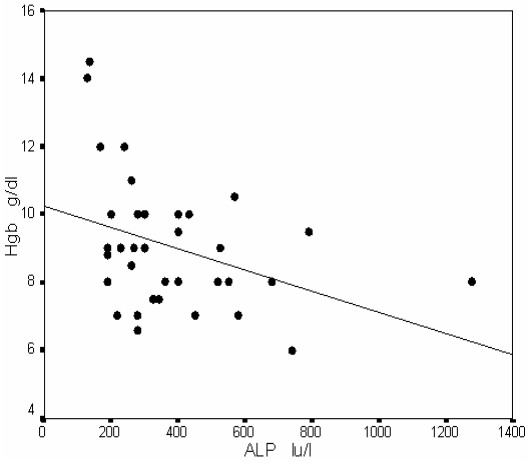

Figure 2: Reverse correlation of ALP with Hgb (r=-0.382, p=0.001)

studies of Grutzmacher[7] and Podjamy[8] a significant increment of Hct was observed following PTX. One of the features of renal osteodystrophy is its refractoriness to treatment with r-HuEpo which can be observed in severe HPTH. In fact, poor response to r-HuEpo in the presence of very high levels of PTH (>500-1000 pg/ml) should prompt radiographic evaluation of the skeleton for SPTH-related osteitis fibrosa. A variety of pathophysiologic mechanisms have been postulated for the contribution of hyperparathyroidism to both anemia and r-HuEpo resistance. In the pre-r-HuEpo era, these centered on a direct toxic effect of PTH on proliferation of red cell precursors in the marrow and antagonism of the effect of endogeneous or exogenous Epo. It is postulated that calcitrol deficiency, direct effect of PTH on Epo release, red blood cell production and loss of erythrocytes, reduce erythropoiesis. Studies of these mechanisms have produced disparate results possibly because SHPTH may have only a relatively minor role in anemia that may be masked by confounding effects of other factors with greater impact. More recent studies have focused on the physical effects of high turnover bone disease on the size of erythron. In the r-HuEpo-treated patients, a clear relationship has been demonstrated between the degree of trabecular fibrosis and r-HuEpo dose. Moreover, the high PTH level could also shift bone cells towards adipocytes. It is suggested that excessive amounts of PTH interferes with normal erythropoiesis by down-regulating the erythropoietin receptors on erythroid progenitor cells in the bone marrow. Therefore, physiologic concentrations of Epo can no longer sustain normal red cell counts with ensuing normocytic normochromic anemia. In primary hyperparathyroidism this effect is observed with very high concentrations of PTH. In SHPTH during chronic renal failure, this effect is more pronounced because Epo synthesis is impaired. attaiing an acceptable Hgb and Hct levels and treatment of SHPTH are two major concerns in hemodialysis centers. Moreover, poor compliance with phosphorus restricted diets, lack of cooperation with regard to using phosphate binders, inadequate hemodialysis, low socio-economic state of some patients and unavailability of newer phosphate binders such as Rena-jel and the drugs decreasing PTH hypersecretion, are problems involved in SHPTH management. Thus, more attention is required to control hyperphosphatemia and PTH hypersecretion with newer drugs which suppress many debilitating side effects of SHPTH, required for the improvement of anemia.

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