CRIMSON PUBLISHERS
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Advancements in
Bioequivalence & Bioavailability

ISSN: 2640-9275

Research Article

Frequency of Anemia and Possible Risk Factors Among Sudanese Children with End Stage Renal Disease

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Submission: September 25, 2018; **Published:** November 13, 2018

Abstract

Background: Anemia is a common Feature of chronic kidney disease, but the management of anemia in children is complex. Erythropoietin and Supplemental iron are used to maintain hemoglobin levels. The aim of this study to determine the Frequency of anemia and possible Risk Factors Among children with End stage renal disease.

Methods: A total of 96 children, 61males (63.5%) and 35 Females (36.5%), were attended at hemodialysis units in Khartoum state were enrolled in the study and Frequency of anemia was estimated by analyzing CBC on blood counter (sysmex). The concentration of iron profile, C-reactive protein and parathyroid hormone was measured using COBAS INTEGRA 400 PLUS and COBAS E411.

Results: 99% of children were anemic, 4.17% of them were suffering from iron deficiency anemia and there are other causes contributing to anemia in ESRD patients which are inflammation and hyperparathyroidism.

Conclusion: The prevalence of anemia in children on hemodialysis in Sudan appears to be higher than that reported in other studies despite extensive use of rHuEPO and iron supplementation.

Keywords: Hemodialysis; Anemia; Erythropoietin; Hemoglobin; Iron; Parathyroid hormone; Children; Khartoum; Sudan

Introduction

Anemia is major complication of end –stage renal disease (ESRD) in children [1]. When severe, it is associated with cardiovascular dysfunction, cardiomyopathy, and death [2] Correction of anemia in children with ESRD improves cardiac dysfunction exercise tolerance and reduces left ventricular hypertrophy [2]. approximately 25% of adult patients maintained on chronic hemodialysis have anemia. Anemia is defined by the National kidney Foundation Dialysis Outcome Quality initiative (K/DOQI) as a hemoglobin value less than 11g/dl [3]. More than 75% of children with anemia maintained on chronic hemodialysis exhibit signs of left ventricular hypertrophy, a harbinger of cardiovascular morbidity in adulthood [4]. The major cause of anemia in patients with chronic kidney disease and end stage renal disease (ESRD) is erythropoietin (EPO) deficiency, resulting from its decreased production from the kidneys [2]. The remarkable development and subsequent introduction of recombinant human erythropoietin (rHuEPO) in 1989 made it possible to safely and effectively treat the anemia of renal insufficiency and practically eliminate the need for repeated transfusion [5] Despite the advances in dialysis care and the use of erythropoietin, anemia continues to be a clinical problem seen in patients with ESRD [3]. It was believed that iron deficiency was the major predictor of EPO hypo responsiveness [6]. Despite the extensive use of erythropoietin and iron supplements, over one third of children aged between 12 to<18 maintained on chronic hemodialysis have a mean hemoglobin of less than 11g/dl [6]. Other factors that have been shown to influence the response to rHuEPO in adult and pediatric patients on dialysis include dosage, route of administration, acute of chronic infection and aluminum intoxication [1]. Refractory anemia appears to be more common in those patients on dialysis who also suffer from protein-energy malnutrition (PEM) or inflammation [6]. Secondary hyperparathyroidism contributes to resistance of rHuEPO in adults [1]. Craig et al showed when serum PTH were markedly elevated in pediatric patients, response to rHuPO will be poor [1].

Rationale

Accurate diagnosis of anemia and iron deficiency is essential in hemodialysis patients, since these conditions are prevalent during chronic disease. Understanding the etiology of anemia and iron deficiency in hemodialysis patients can help health care providers in managing the anemia, which in turn improves their quality of life. Also, there is no published data regarding this study in Sudan.

Objectives

General objective

To determine Frequency of Anemia, iron deficiency anemia and Possible Risk Factors among Children with End-stage of Renal Disease attending Pediatric Hemodialysis Units in Khartoum State.

Specific objectives

A. To determine frequency of anemia by measuring hemoglobin concentration for children with end-stage of renal disease.

B. To determine the presence of iron deficiency anemia among anemic children by measuring iron profile.

C. To find out if there is any correlation between (duration of hemodialysis, level of PTH and level of CRP) and degree of anemia.

Material & Methods

A cross sectional study was conducted in at Soba University hospital, Khartoum children hospital and Omdurman children hospital. Khartoum, Sudan during the period of January 2014 to August 2016.The study population consisted of 96 patients on chronic hemodialysis from pediatric hemodialysis centers. All the patient-specific parameters were recoded, including Age, gender, duration of dialysis (6 month vs.6 months or longer). Blood studies were performed immediately pre-dialysis. Complete blood count, serum iron, ferritin, total iron binding capacity, Transferrin, Transferrin/saturation %, Intact parathyroid hormone (PTH), C-reactive protein were measured. Data on patient rHuEPO dose (unit/Kg/week), and oral iron (mg/Kg) or administration of intravenous iron (mg/Kg/week) were obtained from dialysis charts. All routine laboratories measurements were performed by Sysmex Kx- 21 N using automated methods. Serum Iron profile, intact PTH and CRP were performed by COBAS INTEGRA 400 Plus and COBAS E411. Serum CRP was obtained to indicate the presence of an inflammation state. Anemia was defined as a hemoglobin value less than 11g/dl and severe anemia defined as hemoglobin value less than 8g/dl. Iron deficiency was defined as ferritin ≤100ng/dl or the percentage transferring saturation less than 20% and mean corpuscular (MCV) less 75fl. Serum intact PTH>200pg/ml was considered as high turnover bone disease secondary to hyperthyroidism. The results were analyzed using the statistical Package for Social Sciences (SPSS) program and expressed as mean and standard deviation.

Ethical clearance

The study received ethical clearance from the Research Board at Faculty of Medical Laboratory Sciences, University of AlZaiem AlAzhari, after that the approval from health authorities at the ministry of health in Khartoum was obtained.

Results

The Study group was composed of patients Aged between (5-17 years) (31 Patients were less than 12 years and more 65 patients more than 12 years). The mean age of patients on hemodialysis was 13.2±3.2 years. There were 61 males (63.5%) and 35 females (36.5%). Mean duration of hemodialysis was 28.7±25.6 months (Table 1). Packed cell volumes of most of the patients were less than normal. The mean hemoglobin was 7.38±1.86 (Table 1). Thirty-two patients (34%) had hemoglobin value less than 11g/dl (anemia) and 65% (62 patients) had hemoglobin value less than 8g/dl (severe anemia) (Table 2). One of 4.17% of anemic children had mean transferrin saturation (TSAT) less than 20%. Absolute iron deficiency (defined as a TSAT of less than 20% and a ferritin less than 100ng/ml) was only seen in 4 patients (Figure 1 & Table 3).

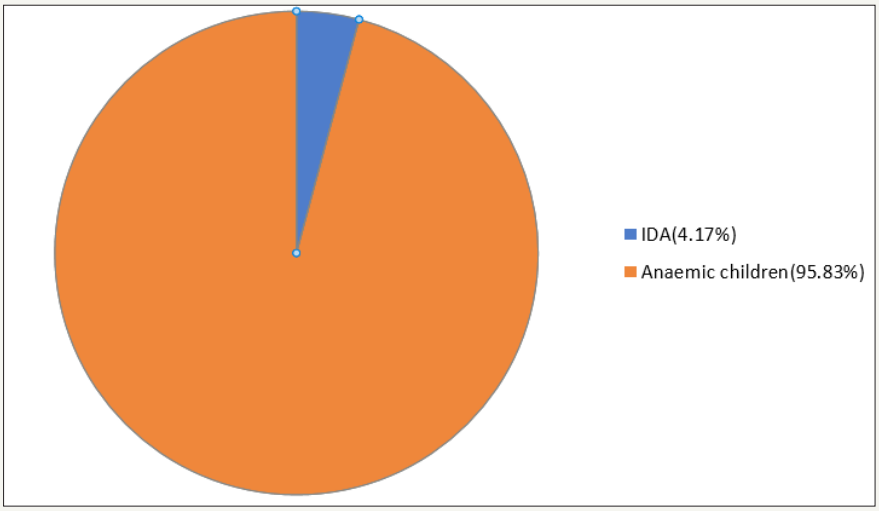

Figure 1: Frequency of anaemia and IDA among children with End stage of renal disease.

Table 1: Mean of age, duration of hemodialysis and hematological parameters among children with End stage of renal disease.

Variable	Mean	Std. Deviation
Age/Years	13.23	3.26
Duration of Dialysis/Months	28.75	25.63
TWBC (cmm)	5.12	20.82

How to cite this article: Abdelmageed A, Abdelrahim M, Muddathir, Rashid A E. Frequency of Anemia and Possible Risk Factors Among Sudanese Children with End Stage Renal Disease. Advancements Bioequiv Availab. 2(1). ABB.000527.2018. DOI: 10.31031/ABB.2018.02.000527

Hb (g/dl)	7.38	1.86
PCV (%)	22.93	5.59
MCV (fl)	85.96	4.91
MCH (pg)	27.63	1.92
MCHC (g/dl)	32.14	1.38
PLT (109 l)	205.81	55.6

Table 2: Frequency of anemia and IAD according to the severity of anemia.

Variable	Anemia Severity		
	Hb<8	Hb 8 to 11	Hb<12
Number of Children	62	32	2
Anemic %	65%	34%	1%
Number of IDA	4	0	0
Iron deficiency%	4.17%	0.00%	0.00%

Table 3: Mean of C-reactive protein and PTH among children with End stage of renal disease.

Variable	Mean	Std. Deviation
CRP (mg/dl)	19.36	40.84
PTH (pg./ml)	148.07	243.53

Discussion

Despite the extensive use of erythropoietin and prescribed iron supplements, over 99% of children maintained on chronic hemodialysis and a mean hemoglobin less than 11g/dl. Patients new to dialysis (treated less than 6 months) were more anemic. Frankenfield et al. [3] showed that 37% (160/435) of HD patients aged between 12 and less than 18 years were anemic in the National 2001 ESRD Clinical Performance Measures Project. Fadrowski et al. [3] demonstrated that more than one third of pediatric patients on dialysis were anemic during the project years of 2000 and 2001 [7]. The 2001 North American Pediatric Renal Transplant Cooperative Study annual report showed that 63% of 1855 pediatric patients on chronic dialysis who were receiving rHuEPO at 6 months of dialysis had hematocrit values of ≤33%(≤11gldl) [8]. In our study more than 99% of patients were anemic. The recommended starting dose of rHuEPO is 50-150U/Kg given three times weekly [2]. Our patients received a mean weekly rHuEPO doses of 158U/Kg, these doses were significantly higher than those received by adults.

Fadrowski et al. [3] showed that an increase in age and dialysis for less than 6 months were 2 factors that enhanced anemia [8]. There was no correlation between age, gender and anemia in our study but patients new to dialysis (treated less than 6 months) were more anemic. Some patients did not respond to rHuEPO therapy even if high doses were used. The main reason for EPO resistance is iron depletion or insufficient access to iron depletion or insufficient access to iron storage pools [9]. Almost all our patients had iron supplements. There are no standards for iron adequacy in concentration >100ng/ml and percentage transferrin saturation of >20% [10]. Serum ferritin >10ng/ml and percentage transferrin saturation as low as 7% are considered normal for healthy children [11]. Serum ferritin >40ng/ml has been reported to be adequate in children on dialysis [12]. According to protocol of adult on dialysis only 4 of our patients had iron deficiency anemia. Severe secondary hyperparathyroidism appears to be an important factor in the severity of anemia in children with chronic renal failure [1]. PTH may be a direct inhibitor of endogenous erythropoietin production [13].

Another mode of action of PTH in ESRD is an increase in red blood cell osmotic fragility, leading to a decrease in red blood cell survival time [14]. Synthetic PTH or serum from hyperparathyroidism patients has been reported to inhibit red blood cell precursors in vitro in some studies [15]. Likewise, hyperparathyroidism may also affect anemia by causing bone marrow fibrosis which reduces the available space for erythroid- forming units [16]. A serum PTH level at 200pg/ml has been shown previously to be strongly predictive of osteitis fibrosa in children [17]. PTH effect on erythropoiesis can be overcome by higher doses of rHuEPO. PTH level at more than 200pg/ml was seen in 14 our patients and 10 of them had PTH level at more 400pg/ml in our study. Several previous studies reported an association between anemia and inflammation in patients on dialysis. Reflected by a high serum concentration of CRP [18]. More cover, IL and TNF-alpha have been shown to inhibit EPO production in vitro and have a suppressive effect on erythropoiesis [19,20]. Uptake of iron is lower than normal in inflammation [21]. Serum level of ferritin a marker of iron stores and appositive acute-phase reactant have been shown to be paradoxically high in patients with ESRD with refractory anemia [22,23]. Increased ferritin production may prevent iron delivery to erythrocyte precursors [22]. Finally, patients with inflammation may be more prone to gastrointestinal bleeding [21]. In this study inflammation existed in 15 patients in which serum ferritin was more than 2000ng/ml in 8 of them.

Conclusion

Frequency of Anemia is high despite of EPO therapy. Frequency of iron deficiency anemia is less compared to Anemia as most of the patients were in iron therapy. Sever hyperthyroidism, malnutrition and inflammation should be considered as other causes (risk factors) of anemia in this study. The results of this study indicate the need for continued improvement in the management of anemia in children undergoing chronic hemodialysis.

Acknowledgement

We are very thankful to all patients participated, to their families, to Pathology department staff at SUH and to Mr. Mosab Nouraldein.

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