EFFECT OF ZINC SUPPLEMENTATION ON ANEMIA AMONG PATIENTS ON REGULAR MAINTENANCE HEMODIALYSIS

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ABSTRACT

Background: Zinc deficiency was reported in patients with chronic kidney disease especially among patients on hemodialysis. The objective was to assess the effect of zinc supplementations on the correction of anemia in those patients.

Patients and Methods: In this study, a total of 105 patients over 18-year old, stable and over 6 months on maintenance hemodialysis were enrolled. Blood samples were collected for biochemical and hematological assessments. The patients with zinc deficiency and anemia of chronic disorder were divided randomly into two groups and completed the study. Group 1 completed their treatment with the addition of zinc to their treatment as food supplementation (elementary zinc 50 mg/day) for 6 weeks and the other without zinc supplementation as a control group. Data collection carried out during the period from 8th January to 1st June 2019 at the kidney diseases center in Duhok city–Kurdistan region/Iraq. Serum zinc level and anemia parameters were determined.

Results: The patients in group 1 that received zinc supplementation showed a significant increase in the mean of serum zinc (mean of percentage 43.12 %) and correspondingly the mean of hemoglobin (mean of percentage 13.06 %).

Conclusion: There was a positive relationship between increase zinc level and the correction of anemia.

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Keywords: zinc, anemia, chronic kidney disease, hemodialysis.

Chronic kidney disease (CKD) is a type of renal disease in which there is a gradual loss of kidney function through months to years. In 2015, 1.2 million deaths are caused by CKD while it was in 1990 around 400,000[1]. There are 5 stages of CKD and the severity of symptoms increased with the progression of the disease. Many factors are contributed to the causing and progression of CKD; like hypertension and diabetes mellitus. The management of the disease is stage-dependent. Hemodialysis is a modality of dialysis that used in managing the end-stage renal disease. Anemia is one of the common complications that worsen with the progression of the disease[2]. Many causes lead to anemia in CKD like iron, folate, vitamin B12 deficiency[3], gastrointestinal bleeding, systemic inflammation, and decrease RBC's life span[4]. Lack of erythropoietin production (a glycoprotein which is necessary for the growth and differentiation of RBC in the bone marrow) by the kidney is the most important and specific etiology causing CKD-associated anemia[5]. Zinc is an essential trace element which is available in approximately 300 specific enzymes with little toxicity in human[6]. Zinc has important physiological functions; including gene expression, immune function, protein synthesis, and behavioral responses[7]. Zinc deficiency has reported in

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40% to 78% of patients with chronic renal failure[8] and may affect disease progression especially diabetic nephropathy[9]. Changes in zinc reservoirs in the body, decreased absorption by the gastrointestinal tract, a decrease in its intake, owing to the fact that dietary restrictions for these patients limit the consumption of foods richer in zinc leading to zinc deficiency[10,11]. The hemodialysis mechanism also leads to more zinc excretion during the filtration process[12]. There are few studies about the zinc status among patients on maintenance hemodialysis and no study about the effect of zinc supplementation on anemia in those patients in Iraq, especially Duhok governorate.

METHODS

Design

This study was carried out from 8th January to 1st June 2019 at the kidney diseases center in Duhok city/Kurdistan region/Iraq. A total of 105 patients (42 males and 63 females) with stable clinical conditions, over 18 years old and more than 6 months duration on maintenance hemodialysis were enrolled in this study. Ten milliliters of the blood sample was obtained from each patient before starting the dialysis, by venipuncture for biochemical [zinc, iron, total iron binding capacity (TIBC), and ferritin] and hematological [hemoglobin (Hb), red blood cell (RBC) counts, and packed cell volume (PCV)] assessments. It was a randomized control study in which 63 patients with zinc deficiency and anemia of chronic disorders were selected. Eight patients were missed from the study due to many reasons. The remaining 55 patients were divided randomly into two groups. Group 1 included 28 patients (10 males and 18 females) and group 2 included 27 patients (9 males and 18 females). Group 1 assigned to receive 50 mg elemental zinc once a day for 6 weeks period as an add on treatment, while group 2 finished the period of study without zinc supplementation as a control group. The laboratory tests were repeated for the entire 55 patients at the end study period. Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 22). A *p*-value of $\leq$ 0.05 was considered statistically significant.

RESULTS

The zinc-treated patients showed a significant increase in the mean of the serum zinc level from 48.25 µg/dL to 68.11µg/dL ($p<0.001$) and the mean of hemoglobin from 8.16 g/dL to 9.17 g/dL ($p< 0.001$). Other parameters are explained in table 1.

Table 1: mean ±SD of serum zinc and related parameters in hemodialysis patients before and after zinc supplementation in the zinc-treated group (n=28).

	Before zinc supplementation		After zinc supplementation		*p*-value
	Mean	SD	Mean	SD	
Hb (g/dL)	8.16	1.30	9.17	1.43	< 0.001
RBC (10^{12}/µL)	2.68	0.50	2.84	0.50	0.040
Ferritin (ng/mL)	763.00	765.37	605.86	551.79	0.043
Iron (µg/dL)	61.46	30.21	59.54	26.33	0.601
TIBC (µg/dL)	220.29	60.62	202.70	56.68	0.264
PCV%	24.96	4.25	25.71	4.87	0.042
Zinc (µg/dL)	48.25	9.41	68.11	13.52	< 0.001

The other group that completed their management without zinc supplementation as a control group showed a significant decrease in the mean of hemoglobin from 8.96 g/dL to 8.16 g/dL (p<0.001). Table 2 illustrated the parameters in the first visit and after 6 weeks for the control group.

Table 2: means +SD of serum zinc and related parameters in hemodialysis patients in the first visit and after 6 weeks of the control group (n=27).

	First visit		After 6 weeks		*p*-value
	Mean	SD	Mean	SD	
Hb (g/dL)	8.96	1.14	8.16	1.16	< 0.001
RBC (10^{12}/µL)	2.91	0.46	2.72	0.47	0.001
Ferritin (ng/mL)	578.40	724.55	523.00	571.29	0.373
Iron (µg/dL)	71.33	26.51	59.19	37.26	0.035
TIBC (µg/dL)	239.19	46.88	228.56	56.80	0.086
PCV%	27.08	3.51	24.93	3.77	< 0.001
Zinc (µg/dL)	47.44	9.55	47.11	8.58	0.831

In the comparison between the two groups, regarding different parameters, the statistical analyses proved the presence of significant differences between the two groups with the favor for the zinc-treated group. The comparisons are illustrated in table 3.

Table 3: means of percentages of change in blood tests between the study groups.

Percentage *	Group	N	Mean	±SD	SE	*P*-value
Hb	Zinc	28	13.06	±13.29	2.51	< 0.001
	(control)	27	-8.88	±7.93	1.53	
RBC	Zinc	28	7.22	±16.17	3.06	< 0.001
	(control)	27	-6.66	±9.36	1.80	
Ferritin	Zinc	28	-16.27	±144.65	27.34	0.434
	(control)	27	-6.37	±36.92	7.11	
Iron	Zinc	28	3.37	±37.17	7.02	0.055
	(control)	27	-16.33	±37.30	7.18	
TIBC	Zinc	28	-2.74	±26.70	5.05	0.753
	(control)	27	-4.52	±12.13	2.33	
PCV	Zinc	28	3.46	±13.86	2.62	0.001
	(control)	27	-7.86	±9.33	1.80	
Zinc	Zinc	28	43.12	±24.69	4.67	< 0.001
	(control)	27	-0.69	±19.00	3.66	

*(Reading after–Reading before)/ Reading before * 100

The figures 1 and 2 show the correlation coefficient (r-value) between zinc-Hb and zinc- PCV among patients after 6 weeks from treating with zinc supplementation (group 1) which was weak and non-significant.

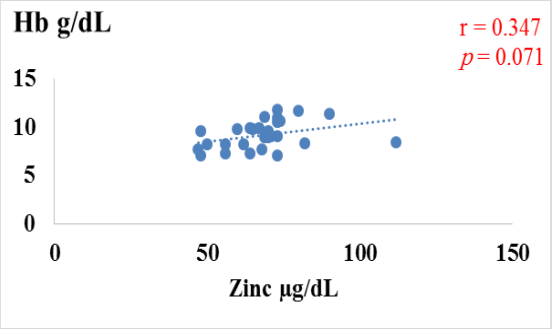

Figure 1: Scatter plot of a correlation coefficient between zinc-Hb in group 1.

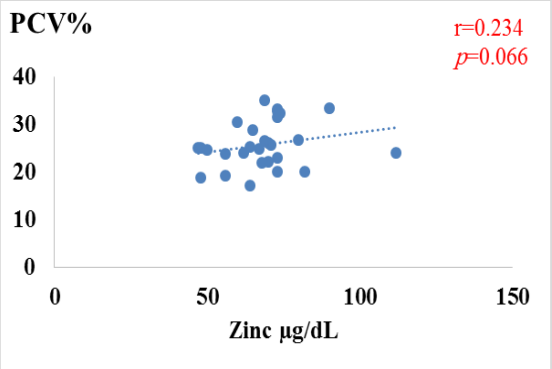

Figure 2 Scatter plot of a correlation coefficient between zinc-PCV in group 1.

DISCUSSION

Over the last few decades, anemia with CKD poses a big concern because of the high rate of morbidity and mortality associated with anemia. The demand is therefore increasingly being placed on the treatment of anemia in patients with CKD, especially those on regular maintenance dialysis [13,14]. The results at the end of the present study showed that the zinc-treated group had a significant increase in the mean serum level of zinc from 48.25µg/dL in day 0 to 68.11µg/dL after 6 weeks (p< 0.001). This result was in agreement to that reported on 38 hemodialysis patients in Nemazi Hospital/Iran in which the mean of zinc was improved significantly from 53.27 µg/dL to 80.38 µg/dL (p< 0.05) [15]. Furthermore, in this study significant increase was found in the mean of hemoglobin after zinc supplementation from 8.16 g/dL to 9.17 g/dL (p < 0.001). This result was also reported in the Iranian study in which the mean of hemoglobin was increased significantly from 9.3 g/dL to 10.1 g/dL (p<0.05) [15]. In the hemodialysis patients, low zinc status may be a possible causative factor for anemia, especially those with erythropoietin-refractory/non-responsive anemia [16]. On the other hand, there was a significant decrease in the mean of ferritin from 763 ng/mL to 605.86 ng/mL (p = 0.043). Since zinc acts as an anti-inflammatory agent, the increase in the plasma zinc concentration may lead to a decrease in the inflammatory condition in patients and this idea is agreed with a study that shows the inverse relationship between zinc concentration and C-reactive protein and inflammatory cytokines after zinc supplementation [17,18]. So, the ferritin as an acute phase reactant protein decreased significantly because of zinc level correction. In the group 2 (control group), the results show that the mean of zinc level was non-significantly decreased from 47.44 µg/dL at day 0 to 47.11 µg/dL after 6 weeks (p = 0.831). This result is agreed with that reported by Rashidi on control group of Iranian patients which declined from 51.9 µg/dL at day 0 to 51 µg/dL after 42 days (p = 0.097), while the mean of hemoglobin showed a significant decrease

from 8.96 g/dL to 8.16 g/dL after 6 weeks ($p< 0.001$) and this result is not the same that noticed in the study of Rashidi that showed no change in the mean of hemoglobin in the control study after 42 days [19] and this decline may be caused by the lack of proper nutritional support and ineffective dialysis. These analytical results of each group individually revealed that the zinc-treated group has beneficial effects in the management of anemia in that period time in comparison to the control group, although the mean of zinc was not reached the normal range and still the mean of hemoglobin refers to anemia. The results of zinc-treated group manifested a better correlation coefficient but still weak and non-significant in the relationship between zinc with hemoglobin and PCV ($r = 0.347$, $p = 0.071$) ($r = 0.234$, $p = 0.066$) respectively. This weak relationship happened may be due to the small sample size of the zinc-treated group (28 patients). In conclusion, this study showed a high positive impact of zinc supplementation on the correction of anemia among maintenance hemodialysis patients.

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پوختە

کارتێکرنا پێدانا زەنك (توتیا) ل سەر کێم خوینیێ لنك نەخۆشێن دیلزەیا خوێناوی یا رێکخستی

پێشەکی: حالەتێن کێمیا زەنکی (توتیا) هاتە توماركرن لنك وان نەخۆشان ئەوێن توشی نەخۆشیا گولچیسکا یا دوم درێژ بووین ب تایبەت دناڤبەرا نەخۆشێن دیلزەیا خوێناوی. ئارمانج ژ ڤەکولینێ هەلسەنگاندنا کارتێکرنا زەنکی یە وەك تەمامکەرەکێ خوراکی ل سەر راستڤەکرنا کێم خوینیێ دناڤبەرا نەخۆشێن دیلزە یا خوێناوی.

نەخۆش و رێك: دڤێ ڤەکولینێدا، (105) نەخۆش هاتنە توماركرن کو تەمەنێ وان ژ 18 سالان زێدەترە، ل سەر تەختەبەندی سەقامگیرن و پتر ژ (6) هەیڤان ل سەر دیلزەیا خوێناوی. نموونەیێن خوینێ هاتنە کۆمکرن بو هەلسەنگاندنێن کیمیا ژیانێ و خوێناوی. پاشی دابەشکرنا وان نەخۆشان ئەوێن توشی کێمیا زەنکی و کێم خوینێ بووین ژبەر نەخوشیێن دوم درێژ بو دوو کومەلان و ڤەکولین هاتە تەمامکرن، کومەلا ئێکێ چارەسەرکرنا خو تەمامکر ب زێدەکرنا زەنکی بو چارەسەرکرنا وان وەك تەمامکەرەکێ خوراکی (زەنك 50 ملگم/ روژ) بو دەمێ (6) حەفتیان و کۆمەلا دووێ یێ تەمامکەرێ زەنکی وەك کۆمەلەکا چاڤدێر. پاشی داتا هاتنە کۆمکرن ژ روژا هەشتێ ژ کانینا دووێ هەتا ئێکێ خزیرانێ 2019 ل بنگەهێ شویشتنا گولچیسکا ل باژێرێ دهوکێ – هەرێما کوردستانێ / عیراق. پاشی دەستنیشانکرنا ئاستێ زەنکی د خوینێدا و نیشانەیێن کێم خوینیێ.

ئەنجام: نەخۆشێن کۆمەلا (1) یێ ئەوێن تەمامکەرێن زەنکی و هەرگرتی زێدەهیەکا مەزن دیارکر د ناڤنجیا زەنکی د خویناڤێدا (ناڤنجیا رێژا سەدی 43,12 ٪) بەرامبەری ناڤنجیا هیموگلوبینی (ناڤنجیا رێژا سەدی 13,6 ٪).

کورتی: پەیوەندیەکا پوزەتیڤ هەبوو دناڤبەرا زێدەکرنا ئاستێ زەنکی و راستڤەکرنا کێم خوینیێ.

الخلاصة

تأثير أعطاء الزنك على فقر الدم عند مرضى الديلزة الدموية المنتظمة

خلفية البحث: سُجلت حالات عن نقص الزنك في المرضى الذين يعانون من مرض الكلى المزمن وخاصة بين مرضى الديلزة الدموية. الهدف من الدراسة هو تقييم تأثي الزنك كمكمل غذائي في تصحيح فقر الدم بين مرضى الديلزة الدموية.

المرضى والطرق: في هذه الدراسة، تم تسجيل 105 مرضى تزيد أعمارهم عن 18 عامًا، مستقرين سريرياً وأكثر من 6 أشهر على الديلزة الدموية. تم جمع عينات الدم للتقييمات الكيمياء الحياتية والدموية. تم تقسيم المرضى الذين يعانون من نقص الزنك وفقر الدم بسبب الأمراض المزمنة بشكل عشوائي إلى مجموعتين وأكملت الدراسة. أكملت المجموعة 1 علاجهم بإضافة الزنك إلى علاجاتهم كمكملات غذائية (الزنك 50 ملغ / يوم) لمدة 6 أسابيع و المجموعة 2 بدون مكملات الزنك كمجموعة مراقبة. تم جمع البيانات خلال الفترة من الثامن من كانون الثاني إلى الأول من حزيران 2019 في مركز غسيل الكلى في مدينة دهوك - إقليم كردستان/ العراق. تم تحديد مستوى الزنك في الدم ومعلمات فقر الدم.

النتائج: أظهرالمرضى في المجموعة 1 الذين تلقوا مكملات الزنك زيادة كبيرة في متوسط الزنك في المصل (متوسط النسبة المئوية 43.12 ٪) وفي المقابل ايضاً متوسط الهيموغلوبين (متوسط النسبة المئوية 13.06 ٪).

الخلاصة: كانت هناك علاقة إيجابية بين زيادة مستوى الزنك وتصحيح فقر الدم.