



## The impacts of parenteral vitamin B1, B6, B12 on hemoglobin levels in chronic kidney disease patients undergoing hemodialysis

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### ABSTRACT

Chronic kidney disease is a disorder of renal function and structure. The glomerular filtration rate was below the normal value and less than 60 ml/minute /1.73 m<sup>2</sup> for more than 3 months. Patients with chronic kidney disease have erythropoietin in small amounts, and cause anemia. Vitamin B1 acts as oxidative decarboxylation reactions, B6 necessary to heme synthesis, and B12 converts homocysteine to methionine. This study aims to measure the impacts of parenteral vitamin B1, B6, B12 on hemoglobin level in chronic renal disease patients undergoing hemodialysis at Bethesda Hospital Yogyakarta and Panti Rapih Hospital Yogyakarta. The design of this study was one group pretest-posttest using secondary data from lab results from medical records. Data were collected from 117 patients using consecutive sampling methods at Bethesda Hospital Yogyakarta and Panti Rapih Hospital Yogyakarta in March 2019. The treatment given was parenteral vitamin B1, B6, B12 twice a week with a dose of 2 ml. Vitamin B was given intravenously after each hemodialysis. Hemoglobin levels were measured 3 times on 1<sup>st</sup> visit (before vitamin B administration), 2<sup>nd</sup> visit (after vitamin B administration), and 3<sup>rd</sup> visit (after vitamin B administration). There were significant differences of hemoglobin levels on 2<sup>nd</sup> visit compared to 1<sup>st</sup> visit (p = 0,000); 3<sup>rd</sup> visit compared to 1<sup>st</sup> visit (p = 0,000) and 3<sup>rd</sup> visit compared to 2<sup>nd</sup> visit (p = 0.010). Parenteral vitamin B1, B6, B12 gave significant impacts on hemoglobin level and was safe for chronic kidney disease patients undergoing hemodialysis.



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### INTRODUCTION

Chronic kidney disease is a progressive decline in renal function for more than 3 months or longer (Wells *et al.*, 2015). Criteria for chronic kidney disease were seen from decreasing value of glomerular filtration rate. Markers of kidney damage are albuminuria (AER  $\geq$  30 mg/24 hours; ACR  $\geq$  30 mg/g [ $\geq$  3 mg/mmol]), urinary sedimentary disorders, electrolytes and other abnormalities due to tubular disorders, and history of kidney transplantation. Glomerular filtration rate is  $<$ 60 ml/min/1.73 m<sup>2</sup> (Kellum *et al.*, 2012).

Prevalence of chronic kidney disease in Yogyakarta is higher than the national average in Indonesia (3.8

per mile) with the prevalence of chronic kidney disease at the age of 65-74 years is dominant (8.23 per mile). Males (3.52 per mile) are more prone to suffer chronic kidney disease than females ([Indonesian Health Ministry, 2018](#)).

Hemoglobin is an oxygen-binding protein found in red blood cells that carries oxygen from the lungs to the tissues. Each hemoglobin molecule is a tetramer consisting of four polypeptide globin chains and contains a part made by an organic protoporphyrin ring and a central ion in the iron ( $\text{Fe}^{2+}$ ) state. Iron molecules in each part can bind and release oxygen to be transported in the body ([Farid and Lecat, 2020](#)). Patients with chronic kidney disease have erythropoietin in small amounts, therefore the bone marrow makes fewer erythrocytes and causes anemia. Blood test, including hemoglobin levels test, is performed to find out decreasing hemoglobin levels and anemia in chronic kidney disease patients ([Budiwiyono et al., 2016](#)).

Vitamin B1 acts as cofactors for oxidative decarboxylation reactions, including the conversion of pyruvate to acetyl coenzyme A (CoA) in the pyruvate dehydrogenase complex. Vitamin B6 forms as pyridoxal, pyridoxine, pyridoxamine, and the 5' phosphates. Pyridoxal-5-phosphate (PLP) is a cofactor to many enzymes and necessary for ( $\delta$ )-aminolevulinatesynthase to initiate heme synthesis. And vitamin B12 plays an important role in converting homocysteine to methionine and for the reaction that converts L-methylmalonyl-coA to succinyl-coA ([Steiber and Kopple, 2011](#)). This research focuses on hemoglobin levels in patients with chronic kidney disease undergoing hemodialysis at Bethesda Hospital Yogyakarta and Panti Rapih Hospital Yogyakarta.

## MATERIALS AND METHODS

### Research subject

Research subject criteria are divided into inclusion and exclusion criteria. Inclusion criteria included male or female, adults (aged > 18 years), had chronic kidney disease who underwent routine hemodialysis twice per week, and did not use routine vitamin B supplements before. The exclusion criteria included subjects who have hypersensitivity to vitamin B, participate in other clinical trials, incomplete medical record data, and pregnant women or planning a pregnancy. This research is a pre-experimental design with one group pretest-posttest design. The sample in this study was collected using nonprobability sampling with a consecutive sampling method, where samples are taken based on inclusion and exclusion criteria until the required number of sam-

ples is met ([Suresh, 2014](#)). The data used in the form of secondary data taken from medical records in March 2019 at Bethesda Hospital.

### Intervention

The treatment given was parenteral vitamin B1, B6, B12 twice a week with a dose of 2 ml. Vitamin B was given intravenously after each hemodialysis. Hemoglobin levels were measured 3 times on 1<sup>st</sup> visit (before vitamin B administration), 2<sup>nd</sup> visit (after vitamin B administration), and 3<sup>rd</sup> visit (after vitamin B administration). Second visit was conducted 2 weeks after the 1<sup>st</sup> visit and 3<sup>rd</sup> visit was conducted 2 weeks after the 2<sup>nd</sup> visit.

### Analysis

Data were analyzed descriptively and statistical analysis was computerized. Descriptive analysis was used to analyse subject characteristics and description of hemoglobin levels in first, second and third visit. Data were statistically analyzed using the SPSS program with non-parametric Wilcoxon test to see the impacts of parenteral vitamin B1, B6, B12 on hemoglobin levels. The p value was significant if  $p < 0.05$ .

### Ethical Approval

This research has passed the ethical approval check and was approved by the Ethics Committee of the Faculty of Medicine, Duta Wacana Christian University with number 906/C.16/FK/2019.

## RESULTS AND DISCUSSION

In this study, a total of 117 subjects were evaluated. Subjects were dominated by male (64.96%) with 45-64 years old being the most common age group (58.12%). Subjects had a history of hypertension (83.76%) and diabetes (32.48%). Table 1 shows the characteristics of the subject. Males have a greater risk of chronic kidney disease than females because females pay more attention to lifestyle than male ([Pranandari and Supadmi, 2015](#)). As age increases, it related to decrease in glomerular filtration rate ([Weinstein and Anderson, 2010](#)).

Subjects with a history of hypertension have a greater risk on developing chronic kidney disease than those who did not have a history of hypertension Figure 1. Higher blood pressure can worsen kidney damage through increased intraglomerular pressure which causes functional and structural disorders of the glomerulus. High intravascular pressure affects the glomerulus through the afferent arteries, then constriction occurs due to hypertension ([Susalit, 2003](#)). Subjects with diabetes mellitus have a greater risk of developing chronic kid-

**Table 1: Baseline Characteristics**

Variable	Criteria	Total (n=117)	Percentage (%)
Sex	Female	41	35.04%
	Male	76	64.96%
Age	18-44	33	28.21%
	45-64	68	58.12%
	> 65	16	13.67%
Hipertension	Yes	98	83.76%
	No	19	16.23%
Diabetes	Yes	40	34.18%
	No	77	65.81%

**Table 2: Patients treatment history**

Treatment History	Treatment Classification	Total	Percentage (%)
Antihypertensive	Calcium Channel Blockers (CCB)	68	68.11 %
	Angiotensin Receptor Blockers (ARB)	51	43.58%
	Diuretic	49	41.88%
Antidiabetic	Insulin	10	8.54 %
Calcium	CaCO3	80	68.37%
Folic Acid	Folic acid	102	87.17%
Eritripoetin	Eritripoetin	98	83.76%

**Table 3: Hemoglobin levels on every visit**

Descriptive Statistics	1st Visit (n=117)	2nd Visit (n=117)	3rd Visit (n=117)
Standard deviation	1.49	1.96	1.87
Mean (g/dL)	9.22	10.33	10.11
Minimal value(g/dL)	5.50	5.50	6.00
Maximal value(g/dL)	13.20	15.7	14.60
Range (g/dL)	7.70	10.2	8.60

**Table 4: p value of hemoglobin levels on every visit**

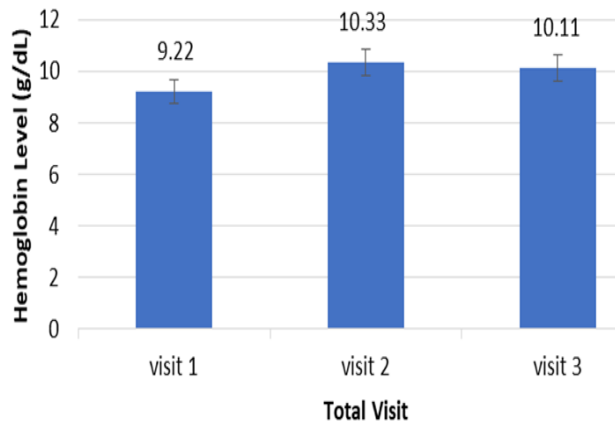
	1st Visit & 2nd Visit	1st Visit & 3rd Visit	2nd Visit & 3rd Visit
VitaminB1, B6, B12	0.000	0.000	0.010

ney disease than those who did not have a history of diabetes mellitus, due to complications of diabetes mellitus, namely diabetes nephropathy. Diabetes nephropathy causes damage to the glomerulus due to denaturation of proteins by high glucose levels (Pranandari and Supadmi, 2015).

The smaller the glomerular filtration rate of patients with chronic kidney disease, the lower the hemoglobin level in these patients (Hidayat *et al.*, 2010). Anemia in chronic kidney disease is mostly characterized by normochromic morphology, having excluded the possibility of anemia due to other causes such as anemia due to hemodialysis, iron

deficiency, folic acid, or vitamin B12, and malignancy (Sukandar, 2006). In the body, vitamin B12 consists of two forms, 5-Deoxyadenosyl cobalamin and methylcobalamin. The methionine synthase needs methylcobalamin as a cofactor, and involved in the conversion of homocysteine to cysteine and 5-Deoxyadenosyl cobalamin acts as cofactor needed to convert l-methylmalonyl CoA to succinyl CoA. These conversions are very important for the extraction of energy and protein. Succinyl CoA is also needed to produce hemoglobin which functions in oxygen transport. (Dowd *et al.*, 1975).

Vitamin B6 deficiency can cause various symp-



**Figure 1: The mean of hemoglobin levels on every visit**

toms, such as higher oxidative stress, and impaired metabolic problems. Deficiency in Vitamin B6 can increase the risk of cardiovascular disease through the mechanism of homocysteine (Shen *et al.*, 2010).

Table 2 shows the history of the patient's treatment history. Patients had a history of antihypertensive medication with a calcium channel blocker (CCB) group of 68 (58.11%), Angiotensin Receptor Blocker (ARB) of 51 (43.58%) and diuretics of 49 (41.88%). Patients with a history of insulin use were 10 (8.54%), CaCo3 was 80 (68.37%) and folic acid was 102 (87.17%). The most treatment used was folic acid, followed by a history of using erythropoietin, antihypertensive drugs, calcium carbonate (CaCo3) and insulin. The use of folic acid beside vitamin B, helps in the role of synthesis of nucleoproteins in the formation and production of red blood cells and maintenance of erythropoiesis (Cronewett, 1990). Providing recombinant erythropoietin therapy helps bone marrow to produce red blood and can increase hemoglobin levels in the blood. A sufficient amount of erythrocytes can increase the capacity to carry oxygen throughout the body (Syai-ful *et al.*, 2013). And hemoglobin was found significantly lower in CCB (calcium channel blockers) users compared to non-users, among chronic kidney disease patients who did not receive renal replacement therapy, iron, erythropoietin, vitamin D, vitamin B12 phosphate binders and folic acid (Cikrikcioglu, 2013).

The results showed significant changes of hemoglobin after parenteral administration of vitamin B1, B6, B12. Changes are indicated by the mean of the hemoglobin level (Obi *et al.*, 2016). The results showed significant changes on hemoglobin levels at 2<sup>nd</sup> visit compared to 1<sup>st</sup> visit (9.22 ± 1.49; 10.33 ± 1.96) and at 3<sup>rd</sup> visit compared to 1<sup>st</sup> visit (9.22 ± 1.49; 10.11 ± 1.87).

Table 3 shows hemoglobin levels at 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> visits. Based on the results of descriptive analysis, the mean of hemoglobin 1<sup>st</sup> visit was 9.22±1.49 g/dL, 2<sup>nd</sup> visit was 10.33±1.96 g/dL, and 10.11±1.87 g/dL at 3<sup>rd</sup> visit.

Table 4 shows there were significant changes in hemoglobin levels on 2<sup>nd</sup> visit compared to 1<sup>st</sup> visit (p = 0,000); 3<sup>rd</sup> visit compared to 1<sup>st</sup> visit (p = 0,000) and 3<sup>rd</sup> visit compared to 2<sup>nd</sup> visit (p = 0.010).

Based on these results it can be said that there were significant impacts on hemoglobin levels after parenteral vitamin B1, B6, B12 administration, but all subjects' hemoglobin levels are still below the normal range of hemoglobin levels. The normal level of hemoglobin in male is 15.7 g/dL with the normal range of 14.0-17.5 g/dL while the normal female level is 13.8 g/dL with the normal range of 12.3-15.3 g/dL (Wells *et al.*, 2015). There was a slight decrease in hemoglobin levels on 3<sup>rd</sup> visit compared to 2<sup>nd</sup> visit (p = 0.010). This may be influenced by chronic kidney disease's progressivity. The limitation of this study was there were no further evaluations on confounding factors.

## CONCLUSIONS

Parenteral vitamin B1, B6, B12 gave significant impacts on hemoglobin level and was safe for chronic kidney disease patients undergoing hemodialysis.

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The authors declare that they have no funding support for this study.

## Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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