



Intravenous neurotropic vitamin b injection in chronic kidney disease patients on dialysis: patient's perspective

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ABSTRACT

Chronic kidney disease is characterized by a decrease in glomerular filtration rate and lasts over 3 months. Meanwhile, patient perspectives include patient compliance in treatment and care programs. Vitamin B combination plays a role in reducing the risk of mortality for cardiovascular disease. This study aims in measuring perspective on patients with chronic kidney disease undergoing hemodialysis to intravenous vitamin B injection. This is a cohort retrospective study of patients on dialysis that were injected with intravenous vitamin B two times a week after dialysis. The subjects studied were chronic kidney disease patients who underwent hemodialysis at Bethesda Hospital Yogyakarta and Panti Rapih Hospital Yogyakarta, Indonesia. This study involved 58 patients, comprising 38 male (65.5%) and 20 females (34.5%). Total 41 patients (70.7%) with age under 60 years. The most common comorbidities were hypertension (86.2%), diabetes mellitus (25.9%), and cardiovascular disease (20.7%). Patients' perspectives on improvement of fatigue symptoms are higher in patients with hypertension comorbidity (88.9%), sleep quality higher in diabetes mellitus comorbidity (80%), daily activity higher in patients with other comorbidity (84.6%) and mood higher in other comorbidity (88.9%). Overall, most of the patients were satisfied with the treatment (98.3%), satisfied that it reduced fatigue (96.6%), said no side effects appeared (91.4%), were confident in the treatment (94.8%), considered it resulted in greater benefit than costs (84.5%). Patients' perspectives in the treatment of intravenous vitamin B combination injections for chronic dialysis patients have satisfactory treatment quality.



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INTRODUCTION

Criteria for defining chronic kidney disease is the onset of the disease over 3 months, with a glomerular filtration rate under 60 mL / min per 1.73 m² with functional and structural abnormalities. Albuminuria occurs as sign of renal damage (Levey and Coresh, 2012). Several diseases can cause chronic kidney disease such as diabetes mellitus, hypertension, chronic glomerulonephritis, obstructive urinary tract infections, obesity and idiopathic. Therefore, early detection of chronic kidney disease is needed (Johnson *et al.*, 2014).

In Indonesia, the number of patients with chronic kidney disease is proliferating. This has become

a severe health, social, and economic problem for patients and patients' families. The prevalence of chronic kidney disease increases with age, with a sharp increase in the 45-54 year age group compared to the 35-44 year age group. Prevalence in male (4.17%) is higher than females (3.52%), higher prevalence for urban communities (3.85%), not attending school (5.73%), not working (4.76%), and farmers/fishermen/laborers (4.64%). The prevalence of chronic kidney disease in Yogyakarta is higher than the national average (3.80%) in Indonesia ([Indonesian Health Ministry, 2018](#)).

One of the most common therapies for patients with chronic kidney disease is hemodialysis ([Kim *et al.*, 2010](#)). Chronic kidney disease has effects on the physical, psychological and functional status of individuals such as changes in lifestyle including financial problems, restrictions on fluid intake and diet, changes in family roles and duties also decreased achievement of long-term goals due to renal dysfunction ([Shasaei and Sheibaei, 2015](#)). Besides diet modification, socioeconomic management of patients often results in failure of therapy and worsens prognosis in patients with chronic kidney disease

Supplementation of vitamins B combination including vitamin B6, vitamin B9 and vitamin B12 intravenously in hemodialysis therapy plays a role in reducing total homocysteine levels by 25% ([Hankey, 2018](#)). High plasma levels of homocysteine in the body are associated with an increased risk factor for mortality and vascular disease ([Jamison *et al.*, 2007](#)). Meanwhile, patient perspective has been examined in terms of the point of view of patients and in terms of what patients think is important that doctor addresses during the consultation. Perspective is about patient's self-perceived impact of the health condition on their life and health condition (based on patient's belief) ([Zanini *et al.*, 2014](#)). This study measures how big the patient's perspective in the injection treatment of the intravenous vitamin B combinations with chronic kidney disease.

MATERIALS AND METHODS

Research subject

The subjects used in this study followed the inclusion and exclusion criteria. The inclusion criteria are male and female patients with chronic kidney disease who undergo hemodialysis and use intravenous combination vitamin B injection treatment and able to communicate. While the exclusion criteria is patients who are not competent in giving informed consent and who move to other hospitals outside the Bethesda Hospital and Rapih Panti

Hospital. Samples were collected using a purposive sampling method, where they were taken based on inclusion and exclusion criteria until the required number of samples were met.

Analysis

The data were analyzed descriptively using median values from the Likert scale. Descriptive analysis was used to analyze baseline characteristics, patient's comorbidity and treatment history, perspectives on symptoms improvement, and satisfactions.

Methods

This was a retrospective cohort study of one group. Retrospective cohort design is a study with exposure-based sampling and absolute effect sizes for risk outcomes. One group means there is no control group ([Dekkers *et al.*, 2012](#)) because a patient's perspective subjectivity has a high variation in treatment. There is no stated hypothesis because of descriptive study.

This study followed up to 122 subjects ([Angela and Pinzon, 2020](#)). After 12 month follow-up, complete data follow-up were received from 122 subjects. There were 36 subjects who did not continue the treatment regularly. The reasons were because 13 patients stopped the treatment, 17 patients died, and 6 patients moved to another hospital. Seventy-seven patients routinely continued the treatment twice every week and 9 other patients also continued, but not routinely using intravenous vitamin B combinations. Based on the corresponding exclusion inclusion criteria, there were 58 patients. This study was conducted at Bethesda Hospital Yogyakarta and Panti Rapih Hospital Yogyakarta, Indonesia, in November to December 2019 with 58 data. Research flow in Figure 1. The vitamin B combination used was Neurobion, and the dose of the vitamin given in the study was 100 mg of vitamin B1, 100 mg of vitamin B6, and 5000 mcg of vitamin B12. Authors got those vitamins from Bethesda Hospital Yogyakarta, Indonesia.

Instrument

The study was conducted using case report form (CRF) questionnaire. CRF is used to collect patient data in clinical trial studies ([Nahm *et al.*, 2011](#)). It has been validated in languages and populations in the area. All authors administered it and were involved in the decision to treat the patients. The CRF has been designed to accurately assess the safety and benefits of the treatment.

Clinical Implications

The data could contribute to medical science related to the patient's perspective on the treatment of

an intravenous combination of vitamin B injection, especially regarding the patient's perspective on improvement of symptoms, patient satisfaction, side effects that can arise, comfort of treatment, patient confidence, and benefits in treatment. As for clinicians, it will be able to provide evaluation of actions and interventions correctness by considering the patient's decision.

Ethical Approvals

Ethical clearance was received from Hospital Bethesda Yogyakarta, Indonesia. Ethics Clearance Committee (Num.15/ KEPK-RSB/1/2020). The confidentiality of the subject will be maintained by not including the patient's name and identity.

RESULTS

Baseline Characteristics

Descriptive analysis was performed on 58 patients with chronic kidney disease who underwent hemodialysis and met the inclusion criteria. The baseline characteristics of the study subjects could be seen in Table 1. Most patients with chronic kidney disease were male (65.5%) under 60 years old (69%), and with marital status of patients being married (91.4%), and most subjects were in public health insurance scheme (96,6%).

Patients Comorbidity and Treatment History

The data on the conditions of comorbid patients could be seen in Table 2. Top three highest comorbidities are hypertensive (86.2%), diabetes mellitus (25.9%), and cardiovascular disease (20.7%). Male sex was more at risk for these three diseases than female. Treatment history follows the patient's comorbidity condition. In addition, patients used anti-hypertensive drugs (78.9%), anti-diabetic (28.9%) and antiplatelet (18.4%)

Patients Comorbidity with Patient Perspectives on Symptom Improvement

Patients comorbidity data on symptoms improvement was measured based on the patient's perspective after using intravenous combination vitamin B injection. It was measured using Likert scale and analyzed using median values. The data could be seen in Table 3. The improvement of fatigue symptoms for hypertensive patients (88.9%), diabetes mellitus (86.7%), patients with other comorbidities (69.2%) and patients who did not have comorbidities (66.7%). Sleep quality was improved in hypertensive patients (70.4%), diabetes mellitus (80%), patients with other comorbidities (76.9%), and patients without comorbidities (66.7%). Daily activity was improved in hypertensive patients (81.5%),

patients with diabetes mellitus (80%), and patients who had other comorbidities (84.5%). Though it did not improve in patients who do not have comorbidities (66.7%). Mood was improved in hypertensive patients (51.9%), patients with comorbid diabetes mellitus (73.3%), patients with other comorbidities (84.6%) and patients without comorbidities (66.7%).

Patients Satisfaction

Patient satisfaction data are measured based on the patient's perspective using a Likert scale and analyzed using median values. It could be seen in Table 4. Satisfaction level regarding the overall condition of the patient is (98.3%). While patients satisfaction with the overall reduction in symptoms of fatigue is (96.6%). As for the intravenous combination of vitamin B injection treatment, the patient did not experience side effects (91.4%). During treatment, patients felt comfortable in the treatment (96.6%), the patients also felt confident in the treatment of vitamin B combination (94.8%). In addition, the patients also felt they obtained more benefits than the costs incurred (84.5%).

Treatment History with Benefits and Costs Incurred

In Table 5, the patient's medical history with the benefits obtained rather than the costs incurred can be seen. Patients who received monotherapy (48.3%) and poly therapy (36.2%) felt that they received greater benefits than the costs incurred.

DISCUSSIONS

This study uses intravenous injection. Intravenous injection has certain benefit, it allows the treatment effect to occur immediately, the speed of delivery is regulated, this helps patients who are unable to handle treatment such as orally or with difficulty swallowing, and large doses can be injected easily to facilitate consistent drug supply (Stoner *et al.*, 2015).

There is a research in North Kerala, India (Jacob *et al.*, 2019) that used 150 subjects in the age range of 18 to 88 years. The results of the study stated that the prevalence of chronic kidney disease is dominated by male (74.7%). Furthermore, there are differences in age division that divides age by 3 age ranges, which are 18-40 years (18%), 41-60 years (50%), and over 60 years (32%). This study divides age based on the definition of elderly in Indonesia. This is suitable to the data obtained by the author. The results of other research in Indonesia (Mihardja *et al.*, 2018) stated that there is significance between the prevalence of kidney dysfunction at productive

Table 1: Baseline characteristics

Variable	Criteria	Total (n=58)	Percentage (%)
Sex	Male	38	65.5%
	Female	20	34.5%
Age	< 60 years	41	70.7%
	≥ 60 years	17	29.3%
Marital Status	Married	53	91.4%
	Not Married	5	8.6%
Health Insurance	Public	56	96.6%
	Private	1	1.7%
	Company	1	1.7%

Table 2: Patients comorbid and treatment history

Variable	Total Patients (n=38)	Male %	Total Patients (n=20)	Female %	Total Patients (n=58)	%
Patient Comorbid	37	97.4	18	90	55	94.8
Hypertension	33	86.8	17	85	50	86.2
Diabetes Mellitus	11	28.9	4	20	15	25.9
Cardiovascular Disease	9	23.7	3	15	12	20.7
Gastrointestinal Disease	2	5.3	1	5	3	5.2
Kidney Infection	2	5.3	0	0	2	3.4
Urinary Tract Infection	1	2.6	0	0	1	1.7
Preeclampsia	0	0	1	5	1	1.7
No Comorbid	1	2.6	2	10	3	5.2
Treatment History						
Anti Hypertension	30	78.9	18	90	48	82.8
Anti Diabetic	11	28.9	3	15	14	24.1
Anti Platelet	7	18.4	2	10	9	15.5
Statin	3	7.9	1	5	4	6.9
No Treatment History	6	15.8	2	10	8	13.8

Table 3: Patient comorbid with patient perspectives on symptoms repairment

Patients Comorbid (n=58)	Hypertension %	Diabetes Mellitus %	Other Comorbid %	No Comorbid %
Fatigue				
Better	24	88.9	13	86.7
Worsen	3	11.1	2	13.3
Sleep Quality				
Better	19	70.4	12	80
Worsen	8	29.6	3	20
Daily Activities				
Better	22	81.5	12	80
Worsen	5	18.5	3	20
Mood				
Better	14	51.9	11	73.3
Worsen	13	48.1	4	26.7

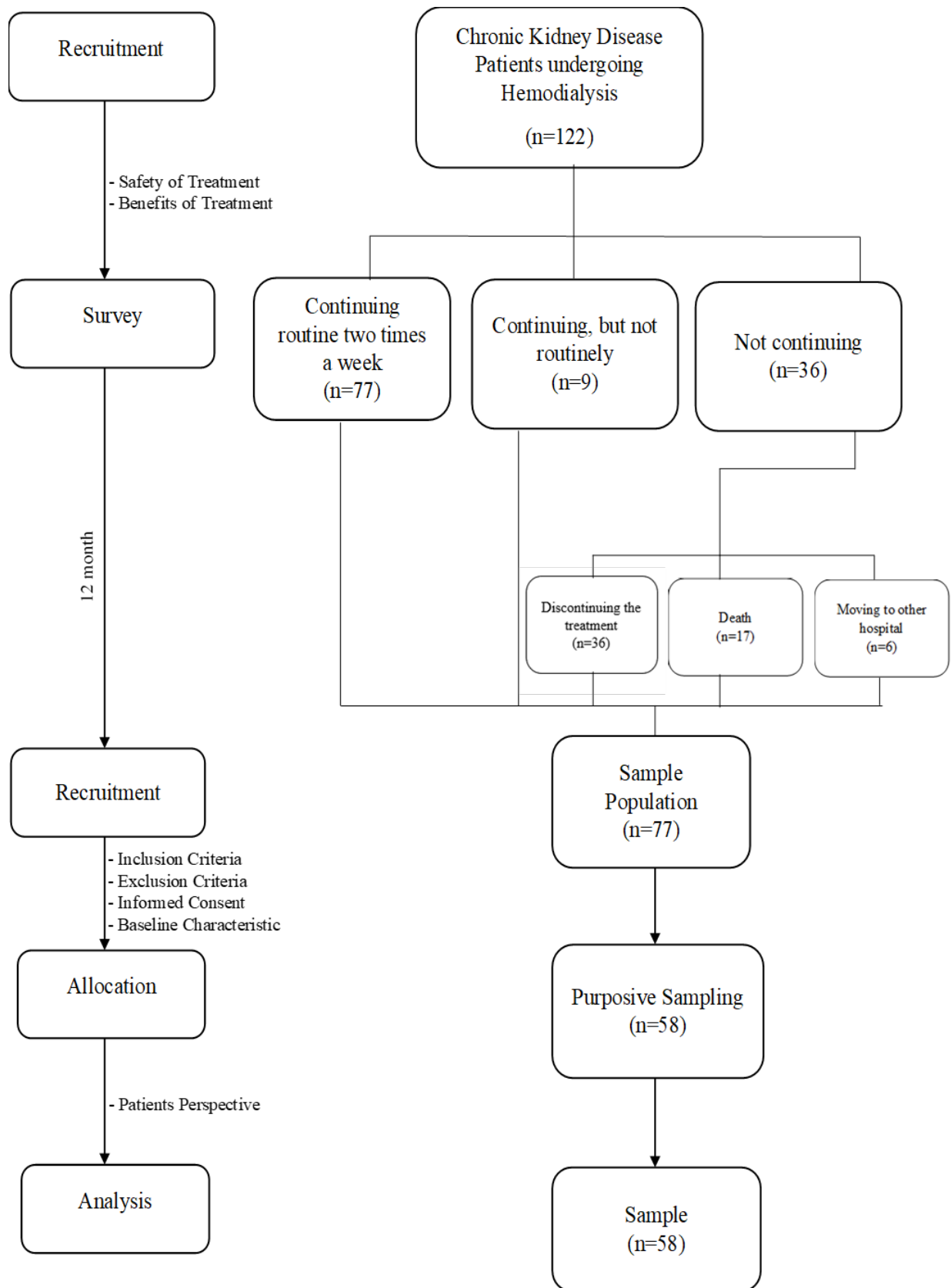


Figure 1: Research Flow

Table 4: Patient satisfaction

Patients Perspective	Total Patients (n=58)	Percentage (%)
Overall Condition of the Patient		
Satisfied	57	98.3
Not Satisfied	1	1.7
Reduction of Fatigue Improvement		
Satisfied	56	96.6
Not Satisfied	2	3.4
Side Effects		
No Side Effect	53	91.4
Side Effects	5	8.6
Inconvenience		
Convenience	56	96.6
Not Convenience	2	3.4
Treatment Confidence		
Not Confidence	3	3.4
Confidence	55	94.8
Benefit > Price		
Yes	49	15.5
No	9	84.5

Table 5: Treatment history with benefits and costs incurred

Total Patients (n = 58)	Benefit > Cost	%	Benefit < Cost	%
Treatment History				
Monotherapy	28	48.3	4	6.9
Polytherapy	21	36.2	2	3.4
No Therapy	0	0	3	5.2

age. Statistically, this significance occurs in diabetes mellitus patient that is not diagnosed early and associated with older age (45-54 years), being male, has high consumption of high glucose beverages and salty foods, and has low or intermediate economic levels. The decrease in glomerular filtration rate is closely related to increasing age (Weinstein and Anderson, 2010). Male patients had 3 highest comorbid conditions. There are hypertension (86.8%), diabetes mellitus (28.9%), and cardiovascular disease (23.7%). This differs from what was obtained from Indonesian National Health Survey (Indonesian Health Ministry, 2018). Female are more at risk for suffering from these three diseases compared to male sex. The prevalence of productive females over 18 years to have hypertension being (36.9% vs 31.3%), diabetes mellitus (1.8% vs 1.2%), and cardiovascular disease (1.6% vs 1.3%). However, the prevalence of chronic kidney disease in male (4.17%) is higher than in female (3.52%)

Factors related to lifestyle and obesity may cause the difference in the results of the three comorbid diseases above. Obesity increases the risk of proteinuria with an increase in sodium reabsorption. It is also one of the risk factors for diabetes mellitus and hypertension. Obesity has a high association with hypertension and diabetes. In Indonesia (Harbuwono *et al.*, 2018), the prevalence of obesity and central obesity was higher in females than male (16.9%). Though other research in China (Wang *et al.*, 2012) stated that the prevalence of general obesity and overweight classified were 15.0% (15.7% for male and 14.3% for female, p value < 0.01) and 19.2% (20.8% for male and 17.7% for female, p < 0.01), respectively, and the overall prevalence rate of abdominal obesity was 37.6% (31.1% for male and female 43.9% for female, p < 0.01). Many conditions influence the difference in obesity prevalence. Some of these conditions include social demographics such as age, gender, socio-economic sta-

tus, and educational background and are associated with several other variables such as diet status and physical activities such as sports. Therefore, epidemiologically, obesity in one country does not always have to be clinically the same to others (Harbuwono *et al.*, 2018). Patients who had hypertension (88.9%), diabetes mellitus (86.7%), patients with other comorbidities (69.2%) and patients who did not have comorbidities (66.7%) experienced increased fatigue of symptom improvement. The effect of vitamin B12 in hemodialysis patients is very significant in reducing fatigue symptoms. Vitamin B12 must be used consistently and for a long time to reduce symptoms of fatigue in patients who have a history of diabetes mellitus (Tayyebi, 2013). Vitamin B12 deficiency is related to long-term use of metformin (de Jager *et al.*, 2010). For patients who have comorbid hypertension, a combination of vitamins B treatments are effective in controlling systolic blood pressure and oxidative stress (França and Vianna, 2010).

Improved sleep quality was obtained in hypertensive patients (70.4%), diabetes mellitus (80%), patients with other comorbidities (76.9%), and patients who do not have comorbidities (66.7%). Patients who have diabetes mellitus comorbidity, can have several disorders that result in decreased quality of sleep. This disorder manifests as symptoms of nocturia, polyuria, neuropathic pain and can be found in association with several other chronic diseases (cardiovascular complications) such as hypertension, depression and obstructive sleep apnea (OSA). Nocturia is closely related to polyuria and the risk of obstructive sleep apnea in patients with comorbid diabetes mellitus. Patients with obstructive sleep apnea will produce negative intrathoracic pressure and stretch the myocardium. Stretching releases atrial natriuretic peptide (ANP) and it causes vasodilation and inhibits aldosterone resulting in excretion of excess sodium and water (Surani, 2015).

Patients who have concomitant hypertension can have poor sleep quality. It is also closely related to other comorbid conditions such as diabetes mellitus. Individuals who have a longer and shorter sleep period than 7 hours of sleep have the same chance of experiencing hypertension. The risk is dominant in the female sex than male (Wang *et al.*, 2015).

Improvement in mood was obtained in hypertensive patients (51.9%), patients with comorbid diabetes mellitus (73.3%), patients with other comorbidities (84.6%) and patients without comorbidities (66.7%). It is corresponding with the literature that giving a combination of vitamins B (injec-

tion) especially vitamin B12 is needed in the process of re-methylation of homocysteine to methionine. Methionine is needed in the synthesis of S-adenosylmethionine (SAM) in the central nervous system (Parletta *et al.*, 2013). The products synthesized from SAM are neurotransmitters related to dopamine, serotonin, and norepinephrine (Bryan, 2004). Thus, deficiency of vitamin B have a direct effect on mood because it reduces the production of neurotransmitters (Calvaresi and Bryan, 2001). In addition, vitamin B12 can reduce arterial stiffness associated with decreased serum asymmetric dimethyl arginine (ADMA) (Koyama *et al.*, 2010). ADMA has a role in increasing oxidative stress and is related to nitric oxide (NO). Increasing the ADMA level will reduce NO synthesis and produces oxidative stress and endothelial dysfunction, which will cause damage to blood vessel function (Sibal *et al.*, 2010).

Daily activities improvement was obtained in hypertensive patients (81.5%), patients with diabetes mellitus (80%), and patients who had other comorbidities (84.5%). But it was not improved in patients who do not have comorbidities (66.7%). Patients suffering from comorbid diabetes mellitus can have other comorbid conditions such as hypertension, osteoarthritis, rheumatoid arthritis and disorders of the neck and shoulders which negatively impact physical quality of life (Physical QoL). Other diseases such as migraines and intestinal disorders result in the most negative impact in decreased quality of mental life (Mental QoL). Thus, it can be said that patients who have comorbid conditions of diabetes mellitus will have reduced quality of physical life, especially those caused by cardiovascular and musculoskeletal disorders. The more comorbid the patient has, the quality of life of this patient will also deteriorate and will affect the daily activities of the patient (Adriaanse *et al.*, 2016). Patients who do not have comorbid conditions felt no improvement in their daily activities. It is because the patients feel the quality of life, both physically and mentally. There are no comorbid conditions in patients that result in decreased quality of life in patients.

The relationship between the patient's perspective and treatment compliance can be seen from the variation in the patient's subjective experience in treatment. The subjective experience includes patient confidence in treatment in the form of an evaluation of a treatment. The form of the evaluation is in the form of effectiveness of treatment which is characterized by a decrease in symptoms and economic burden arising from the duration of the treatment. One cause of non-compliance of patients is drug side effects or lack of information provided

by doctors about the treatment (Pagès-Puigdemont *et al.*, 2016).

The purchase of combination of vitamins B for 1 ampoule (3 cc), costs Rp. 15,300 (\pm \$1.03 USD) and for injection costs Rp. 20,000. (\pm \$2 USD), though this does not include service fees. Patients take intravenous combinations of vitamin B injection twice a week. It can be estimated that patients pay Rp. 70,600 (\pm \$4.73 USD) weekly and if calculated for 1 month, the patient has to pay Rp. 282,400 (\pm \$18.93 USD). If calculated into 1 year, it is approximately about Rp. 3.388.800 (\pm \$230.15 USD), making the patient compliance of the treatment to be very high. In addition, the high level of patient confidence (besides getting greater benefits than the costs incurred) in the treatment of an intravenous combination of vitamin B injection makes it possible to increase the price for intravenous combinations of vitamin B injection, though it could be an economic burden for patients.

Multi morbidity can be defined as having two or more chronic diseases. Patients with chronic kidney disease can have more than one comorbidity (Barnett *et al.*, 2012). Multi morbidity worsens patient care outcomes and adherence, by increasing the burden of treatment and increasing the cost of health services (Gallacher *et al.*, 2014). Patients who received monotherapy (48.3%), poly therapy (29.3%) and did not receive additional therapy (6.9%) felt the benefits outweighed the costs. It means that either monotherapy, poly therapy or not using additional therapy does not burden the patient economically because patients already feel getting benefits greater than the costs incurred.

Research Limitations

The limitations of this study are that we do not measure the duration of chronic kidney disease and the length of dialysis. The longer the chronic kidney disease and dialysis, the longer it will influence the patient's quality of life. The duration of occurrence of comorbid patients such as hypertension, diabetes, mellitus, and other diseases was also not measured. We did not use any control group in this study.

CONCLUSION

Patients' perspectives on the treatment of intravenous vitamin B combination injections for chronic dialysis patients have satisfactory treatment quality. This is based on symptoms repairment including fatigue, sleep quality, daily activity, and mood. Also based on overall condition of patients, occurrence of side effects, inconvenience of therapy, treatment confidence, greater benefit than costs incurred.

Therefore it can be suggested especially for clinicians to use the intravenous vitamin B combination for patients with chronic kidney disease.

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Conflict of Interest

All authors declare no conflict of interest.

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