Quality of Life and Hemoglobin Levels of Hemodialysis Patient at Siriraj Hospital

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ABSTRACT

Objective: To evaluate the relationship of the quality of life (QOL), and hemoglobin (Hb) level of hemodialysis (HD) patients.
Methods: This study was a cross-sectional study. Face-to-face interviews using a Kidney Disease Quality of Life - Short Form (KDQOL-SF™ 1.3) questionnaire (which consisted of SF-36 and kidney disease questionnaires) were conducted during November-December 2009 with 152 patients receiving hemodialysis at Siriraj hospital, Bangkok, Thailand. QOL measures were compared in stepwise Hb levels of ≤9, >9 to 10, >10 to 11, >11 to 12, and >12 g/dl. Scores of QOL and Hb level were examined for the relationship and statistical significance by using ANOVA.
Results: The increasing Hb levels are statistically significant increases in kidney disease domain scores on the kidney disease component of the questionnaire (p=0.042). About the SF36 component, the difference between 5 groups of Hb levels were significant in the general health (p=0.023), role emotion (p=0.015), social functioning (p=0.008), and mental component summary scores (p=0.039).
Conclusion: The difference of the Hb levels were statistically significant differences in the effects of kidney disease, general health, role emotion, and social function scores, and mental component summary scores of the KDQOL-SF questionnaire. However, a long-term assessment should be considered. These findings have implications for the care of hemodialysis patients in terms of the initiation of the Hb target of erythropoietin (EPO) therapy.

Keywords: Quality of life, hemoglobin, kidney disease quality of life - short form, erythropoietin

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Most patients receiving hemodialysis for end stage renal disease (ESRD) currently receive erythropoietin (EPO) or erythropoiesis-stimulating agents (ESAs) for treatment of anemia. Anemia from erythropoietin deficiency is a common complication of chronic kidney disease. It can be treated with EPO administration, red blood cell transfusion (RBCT), or a combination of both.[1] However, the widely accepted treatment in anemia patients is EPO administration. Early studies found that EPO reduced the need for RBCT and improved the quality of life (QOL) in patients with chronic kidney disease (CKD), when compared with no EPO administration.[2,3] EPO agemts are routinely used to treat anemia of chronic kidney disease (CKD), especially in patients who need dialysis. The goal of therapy is to achieve specific hemoglobin (Hb) target levels. Higher doses of EPO are being used to attain higher target levels without evidence of corresponding clinical benefit and possibly resulting in harm. It is remarkable that the three largest studies and the meta-analysis, involving 3,268 subjects, have had a consistent outcome, a 21-48% increased risk for mortality in the higher Hb target group which in each study nearly reached statistical significance.[4-7] The Food and Drug Administration (FDA) in the United States suggest that increases in hemoglobin levels to values more than 12 g/dl may be associated with increased morbidity and mortality and that the benefits of these drugs have not been well documented and this would imply that the FDA asserts a Hb target of only 10 g/dl because this level is far from the range of demonstrated risk[8] while the cost consequences of using EPO to achieve higher Hb targets is increasing. However, many nephrologists believe that EPO improves the quality of life of patients with CKD. In 2007, the US FDA ruled that minimization of blood transfusions and low red blood cell levels were the predominant indications

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for EPO in anemic patients with chronic kidney disease. Regarding the low red blood cell levels, the recommendation of hemoglobin levels is 10 to 12 g/dl.[9] Today, the target hemoglobin levels in chronic kidney disease remain uncertain, as hemoglobin targets above 13 g/dl have been associated with both benefit (quality of life) and harm (cardiovascular events).[10] In November 8, 2007, the FDA stated that for patients with CKD "quality of life claims in the previous labeling were removed, with the exception of improved exercise tolerance and functional ability for chronic renal failure patients". The randomized control trial by CHOIR measured the health-related quality of life in CKD patients in the different target Hb levels of 11.3 and 13.5 g/dl and the results showed no difference in the QOL between the 2 groups. However, previous randomized trials did show an improvement in physical function in CKD patients which have the higher Hb target.[11]

Thailand has been providing the universal health care coverage scheme (UC) since 2001.[12] The scheme protects a population of 47 million who are not eligible for the Civil Servant the Medical Benefit Scheme (CSMBS) or the Social Security Scheme (SSS). Although all anemia treatments for hemodialysis patients are currently covered by CSMBS, SSS and UC, these treatments are inequity for all schemes. Siriraj hospital is the largest medical school in Thailand and must be the therapeutic model for the other hospitals in Thailand. This study is one of a series of studies supported by the Routine to Research (R2R) at Siriraj Hospital to provide scientific evidence about Thai hemodialysis patients for policymakers to make decisions on whether to provide anemia treatments with EPO for hemodialysis patient. This study used the Kidney Disease Quality of Life - Short Form (KDQOL-SF™ 1.3) questionnaire to ask the hemodialysis patients who were included in the study. The KDQOL-SF™ was translated into Thai and back-translated twice into English. The KDQOL-SF™ was developed in 1994 by the Kidney Disease Quality of Life Working Group[11] about a kidney disease specific measure of HRQOL. The KDQOL questionnaire used measured a variety of health-related quality of life domains, the questionnaire included 36 generic items (the SF-36) which represent the general health. For the section of kidney disease, specific questions consisted of 43 items that were the items in the KDQOL-SF™ which consisted of kidney-specific domains such as symptoms and problems, effects of kidney disease on responses to daily life, burden of kidney disease, work status, cognitive function, quality of social interaction, sleep and sexual function. The purpose of this study was to evaluate the relationship between the Hb levels and health-related quality of life in a cross-sectional study of a cohort of hemodialysis patients. The Kidney Disease Quality of Life questionnaire was completed by face to face interview for 152 patients and the data were correlated with Hb levels at the time of completion of the questionnaires.

MATERIALS AND METHODS

The present study had a cross-sectional descriptive design. If the patient gave informed consent, the investigator would administer the study questionnaire as a face-to-face interview which included the KDQOL-SF™ v1.3 (which consisted of SF-36 and kidney disease questionnaires), sociodemographic and clinical data, together with a review of medical records, during November-December 2009 with 152 hemodialysis patients at Siriraj Hospital. The study population was hemodialysis patients who used EPO for at least 6 months with titration of EPO therapy, but excluded the patient who was under 18 years old, changed the modality of dialysis, switched to other anemia treatment method between the study and those who could not answer the questionnaire and/or were not willing to participate in the study. The study was approved by Siriraj Institutional Review Board (protocol number. 323/2552(EC3)). The scores of quality of the KDQOL questionnaire were transformed onto 0 to 100 possible ranges, with higher scores always reflecting better quality of life. The KDQOL questionnaire was used for measuring a variety of health-related quality of life domains, the questionnaire included 36 generic items (the SF-36) which include overall health rating items and 2 domains; 1) the physical domain consisted of physical functioning, role limitations due to physical health problems, pain, and general health perceptions and 2) the mental domain consisted of emotional well being or mental health, role limitations due to emotional health problems, social functioning, and energy/fatigue or vitality. The particular health-related concerns of individuals with kidney disease and on dialysis were: symptom/problems, effects of kidney disease on daily life, burden of kidney disease, work status, cognitive function, quality of social interaction, sexual function, and sleep. Items also included were 3 additional quality of life scales: social support, dialysis staff encouragement, and patient satisfaction.

Patient specific information regarding demographics and clinical laboratory data were collected at baseline and on an ongoing basis at the time of the face to face interview interaction. The demographic data which were obtained included age, gender, marital status, underlying disease (diabetes, hypertension, myocardial infarction and other), and the use of EPO. All patients who agreed to participate in the study and were medically stable were face to face interviewed to complete the Kidney Disease Quality of Life Short Form Questionnaire (KDQOL-SF). The most useful information on target Hb required a study in which a very large group of patients would be randomized to multiple different Hb targets, such as 9,10,11,12, and 13 g/dl[8] and this study separated Hb levels of 152 patients to 5 levels such as Hb ≤ 9, >9 to 10, >10 to 11, >11 to 12, >12 g/dl. The KDQOL questionnaire was used in this analysis. If patients did not have laboratory data within this period and did not answer all the questionnaire completely, they were excluded from this analysis. Differences between parametric data were examined for statistical significance by using ANOVA. The p-value <0.05 was accepted as statistically significant.

RESULTS

The basic demographic data of the 152 patients included in this study are shown in Table 1. Significant representation of all five Hb levels of HD patient was present in the cohort. The mean age of the patients was 57.32 ± 14.52 yrs. Twenty eight percent of the patients had diabetes, 77% had a history of hypertension, and 14% had a history of a myocardial infarction and these percentages were similar in all five Hb levels groups. The basic characteristics of all 5 groups of patients were not significantly different ($p>0.05$) except for the gender ($p=0.006$).

The mean Hbs for all patients were 10.8 g/dl. The mean Hb levels were 8.06 in the ≤ 9 group, 9.62 in the > 9 to 10 group, 10.58 in the >10 to 11 group, 11.60

TABLE 1. Basic characteristic by hemoglobin level.

Parameter	≤ 9 (n = 26)	>9 to 10 (n = 18)	>10 to 11 (n = 40)	>11 to 12 (n = 35)	>12 (n = 33)	P-value
Age (yrs, Mean ± SD)	50.88 ± 14.15	55.06 ± 18.07	58.45 ± 13.57	59.00 ± 14.16	60.48 ± 13.29	0.096
Gender						0.006
Male (%)	38.46	16.67	60.00	62.86	39.39	
Female (%)	61.54	83.33	40.00	37.14	60.61	
Marital status (%)						0.110
Single	65.38	38.89	37.50	34.29	36.36	
Couple	34.62	61.11	62.50	65.71	63.64	
Underlying disease (%)						
Diabetes	34.62	33.33	22.50	25.71	27.27	0.823
Hypertension	73.08	94.44	75.00	77.14	72.73	0.441
Myocardial infarction	11.54	11.11	22.50	5.71	18.18	0.291
Other	3.85	5.56	10.00	14.29	9.09	0.682
Length of HD (yrs, Mean ± SD)	8.73 ± 5.62	7.64 ± 4.28	7.61 ± 5.69	7.87 ± 3.77	6.68 ± 4.59	0.622
Frequency of hemodialysis						0.110
2 times per week (%)	65.38	38.89	37.50	34.29	36.36	
3 times per week (%)	34.62	61.11	62.50	65.71	63.64	

TABLE 2. Clinical laboratory by hemoglobin level (Mean ± SD).

Data	≤ 9 (n = 26)	> 9 to 10 (n = 18)	>10 to 11 (n = 40)	>11 to 12 (n = 35)	> 12 (n = 33)	P-value
Hb (g/dl)	8.06 ± 0.74	9.62 ± 0.33	10.58 ± 0.29	11.60 ± 0.32	12.79 ± 0.55	0.000
Albumin (g/dl)	3.91 ± 0.43	3.99 ± 0.42	3.98 ± 0.37	4.02 ± 0.29	3.91 ± 0.39	0.700
Creatinine (mg/dL)	10.50 ± 2.94	10.70 ± 2.99	10.89 ± 3.34	11.32 ± 2.95	10.43 ± 2.89	0.766
BUN (mg/dL)	68.58 ± 18.60	71.23 ± 17.26	69.99 ± 17.93	7 3.46 ± 15.93	63.87 ± 13.60	0.201

in the >11 to 12 group, and 12.79 in the > 12 group (P <0.001) as shown in Table 2. Albumin, creatinine, and blood urea nitrogen (BUN) levels were not different in the five Hb levels (P> 0.05) and the means of albumin, creatinine and BUN values were similar in all five Hb levels (Table 2).

The score of quality of life in KDQOL-SF questionnaire were transformed onto a 0 to 100 scale range shown in Table 3 between symptom/problem, effects of kidney disease, burden of kidney disease, work status, cognitive function, quality of social interaction, sexual function, sleep, social support, dialysis staff encouragement, patient satisfaction and the SF-36 items which include overall health rating items and 2 domains; 1) the physical domain components consisted of physical functioning, role limitations due to physical health problems, pain, and general health perceptions and 2) the mental domain components consisted of emotional well being or mental health, role limitations due to emotional health problems, social functioning, and energy/fatigue or vitality. The better status patients had the higher score. For our hemodialysis patients, we compared the quality of life measured in 5 groups of patients according to the Hb level ≤9, >9-10 g/dl, >10-11 g/dl, >11-12 g/dl and >12 g/dl. It was found that at the different Hb levels, there were significant differences in the effects of kidney disease scores (p= 0.042).

About SF-36, almost all of the physical domains were not significantly different except the general health component which was significantly different in the different Hb levels as shown in Table 3. For mental domain components, the differences between 5 groups of Hb levels were not significant in the variety of quality of life domains, but the difference was statistically significant in role emotion scores and social functioning scores; p-value = 0.015 and 0.008 respectively.

DISCUSSION

From the controversy of the suggestions between the higher Hb levels in hemodialysis patients achieved with EPO was whether they were associated or not associated with an improved quality of life for these patients.[7,13] The FDA has recently reported that studies examining the quality of life of CKD patients treated with EPO have not been well done and have suggested that the labeling of the drug to indicate an improvement in quality of life was not warranted. However, many nephrologists still believe that the use of EPO has a significant quality of life improvement.[14-16]

In Thailand, hemodialysis patients receive recombinant human EPO for their anemia as a part of routine therapy, but the problem between containing drug expenditure and managing the anemia in the hemodialysis patient is the major issue that many studies cannot agree upon the appropriate target Hb level. Thus, the decision to treat anemic hemodialysis patients depends on the practice guideline that physicians rely on. All hemodialysis patients in this study used EPO for improving the Hb level and quality of life. This study evaluated the relationship between the various KDQOL domains and the difference of Hb levels in a cohort of hemodialysis patients at Siriraj Hospital which is the largest university hospital in Thailand. The improvement in various quality of life domains was mostly associated with Hb levels in the KDQOL-SF scores. The highest score was mostly occurred in the >12 group and the association between Hb levels and the KDQOL scores were significantly different in effect of kidney disease, general health, role emotion, social function and mental component summary scores as shown in Table 3. The limitation of this study was a nonrandomized, unselected cohort study involving 152 hemodialysis patients. Thus,

TABLE 3. Kidney Disease Quality of Life Short Form Questionnaire scores in hemodialysis patients and hemoglobin levels.

Parameter	≤ 9 (n = 26)	> 9 to 10 (n = 18)	>10 to 11 (n = 40)	>11 to 12 (n = 35)	> 12 (n = 33)	P-value
Kidney disease specific						
Symptom/ problem list	74.8	78.6	76.6	77.3	80.1	0.723
Effects of kidney disease	49.0	68.1	62.0	64.2	63.3	0.042
Burden of kidney disease	34.9	43.4	41.7	51.6	46.6	0.274
Work status	51.9	50.0	47.5	54.3	42.4	0.781
Cognitive function	80.0	84.8	82.2	83.2	86.7	0.671
Quality of social interaction	85.1	88.9	82.7	87.2	90.3	0.234
Sexual function	60.0	68.8	72.5	83.9	78.1	0.779
Sleep	58.6	60.8	59.3	60.5	68.6	0.422
Social support	86.5	89.8	84.6	91.4	87.9	0.630
Dialysis staff encouragement	88.9	86.8	88.8	87.1	89.0	0.986
Patient satisfaction	64.6	69.4	63.5	67.4	72.7	0.213
SF-36						
Physical functioning	60.2	57.8	60.0	63.6	67.1	0.836
Role physical	65.4	66.7	87.5	79.3	82.6	0.060
Pain	58.0	69.4	71.5	73.9	74.7	0.162
General health	29.8	45.8	35.4	43.1	44.2	0.023
Emotional well being	72.9	75.3	71.2	80.2	84.1	0.106
Role emotion	59.0	79.6	85.8	79.0	84.8	0.015
Social function	79.8	83.3	93.8	96.1	93.2	0.008
Energy/fatigue	58.7	56.7	59.9	60.9	71.4	0.173
Physical component summary	40.9	41.8	43.9	44.1	45.0	0.397
Mental component summary	48.1	50.9	51.1	53.7	55.9	0.039
Overall health	64.6	69.3	63.6	67.5	72.7	0.235

further study should be done with longitudinal data. Our results can summarize that increasing Hb increases the quality of life in some domains and the increases do not always continue, but can decrease when the Hb increases. Our findings did not have the same conclusion, but were similar to a randomized control trial study that some domains on the quality of life questionnaire increased by increase in Hb, but there were no significant changes in all domains.[6]

Nowadays, there is no evidence to show the best target level of Hb for anemia hemodialysis patient. While it is widely accepted that the renal anemia patients should receive EPO therapy, the appropriate target Hb level is still controversial. Many hemodialysis patients receive recombinant human EPO for their anemia as a part of routine therapy. Since EPO is an expensive therapy, it has created an economic burden on the health care system of every country including our country. Further studies should be focused on the evaluation of the cost effectiveness of EPO use for the different goals of Hb level, and effective measures to control EPO use for all patients.

CONCLUSION

The QOL scores in kidney disease components of the different Hb levels were not significantly different except in the effect of kidney disease, general health, role emotion, social function and mental component summary scores. About the SF36 component, it increases the scores on general health perceptions, role emotion, and social function which were related to the increase of Hb level. The treatment consideration should trade off between the improvement of quality of life and cost consequences since EPO requirements and costs increase as the target level of Hb rises. However, a long-term assessment should be considered.

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