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LABORATORY FINDING AND RESTLESS LEGS SYNDROME IN REGULAR HEMODIALYSIS PATIENTS

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Abstract

Introduction: restless leg syndrome, a complication that increases morbidity and mortality in hemodialysis patients, is a concern. To explore RLS we can start by looking at the baseline characteristics of regular hemodialysis patients.

Aim: To perform baseline characteristic and prevalence of RLS in regular hemodialysis patients.

Metode: This study involved 71 regular hemodialysis patients at the Haji Adam Malik Medan General Hospital using a cross sectional design. Through interviews in accordance with the criteria of the International Restless Leg Syndrome Study Group (IRLSSG) RLS status is enforce. Data of laboratory finding were obtained by laboratory examination. Using the SPSS-21 application, the data has been analyzed.

Result: Various baseline characteristics based on laboratory examination results (Hemoglobin; Calcium; Phosphate; Fibroblast Growth Factors-23; ferritin serum; Serum Iron; Tranferin Saturation; and Total Iron Binding Capacity) and prevalence of RLS in regular hemodialysis patients reach 26 respondents (36.6%)

Conclusion: In regular hemodialysis patients, there is an increase in levels of phosphate, calcium and FGF-23. Almost all patients were anemic. Of 71 respondents, 26 respondents (36.6%) with RLS.

Introduction

Based on data from the Indonesian Renal Registry, the number of new hemodialysis (HD) patients in Indonesia continues to increase from year to year.[1] Hemodialysis is still the main renal replacement therapy aimed to relieving uremic symptoms in patients with chronic kidney disease. Various complications can arise during hemodialysis such as Restless legs syndrome (RLS).[2] The prevalence of RLS reaching 20% in hemodialysis patients cannot be ignored.[3] In addition, there is an increase in morbidity and mortality in hemodialysis patients with RLS compared to HD patients without RLS (32, 3% versus 14.5%; $p < 0.004$).[2] Several studies, such as by Neves et al., have been conducted to determine factors associated with RLS.[3] Age, sex, anemia, iron deficiency and mineral and bone disorders (such as calcium, phosphate and Fibroblast Growth Factor-23 (FGF-23)) considered to be factors related to RLS.[3,4,5] In Indonesia, the RLS data is still limited. Therefore, this study was conducted to perform baseline characteristic of regular hemodialysis patients and prevalence of restless legs syndrome in hemodialysis patients.

Material & Method

An analytic observational study with a cross sectional study design was conducted in May-July 2019. A total of 71 regular HD patients at the Haji Adam Malik Medan General Hospital who met the criteria were sampled this study. Inclusion criteria: 1. undergoing HD at least 3 months; 2. Aged over 18 years. Exclusion criteria: 1. Being hospitalized; 2. there is evidence of infection, malignancy and drugs abuse; 3. Suffering from neurological disorders (eg stroke), venous static, arthritis, leg cramps, discomfort in the feet due to the position and habit of stomping the feet; 4. congestive heart disease class IV according to the New York Heart Association (NYHA) classification; 5. Incomplete data. Sampling was done by consecutive sampling technique.

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This research has been approved by the ethical committee. Patients who have expressed their willingness and signed an informed consent will be collected data through interviews, medical records and blood sampling. RLS is enforced by interview based on the criteria of the International Restless Legs Syndrome Study Group (IRLSSG). Patients diagnosed with RLS will be classified based on the International Restless Legs Syndrome Scale (IRLS) for degree of severity.

Data analysis using the SPSS-21 application. Number or frequency (n) and percentage (%) will be used to categorical variables. Numerical variables normally distributed were presented with the mean and standard deviation , whereas numerical variables that were not normally distributed were presented with the median and data range.

Results

Hemodialysis patients in this study tended to have anemia with mean Hb value 9.83 ± 1.21. The median value of calcium in this study was relatively normal 9.8 (8.0 - 10.9). The mean phosphate value was 5.5 ± 0.58. The median FGF-23 value is 309.0 (217.0 - 2000.0). The mean SI values were 83.9 ± 18.82, and TIBC 216.0 ± 14.82, with ST (%) 38.7 ± 8.38. The median value of ferritin was quite high 340.3 (49.0 - 1000.0).

According to IRLSSG, of 71 respondent, 26 respondents (36.6%) suffered from RLS. The degrees of RLS severity in 2 respondents was mild, 21 respondents was moderate, and 3 respondents was severe. none of the respondents suffered from very severe RLS.

Table 1. ***Baseline characteristic regular hemodialysis patients***

Variabel	n = 71
Laboratory Finding	
Ca (mg/dL)	9,8 (8,0 – 10,9)
P (mg/dL)	5,5 ± 0,58
FGF-23 (RU/mL)	309,0 (217,0 – 2000,0)
Hb (g/dL)	9,83 ± 1,21
SI (µg/dL)	83,9 ± 18,82
TIBC	216,0 ± 14,82
ST (%)	38,7 ± 8,38
Feritin (ng/mL)	340,3 (49,0 - 1000,0)
Status of RLS	
with RLS	26 (34,6 %)
without RLS	45 (63,4 %)
RLS Severity	45 (63,4 %)
Mild	2 (2,8 %)
Moderate	21 (29,6 %)
Severe	3 (4,2 %)
Very severe	0 (0%)

Note: Hb = Hemoglobin; Ca = Calcium; P = Phosphate; FGF-23 = Fibroblast Growth Factors-23; SF = ferritin serum; SI = Serum Iron; ST = Tranferin Saturation; TIBC = Total Iron Binding Capacity; RLS: Restless Legs Syndrome

Discussion

Mineral and bone disorders in regular hemodialysis patients are currently a concern since the association of hyperphosphatemia and vitamin D deficiency with RLS in uremic patients and in the general population is known.[3] In line with the decline in renal function, there is a progressive deterioration of mineral balance which is indicated by changes in the value of calcium, phosphorus and hormones circulating in serum and tissue.[6] In this study, both calcium and phosphate levels were close to normal. This may be supported by adequate dietary management and supplementation. Meanwhile, the level of FGF-23, a marker for mineral and bone disorders, in hemodialysis patients has no clear boundaries. In patients with chronic kidney disease, especially those on dialysis, an increase in FGF-23 is associated with increased of phosphate, increased of PTH and vitamin D intervention.[7] Increased FGF23 is associated with an increased risk of death, cardiovascular disease, hospitalization and heart failure.[7]

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However, the role of FGF23 is not yet fully understood in local mineralization during bone turnover and in systemic mineral metabolism.[7] Apart from its role in mineral and bone disorders, FGF-23 also has an effect on erythopoiesis. Patients with chronic kidney disease also suffer from osteopenia, osteoporosis or osteomalacia where bone components such as osteoblasts, extracellular matrix and minerals are related to the regulation of hematopoiesis function in adult mammals.[8] FGF-23 has a negative effect on erythropoiesis. It has been shown that inhibition of the FGF23 signal stimulates erythropoiesis and induces erythropoietin secretion.[8] In clinical studies, there is an inverse relationship between iron levels and FGF-23.[7]

In this study, almost all patients were anemic. Anemia, which is one of the complications of CKD, occurs in 80-90% of patients with chronic kidney disease.[9] According to the Perhimpunan Nefrologi Indonesia (PERNEFRI) 2011, the Hb value in this study is close to the target.[10] Mean transferrin saturation values above 20% and variations in serum ferritin leads to chronic disease anemia. In general, anemia in CKD is hypoproliferative and takes the form of normositer normochromes.[10] Low erythropoiesis activity is a characteristic of anemia in CKD which is in line with erythropoietin stimulation disorders.[11] Uremic conditions can also inhibit erythropoiesis which contributes to anemia. Other conditions such as shortening of red blood cell life can be caused by mechanical factors and metabolites. Deficiencies in nutrients such as folate and B12 due to anorexia or loss during dialysis are not common due to supplement use in dialysis patients.[12]

In this study, the prevalence of Restless Legs Syndrome (RLS) in regular hemodialysis patients reaches 36.6%. This is in accordance with a study of dialysis patients who diagnose RLS based on IRLSSG where the prevalence of RLS was around 20-62%. RLS in hemodialysis patients had a higher prevalence than the population without dialysis.[2,3] It was found that the prevalence of RLS was around 10-30% in hemodialysis patients.[2,5] Meanwhile, in general population based on RLS data in America RLS is found in 2.5-15% of the American population and around 2-5% in India and other Asian countries.[13] One of the factors associated with RLS is anemia with or without iron deficiency, where in this study we found that almost all respondents had anemia. Apart from that, RLS has also been linked to mineral and bone disorders. And as explained earlier, these three things can be related.

Conclusion

In this study, various laboratory parameters as baseline characteristics of regular hemodialysis patients have been presented. Of the 71 patients studied, it was found that the prevalence of RLS in regular hemodialysis patients reached 36.6% with various baseline characteristics based on laboratory examination results. There were relatively elevated levels of phosphate and calcium, increased FGF-23 and anemia in regular hemodialysis patients. Various limitations in this study in the form of involving only one place (single-center), The use of drugs / supplementation that is needed by the patient such as iron, ESA, phosphate binder, and others cannot be avoided. Finally, this is a cross-sectional study design.

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