ORIGINAL ARTICLE

Renal Tubular Function of the Child with Thalassemia Major who Received Repeated Blood Transfusions

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ABSTRACT A descriptive study was done from December 2, 1994 to January 5, 1995, at the Department of Child Health of Hasan Sadikin General Hospital Bandung. A total of 50 thalassemia major patients who had received 5,000 ml or more of blood transfusions and never received desferrioxamine underwent a renal tubular function test using a radionuclide technique (I-123 Hippuran) to determine the effective renal plasma flow (ERPF). The subjects were divided into two groups according to the amount of transfusion. Group A who received a total of 5,000 to 10,000 ml of blood transfusion consisted of 23 children (11 boys and 12 girls); group B, those who received a total of 10,000 ml or more of blood transfusion, consisted of 27 children (14 boys and 13 girls). The total average of blood transfused for group A and B were 7563.91 (1780.59) and 20,665.93 (6632.39) ml, respectively. The ERPF of all subjects were below the normal standard. The average value of ERPF of group A and B were 205.78 (62.08) and 214.09 (59.44) ml/minute/1.73 m^2, respectively. The correlation between the total amount of blood transfusion and ERPF of the subjects was not significant (Group A had r=0.163, p=0.458; Group B had r=0.084, p=0.934). **[Paediatr Indones 1999; 39: 193-200]**

Introduction

Recent advances in the management of children with beta-thalassemia major have significantly improved both the quality of life and the length of survival; however, the disease still cause significant problems in the future. Blood transfusion is still the main treatment for thalassemic patients. One of the disadvantages of repeated blood

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transfusion is the occurrence of iron overload and iron accumulation in various body organs such as the liver, heart, and kidney. The accumulation of this hemosiderin is detected more in the heart and liver compared to those in the kidneys.[1] With increasing survival of the children with thalassemia major, the effects of iron overload and accumulation of the hemosiderin in those organs become more severe, and eventually will result in dysfunction of the organs.

Previous studies report decreasing of cardiac and liver functions of the thalassemic patients with repeated blood transfusions. Renal function as the consequences of the hemosiderin accumulation has not been studied much. Mastrangello[2] in his study on 10 thalassemic patients aged 13-37 years showed that proteinuria and diminished urine concentrating ability were found in all patients. Landing[3] in his autopsy study on 18 thalassemic patients who received repeated blood transfusions found that tubular abnormalities predominated in those patients with chronic iron overload. The assessment of tubular function such as urine concentrating ability and urine beta-2-microglobulin have been reported. The present study aimed to determine the renal tubular function and the correlation between the total amount of blood transfused and the renal tubular function of the thalassemia major patients receiving repeated blood transfusions using radionuclide technique.

Methods

Our study subjects were thalassemia major outpatients at the Department of Child Health, Hasan Sadikin General Hospital, Bandung who had received packed red cell (PRC) transfusion with a total amount of 5,000 ml or more and had never received desferrioxamine. The subjects were then divided into two groups according to the total amount of blood transfusion. Group A comprised patients who received transfusions with the total amount of 5,000 to 10,000 ml of PRC and Group B consisted of patients who received transfusion with the total amount of 10,000 ml or more of PRC. In all subjects renal tubular function test was assessed by determining the effective renal plasma flow (ERPF) using I-123 hippuran at the Department of Nuclear Medicine, Hasan Sadikin General Hospital Bandung, from December 2, 1994 to January 5, 1995. The results of renal tubular function test from the two groups were analyzed using the t-test, and the correlation between the total amount of blood transfused and effective renal plasma flow (ERPF) value.

Results

Fisty thalassemia major patients consisted of 23 patients from Group A and 27 patients from Group B were enroled to this study. This study showed that all subjects were above three years old. The average age of group A was 6.39 (1.52) years and group B was 9.41 (1.82) years. See Table 1.

Table 1. Characteristics of thalassemia major patients in Group A and Group B

No	Age (years)		Sex		Total amount of PRC (ml)	
	A	B	A	B	A	B
1.	5.5	5.5	F	M	6,850	14,415
2.	5.5	11	M	F	8,425	14,850
3.	7	9	F	M	9,735	13,220
4.	7	13	M	F	9,540	30,400
5.	8	9	F	F	9,825	16,110
6.	8	8	F	F	5,725	13,515
7.	6	7	M	M	5,820	15,810
8.	8	8.5	F	F	9,810	19,000
9.	5,5	8	M	F	6,575	18,660
10.	6	11	M	M	8,740	26,250
11.	4.5	8	M	F	5,040	17,730
12.	10	9	M	F	9,245	14,245
13.	4	8	F	F	5,820	19,080
14.	7	12	M	F	5,245	23,405
15.	4	7.5	M	M	7,575	14,825
16.	5.5	10	M	M	9,450	21,485
17.	6	9	F	M	9,260	15,835
18.	7	10	F	F	9,375	30,970
19.	6	10	M	M	9,375	28,070
20.	5.5	9.5	F	M	6,425	34,705
21.	7	9	F	M	5,025	25,220
22.	9	10	F	M	8,315	29,895
23.	5	8	F	M	5,775	14,215
24.		11		M		26,150
25.		14		F		29,025
26.		10		M		15,185
27.		9		F		15,410

Note: M = male; F = female

Table 2. Results of ERPF value of thalassemia major patients in group A and B

Subject no.	ERPF value (ml/min/1.73m^2)	
	A	B
1.	188.98	263.22
2.	209.66	247.43
3.	142.54	170.78
4.	213.17	135.88
5.	224.50	208.76
6.	211.58	288.24
7.	188.78	145.47
8.	234.92	263.52
9.	312.09	257.82
10.	193.22	205.32
11.	142.39	78.17
12.	260.67	201.44
13.	231.72	300.08
14.	341.84	233.01
15.	288.89	198.37
16.	214.96	274.16
17.	67.11	186.90
18.	229.09	227.96
19.	170.22	327.07
20.	220.40	154.12
21.	182.54	193.96
22.	104.14	246.12
23.	159.36	127.08
24.		206.65
25.		263.98
26.		238.32
27.		136.64

Table 2 showed the results of ERPF value using radionuclide technique with I-123 labeled by hippuran. It was obvious that the ERPF value of all subjects (Groups A and B) were below the determined normal standard for above 3 years old (550-700 ml/min/1.73 m^2). Statistically, the mean of determined normal standard of ERPF was 625 ml/min/1.73 m^2. The average value of ERPF in group A was 205.78 (62.08) ml/min/1.73 m^2 (32.9% of mean normal value of ERPF), below the normal standard of ERPF ($p<0.001$); the average value of ERPF in group B was 214.09 (59.44) ml/min/1.73 m^2 (34.3% of mean normal value of ERPF), below the normal standard of ERPF ($p<0.001$). When total amount of blood transfused is correlated with ERPF value, the following figures are obtained. See Figure 1.

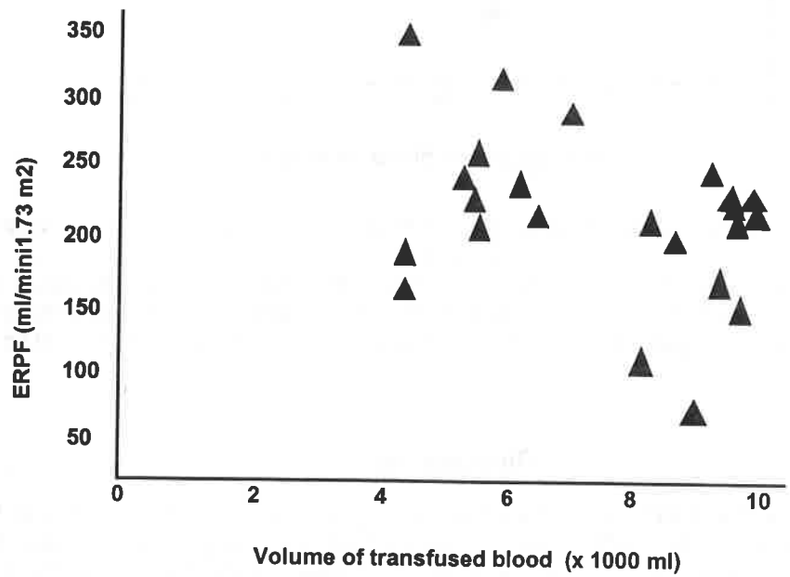

Figure 1. Correlation between total amount of blood transfusion received and ERPF value in group A.

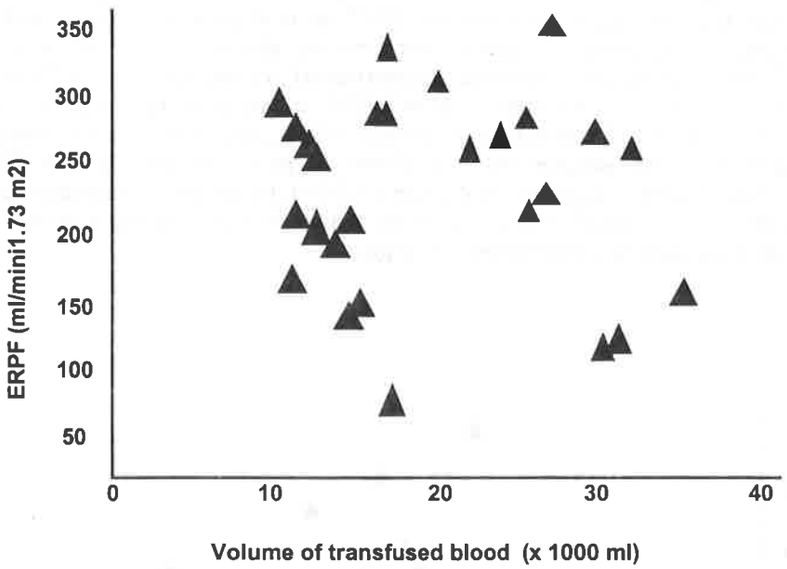

Figure 2. Correlation between total amount of blood transfusion received and ERPF value in group B.

Figures 1 and 2 showed that the observed data were scattered randomly, meaning that there was no significant correlation between the total amount of blood transfusion received and ERPF value (in Group A, r=0.163; p=0.458, and in Group B, r=0.084; p=0.934).

Discussion

Our data show that ERPF value of all thalassemia major patients (Groups A and B) were well below the determined normal standard for age group above 3 years old ($p<0.001$). In other words, there was a decrease of renal tubular function of the patients; renal tubular function for each group was less than 50% of the normal value. When the kidney function is less than 50% of the glomerular filtration rate, we have to be careful in giving medicines, i.e. by adjusting dose. Our study revealed that ERPF of the two groups were below 50% of the normal value. Should we adjust the dose when giving medicines to such patients? There is no answer yet.

Decrease in ERPF value (decrease in renal tubular function) in this study probably

can be associated with Landing's study[3] which showed that thalassemia major patients with repeated blood transfusions will have hemosiderin accumulation in various parts of the kidney, mostly in the tubules.

Study of renal tubular function using radionuclide technique is the most accurate method, because this method can access the tubular function qualitatively and quantitatively, thus explains more clearly than using previous techniques. Mastrangello[2] measured the tubular function using a different method (both after hydropenia and administration of antidiuretic hormone) and found that all subjects under their study losing their ability to concentrate urine. Landing[3] found that urine beta-2-microglobulin of the 21 thalassemia major patients was normal, meaning that there was no decrease of proximal tubular function. While Singadipoera[4] in his study on 17 thalassemia major patients who received repeated blood transfusions found that there was no significant decrease of renal function, using blood urea nitrogen, creatinine and creatinine clearance parameters.

This study revealed that all subjects had ERPF value significantly below normal limit and there was no correlation between the total amount of transfused blood and ERPF value. Actually, in this study a correlation between the total amount of blood transfused and ERPF value is expected. The possible factors which might be able to explain this result is as follows.

Besides type of blood (PRC, fresh whole blood or neocyte), total amount of blood received and whether iron chelating agent was given or not, other factors which need our attention are factors affecting the degree of anemia which finally increasing accumulation of hemosiderin, for example the irregularity of transfusions, infections, and nutritional state of the patients. According to Nicheles[5] a state of tissue hypoxia secondary to anemia may cause cell destruction and enhance accumulation of iron in that tissue. If the anemia is prolonged and continuous, a focus is formed in that organ which will enhance hemosiderin accumulation. In our study, there was no data on the irregularity of transfusions, infections and nutritional state of the patients. Although it is relatively easy to state these data, however, in practice it is difficult to prove.

In summary, we have shown that using radionuclide technique, the renal tubular function in thalassemia major patients who received more than 5,000 ml up to 34,900 ml is significantly disturbed, and there was no correlation between the total amount of blood transfusion received with the decrease of ERPF value.

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