Research of the month : June 2015

Treatment of β-Thalassemia/Hemoglobin E with Antioxidant Cocktails Results in Decreased Oxidative Stress, Increased Hemoglobin Concentration, and Improvement of the Hypercoagulable State

Multidisciplinary research

Treatment of β-Thalassemia/Hemoglobin E with Antioxidant Cocktails Results in Decreased Oxidative Stress, Increased Hemoglobin Concentration, and Improvement of the Hypercoagulable State

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Clinical Study

Treatment of β-Thalassemia/Hemoglobin E with Antioxidant Cocktails Results in Decreased Oxidative Stress, Increased Hemoglobin Concentration, and Improvement of the Hypercoagulable State

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Studies on the antioxidant treatment for thalassemia have reported variable outcomes. However, treatment of thalassemia with a combination of hydrophobic and hydrophilic antioxidants and an iron chelator has not been studied. This study investigated the effects of antioxidant cocktails for the treatment of β-thalassemia/hemoglobin E (HbE), which is the most common form of β-thalassemia in Southeast Asia. Sixty patients were divided into two groups receiving N-acetylcysteine, deferiprone, and either curcuminoids (CUR) or vitamin E (Vit-E), and their hematological parameters, iron load, oxidative stress, and blood coagulation potential were evaluated. Patients were classified as responders if they showed the improvements of the markers of iron load and oxidative stress, otherwise as nonresponders. During treatment, the responders in both groups had significantly decreased iron load, oxidative stress, and coagulation potential and significantly increased antioxidant capacity and hemoglobin concentration. The significantly maximum increase ($P < 0.01$) in hemoglobin concentration was 11% at month 4 in CUR group responders and 10% at month 10 in Vit-E group responders. In conclusion, the two antioxidant cocktails can improve anemia, iron overload, oxidative stress, and hypercoagulable state in β-thalassemia/HbE.

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Table 1: Patient characteristics.

	Curcuminoids cocktail			Vitamin E cocktail		
	Total	Responders	Non-responders	Total	Responders	Non-responders
Number of patients	25	16	9	25	19	6
Age (years)	32.5 ± 1.7	33.9 ± 2.5	30.1 ± 1.7	33.6 ± 2.1	33.0 ± 2.0	31.6 ± 4.3
Female : male, *n*	14 : 11	7 : 9	7 : 2	19 : 6	13 : 5	6 : 1
Splenectomy, *n*	11	7	4	9	6	3
Mean % change of serum ferritin at month 4 from baseline	−28.9	−39.7	+4.1	−33.5	−42.5	+4.7
Mean % change of RBC MDA at month 4 from baseline	−15.8	−24.2	−4.0	−30.1	−37.0	−5.4

The values represent mean ± standard error of the mean.
MDA: malondialdehyde; RBC: red blood cells.

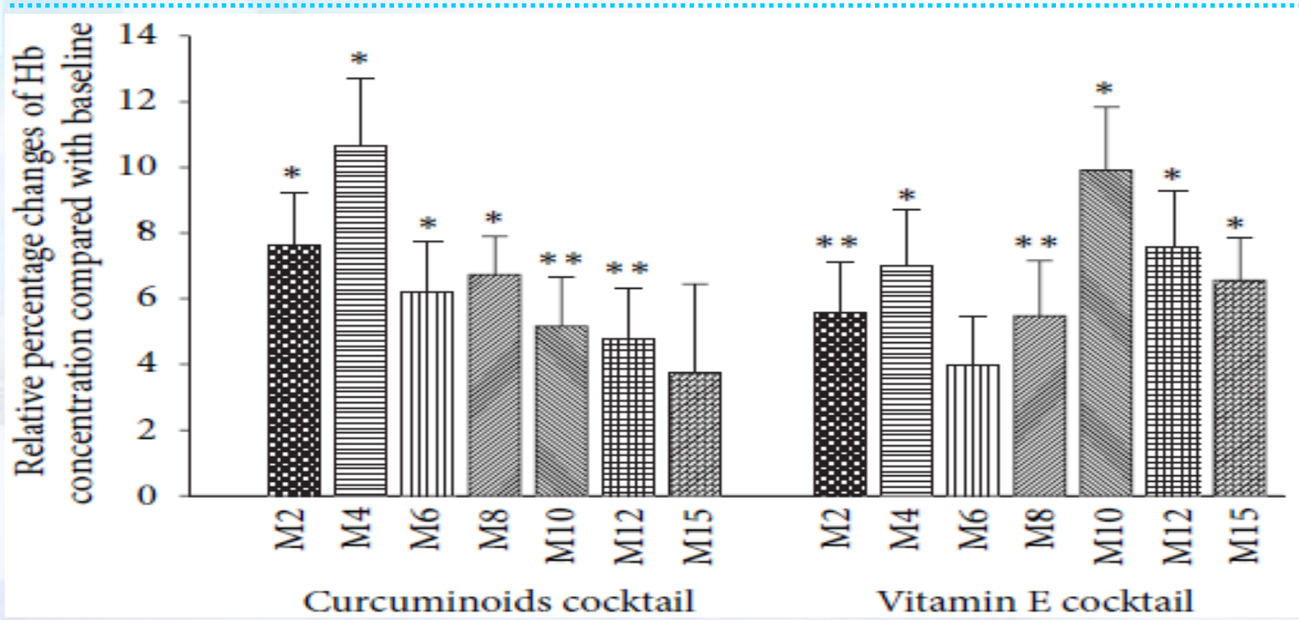

Figure 1: Percentage changes of hemoglobin concentration during and after the treatment period in patients with β-thalassemia/ hemoglobin E who responded to treatment with antioxidant cocktails.

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Table 2: Hematological, iron load, oxidative stress, antioxidant parameters, and markers of hemolysis in responders.

Parameters	Curcuminoids cocktail (n = 16)				Vitamin E cocktail (n = 19)			
	Baseline	Month 6	Month 12	Month 15	Baseline	Month 6	Month 12	Month 15
Hematological parameters								
Hemoglobin (g/L)	61.9 ± 2.3	67.8 ± 2.8[a]	66.9 ± 2.5[a]	63.9 ± 3.8	65.9 ± 3.4	69.6 ± 3.2	71.7 ± 3.5[a]	68.1 ± 3.0
RBC count ($\times 10^{12}$ cells/L)	3.40 ± 0.16	3.51 ± 0.15	3.52 ± 0.18	3.26 ± 0.18	3.63 ± 0.22	3.66 ± 0.19	3.75 ± 0.1	3.71 ± 0.22
Reticulocyte count (proportion of 1)	0.06 ± 0.01	0.03 ± 0.01[a]	0.04 ± 0.01	0.06 ± 0.01	0.05 ± 0.01	0.04 ± 0.01	0.04 ± 0.01	0.07 ± 0.02
Iron load parameters								
Serum ferritin (pmol/L)	3651 ± 855	1921 ± 426[a]	2018 ± 434[a]	2415 ± 598	4767 ± 773	2339 ± 532[b]	2065 ± 655[b]	2765 ± 622[a]
Serum NTBI (μmol/L)	5.3 ± 0.6	2.1 ± 0.2[b]	2.0 ± 0.5[b]	4.8 ± 1.0	4.9 ± 0.6	1.8 ± 0.3[b]	1.8 ± 0.3[b]	5.2 ± 0.7
Oxidative stress parameters								
ROS (%MCF)	51.1 ± 8.8	29.7 ± 3.3[a]	31.6 ± 6.8[a]	33.4 ± 4.8[a]	53.0 ± 7.0	28.6 ± 3.6[a]	33.5 ± 7.4	48.8 ± 15.1
RBC MDA (nmol/g Hb)	1542 ± 165	1150 ± 107[a]	934 ± 81[b]	1469 ± 151	1487 ± 138	815 ± 33[b]	698 ± 24[b]	1175 ± 79
Antioxidant parameters								
RBC SOD (U/g Hb)	5395 ± 278	4318 ± 179[b]	4727 ± 259	5094 ± 334	5051 ± 188	4245 ± 196[b]	4075 ± 219[b]	5097 ± 293
RBC GPx (U/g Hb)	63.7 ± 3.2	48.9 ± 1.9[b]	36.6 ± 1.4[b]	51.6 ± 2.8[b]	62.6 ± 2.6	48.9 ± 2.5[b]	36.6 ± 1.7[b]	47.3 ± 2.1[b]
RBC GSH (mmol/L)	1.74 ± 0.05	2.12 ± 0.06[a]	1.79 ± 0.14	1.76 ± 0.06	1.81 ± 0.04	2.10 ± 0.05[b]	2.04 ± 0.05[a]	1.82 ± 0.05
Markers of hemolysis								
AST (U/L)	43.3 ± 5.3	34.7 ± 3.8	35.5 ± 4.6	36.7 ± 4.0	46.7 ± 5.6	29.3 ± 1.9[b]	26.9 ± 2.6[b]	30.1 ± 3.0[a]
Total bilirubin (μmol/L)	79.4 ± 10.2	58.0 ± 7.7[a]	62.2 ± 10.2	65.7 ± 6.8	71.6 ± 8.7	57.7 ± 6.3	60.0 ± 7.6	66.2 ± 8.2
Indirect bilirubin (μmol/L)	69.3 ± 9.2	45.9 ± 7.2[a]	29.4 ± 0.6	50.3 ± 9.6	60.8 ± 8.4	45.4 ± 6.0	49.1 ± 7.4	54.9 ± 8.0

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Table 3: Procoagulation parameters, markers of platelet activation, and blood coagulation tests in responders.

Parameters	Curcuminoids cocktail ($n = 16$)				Vitamin E cocktail ($n = 19$)			
	Baseline	Month 6	Month 12	Month 15	Baseline	Month 6	Month 12	Month 15
Procoagulation parameters								
PF3-like activity (A_{405})	1.15 ± 0.12	0.86 ± 0.09	0.78 ± 0.10[a]	1.16 ± 0.16	1.24 ± 0.10	0.84 ± 0.08[b]	0.67 ± 0.06[b]	1.17 ± 0.12
PS^+RBC (%)	4.49 ± 0.71	1.90 ± 0.36[b]	1.64 ± 0.44[b]	4.18 ± 0.79	5.41 ± 1.03	2.10 ± 0.65[a]	1.73 ± 0.71[b]	3.55 ± 1.28
PS^+Plt (%)	1.02 ± 0.32	0.56 ± 0.16	0.40 ± 0.14	1.16 ± 0.32	0.61 ± 0.15	0.31 ± 0.06	0.24 ± 0.04[a]	0.61 ± 0.16
Platelet activation								
CD62 expression (%)	21.9 ± 4.0	9.0 ± 1.9[b]	13.8 ± 3.2	18.1 ± 3.9	16.9 ± 3.1	7.8 ± 2.1	12.3 ± 3.3	20.0 ± 4.6
PAC1 expression (%)	3.8 ± 1.0	0.9 ± 0.3[b]	2.0 ± 0.6[a]	2.4 ± 0.7	4.6 ± 1.1	1.1 ± 0.5[a]	2.7 ± 1.0	4.1 ± 1.5
Blood coagulation								
PT (s)	15.1 ± 0.2	14.0 ± 0.2[b]	14.4 ± 0.2	14.5 ± 0.4	14.9 ± 0.2	13.9 ± 0.2[b]	14.2 ± 0.2[b]	14.6 ± 0.2
aPTT (s)	31.3 ± 0.6	28.9 ± 0.6[a]	29.3 ± 0.8[a]	29.6 ± 0.8	30.8 ± 0.3	29.1 ± 0.4[b]	29.0 ± 0.5[b]	29.4 ± 0.5[a]
PT/aPTT	0.50 ± 0.01	0.47 ± 0.01[a]	0.49 ± 0.01	0.50 ± 0.01	0.50 ± 0.01	0.47 ± 0.01[a]	0.49 ± 0.01	0.49 ± 0.01