Differential diagnostic values of serum transferrin receptor, serum ferritin and related parameters in patients with various causes of anemia

This study involved 147 subjects, divided into 4 groups: 50 healthy controls, 54 patients with iron deficiency anemia (IDA); 34 with anemia of chronic disorders (ACD) and 9 with thalassemia. Serum transferrin receptor (sTfR), ferritin, total iron-binding capacity (TIBC), unbound iron-binding capacity (UIBC) and complete blood count were measured in all subjects. In 17 patients with IDA, serum ferritin, sTfR, and hemoglobin were rechecked after iron therapy. sTfR could differentiate patients with IDA from healthy subjects and those with ACD. Serum ferritin was better at distinguishing IDA from other causes of anemia, and was more sensitive than sTfR in indicating the iron repletion in patients with IDA after iron therapy.

Soluble serum transferritin receptor (sTfR) has been introduced as a new tool for diagnosing iron depletion.[1-5] It is applied mainly to distinguish iron deficiency anemia (IDA) from the anemia of chronic disorders (ACD),[5] and is a sensitive index of iron deficiency during pregnancy.[6] In the present study, we tried to compare the differential diagnostic values of sTfR, serum ferritin and other related parameters in different anemic diseases. Four groups of subjects were enrolled. Group A was formed of 50 healthy controls; 35 were male. Group B included 54 patients with IDA, diagnosed either by absence of iron stain in the marrow or a serum ferritin <20 μg/L in females and <40 μg/L in males; 14 of this group were male. Group C included 34 patients with ACD diagnosed according to Bentley's criteria,[7] with C-reactive protein 2.38±2.78 mg/dL (normal range: <0.5 mg/dL); 12 were male. Most of them had collagen disease, 8 had malignancy and 8 had chronic infection. Group D included 9 patients with α- or β-thalassemia trait diagnosed by hemoglobin electrophoresis and hemoglobin (Hb) H staining; 4 were male. In Group B, 17 patients treated with oral iron were consecutively selected to measure the changes of Hb, TfR and serum ferritin after periods of iron therapy (each period lasted ≥ 8 weeks), and to compare the relationships between these changes. Fasting morning blood samples were obtained from all subjects for measurement of sTfR, serum ferritin, total iron binding capacity (TIBC), unbound iron binding capacity (UIBC) and complete blood count (CBC) after informed consent had been signed.

sTfR, serum ferritin, TIBC and UIBC, and CBC were determined by the ELISA technique (IDeA sTfR IEMA, Orion Diagnostica, Espoo, Finland), radioimmunoassay (Clinical Assays™ GammaDab®, Ferritin ^{125}I RIA Kit, DiaSorin Inc. Stillwater, MN, USA; TIBC/UIBC Microtest, Daiichi, Tokyo, Japan), and by an automated hematology analyzer (Sysmex SE9000, Toa Medical Electronics Co. Ltd., Kobe, Japan), respectively. Transferrin saturation was calculated as (TIBC-UIBC)/TIBC. The Kruskal-Wallis test was used to compare each parameter among the 4 groups. All pairwise multiple comparison procedures (Dunn's method) were used to test the significance of differences in each identified parameter between any 2 groups. Pearson's correlation matrix was used to assess the changes of ferritin, sTfR and hemoglobin after iron therapy in the patients with IDA. All parameters except age were significantly different between the 4 groups (Table 1). In the anemic patients, the highest and lowest means of sTfR were found in the patients with IDA (7.39 mg/L) and with ACD (3.00 mg/L), respectively. The highest values of sTfR, sTfR/Fer and sTfR/log Fer were also found in the IDA patients.

Serum ferritin was significantly lower in patients with IDA than in patients without, but was not different among the non-IDA patients (Groups A, C, D, Table 2). Transferrin saturation was significantly lower in patients with IDA than in patients without. sTfR/Fer and sTfR/log Fer were significantly higher in IDA than in non-IDA patients.

Table 1. Means of serum transferrin receptor and other parameters in 4 groups of subjects (Mean ± SD).

	Age (yrs)	sTfR (mg/L)	Fer (μg/L)	T.S. (%)	Hb (g/L)	MCV (fL)	sTfR/ Fer	sTfR/log Fer
Controls	53.6±19.5	2.17±1.13	130±116	38.0±9.8	138±13	90.6±5.5	0.03±0.02	1.2±0.6
IDA	51.1±18.4	7.39±6.62	19.0±25.5	17.0±12.4	98±23	78.0±9.9	1.4±2.7	10.8 ±1.7
ACD	61.7±13.2	3.00±1.72	221±258	31.7±9.0	105±13	86.8±10.1	0.03±0.03	1.5±0.9
Thal	50.9±23.6	4.36±2.75	134±60	38.7±11.9	107±27	68.0±7.5	0.03±0.02	2.0±1.1

sTfR=Serum transferrin receptor; T.S.= Transferrin saturation; Hb=Hemoglobin; MCV=Mean cell volume; Fer=Ferritin; IDA=Iron deficiency anemia; ACD=Anemia of chronic disorders; Thal=Thalassemia.

Table 2. Difference in each parameter between any two groups of subjects*.

Groups	*Ferritin*	*STfR*	*T.S.*	*Hb*	*MCV*	*sTfR/Fer*	*sTfR/log Fer*
A vs B	+	+	+	+	+	+	+
A vs C	-	-	-	+	-	-	-
A vs D	-	-	-	+	+	-	-
B vs C	+	+	+	-	+	+	+
B vs D	+	-	+	-	-	+	+
C vs D	-	-	-	-	+	-	-

**All pairwise multiple comparison procedures (Dunn's method), a difference was regarded as statistically significant when p < 0.05, + indicates p < 0.05; – indicates p > 0.05. T.S.=Transferrin saturation; Hb=Hemoglobin; MCV=Mean cell volume; sTfR=Serum transferritin receptor; Fer=Ferritin. Group A: Healthy controls; Group B: Iron deficiency anemia (IDA); Group C: Anemia of chronic disorders (ACD); Group D: Thalassemia.*

Seventeen patients with IDA treated with oral iron were consecutively selected in order to monitor the changes of hemoglobin, sTfR and serum ferritin after iron therapy. The correlation between the change of serum ferritin and sTfR (r=-0.371, p =0.129) was not significant. Positive and negative correlations were found between serum ferritin and hemoglobin as well as between sTfR and hemoglobin, respectively (r=0.673 and -0.554; p =0.002 and 0.017, respectively). Serum ferritin changed more and faster than sTfR after iron repletion.

In the present study, mean sTfR was highest in the patients with IDA, and was significantly higher in patients with IDA than in those with ACD and healthy subjects. Thus, it could be used to distinguish IDA from ACD as reported by others.[5,7] However, sTfR was not significantly different between IDA and thalassemia, and thus could not distinguish IDA from anemias other than ACD. Serum ferritin could distinguish IDA from other non-IDA anemic patients, but it made no significant discrimination among the patients without IDA. In 17 patients with IDA treated with oral iron, there was no correlation between the change of ferritin and sTfR (r=-0.371, p =0.129) after iron therapy. The change of serum ferritin was more significant than the change of sTfR after iron repletion. Thus, the decrease of sTfR did not occur so rapidly as the increase of serum ferritin after iron repletion. This is compatible with the results of another study.[8] Serum ferritin should be better than sTfR in indicating iron repletion after iron therapy in patients with IDA.

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