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Thyroid Doppler indices in patients with sickle cell disease

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ABSTRACT

Objective: To evaluate the intrathyroidal hemodynamic changes and thyroidal volume in sickle cell disease (SCD) patients. **Methods:** Thirty-two patients with homozygous SCD and 32 control subjects were examined with color Doppler ultrasonography. None of the patients and control subjects had clinical or laboratory evidence of thyroid disease. **Results:** SCD patients had significantly higher resistance index (RI) and pulsatility index (PI) values and lower thyroid volume compared with control group. **Conclusion:** Increased intrathyroidal RI and PI and decreased thyroid volume may be due to impaired thyroidal microcirculation. Further and follow-up studies are needed to explain the relationship between Doppler parameters and thyroid functions.

1. Introduction

Sickle cell disease (SCD) is one of the most common hereditary hemoglobinopathy that is characterized by abnormally shaped (sickled) erythrocytes. The clinical features of SCD originate from as a consequence sickle-shaped erythrocytes, which occur in the deoxygenated state, and adhesion of these cells in microvasculature resulting in hemolytic anemia, chronic tissue ischemia, chronic progressive organ damage, and dysfunction [1,2].

Color Doppler ultrasonography (CDUS) is a noninvasive and reproducible imaging technique that enables quantitative information about blood flow velocities and vascular resistance. In addition it gives information about thyroid volume and morphology with gray scale sonography [3–5]. Changes in the hemodynamic of thyroidal vessels can be determined by these parameters that are more objective for evaluating thyroid function [4,5].

Previous literature describes the application of CDUS in many thyroidal disorders such as Graves' disease, Hashimoto's thyroiditis, spontaneous hyperthyroidism, amiodarone-induced thyrotoxicosis, diffuse goiter, and thyrotropin (TSH)-secreting pituitary adenoma are known to alter blood flow of the thyroid gland [5–10]. Differential diagnosis of destruction-induced thyrotoxicosis from Graves' thyrotoxicosis and amiodarone-induced thyrotoxicosis Type 1 from Type 2 is important for appropriate management, which is provided by CDUS [10,11].

Researchers have suggested that intraparenchymal Doppler measurements may be more reliable for detecting alternations of thyroid microcirculation and disease activity and is a useful index of thyroid function before any invasive tests [4,12]. The main complications in SCD are impairment of microcirculation and functional abnormalities of the organs [1,2].

The purpose of this study was to investigate the intrathyroidal hemodynamic changes and thyroidal volume in SCD and to compare it with control subjects using CDUS. To the best of our knowledge, this is the first study evaluating the intrathyroidal hemodynamics and thyroidal volume in patients with SCD.

2. Materials and methods

2.1. Study population

The study protocol was approved by the ethics committee of our institution, and informed consent was obtained from each of the volunteers or parents.

The study consisted of 32 patients [15, female (F); 17, (male) M] with homozygous SCD in a steady state (mean age±S.D., 25.9±8.6 years; range, 11–45 years) and 32 (18 F, 14 M) similar age and gender control subjects (mean age, 25.9±8.9 years; range, 10–47 years).

The SCD patients were recruited from the center of hemoglobinopathy of the state hospital and/or our hematology outpatient clinic. After enrollment, the medical history of the SCD patients was

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reviewed. The smoking habits, thyroid function, history of vasoocclusive crises, and transfusion of the patients were recorded. Chronic transfusion was defined as at least eight times per year or one transfusion at least every 7 weeks and 3 serum ferritin values within the previous 12 months, which averaged 2.000ng/ml [13,14].

Any SCD patients with a history of chronic transfusion, history of painful crises or history of blood transfusion within the last 3 months, hypertension, diabetes mellitus, liver, kidney, and cardiovascular disease were excluded from the study. In addition, patients with history of thyroid disease or anterior neck swelling and who were taking thyroid or antithyroid therapy, previous thyroid surgery, or radioiodine therapy were excluded. Blood samples were obtained for assessment of thyroid function test and hematological parameters.

Control subjects consisting of randomly selected patients who were routinely attending the radiology department for nonthyroidal ultrasonography and control subjects who had a known history of thyroid, hematologic, or cardiovascular disorder were excluded.

The smoking habits of the patients and control subjects were evaluated according to their history into active smoker or nonsmoker. The body mass index (BMI) was calculated according to the formula: BMI=body weight (kg)/height^2 (m^2).

2.2. Gray scale and Doppler sonography

Diagnostic B mode and a duplex Doppler US examination were performed by using a high-frequency 13–5 MHz linear array transducer (Acuson Antares 5.0, Siemens Medical Solutions, Mountain View, CA, USA). The thyroid screening was performed in a supine position with neck slightly hyperextended. Thyroid echogenicity was described subjectively as compared with the hyporeflective surrounding muscles and parotid glands. The normal echogenicity was defined as normal when it was similar to the parotid glands and higher than adjacent muscles [15].

Thyroid volume of each lobe was calculated after three measurements, the width, thickness, and length, then the volume is calculated by the formula (width×length×thickness×0.52 for each lobe) as previously described [16]. Total volume has been obtained by summation of two volumes. The width and thickness are measured on transverse section of the lobe, and the length is measured on longitudinal section.

CDUS images were obtained in the transverse and longitudinal planes after a 15-min rest period. In order not to underestimate the vascularization intensity, the probe slightly positioned on the skin without any compression. The Doppler parameters were designed to maximize detection of slow flow. Pulse repetition frequency was adjusted manually to its lowest setting without aliasing. Color gain was set to able to detect small vessels and reduce excessive colour noise. The wall filter was adjusted to lowest possible value.

The angle correction was not used because of the tortuosity of small intrathyroidal vessels. The Doppler sample window was set at 1 mm, and the measurements were performed at the level of intrathyroidal arteries in which it allowed to obtain good Doppler spectrum. On each Doppler tracing, measurements were performed only when the waveform modulation and amplitude remained stable on at least three consecutive cardiac cycles. Resistance index (RI) and pulsatility index (PI) were calculated automatically by the Doppler device on spectral Doppler waveform. RI and PI were determined as the following formulas RI=(peak systolic velocity−end diastolic velocity/peak systolic velocity) and PI=[(peak systolic velocity − end diastolic velocity)/TAMaxV], with TAMaxV=time-averaged maximum flow velocity and end diastolic velocity. Intraparenchymal Doppler indices were measured three times for right and left sides (n=6) to derive mean values on each patient and control subjects. All ultrasonographic measurements were obtained by a single radiologist. The operator was blinded to clinical status of the study population at the time of examination.

2.3. Statistical analysis

Continuous data are expressed as the mean±standard deviation (S.D.), and categorical variables are expressed as percentages. The normality of the variables was tested using the Kolmogorov–Smirnov test. Comparisons between two groups were assessed using Student's t test for continuous variables and a chi-square test for categorical variables. The Mann–Whitney U test was used for continuous variables that were not distributed normally. Pearson correlation test was used to assess associations between the Doppler parameters and other variables. Two-sided P values of less than .05 were considered statistically significant.

3. Results

Demographic and laboratory findings of the study population are summarized in Table 1. The patients with SCD and the control subjects were similar in relation to age, gender, BMI, smoking systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate (PR).

Thyroid function tests were normal in SCD patients and control subjects. Although serum concentrations of TSH in our study population was within the normal ranges, TSH level was significantly higher with 2.58±1.29 and 1.17±0.49 uIU/ml (P<.0001) in SCD patients than control subjects. There was no significant difference of free thyroxine (FT4) level between SCD and controls subject (0.85±0.16, 0.85±0.10 ng/dl, P>.05).

In the analysis of the SCD patients, there were no significant relationship between Doppler parameters and ferritin values or haemoglobin (Hb) and haematocrit (Hct) levels (P>.05).

The main CDUS and gray scale sonographic results obtained in the study groups are summarized in Table 2.

In CDUS, patients with SCD had significantly higher intraparenchymal RI and PI values than control subjects (Figs. 1, 2). The mean value of RI and PI of the patients and control subjects were 0.631±0.044 and 0.573±0.048 (P<.0001) and 1.04±0.12 and 0.89±0.13 (P<.0001), respectively. Gray scale sonography showed significant reduced thyroid volume in SCD group compared with control subjects (P<.05). There were no significant relationship between TSH levels and thyroid volume (P>.05). Patients and control subjects had normal diffuse sonographic echogenicity.

4. Discussion

To our knowledge, the current study is the first to use CDUS to evaluate intrathyroidal hemodynamic changes and thyroidal volume

Table 1
Demographic and laboratory findings of the study population

	SCD=32	Control subjects=32	P value
Age (years)	25.9±8.6	25.9±8.9	NS
Gender	15F, 17 M	18 F, 14 M	NS
Weight (kg)	56.3±12.4	62.3±13.4	NS
Height (m)	1.64±0.11	1.68±0.08	NS
BMI (kg/m^2)	20.7±3.2	22.0±3.7	NS
Smoking (n)	9	7	NS
SBP (mmHG)	113±10	117±8.44	NS
DBP (mmHg)	72±10	72.3±6.2	NS
PR	83.2±8.7	79.4±6.6	NS
Ferritin (ng/ml)	406.7±365.6	–	
FT4 (ng/dl)	0.85±0.16	0.83±0.10	NS
TSH (uIU/ml)	2.58±1.29	1.17±0.49	<.0001
Hb (g/dl)	8.79±0.76	13.70±1.22	<.0001
Hct (%)	24.31±3.5	39.90±3.2	<.0001
MCV (fL)	90.14±3.64	90.4±2.1	NS
MCHC (g/dl)	32.50±1.19	31.8±1.9	NS

NS: not significant; MCV: mean corpuscular volume; MCHC: mean cellular Hb concentration.