COMPARING THE SERUM TOTAL ANTIOXIDANT CAPACITY IN CHILDREN SUFFERING FROM HENOCH-SCHÖNLEIN PURPURA IN BOTH ACTIVE AND REMISSIVE PHASE OF THE ILLNESS

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ABSTRACT

Introdution*: In recent studies it has been well documented that oxidative stress plays an active role in pathogenesis of many diseases, including cardiovascular diseases, cancer, atherosclerosis and inflammatory disorders. On the other hand, Henoch-Schönleinpurpura which occurs in 10 out of one hundred thousand children is the most common child-time vasculitis; while the pathogenesis of the disease remains unknown, although it is generally considered a disease due to immunity complexes which is diagnosed by the presence of immunity complexes containing immunoglobulin A in vessels, especially in those of skin, gastrointestinal tract, and glomeruli. And it seems like oxidative stresses play a role indevelopment and clinical course of the illness. So far, few studies have been undergone about the importance of oxidative stress and antioxidant status of the people in development, clinical course and the types and severity of the symptoms of the illness.*

Methodology*: 48 patients, who were diagnosed suffering from Henoch-SchonleinPurpura and were hospitalized in nephrology unit in Motahari hospital, in Orumieh, were studied.During routine blood sampling, serum samples were also taken to measure serum total antioxidant capacity and they were kept at a temperature of minus 70 degree Celsius. Finally, the samples were tested by means of FRAP method.*

Results*: 48 patients suffering from Henoch were included in the study. The serum total antioxidant capacity in acute phase was significantly higher than that of recovery phase according to the results. Also, patients with higher organs involvement in their acute phase, had a significantly higher serum total antioxidant capacity.*

Conclusion*: The results of this study suggest that oxidative stress plays an important role in pathogenesis and disease severity in Henoch patients.*

Key words*: oxidative stress, antioxidant capacity, Henoch-Schönleinpurpura.*

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Introduction

In recent studies it has been well documented that oxidative stress plays an active role in pathogenesis of many diseases, including cardiovascular diseases, cancer, atherosclerosis and inflammatory disorders. Oxidative stress means a condition in which there is an imbalance between oxygen reactive species 1 and physiological antioxidants. As a result, many intra-cellular biomolecules will suffer from oxidative damage. Organisms have different antioxidant systems that help regulating oxygen reactive species and prevent this stress. These antioxidants include water-soluble and fat-soluble molecules such as glutathione, ascorbic acid, uric acid, tocopherol, carotenoids, coenzyme Q, bilirubin, some amino acids and certain plant compounds that exist in different tissues and cells and the overall antioxidant activities of these materials is called the Total Antioxidant Capacity (TAC).

In recent years, extraordinary advancements in biomedical science, has provided the opportunity toidentify the molecular basis of many diseases so that effective steps are taken to treat and prevent

them. The role of oxygen, nitrogen and chlorine reactive species are strongly approved in illnesses conditions; so that nowadays, more than seventy types of pathology, associated with oxidative stress and its biochemical results, such as lipid peroxidation, proteins, nucleic acids and carbohydrates are shown[1-7]. In 1993, Miller and his colleagues invented a test which measured the total antioxidant status, and called it "the total antioxidant capacity" (TAC). The main advantage of this test is its ability to measure the antioxidant capacity of all antioxidants in a biological sample, not just the antioxidant capacity of a particular composition. On the other hand, Henoch-SchonleinPurpura, affecting almost ten per one hundred thousand children a year is the most common acute vasculitis of childhood, which is more common in boys (60%) than girls (40%)[8-13]. Diagnosis of this illness is based on the presence of palpable purpura tissue samples showing immunoglobulin A, or two cases of diffusing abdominal pain, arthritis, or arthralgia, and renal involvement[14]. The pathogenesis is still unknown, though it is generally considered as a disease mediated by immune complexes in which there exists a presence of immune complexes containing immunoglobulin A in the coronary arteries of the body, especially in the skin, gastrointestinal tract and glomeruli[17-15]. And it seems like oxidative stress also plays a role in the incidence and clinical course of the illness[22-18].

On the other hand though Henoch-SchonleinPurpura is often a self-limiting disease, almost 40 percent of children will be stricken by nephritis 4 to 6 weeks after the first manifestation of the disease, which sometimes leads to complications such as high blood pressure, nephrotic syndrome, andeven kidney failure[23].

Little studies have been done about oxidative stress markers and persons' antioxidant status in the incidence, clinical course and types and severities of this illness. In these studies it has been proven that oxidative stress markers in patients suffering from Henoch in the active phase of the illness was higher than the remissive phase of the same people and control group and antioxidant markers were lower but the results were very different in the case of organs involvement[18-25].

Methodology

48 patients suffering fromHenoch-SchonleinPurpura,who based on clinical criteria,had palpable purpura with either of abdominal pain,arthritis or arthralgia and /or renal involvement, admitted in the nephrology unit in Motaharihospital were included in the study- 18 girls and 30 boys.

Inclusion criterion was a diagnosis of Henoch-SchonleinPurpura, and exclusion criteria included severe infection or other systemic diseases and the consumption of NSAIDs before the sampling. Based on the overall status and physical examination at the time of the sampling Patients were categorized into two groups of active and recovery phase of the disease. A serum sample was attained at the time of routine blood sampling for active-phase patients with their consent and the same was done for former patients (now healed). The sampled were kept in a condition of minus 70 degrees Celsius.

Organ involvement in patients was diagnosed with physical examination and laboratory criteria and patients with renal involvement were categorized using hematuria (more than 5 red blood cells per HPF per microliter of urine), proteinuria (more than 150mg/24hrs), an increase in urea and serum creatinine (more than two standard deviations above the normal values on the basis of age) criteria were divided into the following groups:

1. patients with isolated hematuria
2. patients with hematuria with a proteinuria less than the nephrotic syndrome range (less than 50 milligrams per one kilogram of body weight)
3. patients with hematuria with a proteinuria in the nephrotic syndrome range (greater than 50 mg per one kilograms of body weight)
4. Patients with hematuria along with an increase in urea and serum creatinine.

And in the case of each of these patients, serum total antioxidant capacity was measured by FRAP method. This method is based upon recovery of Ferric to ferrous ions by the restoring power of the serum which is measured at a wavelength of 593 nm by spectrophotometer.

Results

This is a descriptive-analytic study studying a group of children with Henoch-SchonleinPurpura in Motahari Hospital in Urumieh. The demographic data of the patients were collected based on hospital records and medical history and physical examination at the time of the sampling and results

are reported as mean ± of standard deviation. Data analysis was performed with SPSS version 22. The Student t-test or Chi-square was used to compare subgroups of patients based on the pattern of distribution of information and the number of samples used and the significant level of P is considered less than 0.05.

Out of 48 patients (18 males and 30 females) with Henoch-SchonleinPurpura, 31 patients (10 girls and 21 boys) were in the recovery phase and 17 patients (8 girls and 9 boys) were in the active phase of the illness.Some of the information about 3 patients was not available. Patients were from 2 to 14 years and mean age was of 6.1±2.7 years. All patients had palpable purpura in the lower organs.

36 patients suffered from gastrointestinal involvement in the form of abdominal pain out of which 5 vomited and 7 had gastrointestinal bleeding (one because of intussusception) and 40 children had severe involvement with arthritis or arthralgia.

27 patients had renal involvement out of which 6 people in form of isolated hematuria, 15 with hematuria with a proteinuria less than the range of nephrotic syndrome, and 2 people with nephrotic syndrome, and one person who hada kidney failure, over whom kidney transplant was performed. 11 patients relapsed.

	Active phase	Remissive phase	Total	P value
Number (percent)	15 (22%)	30 (67%)	45	
Average age (percent)	5.4+-2.2	6.5+-2.9	6.7+-2.1	0.18
Sex (percent)	8.7	20.10	28.17	0.43
Palpable purpura (percent)	15(100%)	30 (100%)	48 (100%)	-
Gustrointestinal involvement (percent)	10	26	36	0.11
Joint involvement (percent)	12	28	40	0.18
Nephritis (percent)	11	16	27	
Isolated hematuria	2	4	6	
hematuria + proteinuria≤ nephrotic	4	11	15	
proteinuria + hematuria ≥ Nephrotic	4	1	5	
Kidney failure	1	0	1	
Relapse	5	6	11	
Corticosteroid treatment	14	23	27	0.16
Response to Corticosteroid	9	19	28	

Table 1: Study group features.

Corticosteroid treatment was used for 37 patients, 28 of whom had responded to the treatment.

Statistically no significant correlation was found between serum total antioxidant capacity and sex, age or recurrence and response to Corticosteroid (P> 0.05).

Serum total antioxidant capacity was significantly lower in patients in the acute phase than those in recovery phase (P = 0.34).

There was no clear relationship between gastrointestinal/joint involvement and serum total antioxidant capacity; while for people in remissive phase and suffering from gastrointestinal and joint involvement there was a higher level of blood TAC. The presence or absence of renal involvement as well as the intensity of the involvementdid not associate with serum total antioxidant capacity in the acute or recovery phase (p = 0.3).

	With gastrointestinal involvement	Without gastrointestinal involvement	P value
Acute phase	989.09	622.26	0.12
Remissive phase	1122.63	744.24	0.038

Table 2: Comparison between serum total antioxidant capacity and gastrointestinal involvement.

Based on the obtained results, the more number of organs in the past for patients in the remissive phase, higher serum total antioxidant capacity will be, and no such relationship was found in the active phase.

	With gastrointestinal involvement	Without gastrointestinal involvement	P value
Acute phase	867.45	864.26	0.94
Remissive phase	1106.45	592.32	0.041

Table 3: Comparison between serum total antioxidant capacity and gastrointestinal involvement.

P Value	Without nephritis	With nephritis		
0.9	829.62 ±421.3	683.35 ± 153.5		Acute phase
		995.47 ±511.1	G2	
		863.51	G3	
		982.74	G4	
0.21	984.76 ±310.1	1191.89 ± 323.9	G1	Remissive phase
		1094.21 ± 358.6	G2	
		1574.78	G3	
			G4	

Table 4: Comparing the serum antioxidant capacity and renal involvement.

P Value	Three organs	2 organs	One organ	
0.39	1070.8 ±286.9	726.55 ±435.8	845.05 ±439.02	Acute phase
0.007	1258.9 ±299.7	1003.04 ±302.2	670.92 ±129.8	Remissive phase

Table 5: Comparing the serum antioxidant capacity and number of organs.

Discussion and conclusion

Henoch-Schonlein Purpura is the most common systemic vasculitis in childhood. Although many causes have been proposed to explain the etiology and pathogenesis of the disease, but none of these assumptions are conclusive[27]. Despite the numerous studies done on the role of oxidative damage in inflammatory diseases, little clinical research study about this issue is available in the case of vasculitis[29, 28]. The release of reactive oxygen species from inflammatory cells, causes oxidative stress and hence tissue damage. Henoch-Schönleinpurpuraseems to have oxidative damage like any other inflammatory disease.

As shown in studies of Demircin, Erdogan, Chen, Ece and gurses, antioxidant markers in the acute phase are significantly lower than those in remissive phase. Our study confirms this subject, so it is also evidence on the role of oxidative stress in diseases.

In a study conducted by Yilmaz and his colleagues in 2009 in Turkey, it has been shown that polymorphisms in the gene PON-1, being an antioxidant enzyme, changes the incidence of Henochin a way that the genotype QQ increases the risk of Henoch ($p = 0.000$).However, no evidence has been found about this gene and the clinical course and renal involvement; so this also emphasizes the role of oxidative damage in the pathogenesis of Henoch[18].

Also, in our study the bigger number of organs involved in the patients recovered in the past, more serum antioxidant capacity there was. This was also significantly meaningful for joint and gastrointestinal involvement and lower connection with renal involvement was perhaps due to the low number of patients with severe renal involvement ($n = 3$) versus milder cases.

There are several compensatory mechanisms that limit oxidative damages. Antioxidants are chemical compounds that bind to free oxygen radicals and prevent damages to healthy cells. With a reduced serum total antioxidant capacity in patients with acute phase compared to those in recovery phase we can conclude that an overcome of oxidative stress over the compensatory mechanisms causes their disease and people with more organ involvement are victims of more severe oxidative stress and need more powerful compensation.

Different Endogenous and exogenous causes have been presents for increased oxidative stress; BMI, gender, race, specific mutations in mitochondrial DNA, chronic diseases, exposure to cigarette smoke, the high level of non- saturated fat in diet, low intakes of fruits and vegetables, low physical activity and prolonged immobility, acute psychological stresses, low levels of ascorbic acid and carotenoids in blood, lowblood transferrin and high cholesterol are some of them[30].

The results of this study suggest a role of oxidative stress in incidence and severity of Henoch-SchonleinPurpur and the serum antioxidant capacity in the recovery from the disease; based upon which effective steps can be taken to prevent and treat the illness. And more and broader studies about the subject are necessary.

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