ERYTHROCYTE SEDIMENTATION RATE DETERMINATION IN CHILDHOOD ASTHMA DUE TO HOUSE DUST ALLERGY

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ABSTRACT

Background: Allergy is a disease of inflammation. The evidence of elevated erythrocyte sedimentation rate in asthmatic patients due to house dust allergy and its correlation with house dust positivity have not been fully elucidated. Objective: To investigate the findings of erythrocyte sedimentation rate elevation and its correlation with positivity reaction of house dust allergen. Methods: The study is an observational retrospective study. The patients were asthmatic children visiting the pediatric allergic outpatient clinic, during the period of 1 January 2000-31 December 2000. Included in this study were asthmatic patients with positive house dust skin test reaction. Blood examinations were taken from the patients including erythrocyte sedimentation rate on the first visit to the hospital. Results: Seventy-three children (40 boys and 33 girls) were enrolled in this study. Increased erythrocyte sedimentation rate were noted in 26 patients (49%) with positive house dust skin test reaction. Coefficient correlation between House Dust and erythrocyte sedimentation rate (1 hour) was –0.087 (p=0.467) and coefficient correlation between House Dust and erythrocyte sedimentation rate (2 hour) was -0.203 (p=0.121). Conclusion: This indicates that elevated erythrocyte sedimentation rate possibly could be used as one of parameters of allergic reactions. There is no correlation between either 1 hour or 2 hour erythrocyte sedimentation rate and House Dust positivity reaction.

Keywords: Childhood Asthma, erythrocyte sedimentation rate, and house dust allergy.

Abbreviations used
ESR: Erythrocyte Sedimentation Rate
HD: House Dust
Hb: Hemoglobin concentration
CRP: C-reactive protein

INTRODUCTION

The laboratory examination that is a simple, inexpensive and frequently ordered in clinical medicine is ESR determination. (Brigden, 1999; Wolfe, 1994). The routine laboratory tests done to the children, referred to the pediatrician for evaluation of allergy are: hemoglobin concentration, leukocyte count, differential count, ESR, mantoux test, skin testing, and chest x-ray. (DeVries, 2000; Santosa, 1980). An increased ESR is associated with some condition such as: anemia, macrocytosis, tilted ESR tube, infection, inflammation, malignancy, etc. (Brigden, 1999).

Degranulation of mast cell is triggered by IgE-antigen binding. Then, some mediator such as histamine, neutrophil chemo tactic factor, and eosinophil chemo tactic factor are released and synthesis of leukotriens and prostaglandin occurred. All of these events increase vascular permeability so interstitial exudation and chronic inflammatory reaction occurred. (Rote, 1994; Leung, 1996). Skin test is one of the important diagnostic procedures in allergy patients. Food skin testing can be positive but it does not mean anything. Positive House reaction is more relevant with the clinical symptoms (Partana, 1980). The purpose of this study is to determine whether there is increase of ESR and if it does so, whether there is correlation with the positivity of house dust skin test reactivity.

METHODS

Patients: all of the children referred to the children allergic clinic Dr Soetomo hospital for 1 year (January 1, 2000 until December 31, 2000). Retrospective evaluation about sex, age, eosinophil, hemoglobin concentration, leukocyte, ESR 1 hour, ESR 2 hours (Westergreen method) and diameter of house dust reaction was done.

Inclusion criteria: Asthmatic patient either boy or girl with positive house dust skin test reaction and available diameter of reaction. Exclusion criteria:
1. Incomplete data
2. Anemia (Hb < 10 g/dl) or policytemia (Hb > 15 g/dl), leukocytosis (leukocyte count > 11.000/ cmm) or leukopenia (leukocyte count< 4.000 / cmm).
4. Tuberculosis.

Spearman correlation coefficient was calculated because of skew distribution. Data were analyzed using Version 10.0 of SPSS. Statistical significance was declared at the 0.05 levels.
RESULTS

A total of 323 patients were referred to the children allergic clinic Dr Soetomo hospital. Positive house dust reaction was noted in 123 patients. 50 of them were excluded, 39 because of incomplete data, 5 because of leukocytosis, 3 because of leukopenia, 1 because of anemia and 2 because of polycythemia. A number of 73 patients were enrolled in this study. 40 of them are male and 33 are female with age ranged from 1 year to 14 years. An increased ESR in 1 hour was found in 36 patients (49%) and normal ESR was found in 37 patients (51%).

Table 1. Characteristic of laboratory results.

<table>
<thead>
<tr>
<th>No</th>
<th>Variable</th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hemoglobin conc.</td>
<td>10.4-14.9</td>
<td>12.9</td>
<td>0.9</td>
</tr>
<tr>
<td>2</td>
<td>Leukocyte count</td>
<td>4,000-10,900</td>
<td>6,995</td>
<td>1,954.8</td>
</tr>
<tr>
<td>3</td>
<td>ESR 1</td>
<td>3-80</td>
<td>21.3</td>
<td>16.02</td>
</tr>
<tr>
<td>4</td>
<td>ESR 2</td>
<td>5-119</td>
<td>37.6</td>
<td>23.6</td>
</tr>
<tr>
<td>5</td>
<td>Eosinophil</td>
<td>0-6 %</td>
<td>1.3 %</td>
<td>1.2 %</td>
</tr>
<tr>
<td>6</td>
<td>Diameter of House dust reaction</td>
<td>2.2-30.5</td>
<td>15.3</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Table 2. Correlation between ESR & positive HD reaction

<table>
<thead>
<tr>
<th>No</th>
<th>Variable</th>
<th>Coeff correlation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ESR 1 hour &amp; HD</td>
<td>-0.087</td>
<td>0.467</td>
</tr>
<tr>
<td>2</td>
<td>ESR 2 hour &amp; HD</td>
<td>-0.203</td>
<td>0.121</td>
</tr>
</tbody>
</table>

DISCUSSION

ESR determination is a simple method, inexpensive and widely used in the laboratory examination. The principle is measurement of decreased level of erythrocyte after 1 hour and 2 hour in vertical tube because of gravitation. There are 2 methods: Wintrobe and Westergreen. Normal value of ESR: Wintrobe: male 0-10 mm/hour, female 0-15 mm/ hour. Westergreen: male 0-13 mm/hour, female 0-20 mm/ hour. (Brigden, 1999; Kjeldberg,1993).

Factors that increased ESR are: old age, female, pregnancy, anemia, macrocytosis, technical factor, increasing fibrinogen level due to infection, inflammation or malignancy. Factors that decreased ESR are severe leukocytosis, polycythemia, anisocytosis, spherocytosis, and technical factor. (Brigden, 1999).

Children with inflammation due to infection or other tissue damage (immunology process, trauma, ischaemia, or malignancy) develop a systemic response, which includes fever, a neutrophil leukocytosis, and an increase concentration of several plasma proteins of hepatic origin. These changes are collectively known as the acute phase response and are mediated by cytokines, such as interleukin-1 and tumor necrosis factor, which are synthesized by macrophages, mast cell or basophile. (Leung, 1996; Stuart, 1988). The term acute phase is ill defined but refers to the intensity rather than the duration of inflammatory response so that a child with chronic disease may also show an increase in acute phase reactants, either intermittently or persistently. These acute phase proteins are: C-reactive protein, serum amyloid A protein, alpha-1-antichymotripsin rise within 6 to 10 hours of injury, show large incremental increases of 10 to 1000 fold over their normal values, have short half lives, and behave consistently in different forms of inflammation. Orosomucoid, alfa-1-antitrypsin, haptoglobin and fibrinogen rise after 24 to 48 hours, rarely increase more than twofold, have long half lives and with exception of orosomucoid, show variable catabolism in some diseases. C3, C4, and caeruloplasmin generally show poor and inconsistent acute phase responses. (Stuart, 1988).

The relative contribution of different plasma proteins to erythrocyte sedimentation rate is fibrinogen 55 %, alpha-2-macroglubulin 27 %, immunoglobulins 11 % and albumin 7%. Thus, in parallel with changes in fibrinogen, ESR test respond slowly to inflammation,
not showing an increase until 24 hours or more after the onset and falling slowly to normal with a half time of 96-144 hours on resolution of inflammation. It has the advantage of being less affected by acute events, such as a viral infection, that cause a transient increase in sensitive acute phase proteins such as CRP. (Stuart, 1988).

A factor of importance in affecting the sedimentation rate in the diseased state is the size of the sediment particle. The larger the volume of the particle, the smaller the relative surface area. In the presence of rouleaux formation aggregates of large volume but relatively small surface area are produced, accelerating the sedimentation rate. Rouleaux formation may result from changes in the negative charge of red cells, which in turn is a function of sialic acid groups of the cell membrane. This charge may be attenuated by the dielectric effect of proteins in the surrounding plasma, especially asymmetric macromolecules such as fibrinogen and gamma globulin. Thus alterations in the ESR generally reflect alterations in this plasma protein. Indeed, the addition of fibrinogen to normal plasma leads to a greatly increased sedimentation rate. (Kjeldberg, 1993). Increased ESR was found in 36 (49%) patients indicating that in the allergic patients, the ESR could be increased. As mention before it may be due to the mediator IL-1 and TNF produced by mast cell, basophile and macrophage. (Leung, 1996; Kjeldberg,1993; Stuart, 1988) Then, these mediators stimulate the liver to produce acute phase proteins, such as fibrinogen. (Stuart,1988) Increasing level of fibrinogen will increase positive charge of dielectric plasma protein and rouleaux formation will be found. These rouleaux formation increases the ESR. (Kjeldberg, 1993).

In allergic reaction, there is binding of allergen and IgE in the mast cell and basophile surfaces These binding trigger releasing of mediators, such as histamine, protease, heparin proteoglikan, eosinophil and neutrophil chemo tactic factor. Stimulation to the mast cell and basophile also trigger releasing of leukotriene C4, D4, E4, prostaglandin D2, and platelet activating factor (PAF). These effects include increased vascular permeability and vasodilatation, bronchial smooth-muscle contraction, increased mucous production, as well as increased chemo taxis of eosinophils, neutrophils, and mononuclear cells. (Leung, 1996)

Recently, it has also been found that cross-linking of IgE on these same cells results in the synthesis and release of a variety of cytokines including IL-1, IL-3, IL-4, IL-5, IL-6, GM-CSF, and TNF. These cytokines play a critical role in the induction of late-phase allergic responses, regulation of IgE synthesis promotion of mast cell differentiation and survival, and the sustaining of chronic allergic inflammation by modulating leukocyte effectors function and expression of cellular adhesion molecules. (Leung, 1996)

There are 3 ways to do the skin-testing, intradermal, prick test, and scratch test. (Owmby, 1996; Munasir, 1996). In this study we used the scratch test. The best area to perform the skin testing is volar forearms, 2 cm from elbow fold and wrist. The scratchier is lightly pressed into the epidermis, and the tip of the scratcher then attenuated, producing a small-punctuated laceration. The lesion should not be deep enough to produce visible bleeding. After the scratch has been made the extract can be dropped to the spotted lesion. The scratch test has higher specificity than intradermal test but the sensitivity is lower in the lower concentration and potency. (Munasir, 1996).

After the allergen has been introduced into the skin, the allergen diffuses through the skin and interacts with IgE antibody bound to mast cells. If the allergen binds to two or more IgE antibody molecules bound to a mast cell bridging the IgE molecules, a signal is generated initiating mediator release from the cell. Most of the immediate skin response is due to the release of histamine. The central wheal of the skin response is due to histamine induced vasopermeability and secondary edema. The central erythematic results from histamine-induced arteriolar vasodilatation and circumferential erythematic results from the stimulation of nerve receptors and a resulting axon reflex vasodilatation. Maximal reaction occurs after 15 to 20 minute and then can be followed by late reaction after 4 – 8 hours. (Owmby, 1996; Munasir,1996). Other study showed that Langerhans epidermal cell could express FceRI (receptor for IgE); so in vitro the Langerhans epidermal cell bound IgE can capture the house dust mite for allergen presentation. (Leung, 1996). Most of the visible skin testing can be blocked by antagonist receptor H1, but for the complete inhibition need antagonist H1 and H2. (Owmby, 1996; Munasir, 1996). Variation results of positive house dust reaction in this study ranged from 2.2 to 30.5 mm (mean 15.3 mm, deviation 6.7 mm). The variation of positive reaction can be affected by age, which is affecting the reactivity of the skin. The younger age, the lower reactivity of the skin can be found (11) In this study the age of subject ranged 1 year until 14 years.

We found, there is no significant correlation between house dust reaction and ESR (coefficient correlation HD & ESR 1 hour: -0.087, p = 0.467 and coefficient correlation HD & ESR 2 hours: -0.203, p=0.121). As mention before, after the allergen has been introduced into the skin, the allergen diffuses through the skin and
interacts with IgE antibody bound to mast cells. If the allergen binds to two or more IgE antibody molecules bound to a mast cell bridging the IgE molecules, a signal is generated initiating mediator release from the cell. Most of the immediate skin response is due to the release of histamine. (Leung, 1996). Fibrinogen, as one of the acute phases protein produced by liver, increases after 24 – 48 hour and in parallel with changes in fibrinogen concentration ESR respond slowly to inflammation. (8,9) The increased of ESR in this study may be due to inflammation process of allergy so mediator IL-1 mediates the high level of fibrinogen produced by liver, and TNF produced by mast cell and basophile. (Leung, 1996; Kjeldberg, 1993).

CONCLUSION

This indicates that elevation of erythrocyte sedimentation rate possibly could be used as one of parameters of allergic reactions. There is no correlation between either 1 hour erythrocyte sedimentation rate or 2 hour erythrocyte sedimentation rate and house dust positivity reaction.

REFERENCES

DeVries TW. Routine laboratory test unnecessary for children referred for recurrent wheezing and/or asthma. Ned Tijdschr Geneeskd 2000; 144:2107-11.