Original Article *Iran J Ped Hematol Oncol. 2017, Vol7.No3, 149-153*

Evaluation of Immunoglobulin-A Level in Children with Acute Lymphoblastic Leukemia

Robab Sheikhpour PhD[1], Azam Hashemi MD[1], Elham Akhondzadeh MSc[2], Zohreh Khanjarpanah BSc[2], Mahnaz MirAkhor BSc[2], Razieh Akhond Zardini MSc[3]

1. Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Department of Pediatric, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
3. Infectious Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

*Corresponding author: Dr. Robab Sheikhpour, Address for correspondence: Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. E-mail: R.Sheikhpour@yahoo.com

Received: 25 March 2017 **Accepted:** 12 June 2017

Abstract

Background: Acute lymphoblastic leukemia (ALL) is the most common type of leukemia among children. Immunoglobulin A is the most numerous immunoglobulin isotype in mucosal secretion. Immunoglobulin A (IgA) deficiency can increase risk of cancer in patients. Since few studies have been done on relation between serum IgA and ALL, this study was attempted to evaluate serum IgA in ALL patients.

Materials and Methods: In this descriptive analytical study, 28 pediatric patients diagnosed with ALL with mean age of 6.75± 3.29 ranged from 1 to11 years old and 28 controls with mean age of 7.31± 4.12 ranged from 2 to 12 years old were chosen from Shahid Sadoughi Hospital. Serum IgA was measured by immunotorbidometric method (Pars Azmoon Kit, Iran). Pearson and Independent t test were used for the analysis of data.

Results: In this study, the mean level of IgA was lower in patients with ALL (82.5± 21.3 mg/dl) in comparison to control group (113.2± 26.62 mg/dl). Moreover, there was significant difference between two groups ($P<0.01$). Regarding patients age, no significant difference was seen either ($P>0.05$).

Conclusion: According to the results of the present study, the serum level of IgA was significantly lower in ALL pediatric patients than the control group; however, it was in normal range in both groups. More studies are needed to strongly conclude IgA deficiency as a new risk factor or as a new marker of ALL in children. Other immunoglobulins are recommended to be considered in patients with ALL in further studies.

Key Words: Acute Lymphoblastic Leukemia, Immonoglobulin, IgA deficiency

Introduction

One of the most fatal diseases in human beings is cancer with the death of about 30000 persons annually in Iran (1, 2). Leukemia as a common and important cancer starts in blood (3). Acute lymphoblastic leukemia (ALL) is the most common type of leukemia among children (4). So that incidence peak of ALL is between 2 to 5 years old. The survival rate of ALL in children has been improved nearly 90% (5). Moreover, the annual incidence of ALL has increased 0.8% per year from 1975 to 2006 (6). It is estimated that 6000 new cases of ALL are recognized annually in the United States (5). ALL as multi-factorial disease arises from interaction between exogenous or endogenous exposures, genetic susceptibility, and chance (5). These factors account for the approximately 1 out of 2000 risk of childhood ALL (5). Treatment of ALL involves short-term intensive chemotherapy, including high-dose methotrexate, cytarabine, cyclophosphamide, dexamethasone or prednisone, vincristine, L-asparaginase, and/or an anthracyclin and radiation therapy. These treatments are used for patients who show evidence of Central Nervous System (CNS) or testicular leukemia, although this approach is controversial at the current time, especially in children (7). Moreover, immunoglobulin A (IgA) is the most numerous immunoglobulin isotype in mucosal secretion (8). IgA exists in two

isotypes, IgA1 and IgA2 which are glycosylated proteins (10). IgA1 predominates in serum (~80%); while, IgA2 is higher in secretion than serum (11). Prevalence of immunoglobulin-A deficiency (IgA-D) is diverse in different geographical regions (12). This deficiency is altered from 1/500 in Caucasians to 1/18,500 in Asia (13). IgA deficiency as the commonest type of immunodeficiency is associated with autoimmune disease (12). Moreover, it is linked to lymphoma or lymphoproliferative malignancy (LPM) in both rheumatoid arthritis and celiac disease (CD) (14). Moreover, IgA deficiency in patients increases the risk of cancer and death (14). So that cancer is the most common cause of death in patients with IgA deficiency (14). Since, few studies have been done on the relation between IgA level and ALL in children; the aim of this study was to evaluate immunoglobulin-A level in children with Acute Lymphoblastic Leukemia.

Materials and Methods

Sample Collection

In this descriptive analytical study, 28 children with ALL (newly diagnosed patients) and 28 controls were chosen based on Cochran's formula from Shahid Sadoughi Hospital from 2014 to 2015. Children with ALL who were diagnosed using aspiration of bone marrow were recruited for this study. Informed written consent was taken from the participants. Ethics committee approval was obtained by Yazd University of Medical Sciences (IR.SSU.Medicine.Rec.1395.2).

Blood Collection and immunoglobulin-A (IgA) assay

Blood samples were obtained from patients after at least 8 hours fasting. Serum was separated from the clots after complete coagulation (1 h in room temperature) by low speed centrifugation (15 min at 2000 g) and stored in -70°C refrigerator. Serum IgA was measured by immunotorbidometric method (Pars Azmoon Kit, Iran). In this method, IgA concentration was evaluated by photometric reaction between antibodies and IgA.

Statistical analysis was performed using SPSS (version 19). Pearson and Independent t test were used for analysis of data. P-values< 0.05 were considered statistically significant.

Results

In this study, the mean age of case group was 6.75± 3.29 ranged from 1 to11 years and mean age of control group was 7.31± 4.12 ranged from 2 to 12 years old. Fifteem patients (53.57%) were female and 13 patients (46.4 %) were male.

The normal range of IgA was 70 - 400 mg/dl.

The mean level of IgA in patients and control group is shown in Table I.

As shown in Table I, the mean level of IgA was lower in patients with ALL in comparison to control group. However, there was significant difference between IgA in patients with ALL and control (P=0.000).

The mean level of IgA in male patients and control group was 82.5± 21.3 and 113.2± 26.62 mg/dl, respectively.

Moreover, no significant relation between IgA and age was observed (P=0.45).

Table I: The mean level of IgA in patients and control group.

IgA mean in children with ALL n=28	IgA mean in control group n=28	p-value
82.5± 21.3 mg/dl	113.2± 26.62 mg/dl	0.000

Discussion

The result of this study showed that the mean level of IgA was lower in patients with ALL in comparison to control group. Moreover, significant difference was seen in patient and control group in terms of IgA level. Okpala et al., evaluated the level of immunoglobulin A by single radial immunodiffusion method in patients with ALL. They showed that the level of serum IgA was lower than control group, although it was not statistically significant (15). Potapnev et al., in another study evaluated serum IgA in 68 children with primary B-lineage ALL and 46 healthy children. They reported no significant difference between ALL patients and control group regarding mean level of serum IgA (16). Martin Ibanez evaluated serum IgA, IgG, and IgM in 50 patients with ALL and reported that immunoglobulin concentration was normal in ALL's onset (17). Ludvigsson et al., reported that individuals with IgA deficiency are at moderately increased risk of cancer, especially risk of gastrointestinal cancer (14). They also reported that children with IgA deficiency are not at increased risk of cancer (14). Welch et al., reported that low level of serum IgA is associated with worse prognosis for survival in children (18). Luczynski et al., carried out a study on 40 children with ALL aged 2-15 years old. The level of IgA was measured using flow cytometry. The results of aformentioned study showed reduced level of IgA in patients during maintenance therapy in comparison to healthy children (19).

Haraldsson et al., evaluated serum IgA in 10 patients with acute lymphoblastic leukemia before, during, and after antileukemic therapy. The results showed that concentration of IgA decrease during treatment but recovere slowly after cessation of the therapy in patients with ALL (20). Van Tilburg et al.,, evaluated the level of immunoglobulins in patients with ALL and showed that decreased chemotherapy is advantageous for recovery of immunoglobulin which may prevent the susceptibility for infections (21).

Ludvigsson et al., reported that IgA deficiency increase risk of infections in individuals (22). They believed that relation between IgA deficiency and infections is due to reduced mucosal defense mechanisms, because IgA is the most important immunoglobulin at mucosal surface (22). Salavoura et al., also reported that IgA deficiency is associated with high frequency of epithelial tumors, because of defective defense of mucosa against pathogens especially in respiratory and gastrointestinal tract (23).

Conclusion

According to the results of the present study, the serum level of IgA was significantly lower in ALL pediatric patients than the control group; however, it was in normal range in both groups. More studies are needed to strongly conclude IgA deficiency as a new risk factor or as a new marker of ALL in children. Other immunoglobulins are recommended to be considered in patients with ALL in further studies.

Acknowledgments

This study was induced from an approved project by the Hematology and Oncology Research Center of Shahid Sadoughi University of Medical Sciences. We are thankful of the staff in Pediatric Oncology Ward of Shahid Sadoughi Hospital for their kind cooperation.

Conflict of interest

The authors declare that there is no conflict of interest.

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