

Salivary Immunoglobulin A Assessment in Lymphoma Patients before and after Chemotherapy

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ABSTRACT

Background: Lymphomas are group of diseases caused by malignant lymphocytes that accumulate in lymph nodes and caused the characteristics lymphadenopathy. Occasionally, they may spill over into blood or infiltrate organs outside the lymphoid tissue. The major subdivision of lymphomas is into Hodgkin lymphoma and non-Hodgkin lymphoma and this is based on the histologic presence of Reed-Sternberg cells in Hodgkin lymphoma. Salivary immunoglobulin A is the prominent immunoglobulin and is considered to be the main specific defense mechanism in oral cavity. The aim of this study was to determine the level of salivary immunoglobulin A in lymphoma patients before and after chemotherapy treatment.

Subjects, materials and methods: The study included 25 patients (15 male and 10 female) with non-Hodgkin lymphoma(B-cell type) , 25 patients(16 male and 9 female) with Hodgkin lymphoma and 25 (15 male and 10 female) healthy control group. Whole un-stimulated saliva was collected to determine the level of salivary immunoglobulin A, which measured by Enzyme Link Immunosorbent Assay.

Results: The level of salivary immunoglobulin A was significantly higher in pre-treatment patients in comparison with control group, and there was a significant decrease after chemotherapy treatment when compared to their base line levels in both study groups.

Conclusion: The salivary immunoglobulin A was higher in lymphoma patients than control, then its level showed obvious decrease after chemotherapy treatment.

Key words: Non-Hodgkin, Hodgkin Lymphoma, salivary immunoglobulin A. (J Bagh Coll Dentistry 2016; 28(3):65-68).

INTRODUCTION

Lymphomas are a group of diseases caused by malignant lymphocytes that accumulate in lymph nodes and cause the characteristics clinical features of lymphadenopathy. Occasionally, they may spill over into blood (Leukemicphase) or infiltrate organs outside the lymphoid tissue. The major subdivision of lymphomas is into Hodgkin lymphoma(HL) and non-Hodgkin lymphoma (NHL)and this is based on the histologic presence of Reed-Sternberg (RS) cells in Hodgkin lymphoma⁽¹⁾.

Non-Hodgkin's lymphomas are a heterogeneous group of lymphoproliferative disorders originating in B, T, or natural killer lymphocytes. The B-cell lymphomas represent about 80% to 85% of the cases, with 15% to 20% being T-cell lymphomas; natural killer lymphomas are rare⁽²⁾.

Hodgkin's lymphoma is a lymphoproliferative malignancy of B-cell origin. According to the WHO classification, Hodgkin's lymphoma is divided into a classical variant and a nodular lymphocyte predominant variant. Classical HL is separated into four subtypes: lymphocyte rich type, nodular sclerosis type, mixed cellularity type and lymphocyte depleted type⁽³⁾. Immunoglobulin A (IgA) is an antibody that plays a critical role in mucosal immunity⁽⁴⁾.

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Immunoglobulin A accounts for more than 70 percent of total immunoglobulin in the body; although its concentration in the serum is relatively low. IgA is concentrated in mucosal secretions, including nasal and pulmonary secretions, saliva, tears, breast milk, and secretions of the genitourinary and intestinal tracts⁽⁵⁾.

Salivary IgA is the prominent immunoglobulin and is considered to be the main specific defense mechanism in oral cavity⁽⁶⁾. It is the first line of host defense against pathogens which invade mucosal surfaces, these antibodies could help oral immunity by preventing microbial adherence, neutralizing enzymes, toxins, and viruses; or by acting in synergy with other factors such as lysozyme and Lactoferrin⁽⁷⁾.

MATERIALS AND METHODS

Sample

A comparative study was performed in the oncology unit of Al-Sadder Medical City in Al-Najaf. The study samples consist of (50) patients with lymphoma with age range (20-50) years and divided into:

1. The first group consisted of (25) patients with Hodgkin lymphoma taking adriamycin, bleomycin, vinblastine and dacarbazine (ABVD) chemotherapy regimen.
2. The second group consisted of (25) patients with non-Hodgkin lymphoma

(B cell type) taking rituximab (R) in combination with cyclophosphamide, hydroxodaunorubicin, vincristine (oncovine) and prednisolone (R-CHOP) chemotherapy regimen.

Exclusion criteria

- Diabetic patients.
- Pregnant women.
- Heavy smokers and alcoholism.
- Patients with severe periodontal disease.
- Patients under radiotherapy.
- Other metabolic disease and patients taking other medications suppress the immunity.

The whole saliva was collected to evaluate the level of salivary immunoglobulin A, at two times interval: first before taking medical treatment (at the time of diagnosis) and second after receiving three cycles of medications (28 days for each cycle of ABVD and 21 days for each cycle for R-CHOP). The study time was from the period (11/2013 – 5/2014). Control group consist of (25) looking healthy and age, sex match with patient groups.

Saliva collection

Unstimulated saliva had been obtained by having the subject seated quietly with his or her head flexed forward and the subject gently spit into a collection container for a specified amount of time. This method of collection is considered the “gold standard” for obtaining many components of saliva⁽⁸⁾.

To avoid circadian variations, saliva samples were collected between 9 a.m. and 1.00 p.m. In order to obtain a sample of total saliva, the

patients were instructed not to eat or drink (except water) for 1 hour⁽⁹⁾.

Saliva samples were kept in ice during the collection. In order to reduce bubble and foam, samples were centrifuged at speed of (3000-3500 RPM) and supernatant stored at -20°C freezer until immunological analysis⁽¹⁰⁾.

Determination of Salivary IgA

The level of salivary IgA in saliva was determined using Secretary immunoglobulin A ELISA kits – Cloud- Clone Corp (USA).

Statistical analysis

Statistical analyses were performed using Excel program (2010) from Microsoft Co.

RESULTS

The IgA mean values was variant among control group (240) µg/ml, NHL patients at the time of diagnosis (301) µg/ml and after receiving three cycles of R-CHOP (220) µg/ml as shown in figure (1), with significant relationship ($P < 0.05$) between pre-treatment patients and control group and highly significant difference ($P < 0.001$) between pre-treatment and post-treatment patients, as shown in table (1).

This study also showed different levels of salivary IgA among control group (240) µg/ml, HL patients at the time of diagnosis (296) µg/ml and after receiving three cycles of ABVD (225) µg/ml as shown in figure (2), and there was significant increase ($P < 0.05$) in pre-treatment patients in comparison to control group and highly significant difference ($P < 0.001$) between pre and post-treatment patients, as shown in table (1).

Table 1: The mean values ± SD of salivary IgA for NHL and HL patients and control group with their comparison significant

Variable	NHL pre-treatment	NHL post-treatment	NHL pre-treatment	Control	NHL post-treatment	Control
IgA Mean ±SD	301±79.5	220±56	301±79.5	240±116	220±56	240±116
P-value	0.0001 **		0.035 *		0.44^	
Variable	HL pre-treatment	HL post-treatment	HL pre-treatment	Control	HL post-treatment	Control
IgA Mean± SD	296±75	225±48	296±75	240±116	225±48	240±116
P-value	0.0002 **		0.047 *		0.56^	

NHL= Non-Hodgkin lymphoma, HL= Hodgkin lymphoma, *= Significant, **=highly significant, ^ = non significant, SD= standard deviation.

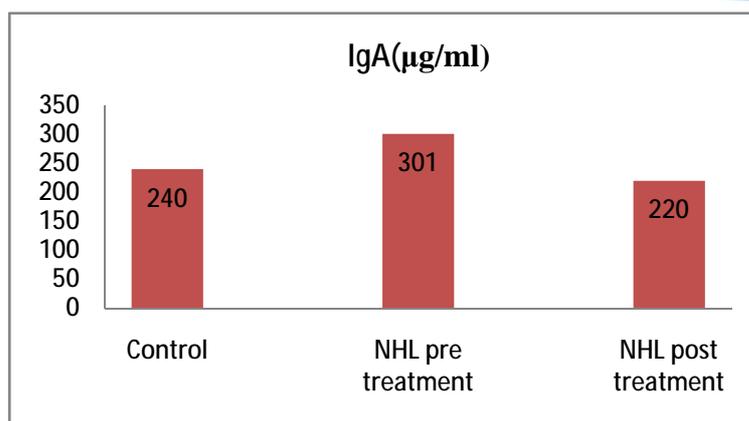


Figure 1: The different levels of IgA mean values in µg/ml for control group, NHL patients before treatment and after three cycles of R-CHOP.

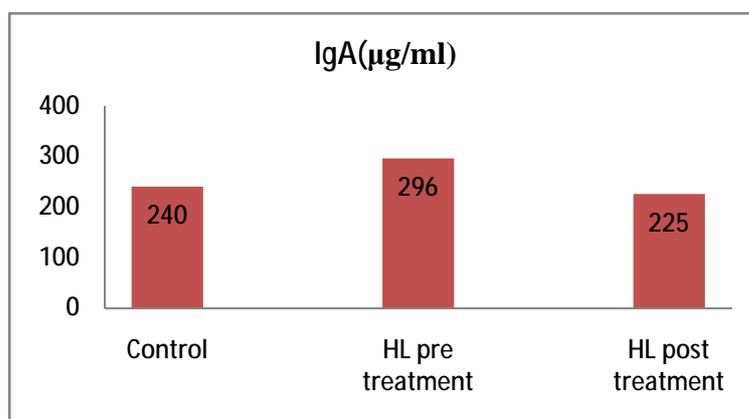


Figure 2: The different levels of IgA mean values in µg/ml for control group, HL patients before treatment and after three cycles of ABVD

DISCUSSION

The present study showed a significant elevation of salivary IgA level in pre - treatment patients with malignant lymphoma when compared with those of the control, this finding didn't match with Ellison et al. ⁽¹¹⁾ and Biggar et al. ⁽¹²⁾ as they found in their studies a significant decrease in serum level of immunoglobulin including IgA in lymphoma patients before starting therapy. While Timucin et al. ⁽¹³⁾ reported that total serum IgA concentration was found to be within normal ranges in all NHL & HL patients.

This difference may be explained by first: change in oral microflora and this may lead to local increase of salivary IgA secretion, this was documented by Ye et al. ⁽¹⁴⁾ as they said the patients with malignancies exhibited a less diverse and significantly different bacterial community in their oral cavity when compared to control group, second; there does not appear to be any correlation between serum and Salivary immunoglobulins. This may suggest that extra-vascular transfer of immunoglobulin A primarily

depends on the mucosal status of the individual and not necessarily the serum level ⁽¹⁵⁾.

The current study showed a significant decrease in the salivary IgA level in lymphoma patients after chemotherapy treatment in comparison with its baseline level, this agree with the result of Pekka et al. ⁽¹⁶⁾ and Erika et al. ⁽¹⁷⁾ when they noticed a significant decrease in the salivary IgA level during chemotherapy.

The lower level of salivary IgA may be a result of impairing the normal function of the human immune system by chemotherapy which can cause major alterations in the oral defense mechanisms that are likely to play a role in the decrease of salivary contents of immunoglobulins ⁽¹⁸⁾.

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