ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN-POLONIA
VOL. LXI, N1, 28 SECTIO D 2006

Chair and Department of Conservative Dentistry, Medical University of Lublin

TERESA BACHANEK, BARBARA DROP, KATARZYNA JARMOLIŃSKA, EWA WOLAŃSKA

The saliva immunoglobulin level in patients with diseases of the leukocytic system (a preliminary report)

The term "leukocytic system" includes the cells defined as neutrophils, eosinophils, basophils, macrophages, lymphocytes and plasmacytes. The leukocytic system is an essential element of the immune system. The individual morphotic elements of this system are involved in: phagocytosis, production of antibodies and phenomena of cellular immunity such as rejection of tissue and organ transplants and antineoplastic immunity (9, 14).

The diseases of the leukocytic system include: leukocytopenia, leukocytosis, leukemia, myelofibrosis and lymphoreticular conditions. Their clinical signs result not only from the disease itself but also from myeloblastic effects of the drugs used, e.g. in chemotherapy. The condition of immunosuppression favours infections and the oral cavity is likely to become the entry of viral, fungal or bacterial infections. The balance of the oral cavity is mainly maintained by the saliva which provides mechanical, non-immunological – non-specific and immunological – specific protection (2, 4).

The aim of the study was to evaluate the saliva immunoglobulin level in the following diseases of the leukocytic system: acute lymphoblastic leukemia – ALL, chronic lymphoblastic leukemia – CLL, acute myeloblastic leukemia – AML, chronic myeloblastic leukemia – CML, malignant lymphoma, malignant lymphogranulomatosis, bone marrow aplasia, myeloma.

MATERIAL AND METHODS

Thirty-six patients treated in the Department of Haematooncology and Bone Marrow Transplantation and the Clinic of Paediatric Oncology and Haematology, Medical University of Lublin were examined (18 aged 16 years and 3 months and 18 aged 49 years and 11 months on average).

The oral mucosa, parodontium, mineralized tissues of teeth were examined and the saliva was collected to determine the level of immunoglobulins. The immunological examinations were conducted in the Interfaculty Chair and Department of Laboratory Diagnostics, Medical University of Lublin. The levels of IgA, IgG, IgM were determined by the diffusion method according to Mancini on low concentration plates, Behring-Partigen LC. The 2 ml saliva samples were collected in the morning, at least 1 ½ h after meal. Immediately after the collection they were placed in the container with ice and transported to the laboratory where they were centrifuged at 5,000 revolutions for 15 min. and placed on the plates; after 72–100 h of storage at room temperature the precipitate diameter was read. In the immunodiffusion method precipitation bands occur due to the reaction between antigens and the homologous antibody during their migration through the gel. The higher the antibody concentration the higher the diffusion and precipitate zone. The medium/agar with serum contains standard antibody concentrations while the saliva is an antigen.

The patients were divided into 4 groups according to sex and age. The patients under the age of 25 were qualified to the younger group and those over 25, to the older group: Group I – boys, Group II – girls, Group III – men, Group IV – women.

RESULTS

The results obtained were compiled in Tables 1–4. Table 1 presents the leukocytic system diseases in the individual age groups considering sex. Table 2 presents average saliva IgA, IgG and IgM concentrations in group I and II patients, i.e. younger subjects taking sex into account. In ALL and CLL lower IgA and IgM levels were observed both in boys and girls compared to the accepted normal values. In both groups, however, there was a slight increase in the IgG level. The patient with bone marrow aplasia showed a significant decrease in IgA and IgG levels and his IgM level was found to be below the detection limit. In the remaining groups of diseases the results did not differ or were slightly different from the accepted standards. Table 3 presents average values of saliva immunoglobulin concentrations in group III and IV patients, i.e. older subjects taking sex into account. In all types of leukemias higher IgG levels and lower IgA and IgM levels were observed in women. In patients with myeloma the immunoglobulin level was several times higher compared to the accepted norms. Table 4 shows average values of saliva immunoglobulin concentrations according to age. Higher saliva immunoglobulin levels observed in younger patients compared to older subjects with AML are consistent with the results of other authors.

Table1. Number of patients with leukocyte system diseases

	Groups			
Disease entity	I	II	III	IV
Acute lymphoblastic leukemnia	7	6	-	-
Chronic lymphoblastic leukemia	-	-	2	4
Acute myeloblastic leukemia	-	2	3	4
Chronic myeloblastic leukemia	-	-	-	1
Malignant lymphoma	-	1	-	1
Malignant lymphogranulomatosis	-	1	-	-
Bone marrow aplasia	1	-	-	-
Myeloma	-	-	1	2
Total	8	10	6	12

Table 2. Mean values of saliva immunoglobulin concentration in patient from groups I and II

Disease entity	N	Group I			N	Group II		
		IgA	IgG	IgM		IgA	IgG	IgM
Acute lymphoblastic leukemnia	7	3.814	7.185	0.242	6	5.533	6.033	0.766
Chronic lymphoblastic leukemia	-	-	-	-	-	-	-	-
Acute myeloblastic leukemia	-	-	-	-	2	4.100	6.250	uind
Chronic myeloblastic leukemia	-	-	-	-	-	-	-	-
Malignant lymphoma	-	-	-	-	1	6.600	2.440	uind
Malignant lymphogranulomatosis	-	-	-	-	1	4.000	3.003	uind
Bone marrow aplasia	1	2.300	3.001	uind	-	-	-	-
Myeloma	-	-	-	-	-	-	-	-

uind – unindicatable

Table 3. Mean values of saliva immunoglobulin concentration in patient from groups III and IV

Disease entity	N	Group III			N	Group IV		
		IgA	IgG	IgM		IgA	IgG	IgM
Acute lymphoblastic leukemnia	-	-	-	-	-	-	-	-
Chronic lymphoblastic leukemia	2	2.800	2.900	uind	4	3.075	5.225	uind
Acute myeloblastic leukemia	3	3.500	4.666	uind	4	3.825	5.975	0.225
Chronic myeloblastic leukemia	-	-	-	-	1	3.201	4.500	uind
Malignant lymphoma	-	-	-	-	-	-	-	-
Malignant lymphogranulomatosis	-	-	-	-	1	4.200	3.200	uind
Bone marrow aplasia	-	-	-	-	-	-	-	-
Myeloma	1	20.100	10.300	2.000	2	26.500	9.950	2.000

uind – unindicatable

Table 4. Mean values of saliva immunoglobulin concentration in patient from groups I, II, III and IV

Disease entity	N	Group I,II			N	Group III,IV		
		IgA	IgG	IgM		IgA	IgG	IgM
Acute lymphoblastic leukemnia	13	4.673	6.609	0.505	-	-	-	-
Chronic lymphoblastic leukemia	-	-	-	-	6	2.983	4.450	uind
Acute myeloblastic leukemia	2	4.100	6.250	uind	7	3.685	5.414	0.128
Chronic myeloblastic leukemia	-	-	-	-	1	3.200	4.500	uind
Malignant lymphoma	1	6.600	2.440	uind	-	-	-	-
Malignant lymphogranulomatosis	1	4.000	3.003	uind	1	4.200	3.200	uind
Bone marrow aplasia	1	2.300	3.001	uind	-	-	-	-
Myeloma	-	-	-	-	3	24.366	10.066	2.000
The healthy examination acc. to Sikorska	-	6.856	5.809	1.100	-	-	-	-
The healthy examination acc. to Chałas	-	-	-	-	-	5.400	3.200	1.400

uind - unindicatable

DISCUSSION

The immune system provides protection, homeostasis and control and its functions are mediated by numerous morphologically and functionally differentiated cells. Each of its functions has to be carried out differently, which is reflected in various detector and effector mechanisms. Therefore the immune response was divided into: specific, non-specific, cellular-late and humoral-early (6, 7, 10, 11).

In the humoral response the synthesis of specific immunoglobulins takes place in lymphocytes B and plasmocytes. Immunoglobulins are glycoproteins specifically directed against an antigen which caused their production. Three out of 5 known immunoglobulin classes are present in the saliva. Immunoglobulin A occurring in the saliva is produced by the plasmocytic cells of the salivary secretory epithelium. Immunoglobulin G produced by lymphocytes B and plasmocytes enters the saliva from the intercellular space. Immunoglobulin M is partly synthesized

by lymphocytes B in the parotid gland but its substantial amount enters the saliva from the tissue fluid (6, 13).

The available literature provides different values of saliva immunoglobulin levels, which results from different determination methods used (3). In our study the results obtained were referred to the saliva examinations in healthy young individuals (average age 15 years) conducted by Sikorska. The level of IgA was found to be 6.856 mg%, of IgG – 5.809 mg% and of IgM – 1.100 mg%. In the study by Chalas the levels of these saliva immunoglobulins in healthy adults (average age – 39.09) was: 5.400 mg%, 3.200 mg% and 1.400 mg%, respectively. The studies of both authors and ours were conducted using the same method and in the same laboratory conditions (1, 12).

Many authors emphasize the differences in immunoglobulin levels depending on age. An increase in the concentration of all classes of immunoglobulins is a response to an external or internal antigen stimulus. Increased concentration of one of Ig classes may result from neoplastic growth of the homogenous population of cells of the lymphatic and reticuloendothelial system (3, 5, 8, 10).

Our studies showed decreased IgA and IgM levels in both age groups and in both sexes in myeloblastic, lymphoblastic leukemias, acute and chronic, malignant glanulomatosis, lymphoma and bone marrow aplasia. On the other hand, increased IgG levels were observed in both types of acute and chronic leukemias. In myeloma an increased immunoglobulin level is observed in blood plasma. In our study in adult patients the level of IgA increased fivefold, of IgG threefold and of IgM twofold.

CONCLUSIONS

1. In both types of leukemias the level of IgG increases in younger patients compared to healthy individuals.
2. In chronic leukemia the IgG level in men decreases markedly; it is also lower in women compared to the younger group.
3. In both types of leukemias, irrespective of their course, the IgA level is lower in both age groups and in both sexes compared to the levels in healthy individuals.
4. In myeloma the levels of all immunoglobulins were substantially increased.
5. In the remaining diseases of the leukocytic system the level of IgA and IgG is lower in both age groups and both sexes in comparison with the levels observed in healthy individuals.

REFERENCES

1. Chałas R.: Ocena stanu uzębienia jamy ustnej oraz wybranych składników śliny pacjentów leczonych z powodu stwardnienia rozsianego preparatem 2-CDA. Praca doktorska, AM w Lublinie 2000.
2. Hall H. D.: Ochronne i regenerujące funkcje ludzkiej śliny. Quintessence. t. II, 6, 403, 1994.
3. Ilewicz L. et al.: Poziom IgG w ślinie u kobiet zatrudnionych w zakładach cukierniczych ZPC „Skawa" SA w Wadowicach. Mag. Stomat. 2, 8, 2002.
4. Karolewska E. et al.: Poziomy nieswoistych czynników obronnych śliny u dzieci z biała-czkami – doniesienie wstępne. Czas. Stomat., LVI, 6, 403, 2003.
5. Konopka T. et al.: Zmiany w jamie ustnej w przebiegu białaczek u dzieci. Czas Stomat., LVI, 4, 217.
6. Mackiewicz S.: Immunologia. PZWL, Warszawa 1991.
7. Mackiewicz S.: Immunoglobuliny: podstawowe funkcje biologiczne i zastosowanie lecznicze. Podst. Nauk Med., t. VI, 135, 1993.
8. Manson-Rehemtulla B. et al.: Analyses of salivary components in leukemia patients receiving chemotherapy. Oral Surg. Oral Med. Oral Pathol., 73, 35, 1992.
9. Orłowski W.: Nauka o chorobach wewnętrznych. PZWL, t. VII, 140, Warszawa 1988.

10. Pawelski S., Maj S.: Normy i kliniczna interpretacja badań diagnostycznych w medycynie wewnętrznej. PZWL, 89, Warszawa 1993.
11. Ptak W.: Podstawy immunologii. PZWL, Warszawa 1976 .
12. Sikorska-Jaroszyńska M.: Poziom immunoglobulin wybranych białek ostrej fazy i laktoferyny w ślinie a stan twardych tkanek zębów u młodzieży. Praca doktorska, AM w Lublinie, 1998.
13. Streenbny L. M.: Saliva in health and disease: an appraisal and update. Int. Dent. J. 50, 140, 2000.
14. Sulik J.: Trudności w rozpoznaniu ostrej białaczki limfoblastycznej u dziecka – opis przypadku. Czas. Stomat., LV, 2,128, 2002.

SUMMARY

The leukocytic system is an essential element of the immune system. The aim of the study was to evaluate the saliva immunoglobulin level in the following diseases of the leukocytic system: acute lymphoblastic leukemia, chronic lymphoblastic leukemia, acute myeloblastic leukemia, chronic myeloblastic leukemia, malignant lymphogranulomatosis, bone marrow aplasia, myeloma, malignant lymphoma. Thirty-six patients treated in the Department of Haematooncology and Bone Marrow Transplantation and the Clinic of Paediatric Oncology and Haematology, Medical University of Lublin were examined (18 aged 16 years and 3 months and 18 aged 49 years and 11 months on average). Saliva was collected to determine the level of immunoglobulins. The levels of IgA, IgG, IgM were determined by the diffusion method according to Mancini on low concentration plates, Behring-Partigen LC. The patients were divided into 4 groups according to sex and age. In both types of leukemias the level of IgG increases in younger patients compared to healthy individuals. In chronic leukemia the IgG level in men decreases markedly; it is also lower in women compared to the younger group. In both types of leukemias, irrespective of their course, the IgA level is lower in both age groups and in both sexes compared to the levels in healthy individuals. In myeloma the levels of all immunoglobulins were substantially increased. In the remaining diseases of the leukocytic system the level of IgA and IgG is lower in both age groups and both sexes in comparison with the levels observed in healthy individuals.

Poziom immunoglobulin śliny u pacjentów z chorobami układu białokrwinkowego (doniesienie wstępne)

Układ białokrwinkowy stanowi podstawowy element systemu odpornościowego. Objawy kliniczne chorób tego układu mogą wystepować w jamie ustnej. Celem pracy była ocena poziomu immunoglobulin śliny w białaczkach limfoblastycznych i mieloblastycznych ostrych i przewlekłych, szpiczaku plazmocytowym, zaniku szpiku, ziarnicy złośliwej, zaniku szpiku. Zbadano 36 pacjentów leczonych w Klinice Hematoonkologii i Transplantacji Szpiku oraz Klinice Onkologii i Hematologii Dziecięcej AM w Lublinie (18 osób o średniej wieku 16 lat i 3 miesiące oraz 18 osób o średniej wieku 49 lat i 11 miesięcy). Od chorych pobierano ślinę w celu oznaczenia poziomu immunoglobulin. Stężenie IgA, IgG, IgM oznaczano metodą dyfuzji krążkowej wg Manciniego, na płytkach do niskich stężeń firmy Behring-Partigen LC. Badanych pacjentów podzielono na cztery grupy w zależności od płci i wieku. Na podstawie przeprowadzonych badań stwierdzono, co następuje: W obu typach białaczek poziom immunoglobuliny IgG wzrasta w grupie pacjentów młodszych w porównaniu z grupą ludzi zdrowych. W białaczkach przewlekłych poziom IgG w grupie mężczyzn znacznie maleje i jest także niższy u kobiet w porównaniu z grupą młodych. W obu typach białaczek bez względu na przebieg poziom IgA jest niższy w obu grupach wiekowych i u obu płci w porównaniu z grupą osób zdrowych. W szpiczaku plazmatycznym poziomy wszystkich immunoglobulin wykazują znaczny wzrost. W pozostałych chorobach układu białokrwinkowego poziom IgA i IgG jest niższy w obu grupach wiekowych i u obu płci w stosunku do stężeń obserwowanych u osób zdrowych.