J. Elem. s. 227–236 DOI: 10.5601/jelem.2011.16.2.06

EVALUATION OF TITANIUM CONTENT IN MUCOSA COVERING TWO-STAGE INTRAOSSEOUS IMPLANTS*

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Abstract

Widely used biomaterials, including titanium and its alloys, manifest a range of the physicochemical properties which determine the way they are exploited. According to the literature, titanium dental implants, considered biocompatible with the human body, under certain conditions, may cause inflammatory or allergic reactions.

The aim of the study has been to evaluate the content of titanium in the mucosa covering two-stage intraosseous implants of the Osteoplant-Hex® system. The content of titanium ions in the examined samples containing segments of mucosa collected from those dental implants was determined with an inductively-coupled plasma emission spectrometer VISTA-MPX produced by VARIAN ICP. A diverse titanium content in the mucosa adjoining the implants has been revealed during their healing period. The determined concentration of titanium ranged from 0.00 to 122.59 μg g^{-1}. As the conducted research suggests, such a wide range may result from differences in the implant location, sex and age of patients. Therefore, the authors tried to find a relationship between the results and those variables.

Key words: titanium, implants, allergy.

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* This work was partially funded by the UM-UAM grant 501-03-02208682-02514.

OCENA ZAWARTOŚCI TYTANU W BŁONIE ŚLUZOWEJ POKRYWAJĄCEJ DWUETAPOWE WSZCZEPY ŚRÓDKOSTNE

Abstrakt

Szeroko stosowane współcześnie biomateriały, w tym tytan i jego stopy, wykazują wiele cech i właściwości fizykochemicznych, które determinują sposób ich wykorzystania. Jak wynika z piśmiennictwa, wszczepy tytanowe stosowane w stomatologii, uważane za biokompatybilne z ustrojem, mogą w określonych warunkach wywoływać reakcje zapalne lub alergiczne.

Celem pracy była ocena zawartości tytanu w błonie śluzowej pokrywającej dwuetapowe wszczepy śródkostne systemu Osteoplant-Hex®. Zawartość jonów tytanu w badanych próbkach zawierających wycinki błony śluzowej pobrane nad wszczepami stomatologicznymi oznaczono na spektrometrze emisyjnym z indukcyjnie sprzężoną plazmą VISTA-MPX firmy VARIAN ICP. Wykazano zróżnicowaną zawartość tytanu w błonie śluzowej kontaktującej się z implantami w okresie ich wgajania. Oznaczono stężenia tytanu od 0,0 do 122,59 μg g^{-1}. Jak wynika z badań, duża rozpiętość wyników może być uzależniona od lokalizacji wszczepu, płci pacjentów, a także wieku, i dlatego podjęto próbę powiązania uzyskanych wyników z kilkoma potencjalnymi parametrami.

Słowa klucze: tytan, implanty, alergia.

INTRODUCTION

Titanium, a light metal of high mechanical resilience, resistant to corrosion, is commonly considered to be well-tolerated in the tissue environment. Thus it fulfills the requirements for modern metallic biomaterials applied in medicine. Owing to good osteointegration and biotolerance, titanium and its alloys are used to produce elements applied for example in dentistry and other branches of medicine (ORLICKI, KŁAPTOCZ 2003, SINGH, DAHOTRE 2007, RUSINEK et al. 2008).

To reconstruct teeth losses, present-day prosthetics more and more frequently uses titanium intraosseous implants as denture bases. Similarly to other countries, the number of implants in Poland increases proportionally to the society's affluence and the rise in the number of dentists performing implantation procedures.

In the last 40 years, descriptions of cases suggesting side effects of the use of implants, including those made of pure titanium, have appeared (UNGERSBÖCK et al. 1994, MÜLLER, THON 2006, STEJSKAL et al. 2006, PRYLIŃSKI, LIMANOWSKA-SHAW 2007, TOMIZAWA, HANAWA 2007, RUSINEK et al. 2008). They have usually comprised reactions such as metalosis or fistulas, often in the form of eczema, rash or itch surrounding the implant, thus suggesting allergy (SINGH, DAHOTRE 2007, RUSINEK et al. 2008). Most of these phenomena have been observed in the case of orthopaedic implants, and have resulted from contact with nickel, chromium and cobalt allergens, but also titanium ones, yet less frequently. Allergic reactions to metal dentures take form of bone or marrow inflammation without any changes to the skin (ŚPIEWAK, BREWCZYŃSKI 1993, POHLER 2000, MÜLLER, THON 2006, SINGH, DAHOTRE 2007). The problem also concerns, although to a lesser extent, titanium intraosseous dental implants. In these cases, allergic symptoms have caused unpleasant, long-term effects such as skin changes, receding after the removal of the allergen; however, it is believed that the reaction may sometimes be so serious that it causes complications leading even to the implant rejection (MÜLLER, THON 2006, ŚPIEWAK 2007). A strong allergic reaction in the form of eczema has been observed in a toothless patient with very good general medical examination results after the insertion of 2 dental implants. The changes on her skin and mucosa have totally vanished shortly after extraction of the titanium implants (MÜLLER, THON 2006, EGUSA et al. 2008). The suggested oversensitivity to titanium may turn out to be a reaction of the organism to trace quantities of other metals such as nickel, cobalt or palladium since implants declared to be purely titanium quite often contain minor additives (STEJSKAL et al. 1999, THON et al. 2006). The mechanism of allergic reactions related to titanium has not been scientifically proven so far (LALOR et al. 1990, RUSINEK et al. 2008) for the implanted material may be subject to various physicochemical alterations (e.g. under the influence of the environment) and, therefore, the reaction to it may also differ.

Analysing the allergy to titanium and its compounds, it is considered that the released particles/ions as haptenes merge with tissue proteins and may induce an IgE-dependent allergy. This phenomenon has not, however, been completely confirmed in literature thus far (FRIEDMANN 2006). It is thought that titanium may cause allergy in a similar way to other metals through T-lymphocyte-specific sensitivity evoking oversensitivity type IV.

The aim of the study has been to evaluate the content of titanium in the mucosa covering two-stage intraosseous implants Osteoplant-Hex® and to try to relate the release of this element to tissues to some selected factors. Attention has been paid to the purposefulness of the abovementioned study considering the potentially detrimental influence of titanium on the human organism in certain clinical situations. Most of the experimental studies into implants have been conducted on animal material. There is, nevertheless, little experimental research connected to the reactions of human tissues to titanium implants in literature.

MATERIAL AND METHODS

The research material included segments of mucosa covering two-stage screw intraosseous titanium implants Osteoplant-Hex®. The implantation procedures were carried out with the use of the closed healing method. After 4-6 months, i.e. the osteointegration period, a procedure of implant exposure was conducted through excision of the mucosa covering the implant bearing surface in order to place the healing screw in the implant. The exposure was performed with a scalpel to exclude the possibility of metal particles getting from mechanical damages into the research material. Prior to implantation, a segment of the mucosa from the area of the planned implant bed was collected. This fragment as well as the segments of mucosa taken from the alveolar ridge during other surgical procedures constituted a control group and came from patients who did not have metal restorations in their oral cavities.

The phases of the clinical studies were conducted with the consent of the Bioethics Commission of Karol Marcinkowski University of Medical Sciences in Poznan.

The content of titanium ions in the investigated samples containing the segments of mucosa from above the dental implants was determined, after previous mineralization in a microwave oven MDS – 2000, on an inductively-coupled plasma emission spectrometer VISTA-MPX produced by VARIAN ICP. The mineralization was conducted in Teflon bombs in a mixture of 65% HNO_3 + H_2O_2 (5:2), at 60 psi and a power of 40. After the mineralization, the samples were quantitatively transferred into 10ml flasks, filled up with redistilled water and then, the content of titanium was determined.

The parameters for ICP-OES determination have been compiled in Table 1.

The results of the studies were analysed statistically. Due to the fact that the variable distributions did not fulfil normality conditions, nonparametric tests were applied as they are not very sensitive to outlying observations. The Mann-Withney test was used to compare two groups, e.g. women

Table 1

The operating parameters for determinations of ICP-OES

Method parameters	Value
RF, power (kW)	1.20
Plasma flow (L min^{-1})	15.0
Nebulizer flow (L min^{-1})	0.9
Viewing height (mm)	12
Pump rate	15
Rinse time (s)	10
Auxiliary flow (L min^{-1})	1.50
Replicate read time (s)	5.0
Instrument stabilization (s)	15
Sample uptake delay (s)	30
Element – emission line (nm)	Ti - 336122

and men, maxilla-mandible. The Kruskal-Wallis test was applied to compare a larger number of groups. Spearman's rank correlation coefficient was used to assess the relationship between variables (dependence on age in the investigated group).

RESULTS AND DISCUSSION

The results have been analysed in order to evaluate the accumulation of titanium in the mucosa covering two-stage intraosseous implants during their healing period and to determine the relation between the results obtained and such parameters as the implant location (maxilla, mandible), sex and age of the patients. The comparison of the results obtained from individual patients who had had a larger number of implants inserted enabled us to identify intra-individual dependencies.

The results of titanium determination for the study group (24 samples) and the control group (21 samples) have been compared in Table 2 and Figure 1. The results of the implanted group indicate that the content of titanium in soft tissues is over 10 times greater than in the control group, which may prove translocation of titanium ions from the implant to the tissues of the human organism.

Table 2

Average Ti results of the test and control groups

Parameters	Average content of Ti ($\mu g\ g^{-1}$)
Osteoplant-Hex®	9.765
Control group	0.818

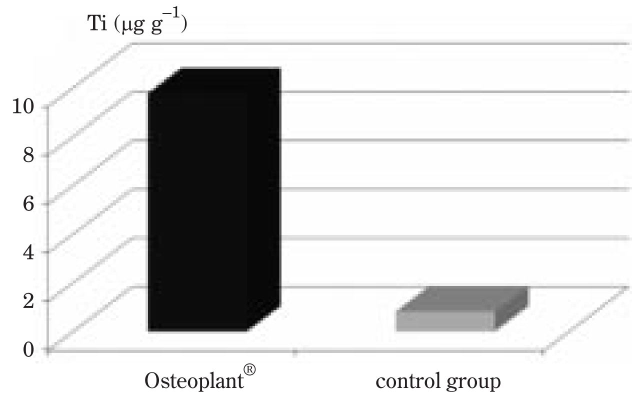

Fig. 1. Graphic presentation of the average results of the titanium content for the test and control groups

Table 3

Characteristics of the research material and results for the Osteoplant system

Patients	Sex		Average age	Implant number in a given location		Average result for group Ti (μg g^{-1})
	F	M		maxilla	mandible	
24	14	10	54.166	17	35	9.765

Table 4

Results for different implant locations in patients with more than 2 implants

Patient's numbers	Maxilla			Mandible		
	1-3	4-7	average	1-3	4-7	average
1					22.4 21.6	22.00
2		6.6 12.9 28.9 20.5	17.23			
3		0.4 0.4 48.1*	16.3			
4					20.8 12.7 5.0	12.83
5					BDL 3.6	3.6
6				9.7 2.0 8.9 13.5		8.53
7	1.0 122.59	19.5	106.20		1.5 6.1 1.4	3.00
8				1.02	5.91 0.29 0.68 0.49	1.62
9				4.38 1.34	3.02 6.91 1.77	19.19
10					0.44 1.26	0.85
11					6.27 0.47 BDL	2.25
			46.58			8.21

Some of the patients participating in the study had more than two intraosseous implants inserted. Different results were obtained for the samples taken from one patient, both from distant and close locations of the implants. The results presented in Table 4 may prove intra-individual variation and a predisposition to ion migration or they may stem from heterogeneity of the inserted titanium implants.

The segments of mucosa which were subject to the study on the titanium content had been collected from patients at different age. They were divided into two representative groups: a younger one – up to the age of 60, and an older one – over the age of 60. The results of the content of titanium in the mucosa depending on the patient's age have been compared in Table 5 and Figure 2. They suggest no interdependence between the titanium ions release and age, neither among men nor women. Nonetheless, it has been noticed that the titanium content was several dozen percent lower among men than among women in both age groups. Considering the small number of the examined patients, it is difficult to draw any unambiguous conclusions, though.

Table 5

Average values obtained for groups of patients up to and over the age of 60

Age group	Sex	Quantity	Ti values		Average Ti value
			min	max	
Up to the age of 60	F	9	BDL	122.59	10.49
	M	5	0.2	20.8	4.45
Over the age of 60	F	5	BDL	48.1	10.24
	M	5	0.44	22.4	7.84

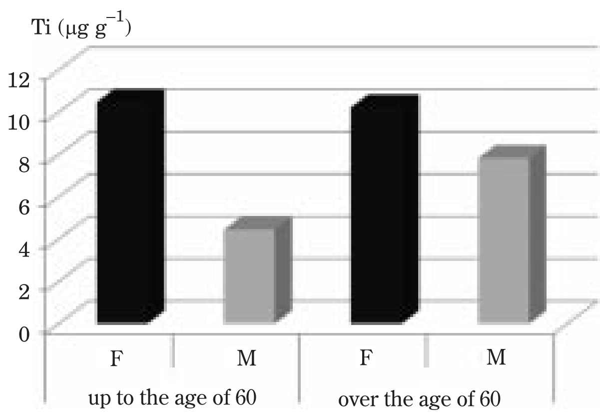

Fig. 2. Graphic presentation of the titanium content in mucosa depending on patients' age

Spearman's test suggests no correlation between age and the results obtained from the examined groups. The correlation coefficient was equal 0.003, while the relevance coefficient was close to 1.

The dependence of the results obtained on the patients' sex was another analysed factor. Women prevailed among the examined people and had a total of 30 implants inserted. The comparison of the results of the titanium content in the mucosa depending on the patient's sex has been presented in Table 6 and Figure 3.

The analysis of the results obtained in the study enables us to conclude that in both groups of patients, i.e. those up to the age of 60 as well as those over the age of 60, the titanium content is lower in men.

On the basis of the Mann-Withney test, it may be stated that there is no significant statistical difference (P=0.05) between the examined groups of women and men.

Table 6

Results for the examined groups of women and men

Sex	Number of patients	Average age	Number of implants	Average result for group ($\mu g\ g^{-1}$)
F	14	49.45	30	10.40
M	10	54.36	22	6.14

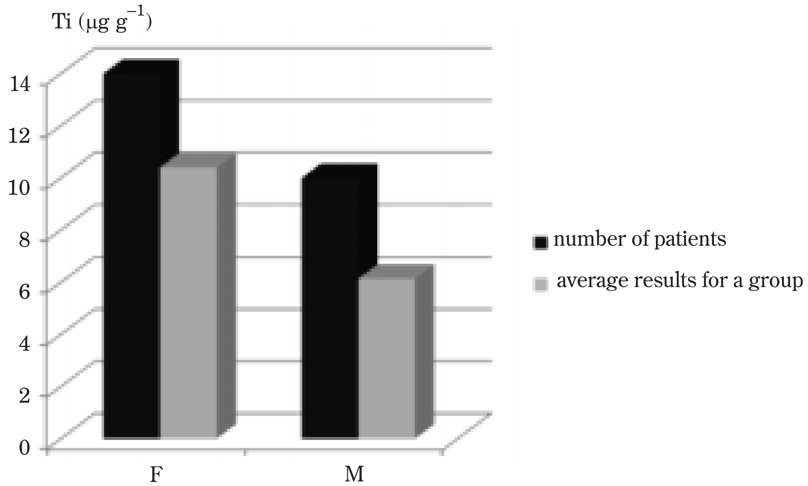

Figure 3. Graphic presentation of the titanium content in mucosa depending on patients' gender

CONCLUSIONS

1. Ions of titanium were found to migrate into the soft tissues surrounding Osteoplant-Hex dental intraosseous implants despite the biocompatibility of that metal.

2. No statistically significant correlation was observed between the amount of titanium ions released into the soft tissues and such factors as the mandibular or maxillary location of the implants, the gender or age of the patients.

3. The presence of titanium ions in the soft tissues did not cause any clinically recognizable changes in the oral cavity over a period of 4 to 6 months.

4. It is possible that the use of titanium intraosseous implants by allergic patients may lead to a negative reaction of the tissues of the masticatory organ due to the migration of various ions.

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