

VENOSTASIS TEST AS A METHOD OF CHOICE TO EVALUATE BLOOD FIBRINOLYTIC CAPACITY DURING THIRD MOLAR SURGERY

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Abstract: The aim of our research was to evaluate the fibrinolytic capacity during oral surgical interventions – operative extraction of semi-impacted third molars having caused blood fibrinolysis activity.

With the intention of establishing the condition of the blood vessels' endothelium before oral surgical interventions, the influence of surgical procedures upon the endothelium, and the response of the endothelium after interventions, the venostasis test (venous stasis) was conducted in all the subjects. This test measures the global fibrinolytic activity of the plasma, caused by anoxia.

In order to realize the aim, the first blood sample was taken before the beginning of the test, and then the indicated oral surgical intervention was performed. Immediately after the completion of the surgery, the venostasis test was carried out, lasting for five minutes, and right after the test a second sample of blood was taken. Using the method of fibrin plates, the level of the activators and inhibitors of the plasminogen was established afterwards.

The average values of the pro activators and inhibitors of fibrinolysis from the venostasis test, in all subjects, showed increased values compared to the same ones in the control group, in all researched relations. Statistically, a significant difference was established after interventions were performed.

These findings support the fact of possible damage to the blood vessels' endothelium and a change of the fibrinolytic capacity in the perioperative period of third molar surgery.

Key words: third molar impaction, oral surgery, fibrinolytic system, stress.

Introduction

Alveolar osteitis after operative extraction of third molar mandible impaction and semi-impaction is characterized by excess fibrinolysis, leading to early dissociation of the clot. Following the removal of mandibular teeth, especially the third molars nowadays, a post-operative complication may occur, namely alveolitis [19, 30, 31]. Alveolar osteitis, commonly referred to as dry socket, is by far the most common complication following dental extraction [5]. It represents a breakdown of healing after clot formation but before wound organization [10]. In the scientific literature, there are two different groups of authors: the first [2, 4, 13, 15] emphasizes the etiology and the pathogenesis of the dry socket, as well as the influence of surgery stress and the operative trauma over certain parameters of the blood coagulation and fibrinolysis [1, 6, 10]. The second group of research authors [7, 9, 11] had the aim of preventing the alveolar osteitis and, if the healing was prolonged, finding which treatment would be the most useful. On the other hand, Turcotte [30] and many other authors [3, 23] in their articles review the pertinent literature concerning this condition and discuss its etiology [5], symptoms [4, 15, 18] and treatment [8].

Many scientific authors [17, 18, 22, 24] in their researches set the aim of evaluating the influence of surgery stress and operative trauma [32] over certain parameters of the blood coagulation and fibrinolysis.

According to Grand [13], acute physical stress such as major surgery, the insulin-induced hypoglycemia and physical exercises are connected to the acute increase of the concentration of the factor VIII in the circulation as well as increased blood fibrinolytic activity. The mechanisms that are included in the production of these answers are partly under hormone control, and it is obvious that the changes are mediated by the neurohormones [25] adrenalin and arginine vasopressin [14].

Kehlet [18] emphasized that surgery trauma and modified the effects of pain are the reason for the start of possible complications such as infections and haemorrhage. Precisely as a consequence of the activation of the humoral substances prostaglandin, kinin, leukotren, interleukin-1, as well as the tumour necrotic factor, the creation of the above-mentioned complications is made possible. Interleukin-1 as a mediator of an inflammatory reaction, and the tumor necrotic factor lead to pro-coagulation changes in the one-body cells [12]. The synthesis and the secretion of the thromboplastin [12], antigen activity of F VIII: factor v. Willebrand, is present as well as activity of the inhibitor of the plasminogen-1 (PAI-1) activator [26, 28] with the same time decreased production and secretion of the tissue type plasminogen activator (t-PA).

In modern scientific books knowledge [16, 20, 21] there is an elaboration of accidentally discovered cases with prolonged bleeding after completed

extraction when often rare deficits of some coagulation factors or fibrinolytic inhibitors are discovered [29].

The basic aim of this research was to carry out clinical evaluation of the fibrinolytic capacity in the subjects during oral surgical interventions – operative extractions of semi-impacted third molars in the mesio-angular position, having caused activity of fibrinolysis. The general aim of the study was to evaluate the correlation between third molar surgery, as psychophysical and operative trauma, and the blood fibrinolytic activity during the oral surgical interventions. The second aim was to confirm whether the possible changes in the level of the activators/inhibitors of the fibrinolytic system could be specified by clinical results from laboratory tests (or not), and how its value could be an influence on the clinical outcome after semi-impacted third molar surgery.

This study had the intention of estimating the condition of the blood vessels' endothelium before oral surgical interventions, the influence of the procedures (extraction of the semi-impacted third molar) upon the endothelium, and the response of the endothelium after the interventions.

Material and Method

For realization of the aim, this study included an examined group of 50 subjects, healthy patients, both male and female, aged between 25–35. According to the data of anamnesis, clinical and radiographic examination, indications for operative extraction were set up (bilateral semi-impacted third molars in meso-angular position). The surgical interventions were carried out over 35–40 min, and the trauma was similar in the examinees, according to the operative protocol. The interventions in the examined group were realized during the morning hours at the Dental Medicine Department, Goce Delcev University, Stip, and at the Oral Surgery Clinic, Faculty of Dentistry, Skopje, R. Macedonia in the period 2005–10.

The control group consisted of 35 examinee blood donors, both male and female, aged between 25 and 30, healthy patients, who had not had any dental intervention. All examinees agreed to be included in our research.

With the intention of determining the cause activity of fibrinolysis, all the subjects took the venostasis test. With the help of this test, the fibrinolytic capacity of the subjects was investigated. The test was performed in order to determine the condition of the endothelium before the interventions, the influence of the surgical procedures upon the endothelium, and its response after the interventions. This test measures the global fibrinolytic activity of the plasma, caused by anoxia.

Before the beginning of the test, a first blood sample was taken, and then the indicated oral surgical intervention was performed. Immediately after the completion of the surgery, the venostasis test was carried out lasting for five minutes, and right after the test, a second sample of blood was taken.

Two blood samples were taken from the subjects from the control group : before and after the test, without any kind of dental procedures having been performed.

Blood samples were instantly distributed and analyzed at the Blood Transfusion Institute, of Hemostasis and Thrombosis Department, at the Republic Institute of Transfusion, Faculty of Medicine, Skopje. Using the method of fibrin plates (Figure1), the level of the activators and inhibitors of the plasminogen was established afterwards.

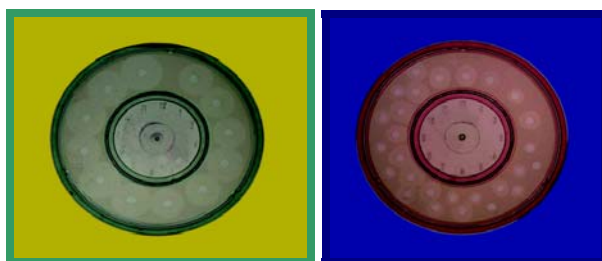


Figure 1 – Fibrin plates with activators and inhibitor of fibrinolysis

Control visits were made on the first, second and seventh day after the oral surgical interventions, recording the presence of oedema, haematoma, pain, dry socket and prolonged bleeding.

For statistical elaboration and analysis of the obtained data, the Statistica statistics program was used.

Results

Results from the average values of the venostasis test in the examined group (before and after the oral surgical interventions of semi-impacted third molars) and the same values of the control group are given in Table 1. The values of the activators from the venostasis test before (77.67%) and after (57.90%) the operative intervention, analyzed with the "t"-test, point to a relation with a high statistically significant difference ($t = 6.80$ and $p < 0.01$). The average values of the inhibitors after (72.25%) the operative intervention, compared to the average values of the inhibitors before (73.52%) the operative intervention, show that there is no statistically important difference ($t = 0.29$ and $p > 0.05$).

Table 1

Differences of the average value of the fibrinolytic parameters before and after venostasis test in examined and control groups

Research group No = 50				
Parameters (%)	\bar{X}	SD	t	p
activators-before	77.67	18.98	6.80	p < 0.01**
activators-after	57.90	9.95		
inhibitors-before	73.52	21.14	0.29	p < 0.05*
inhibitors-after	72.25	22.96		
Research group / control group No = 50 / No = 35				
activators-before res. gr./cont. gr.	77.67/21.08	18.98/7.07	15.75	p < 0.01**
activators-after res. gr./cont. gr.	57.90/21.08	9.54/7.07	16.73	p < 0.01**
inhibitors-before res. gr./cont. gr.	73.52/41.60	21.14/14.15	7.56	p < 0.01**
inhibitors-after res. gr./cont. gr.	72.25/41.60	22.96/14.15	6.83	P < 0.01**

Comparing the values of the activators and inhibitors from the venostasis test in all subjects before and after the oral surgical interventions, we obtained results that show a high statistic significance in all relations, except in the analysis of the values of the inhibitors before/after the intervention.

The analysis of the values of the activators from the venostasis test before and after the oral surgical intervention compared to the values of the activators of fibrinolysis in the control group are significantly higher in all relations, and show a high statistical significance (Table 1 and Figures 1, 2). The differences of the average values of the activators and inhibitors were tested before and after the oral surgical interventions with the same parameters in the control group. The analyses of the average values of the activators of fibrinolysis from the venostasis test, before (77.67%) and after (57.90%) the oral surgical intervention, and the average values of the activators of fibrinolysis in the control group, show a high statistical significance in both researched relations ($t = 15.75$; $t = 16.73$ and $p < 0.01$).

The average values of the inhibitors before (73.52%) the intervention in the examined group significantly differ from the average ones in the control group (41.60%), and the analysis shows a high statistically significant diffe-

rence ($t = 7.56$ and $p < 0.01$). The average values of the inhibitors of fibrinolysis after (72.25%) the intervention also significantly differ compared to the average values of the inhibitors of fibrinolysis in the control group (41.60%). The "t"-test shows a high statistical significance ($t = 6.83$ and $p < 0.01$). After the first and second day following the operative extractions of semi-impacted third molars, no prolonged bleeding was seen among the examinees.

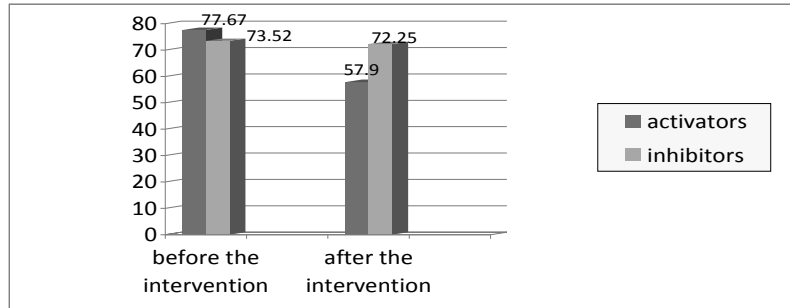


Figure 2 – Display of the average values of fibrinolytic parameters before and after oral surgical interventions of semi-impacted third molars

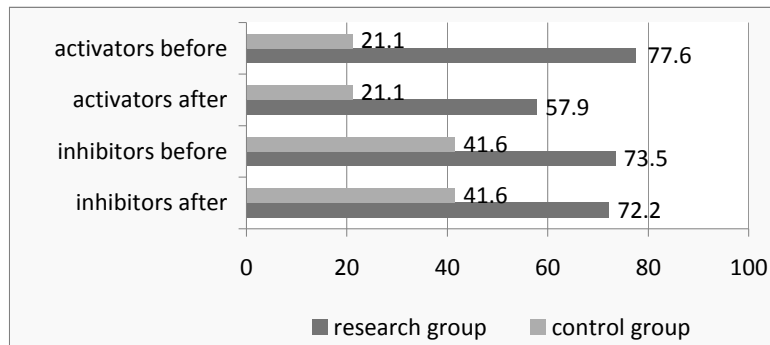


Figure 3 – Display of the differences of the average values from the venostasis test before and after interventions in research and control group

The data of the examined group concerning the appeared oedema, haematoma, pain and alveolitis during the control investigations after the first, second and seventh day is shown in Table 2. With the Spearman coefficient of correlation, the linear connection between the values of activators and inhibitors were determined after the operative extractions of semi-impacted third molars with the parameters from the control examinations.

Table 2

Presence of clinical outcome after operative extractions of semi-impacted third molars in examined group

(n = 50)	First day				Second day				Seventh day			
	oedema		hematoma		oedema		hematoma		oedema		hematoma	
	N ⁰	%	N ⁰	%	N ⁰	%	N ⁰	%	N ⁰	%	N ⁰	%
absence	24	47.5	50	100	35	75	50	100	50	100	50	100
presence	26	52.5	0	0	15	25	0	0	0	0	0	0
	pain		dry socket		pain		dry socket		pain		dry socket	
	N ⁰	%	N ⁰	%	N ⁰	%	N ⁰	%	N ⁰	%	N ⁰	%
	absence	22	42.5	40	100	27	55	35	75	50	100	40
presence	28	57.5	0	0	23	45	15	25	0	0	10	12.5

Table 3

Spearman coefficient of correlation between activators and inhibitors after interventions and parameters of control examinations in examined group

Parameters	Spearman R.	p
activators after interv. / edema 24 h	- 0.049	p = 0.76
activators after interv. / edema 48 h	0.043	p = 0.79
activators after interv. / edema 7 days	/	/
activators after interv. / hematoma 24 h	/	/
activators after interv. / hematoma 48 h	/	/
activators after interv. / hematoma 7 days	/	/
activators after interv. / dry socket. 24 h	/	/
activators after interv. / dry socket 48 h	0.005	p = 0.97
activators after interv. / dry socket 7 days	0.101	p = 0.53
inhibitors after interv. / edema 24 h	- 0.357	p = 0.02
inhibitors after interv. / edema 48 h	- 0.233	p = 0.14
inhibitors after interv. / edema 7days	/	/
inhibitors after interv. / hematoma 24 h	/	/
inhibitors after interv. / hematoma 48 h	/	/
inhibitors after interv. / hematoma 7 days	/	/
inhibitors after interv. / dry socket 24 h	/	/
inhibitors after interv. / dry socket 8 h	- 0.32	p = 0.04
inhibitors after interv. / dry socket 7 days	- 0.167	p = 0.30

The coefficients of correlation shown in Table 3 showed a modest connection. There is a domination of the values of the relation of inhibitors after / oedema first day; inhibitors after / oedema second day; inhibitors after / alveolitis seventh day; activators after / alveolitis seventh day.

Discussion

The exact pathogenesis of dry socket is not well understood [5, 15]. However, disintegration of the blood clot by fibrinolysis remains the most widely accepted theory. Several contributing factors have been reported to be associated with an increased risk of dry socket. They include traumatic extraction, preoperative infection [33], smoking and sex, site of extraction, use of oral contraceptives, and use of local anaesthetics with vasoconstrictors, inadequate postoperative irrigation, and low level of operator experience [4]. Several methods have been advocated to reduce the incidence of dry socket, including the use of antiseptic mouthwashes, antifibrinolytic agents, antibiotics, steroids, clot-supporting agents and other intra-alveolar dressings and medicaments [9, 15].

The extraction of impacted mandibular third molars is a common procedure in oral and maxillofacial surgery. The reasons for extracting these teeth include acute or chronic pericoronitis, the presence of cysts or a tumour, periodontal problems and the presence of a carious lesion on the second or third mandibular molar. In some cases, extraction is performed in preparation for orthodontic treatment or orthognathic surgery. In North America, extraction of impacted mandibular third molars is often intended to prevent future complications. Before any such procedure, the patient must be informed of the reason for the surgery and the associated risks [2].

Several complications are associated with extraction of impacted mandibular third molars, the most common being alveolitis, infection [2, 6] and paraesthesia of the inferior alveolar nerve [22, 23]. Haemorrhage during or after surgery and paraesthesia of the lingual nerve are the relatively rare surgical techniques which seem to play a major role in the occurrence of the latter problem.

The maintenance of haemostatic homeostasis is one of the most dynamic processes in the human organism. As a result of that constant balance between the blood coagulation mechanisms and those that prevent it, uninterrupted circulation of the blood is enabled [27]. In the researches of most authors from the contemporary scientific literature an essential role is given to the fibrinolytic system in the process of haemostasis. The influences of surgical stress and operative trauma upon the activators and inhibitors of fibrinolysis are analysed in their researches [2].

The venostasis test (venous stasis) was introduced by Swedish researchers from Malmö: Nilsson & Robertson in 1968 [9, 27]. It is considered that after the venostasis, half of the fibrinolytic activity of the blood is owed to the activity of the tissue activator, referring to the external route of activation of the fibrinolysis, and the second half belongs to the internal activation that dominates while still. In fact, the local stimulation of fibrinolysis is dosed with this test. Bachmann, in the research of Sindet-Pedersen, 1999 [27] explains the mechanism of releasing the activators of fibrinolysis as a consequence of distension of the blood trough and/or the neuroreflex or the metabolic mechanism. At first, the venostasis test was carried out lasting for 20 minutes, but later on, because of severe pain caused by anoxemia, most authors [9, 11] investigated for various and shorter times, and had concluded that the same effect gained in 20 minutes could also be obtained in 5, 10 and 15 minutes. It should be stressed that the comparison of the results from the test is very difficult and sometimes impossible, because of the variety of criteria concerning the type of responders, the time of the stasis and the method used for the evaluation.

In our research there is an attempt to give an answer to the question of whether the oral surgical interventions similar to the intensity of the surgical trauma, carried out on healthy individuals (with an intact system of haemostasis) under local anaesthesia can cause changes to some parameters of the haemostasis, in other words in the fibrinolytic blood behaviour.

Bearing in mind the complexity of the system for haemostasis, our mean was that the research enabled us to obtain a real clinical evaluation of the physiological activity of the blood fibrinolytic system during surgical extractions of semi-impacted third molars.

The acquired results in this study have a logical explanation, if we consider that the values of the activators and inhibitors of fibrinolysis from the venostasis test before and after the interventions, compared to the values of the control group, are within the limits of normal values (60–100%). Still, from these results it can be clearly noticed that the oral surgical interventions had a statistically significant influence upon the researched parameters of the fibrinolytic system. Our findings for the presence of oedema and haematoma in the period after the intervention show that there is a moderate correlation of the same with the values of activators and inhibitors after the extractions. In the period after the extractions no haemorrhage was noticed, which was confirmed at the control examinations. This finding is normal as the examinees have an intact system of haemostasis.

Still, most authors [2, 5–9, 12, 13] agree with one thing: this test should have a diagnostic value. In the case of existing thrombosis or exhausted reserves of endothelium, it can show lower fibrinolytic activity, or it can have a prognostic importance – to predict the possible risk of the occurrence of a thrombotic insult, if the patient is out of a thrombotic episode.

Conclusions

- Oral surgical interventions (operative extractions of the semi-impacted mandible third molars) have an influence upon the fibrinolytic capacity with the release of proactivators and inhibitors of the fibrinolytic system.
- The venostasis test shows an increase in the values of the proactivators of fibrinolysis in the subjects, which is probably owing to a larger release of the blood vessels' endothelium.
- Statistically, after the completion of procedures in the research group, a highly significant difference is confirmed, which also points to the stage of possible damage to the blood vessels' endothelium and the fibrinolytic capacity during third molar surgery.

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Резиме

ТЕСТОТ НА ВЕНСКИ ЗАСТОЈ КАКО МЕТОД ЗА ПРОЦЕНА НА ФИБРИНОЛИТИЧКИОТ КАПАЦИТЕТ НА КРВТА ВО ТЕКОТ НА ХИРУРШКИ ТРЕТМАН НА ТРЕТИТЕ ИМПАКТИРАНИ МОЛАРИ

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Целта на испитувањето беше да се изврши клиничка проценка на фибринолитичкиот капацитет на испитаниците во текот на оралнохируршките интервенции – оперативно вадење на полуимпактирани трети молари при предизвикана активност на фибринолиза.

Со цел да се утврди состојбата на ендотелот на крвните садови пред оралнохируршките интервенции, влијанието на хируршката процедура врз ендотелот, како и одговорот на истиот по интервенциите кај сите испитаници беше спроведен тестот на венски застој. Со овој тест се мери глобалната фибринолитичка активност на плазмата предизвикана со аноксија.

За реализацијата на целта, првиот примерок крв беше земен пред изведување на тестот, потоа беше изведена индицираната оралнохируршка интервенција. Веднаш потоа беше изведен тестот на венски застој, така што веднаш по него беше земен вториот примерок на крв. Потоа со методот на фибринска плоча беше утврдено нивото на активаторите и инхибиторите на плазминогенот.

Средните вредности на проактиваторите и инхибиторите на фибринолизата од тестот на венски застој покажа зголемени вредности во однос на истите кај контролната група во сите испитувани релации, така што беше утврдена статистичка сигнификантна разлика по извршените интервенции.

Овие наоди одат во прилог на можното оштетување на ендотелот на крвните садови и промена на фибринолитичкиот капацитет во периоперативниот период на хируршкото отстранување на третите импактирани молари.

Клучни зборови: импактиран трет молар, орална хирургија, фибринолитички систем, стрес.

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