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DYNAMICS OF CHANGES IN BIOCHEMICAL MARKERS OF BLOOD SERUM AFTER REMOVAL OF MANDIBULAR MOLARS AND AUGMENTATION OF THE ALVEOLAR PROCESS

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The article describes the dynamics of connective tissue markers in blood serum (glycoproteins and chondroitin sulfates) under the conditions of mandibular molars extraction and augmentation of the alveolar process. According to the obtained data, it was established that the operation of tooth extraction and augmentation of the bone defect of the alveolar process of mandible caused more significant changes in the content of blood serum glycoproteins than chondroitin sulfates. The minimal changes in the studied parameters were observed in the second experimental group (when augmentation of the bone defect of the mandibular alveolar process with bone substitute of animal origin granules in combination with keratoxenoimplantant was performed after the molar extraction), the most significant changes were noted in the control group, in which no augmentation of the alveolar process was performed at all.

Key words: tooth extraction, alveolar process augmentation, biochemical markers.

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ДИНАМІКА ЗМІН БІОХІМІЧНИХ МАРКЕРІВ СИРОВАТКИ КРОВІ ПІСЛЯ ВИДАЛЕННЯ МОЛЯРІВ НИЖНЬОЇ ЩЕЛЕПИ ТА АУГМЕНТАЦІЇ АЛЬВЕОЛЯРНОГО ВІДРОСТКА

У статті описано динаміку змін сполучнотканинних маркерів сироватки крові (глікопротеїнів та хондроїтинсульфатів) за умов видалення моляра нижньої щелепи та аугментації альвеолярного відростка. За отриманими даними встановлено, що операція видалення зуба та аугментації кісткового дефекту альвеолярного відростка нижньої щелепи викликала більш значні зміни вмісту глікопротеїнів сироватки крові, ніж хондроїтинсульфатів. Мінімальні зміни досліджуваних показників спостерігали у другій дослідній групі (за умов аугментації кісткового дефекту альвеолярного відростка нижньої щелепи гранулами кісткового замінника тваринного походження у поєднанні з кератоксеноімплантантом після видалення моляра), найбільш значні зміни відзначені у контрольній групі, в якій аугментація альвеолярного відростка не проводилася взагалі.

Ключові слова: видалення зуба, аугментація альвеолярного відростка, біохімічні маркери.

The study is a fragment of the research project "Clinical-laboratory substantiation of the use of modern medical technologies in the diagnosis, treatment and prevention of diseases of the mouth and maxillofacial area", state registration number 0121U113582.

Secondary adentia is a significant problem of modern dentistry. After the tooth extraction, dimensional changes occur in the alveolar bone, which leads to remodeling of the bone tissue and reduction of its volume in various directions [3, 11]. The alveolar ridge under the background of adentia is not exposed to the functional load, its own tooth and their supporting structures, which leads to bone resorption. This combined effect forms the horizontal and vertical atrophy of the alveolar process [4, 8]. Bone resorption can make it impossible to carry out the surgical stage of dental implantation due to insufficient space or creates unfavorable aesthetic and functional conditions for prosthetics [2, 3].

Reparative regeneration after tooth extraction begins with the formation of a stable blood clot in the alveola, which is then filled by epithelium, which promotes osteoregeneration [9, 13]. The fibrin forms a natural support structure inside the blood clot that promotes the formation of osteoid and its subsequent calcification. This process is completed in about 120 days; periosteum is completely stabilized after about 180 days [14]. However, the processes of remodeling, namely the mineralization of new bone tissue, occur during periods that are very different and unpredictable in different patients. Thus, it was observed the average horizontal degeneration of the alveolar process in the amount of 3.8 mm and vertical – 1.2 mm during the first six months after extraction [15].

According to literature data, 29–63 % of horizontal and 11–22 % of vertical bone loss occurs during the first 6 months after tooth extraction without the use of alveolar process preservation techniques. Current reconstructive approaches to alveolar process augmentation include several methods with varying success rates, such as interpositional grafts, bone grafting with overlays, ridge splitting, guided bone regeneration, and distraction osteogenesis [12].

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In an attempt to reduce the need for modern surgical procedures and simplify the treatment plan, several surgical techniques have been developed to reduce post-extractive alveolar atrophy [5, 7, 10]. Conservation of the alveolas with the use of various biomaterials is the most common procedure aimed at controlling bone tissue resorption after tooth extraction. Several methods are used to reduce bone tissue resorption after tooth extraction. In particular, bone substitutes (autografts, allografts, xenografts or alloplastic materials), resorbable and non-resorbable membranes [2, 6, 8].

The purpose of the study was to determine the changes of connective tissues markers in the blood serum after the extraction of mandibular molars in combination with augmentation of alveolar process.

Material and methods. The study involved 75 patients of Sumy City Clinical Dental Polyclinic. Patients were separated into 3 groups. Patients to whom it was conducted mandibular molars extraction by classic methodic (control group, 25 people); additionally underwent alveolar augmentation with "Cerabone" granules ("Botiss biomaterials", Germany) (1st group, 25 people); and the use of "Cerabone" granules in combination with a keratoxenoimplant (2nd group, 25 people).

To determine the changes in connective tissue under the conditions of removal of mandibular molars and augmentation of the alveolar process, the following markers in blood serum were studied: glycoproteins and chondroitin sulfates. The study was conducted on the first day (during the extraction of mandibular molar and augmentation of the alveolar process), on the seventh and fourteenth day, and on the first, second, and third months of the postoperative period. The last period of observation had corresponded to the time of the surgical stage of dental implantation.

Glycoprotein content in blood serum was determined by the Steinberg-Dotsenko's method. The principle of this method: solutions of fructose (since glucose turns into fructose when boiling) in the presence of ammonium molybdenum and concentrated acids give a blue color, the intensity of which depends on the amount of glycoproteins in blood serum. The content of chondroitin sulfates was determined by the Nemeth-Csoka's method in the modification of L.I. Slutsky. The principle of this method is based on the formation of turbidity with rivanol, the intensity of which depends on the content of chondroitin sulfates [1].

Statistical processing of data was performed using the Statistica 6.0 software package (StatSoft Inc., USA), using the Student's t-criteria.

Results of the study and their discussion. On the first day of the study (during the tooth extraction), no probable changes of glycoprotein content in the blood serum were noted (Table 1).

Table 1

The content of glycoproteins in blood serum for different terms of reparative osteogenesis, g/l (M±m)

Term of study	group 1 (n=25)	group 2 (n=25)	group 3 (n=25)
1-st day	0.42+0.008	0.42+0.007	0.42+0.007
7-th day	0.49+0.007 *	0.50+0.005 *	0.49+0.006 *
14-th day	0.47+0.003 *	0.46+0.004 * ***	0.49+0.004 *
1-st month	0.44+0.006 ** ***	0.44+0.008 **	0.47+0.005 * ***
2-nd month	0.44+0.008	0.43+0.007	0.5+0.009
3-d month	0.43+0.006	0.43+0.005	0.44+0.007

Notes: 1.* – $p<0.05$ compared to the first day of the study; 2. ** – $p<0.05$ compared to the control group for the same period of reparative osteogenesis; 3. *** – $p<0.05$ compared to the previous term of reparative osteogenesis.

On the 7th day after the removal of the mandibular molars in all groups, a probable increase in the studied indicator was noted by 16.7 %, 19.0 % and 16.7 %, respectively for 1-st, 2-nd and 3-d groups. The indicator in the first and second experimental groups did not undergo a probable difference relative to the control for a similar period of the postoperative period.

14 days after the operation of mandibular molars removal and augmentation of the alveolar process, a probable increase of the glycoproteins content in the blood serum compared to the first day of the study was noted in the first group (carrying out the augmentation of the alveolar process with "Cerabone" granules) by 11.9 %, in the second group (under the conditions of combined use of "Cerabone" granules with keratoxenoimplant) by 9.5 % and in the control group by 16.7 %. When compared with the control group for the same period of reparative regeneration, a probable decrease in the content of serum glycoproteins was noted in the second group by 6.1 %, the indicator of the first group did not have the probable changes.

One month after the removal of the mandibular molars, a probable increase of the content of glycoproteins in the blood serum compared to the first day of the study was observed only in the control group by 11.9 %.

When using "Cerabone" granules as a monotherapy (the first group) and in combination with a keratoxenoimplant for alveolar augmentation (the second group), a probable decrease in the level of the

studied indicator by 6.4 % was observed for both groups relative to the same period of reparative osteogenesis in the control group. There was also a probable decrease in the content of serum glycoproteins relative to the previous period of the study (the 14th day after the operation of tooth extraction and augmentation of the alveolar process) in the first and control groups by 6.4 % and 4.1 %, respectively.

No significant changes in the content of blood serum glycoproteins were founded relative to the first period of the supervision and control in all three groups on the second and third months of the study (during the surgical stage of dental implantation).

Thus, probable changes in glycoproteins relative to the first term of the study were noted at all groups only on the 7th and 14th day of the study and were preserved in the control group after a month of supervision. In the second and third months of the study (at the time of the surgical stage of dental implantation), this indicator reached constant values in all three groups.

When examining the content of chondroitin sulfates in the blood serum on the first day of the study, no significant difference in the indicator was noted in the all studied groups (Table 2).

Table 2

The content of chondroitin sulfates in blood serum for different periods of reparative osteogenesis, g/l (M±m)

Term of study	group 1 (n=25)	group 2 (n=25)	group 3 (n=25)
1-st day	0.061+0.005	0.062+0.005	0.061+0.004
7-th day	0.075+0.005 *	0.075+0.004 *	0.079+0.004 *
14-th day	0.074+0.004 *	0.073+0.006	0.076+0.004 *
1-st month	0.065+0.002 ** ***	0.065+0.002 **	0.073+0.003 *
2-nd month	0.064+0.005	0.064+0.004	0.066+0.005
3-d month	0.062+0.004	0.062+0.003	0.063+0.003

Notes: 1.* – $p<0.05$ compared to the first day of the study; 2. ** – $p<0.05$ compared to the control group for the same period of reparative osteogenesis; 3. *** – $p<0.05$ compared to the previous term of reparative osteogenesis.

On the 7th day after the operation of mandibular molar extraction, a probable increase in the level of the studied indicator by 29.5 % was observed in the control group.

During the augmentation of the alveolar process with “Cerabone” granules, the content of serum chondroitin sulfates increased by 23.0%. When augmenting the alveolar process with “Cerabone” granules in combination with a keratoxenoimplant, a statistically significant increase of this marker by 21.0 % was noted.

On the 14th day of the postoperative period, a statistically significant increase in the level of chondroitin sulfates in blood serum by 24.5 % was observed in the control group.

Under the conditions of using “Cerabone” granules for the augmentation of the alveolar process, a statistically significant increase of this index by 21.3 % was also noted compared to the first day of the study. With the combined use of “Cerabone” granules with a keratoxenoimplant to replace the bone defect of the alveolar process, no changes in the content of serum chondroitin sulfates were observed at this stage of reparative osteogenesis.

Also, it was not noted the significant difference of the studied marker between the first and second experimental and control groups.

In the first month of the postoperative period, an increase in the level of the studied indicator by 19.7 % compared to the first day of the study was noted only in the control group. Changes in the level of chondroitin sulfates in the blood serum in the first and second experimental groups in a similar comparison had no statistically significant differences. At the same time, the content of chondroitin sulfates in blood serum in the first group was characterized by a significant decrease by 12.2 % relative to the previous period of reparative regeneration. Also, it was noted a probable decrease of this indicator in both experimental groups by 11.0 % compared to the control group for the corresponding period after tooth extraction.

It should be noted that at all other periods of the study, no significant difference in the content of chondroitin sulfates in blood serum was observed in the first and second experimental groups relative to the control group at the same period of the postoperative period.

On the second and third month of the postoperative period, the level of the studied indicator in blood serum had no significant changes in all three groups.

Thus, a significant increase in the content of chondroitin sulfates in blood serum was observed on the 7th day in all groups of patients, on the 14th day - in the first experimental and control groups. On the 1st month of the postoperative period, probable changes compared to the first day of observation were noted only in the control group.

So, according to the results of the study, no probable changes in the content of glycoproteins and chondroitin sulfates in the blood serum were recorded during the first tooth extraction operation, this is due to the fact that the treatment according to the classical and author's methods was carried out after the collection of blood serum for further research. Such results correlate with the data of other researchers [7, 13].

The greatest changes in connective tissue markers in blood serum were noted on the 7th, 14th, and one month after the tooth extraction. Moreover, it should be noted that on the 2nd and 3rd month (at the time of the surgical stage of dental implantation), the studied markers reached normal values. Similar data of positive marks of bone-graft materials using were noted during analyzes of literature data [8].

It was found that the smallest changes in the studied indicators were established in case of augmentation of the bone defect of the mandibular alveolar process with "Cerabone" granules in combination with a keratoxenoimplant. It was a contrast to the control group, in which the augmentation of the alveolar process was not carried out, where the changes of connective tissues markers of blood serum reached the maximum values.

Conclusion

Therefore, the operation of tooth extraction (classic technique) and augmentation of the bone defect of the alveolar process of the mandible (the author's technique) caused more significant changes in the content of blood serum glycoproteins than chondroitin sulfates.

The minimal changes in the studied parameters were observed in the second experimental group (when augmentation of the bone defect of the mandibular alveolar process with "Cerabone" granules in combination with keratoxenoimplantant was performed after the molar extraction), the most significant changes were noted in the control group, in which no augmentation of the alveolar process was performed at all. Moreover, both indicators reached the norm already in the second month of the postoperative period in all three studied groups.

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