POSTTRAUMATIC DENSITY OF THE BONE TISSUE OF THE RAT’S MANDIBLE WITHOUT PATHOLOGY, ON THE BACKGROUND OFNALBUPHINE INTAKE AND AFTER LINCOMYCINTREATMENT

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ABSTRACT
Numerous dental manipulations are accompanied by bone injuries. Various types of drug correction are widely used for correction and optimization of bone tissue reconstruction after bone-traumatic injury. The evaluation of the course of reparative osteogenesis becomes possible with the x-ray methods which gives the possibility to evaluate and predict early quantitative and qualitative changes in various pathological conditions, as well as to trace their dynamics in clinical and experimental conditions. In our research we have found out the peculiarities of the density dynamics of the bone tissue of the mandible after causing bone-traumatic injury to intact animals and animals that have been taking nalbuphine for a long time, as well as after treatment with lincomycin.

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Introduction. Numerous dental manipulations, in particular tooth extraction, resection of the tooth root, implant placement, etc., are accompanied by bone injuries. The reason of the most common causes of patients’ referral to the clinic of maxillofacial surgery include jaw injury with the break of bone integrity [1, 3, 6, 9, 12]. Data from numerous scientific studies indicate that there are many factors that affect the course of reparative osteogenesis - concomitant or background diseases, bad habits, patient's age, alcohol or drug dependence [7, 8, 10, 11, 12, 13, 14, 15, 16]. Various types of drug correction are widely used for correction and optimization of bone tissue reconstruction after bone-traumatic injury [13, 15, 16, 17, 18]. The evaluation of the course of reparative osteogenesis becomes possible with the x-ray methods usage, in particular - dental radiovisiography, which has become widely used in modern dentistry [4]. This method allows not only to find out the quality of bone tissue, but also to evaluate and predict early quantitative and qualitative changes in various pathological conditions, as well as trace their dynamics in clinical and experimental conditions [4, 7, 14,].

Purpose of our study: to find out the peculiarities of the density dynamics of the bone tissue of the mandible after causing bone-traumatic injury to intact animals and animals that have been taking nalbuphine for a long time, as well as after treatment with lincomycin.

Material and methods. The study was performed on 80 sexually mature, non-breeding male rats with a body weight of 180-200 g and 3.5 months old. Experimental animals were kept in the
vivarium of the Danylo Halytsky Lviv National Medical University. All studies were conducted in accordance with the provisions of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (Strasbourg, 1986), Council Directive 86/609/EEC (1986), Law of Ukraine No. 3447-IV “On the Protection of Animals from Cruel handling”.

All experimental animals were divided into 6 groups:
- Group 1 - intact animals that had bone-traumatic injury (15 animals);
- Group 2 - animals with the modeled opioid dependence (15 animals);
- Group 3 - animals with opioid dependence and with the bone-traumatic injury (15 animals);
- Group 4 - animals that were treated with lincomycin after a bone-traumatic injury (15 animals);
- Group 5 - animals with opioid dependence, which were treated with lincomycin (15 animals) after bone-traumatic injury;
- Group 6 - control (5 animals).

The injury was modeled by breaking the integrity of the bone tissue of the mandible in the area of molars with the help of dental drill. The operation was performed under thiopental anesthesia [5].

Opioid dependence was modeled by the administration of a narcotic analgetic Nalbuphine on a daily basis (once a day at the same time interval). Nalbuphine was administered intramuscularly according to the following schedule: 1 week - 8 mg / kg, 2nd week - 15 mg / kg, 3rd week - 20 mg / kg, 4th week - 25 mg / kg, 5 -this week - 30 mg / kg, 6th week - 35 mg / kg [2]. Lincomycin (30% solution) was administered intraperitoneally at a dosage of 25 mg / kg once a day for 6 days after bone injury.

Control of the quality of bone tissue of the mandible in the area of injury was carried out using a dental radiovisiographer Siemens with the software Trophy Radiology. The unit of measurement of tissue density was taken the conventional unit of gravity (CUG).

Investigations of the quality of bone tissue of the mandible were performed weekly to all animals of all experimental and control groups.

For each group, the arithmetic mean value of the researched indicator, the variance and the confidence interval at the level of reliability of P = 95% were determined.

**Research results.** An analysis of the density of the bone tissue of the rat's mandible after bone-traumatic injury made it possible to determine the presence of an express dynamics of the investigated index (Table 1).

|            | M    | Dysp | Δ   | M-Δ  | M+Δ  |
|------------|------|------|-----|------|------|
| control    | 75,33| 177,87| 14  | 61,34| 89,33|
| 1 week after trauma | 107,67| 689,87| 27,56| 80,1 | 135,23|
| 2 week after trauma | 152  | 394,8 | 20,85| 131,15| 172,85|
| 3 week after trauma | 99,5 | 820,7 | 30,06| 69,44| 129,56|

The obtained data indicate that, after two weeks after injuries, the density of the mandibular bone tissue in the traumatized area gradually increases and by the end of the second week doubles in comparison with the norm. During the third week after the injury, the investigated index is reduced, but remains slightly higher than in intact animals.

Dynamics of density of bone tissue of the mandible of the rat after bone destruction with the subsequent treatment with lincomycin is similar - the observed index increases within two weeks after the injury and decreases to the end of the third, but its absolute values are much lower than in animals not treated with lincomycin (Table 2).

|            | M    | Dysp | Δ   | M-Δ  | M+Δ  |
|------------|------|------|-----|------|------|
| control    | 75,33| 177,87| 14,00| 61,34| 89,33|
| 1 week after trauma | 92,33| 739,87| 28,55| 63,79| 120,88|
| 2 week after trauma | 104,00| 722,80| 28,21| 75,79| 132,21|
| 3 week after trauma | 95,17| 1326,97| 38,23| 56,94| 133,40|

To reveal the peculiarities of changes in the quality of bone tissue of the mandible on the background of prolonged nalbuphine intake, we analyzed the dynamics of this indicator for 6 weeks of dosing (Table 3).
The analysis of the obtained data showed that after two weeks of nalbuphine intake, the studied index gradually increases, and during the third week it decreases practically to norm. During the fourth and fifth weeks the bone density increases again, and in the sixth week it decreases and only slightly exceeds the norm (Table 3).

Table 3. Dynamics of density indices of bone tissue of the rat's mandible on the background of the nalbuphine intake

|                           | M   | Dysp | Δ    | M-Δ  | M+Δ  |
|---------------------------|-----|------|------|------|------|
| Intact animal             | 75,33 | 177,87 | 14   | 61,34 | 89,33 |
| 1st week of the experiment| 78,17 | 191,77 | 14,53 | 63,63 | 92,7  |
| 2nd week of the experiment| 85,67 | 809,47 | 29,86 | 55,81 | 115,52|
| 3rd week of the experiment| 75,5  | 333,1  | 19,15 | 56,35 | 94,65 |
| 4th week of the experiment| 82,33 | 433,07 | 21,84 | 60,49 | 104,17|
| 5th week of the experiment| 83,17 | 380,97 | 20,48 | 62,68 | 103,65|
| 6th week of the experiment| 79,5  | 537,5  | 24,33 | 55,17 | 103,83|

Since the bone density of the mandible after three weeks of nalbuphine intake is as close as possible to normal values, this term was chosen for causing a bone-destroying trauma to animals with nalbuphine dependence. The obtained data suggest that the dynamics of bone density after bone-traumatic injury with the use of nalbuphine is quite different from that of intact animals. One week after the trauma, the investigated index practically does not change, after two weeks it increases somewhat and its extension continues until the end of the experiment - after 3 weeks after injury, the density of bone tissue with the use of nalbuphine is almost twice as high as in intact animals (Table 4).

Table 4. Dynamics of the bone tissue density indices of the rat's mandible after a bone-traumatic injury on the background of the nalbuphine intake

|                           | M   | Dysp | Δ    | M-Δ  | M+Δ  |
|---------------------------|-----|------|------|------|------|
| Control                   | 75,33 | 177,87 | 14   | 61,34 | 89,33 |
| 3 week of the nalbuphine intake / before trauma | 75,5  | 333,1  | 19,15 | 56,35 | 94,65 |
| 4 week of the nalbuphine intake / 1 week after trauma | 74,5  | 421,1  | 21,54 | 52,96 | 96,04 |
| 5 week of the nalbuphine intake / 2 week after trauma | 86    | 1128,4 | 35,25 | 50,75 | 121,25|
| 6 week of the nalbuphine intake / 3 week after trauma | 133,5 | 3108,3 | 58,51 | 74,99 | 192,01 |

The study of the lincomycin influence on the condition of the bone tissue of the rat's mandible after the bone-traumatic injury conducted on the background of prolonged nalbuphine intake, made it possible to establish that, after a traumatic injury, the density of bone tissue drastically increases and gradually decreases over the next two weeks, only slightly exceeding the norm at the end of the experiment (Table 5).

Table 5. Dynamics of bone tissue density indices of the rat's mandible after the bone injury on the background of the nalbuphine intake with the following lincomycin correction

|                           | M   | Dysp | Δ    | M-Δ  | M+Δ  |
|---------------------------|-----|------|------|------|------|
| Control                   | 75,33 | 177,87 | 14   | 61,34 | 89,33 |
| 3 week of the nalbuphine intake / before trauma | 75,5  | 333,1  | 19,15 | 56,35 | 94,65 |
| 4 week of the nalbuphine intake / 1 week after trauma | 112,33 | 3299,87 | 60,28 | 52,05 | 172,62|
| 5 week of the nalbuphine intake / 2 week after trauma | 91,67 | 401,47 | 53,25 | 50,75 | 121,25|
| 6 week of the nalbuphine intake / 3 week after trauma | 86,17 | 496,57 | 23,39 | 62,78 | 109,55|

Comparison of the dynamics of bone density of the rat's mandible three weeks after bone-traumatic injury in animals of different experimental groups showed that in animals without background pathology the dynamics of the studied index was similar to both in the treatment of lincomycin and without its use - the maximum value of bone density reached through two weeks after the injury and decreased during the third week (Fig. 1). However, the absolute values of the studied index for all three weeks after the injury were significantly lower in animals treated with lincomycin (Fig. 1).
Animals with background opioid dependence had quite different dynamics of density of bone tissue after injury in the groups where the treatment was conducted with lincomycin and where it was not used. In animals that had not been treated with lincomycin after injury, but continued nalbuphine intake, bone density declined slightly during the first week after injury, increased somewhat during the second week and increased rapidly during the third week. In animals treated with lincomycin, the dynamics of the studied index was quite different - bone density increased significantly during the first week and gradually decreased to the third (Fig. 1).

![Fig. 1. Dynamics of density of bone tissue of rat's mandible during three weeks after bone-traumatic injury in animals of different experimental groups.](image1)

An analysis of bone density indices after bone-traumatic injury to animals of different experimental groups at different periods of the experiment shows that during the first week after the injury, the biggest difference from the norm was registered in the group of animals which were treated with lincomycin on the background of nalbuphine use; during the second week - intact injured animals; during the third week - animals that were injured on the background of nalbuphine use without correction by lincomycin (Fig. 2).

![Fig. 2. Comparison of the indices of bone density of rat mandible in animals of different experimental groups within three weeks after a bone-traumatic injury.](image2)
Throughout the experiment, the density of bone tissue after injury was higher than in norm in all experimental groups, with the exception of animals with nalbuphine addiction without correction of lincomycin one week after injury.

**Conclusions.**

1. The application of a bone-traumatic injury leads to an expressed dynamics of bone density of bone tissue and the area of injury, which indicates a change in its quality.

2. Dynamics of density of bone tissue of the mandible after bone-traumatic injury in intact animals, animals with the nalbuphine addiction and animals with the treatment of lincomycin, is different.

3. Three weeks after bone-traumatic injury, the bone density in opioid-dependent animals, which had not been treated with lincomycin, exceeded the norm by half; in animals of other experimental groups, the test indicator was only slightly higher than normal.

4. For persons who have been using nalbuphine for a long time or having opioid dependence, after treatment of bone loss, it is necessary to treat with lincomycin, since the experimental groups, the test indicator was only slightly higher than normal.

5. It is necessary to conduct further studies on the effect of osteoporosis on bone density of the mandible after treatment of bone loss, since the results of the present study are limited to the period from 2005 to 2014.

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