

1. Introduction

The thesis is devoted to the comprehensive study of the problem of delayed union of bone tissue in patients with mandibular fractures (MF). The urgency of the research is due to the significant prevalence rate of this complication, which, according to statistical data, is observed in 2.4–26 % of MF [1–3].

Most authors mark absence of the unique approach in relation to etiologic factors and nosotropic mechanisms of delayed union of bone tissue in patients with mandibular fractures. Unfortunately, many existing researches have fragmentary character.

From experience of leading maxilla-facial surgeons, a diagnosis of delayed union of MF usually is resultants and only establishes absence of consolidation in a term over 50 days [4]. Until this they try to improve immobilization due to additional bandages, additional operations (osteosynthesis) or continue to keep the intermaxillary fixing for indefinite term (sometimes to 2 months). Nevertheless, not all the time problem of osteoreparation is fixed in a medical document and we do not have objective statistics of disease [5].

Without regard to certain advantages of osteosynthesis, however in most researches it was not set meaningful dependence of delayed union of MF on the select method of treatment [6–8].

Growth of cases of delayed union of MF in the last years conditioned by the row of factors, between them the special attention is spared general factors, abuse of alcohol and narcotic substances, smoking.

Also generally known, that somatic pathology negatively influences on osteoreparation. It is in fact that among patients with MF year-to-year grows part of patients with concomitant pathology [9, 10].

Thus, it should be noted, that decision of this problem yet very much far from the final decision and there is an urgent requirement in the comprehensive analysis of role of general and local factors of origin of delayed union of MF.

DELAYED UNION OF MANDIBULAR FRACTURES: ANALYSIS OF 74 CLINICAL CASES

Natalya Idashkina

PhD, Associate Professor

*Department of oral surgery, implantology and periodontology
State Institution "Dnipropetrovsk Medical Academy of
the Ministry of Health of Ukraine"
9 Vernadsky str., Dnipro, 49044, Ukraine
idashkina@ukr.net*

Abstract: Delayed union of bone tissue in patients with mandibular fractures is observed in 2.4–26 % of clinical cases. Solution of this problem yet very much far from the final solution and there is an urgent requirement in the comprehensive analysis of role of general and local factors of origin of delayed union MF.

Methods. Modern clinical, laboratory and microbiological research methods were used in the work. Densitometry conducted on computed tomograph Planmeca Promax 3d (Finland) (85 kV 5–7 mA). The basal values of immunoglobulins of the main classes and interleukins IL-1 β , FNT- α , IL-4, MDA, SOD and catalase activity, POL, β -Cross Laps and osteocalcin in peripheral blood were determined in 74 patients with delayed consolidation of the mandibular fractures. Correlation analysis of local and general (concomitant somatic pathology) factors, and clinic-laboratorial parameters in patients with delayed consolidation of the mandibular fractures is conducted.

Results. There is a high correlation between β -Cross Laps (negative) and osteocalcin (positive) and bone mineral density. The mean inverse correlation relationship was established between the MDA and catalase activity and BMD ($r=-0.57$), and the high correlation of these indices with markers of bone remodeling (positive to β -Cross Laps ($r=0.80$ and $r=0.87$, respectively) and negative to osteocalcin ($r=-0.80$ and $r=-0.84$, respectively). High direct correlation between FNT- α indices and POL, MDA, and catalase indices, as well as very strong with β -Cross Laps (positive) and osteocalcin (negative), and also with high-correlation ligaments of sIgA and IL-1 β .

Discussion. Convincing clinical and laboratory data were obtained that the combined effect of local and general (concomitant somatic pathology) factors on the basis of the activation of inflammation processes, which increase the indirect influence on immune factors, processes of radical oxidation and bone metabolism, is resulted to delayed union. It was also found that clinical signs of the development of consolidation complications in patients with MF include increased signs of inflammation (oedema, exudation, etc.) up to the 3rd day and preservation of even moderate signs of inflammation (inflation, local hyperemia, and others) after the 7th day, BMD below 600 HU. Among the local factors that increase the infectious risk and inflammatory reaction, the following clinical situations should be distinguished: comminuted fracture; the presence of a tooth in the line of fractures; partially edentulous with loss of antagonist teeth (according to Eichner); complete adentia with mandible atrophy.

Keywords: mandibular fracture, delayed union, pathogenesis, risk factors, reparative osteogenesis, prognosis and treatment of complications.

Aim of research was to study of clinical and basic pathogenetic features of delayed union of bone fragments at the patients with mandibular fractures.

2. Methods

For period from 2012 to 2017 in the clinic of Dnipropetrovsk Medical Academy (Department of Oral surgery, implantology and periodontology) a group from 74 patients was selected, in which mobility in the area of break was saved in 1 month after a reposition and fixation of bone fragments.

Modern clinical, laboratory and microbiological research methods were used in the work.

Densitometry conducted on computed tomograph Planmeca Promax 3d (Finland) (85 kV 5–7 mA).

Images saved in the format DCOM and opened in viewing software Romexis Viewer. It allowed the revision of image in any plane, determination of bone mineral density (BMD) on the select area of jaw in Hounsfield's units (HU).

The estimation of jaws BMD was conducted by U. Lekholm and G. Zarb classifications (1985), and by S. Mish (1990).

BMD more than 850 HU was examined as an intact dense bone; indexes from 350 to 850 HU were accounted as relatively intact bone; less than 350 HU as a local osteoporosis.

The basal values of immunoglobulins of the main classes and interleukins IL-1 β , FNT- α , IL-4, MDA, SOD and catalase activity, POL, β -Cross Laps and osteocalcin in peripheral blood were determined in 74 patients with delayed consolidation of the mandibular fractures.

During research for an estimation and analysis of the results, the methods of descriptive statistics were used. For the estimation of normal distribution we used the coefficients of symmetry and variation, Kolmogorov-Smirnov's test, histograms with the line of the expected normal function of compactness. In case if dates submitted normal distribution, they were described as a mean arithmetic value and standard deviation. For the

estimation of authenticity of results calculated the t-criterion of Student's. Differences considered reliable if $p < 0.05$.

For a cross-correlation analysis we used a grade method, the estimation of correlation relationship was carried out coefficient of correlations, calculated an error by Spearman; authenticity was determined according to the tables of standard correlations coefficient, if by the certain number of freedom degrees ($n-2$), it was more or equal tabular (the degree of faultless prognosis of $p \geq 95\%$) considered its reliable.

3. Results

The study of 74 patients with delayed union of MF was conducted. The main criterion for inclusion was the mobility of fragments in the fracture zone in 1 month after repositioning and fixation. All patients filled out the designed specific questionnaire, which separated the local and general factors that best of all correlated with the development of this complication. According to the results of the conducted analytical studies, the following conclusions were made: the development of delayed union of MF correlated with the general factors (patients with somatic pathology, head injury ($p \geq 95\%$) and polytrauma ($p \geq 95\%$)), as well as with substance abuse (alcohol abuse ($p \geq 95\%$) and narcotic substances ($p \geq 95\%$)) (Fig. 1).

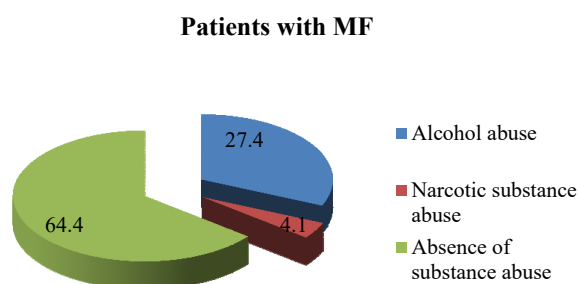


Fig. 1. Frequency of substance abuse in patients with delayed union of MF

Among the local factors, the first was inflammation in the area of MF ($p \geq 95\%$), which was most often caused by untimely treatment of patients, communicated fracture, traumatic surgical interventions and others. The overwhelming majority of patients with delayed union of MF (86.5%) received antibiotics over ten days. The risk group included young patients (from 18 to 25 years old) ($p \geq 95\%$) and older than 45 years ($p \geq 95\%$). Problem areas for consolidation were the mental department (31.1%) and the angle of the mandible (25.7%) (Table 1).

The initial levels of the basal classes of immunoglobulins and IL-1 β , TNF- α , IL-4, MDA, SOD and catalase activity, LPO, β -Cross Laps and OCC in peripheral blood were determined for the analysis of the role of the immune mechanisms, the features of LPO/AOA and the bone remodeling processes in the implementation of delayed union of MF in all patients with this pathology.

Concentrations of IL-1 β and TNF- α were significantly increased in comparison with healthy subjects, and the concentrations of sIgA, IL-4 were reduced. The IL-1 β value in the group of patients with delayed union of MF was 120.96 ± 16.89 pg/ml ($p < 0.05$), TNF- α was 95.02 ± 6.23 pg/ml ($p < 0.05$), IL-4 – 0.97 ± 0.18 pg/ml ($p < 0.05$), sIgA – 0.25 ± 0.08 g/l ($p < 0.05$).

A statistically significant decrease of SOD activity and increase of catalase activity, MDA and LPO/AOD was established in relation to the group of healthy persons also. The activity of SOD value in patients with delayed union of MF was 11.03 ± 0.87 IU/mg Hb ($p < 0.05$), catalase activity – 690.57 ± 20.97 IU/mg Hb ($p < 0.05$), MDA – 4.19 ± 0.43 mmol/l ($p < 0.05$), LPO – $29.67 \pm 1.67\%$ ($p < 0.05$), AOA – $11.08 \pm 0.60\%$ ($p < 0.05$).

The values of β -Cross Laps and OCC in patients with delayed union of MF were 2.36 ± 0.21 ng/ml ($p < 0.05$) and 27.36 ± 2.55 ng/ml ($p < 0.05$), respectively, and were significantly different from the control group indicators.

BMD in all patients with MF was significantly lowered, the value in the group was 597.91 ± 54.03 HU and most informatively reflected the clinical and radiological picture of delayed union of MF in terms of more than one month after fragments repositioning and fixing.

Table 1

Correlation between general and local factors and delayed union of MF

Factor	Delayed union of MF (n=74)	
	Number of patients	%
1	2	3
Sex		
Male	71	96.0 \pm 0.9
Female	3	4.0 \pm 21.9
Age (years)		
18–25	29	39.2 \pm 4.0
26–45	33	44.6 \pm 6.1
46–60	12	16.2 \pm 7.3
Concomitant pathology		
No pathology	18	24.3 \pm 6.9
Gastroenteric tract pathology	17	23.0 \pm 17.7
Vascular heart disease	28	37.8 \pm 7.9
ENT-organ disease	11	14.9 \pm 15.7
Endocrine diseases	2	2.7 \pm 35.2
Respiratory problems	7	9.5 \pm 15.5
Diseases of the genitourinary system	6	8.1 \pm 7.7

TECHNOLOGY TRANSFER: INNOVATIVE SOLUTIONS IN MEDICINE, 2019

Continuation of Table 1

1	2	3
Connective tissue pathology (arthritis, arthrosis)	6	8.1±7.7
MF conn CCT	22	29.7±16.1
MF conn polytrauma	8	10.8±20.5
Social habits		
Tobacco smoking	44	59.5±9.3
Alcohol abuse	36	48.6±11.8
Narcotic substances	2	2.7±35.2
Duration of course of antibacterial therapy (days)		
5	3	4.0±21.9
7	7	9.5±15.5
10–14	16	21.6±17.9
>14	48	64.9±8.1
Delayed treatment (days)		
0	11	14.9±15.7
1	29	39.2±4.0
2–3	14	18.9±18.6
4–5	16	21.6±17.9
>5	4	5.4±21.7
Localization of MF		
Unilateral	59	79.7±4.7
Bilateral	15	20.3±18.3
Treatment		
MMF	54	73.0±6.2
Osteosynthesis	20	27.0±16.7
Complication of MF before reposition		
No complication	7	9.5±15.5
Oedema or hematoma	64	86.5±3.1
Open wound of skin or mucosa	36	48.6±11.8
Sensory abnormalities of lower alveolar nerve (atypical pain, paresthesia)	16	21.6±17.9
Abscesses and phlegmon	5	6.8±21.5
Suppuration of bone wound	24	32.4±15.5
Posttraumatic osteomyelitis	0	-
Fragments displacement (D>2 cm)	32	43.2±13.0
Complication of MF after reposition		
No complication	2	2.7±35.2
Oedema or hematoma, more than 7 days	69	93.2±1.6
Sensory abnormalities of lower alveolar nerve (atypical pain, paresthesia)	16	21.6±17.9
Abscesses and phlegmon	6	8.1±7.7
Suppuration of bone wound	8	10.8±20.5
Posttraumatic osteomyelitis	7	9.5±15.5
Fragments displacement (D>0.5 cm)	16	21.6±17.9
Local factors		
Comminuted fracture	14	18.9±18.6
A tooth in the line of fractures	17	23.0±17.7
Exacerbation periodontal disease	53	71.6±6.5
Chronic apical periodontitis	34	46.0±12.4
Partial adentia	18	24.3±17.4

Correlation analysis of clinical and laboratory parameters in patients with delayed union of MF allowed to determine specificity regularities. There was a high correlation between β -Cross Laps (negative) and OCC (positive) ($r=-0.70$ and $r=0.69$, respectively) and BMD. That is, in patients with delayed union of MF imbalance of bone remodeling processes led to slowing of osteoreparative processes and delaying of fragments consolidation. The average reverse correlation relationship existed between the MDA and catalase activity and BMD ($r=-0.57$), while these indices had a high correlation with markers of bone remodeling (positive for β -Cross Laps ($r=0.80$ and $r=0.87$ respectively) and negative for OCC ($r=-0.80$ and $r=-0.84$ respectively)). The established correlation relationship has shown that bone metabolism disorders in patients with mandible injuries are progressing under the indirect influence of unmediated oxidative stress. There was a high direct correlation between the indices of TNF- α and the indices of LPO, MDA, catalase ($r=0.75$, $r=0.82$ and $r=0.87$ respectively), and very strong with β -Cross Laps (positive) ($r=0.96$) and OCC (negative) ($r=-0.95$). In addition, the LPO had high correlation relationship with sIgA ($r=-0.77$) and IL-1 β ($r=0.71$).

4. Discussion and conclusions

The detailed analysis of general and local factors of delayed union of MF allowed complementing and expanding our knowledge about of etiologic factors and nosotropic mechanisms of this complication.

As well as most researchers, we did not set correlation between gender and complications of reparative osteogenesis for patients with MF. Among patients, men prevailed (96 %), but such statistics were only investigation of that well-known fact, that men have traumatic damages of facial bones more frequently.

Among patients with delayed union of MF were representatives of three age-dependent groups, which attribute to the socially active population and traditionally have most indexes of traumatism. In addition, aged patients absented in research, but this fact can have analogical explanation – the numbers of traumatism in this group were considerably lower.

The correlation was also set for young persons (group from 18 to 25 years) and for patients older 45 years ($p \geq 95$ %). However, if the information about the risks of delayed union of MF for patients after 45 were also resulted in previous works, the facts of high level of reparative osteogenesis complications for the persons of young age with the traumas of jaws have not described yet.

As well as in works of Adell R., Eriksson B. (1987) and Mathog R. H., Toma V. (2000) we set the correlation between delayed union of MF and abuse of alcohol ($p \geq 95$ %) and narcotic substances ($p \geq 95$ %), presence of concomitant pathology ($p \geq 95$ %). We also set statistical dependence between delayed union and CBT ($p \geq 95$ %), polytrauma ($p \geq 95$ %).

K. B. Dyusupov and V. O. Kenbaev (2012) observed delayed union of MF after osteosynthesis on 4.6 % more frequent then after a splintage [12]. However, we did not set correlation between this complication and selected method of treatment.

Johanna Snäll, Satu Apajalahti (2015), described the role of postoperative infection for delayed union of MF [9].

It was set in our research, that inflammatory process in the area of fracture ($p \geq 95$ %) initiated the low consolidation in most patients. However, in 32.4 % patients inflammation began before hospitalization as suppuration of bone wound, due to mobility of fragments and late recourse for medical help, 5 patients (6.8 %) had abscesses and phlegmons in soft tissues as a purulent complication, what required additional surgical interventions.

Different inflammatory reactions was fixed in 86.5 % patients, 48.6 % patients had wounds of skin or mucosa, which needed of stitching, but in 5 (6.8 %) patients with late treatment for medical care, debriding was not carried out, because of purulent exudation.

At majority of cases, duration of course of antibacterial therapy exceeded two weeks. Most often were prescribed antibiotics: lincomycin, ceftriaxone, cefazolin, metronidazole. It follows to consider such prolongation of terms of treatment indirect proof of presence of durable inflammatory process after a reposition and fixation of bone fragments. On the other side, increase of antibiotics load resulted in disbiotic changes and immune suppression.

Such relationships indicated that secondary immunodeficiency and oxidative stress leading to immuno-structural imbalance and activation of LPO and increased synthesis of proinflammatory cytokines IL-1 β and TNF- α are based on the unbalanced bone remodeling processes and the delayed consolidation of bone fractures. The general provisions relative the specification of the etiology and pathogenesis of delayed union of MF were formulated, whereby the combined effect of local and general (concomitant somatic pathology) factors, which increase the indirect effect of injury on immune factors, free-radical oxidation processes and bone metabolism is formulated.

It was also found that clinical signs of the development of consolidation complications in patients with MF include increased signs of inflammation (oedema, exudation, etc.) up to the 3rd day and preservation of even moderate signs of inflammation (inflation, local hyperemia, and others) after the 7th day, BMD below 600 HU.

Convincing clinical and laboratory data were obtained that the combined effect of local and general (concomitant somatic pathology) factors on the basis of the activation of inflammation processes, which increase the indirect influence on immune factors, processes of radical oxidation and bone metabolism, is resulted to delayed union. Among the local factors that increase the infectious risk and inflammatory reaction, the following clinical situations should be distinguished: comminuted fracture; the presence of a tooth in the line of fractures; partially edentulous with loss of antagonist teeth (according to Eichner); complete adentia with mandible atrophy.

The results of the study allowed introducing into the clinical practice the developed personified algorithm of early diagnostics, prophylaxis and treatment of delayed union of MF.

Conflict of interests

No conflict of interest.

References

1. Adell, R., Eriksson, B., Nylén, O., Ridell, A. (1987). Delayed healing of fractures of the mandibular body. *International Journal of Oral and Maxillofacial Surgery*, 16 (1), 15–24. doi: [http://doi.org/10.1016/s0901-5027\(87\)80026-7](http://doi.org/10.1016/s0901-5027(87)80026-7)
2. Mathog, R. H., Toma, V., Clayman, L., Wolf, S. (2000). Nonunion of the mandible: An analysis of contributing factors. *Journal of Oral and Maxillofacial Surgery*, 58 (7), 746–752. doi: <http://doi.org/10.1053/joms.2000.7258>

3. Ostrander, B. T., Wang, H. D., Cusano, A., Manson, P. N., Nam, A. J., Dorafshar, A. H. (2018). Contemporary Management of Mandibular Fracture Nonunion – A Retrospective Review and Treatment Algorithm. *Journal of Oral and Maxillofacial Surgery*, 76 (7), 1479–1493. doi: <http://doi.org/10.1016/j.joms.2018.01.027>
4. Holt, G. R. (Ed.) (2012). Resident Manual of Trauma to the Face, Head, and Neck. Available at: <https://www.entnet.org/sites/default/files/ResidentTraumaFINALhighres.pdf>
5. Matros-Taranets, I. N., Alekseev, S. B., Kalinovsky, D. K. (2001). Complications of traumatic injuries in the maxillofacial region: infrastructure, occurrence conditions, treatment. *Vestnik of hygiene and epidemiology*, 5 (1), 21–25.
6. Kulitska, O. V. (2015). Peculiarities of treatment of mandibular fractures of the lower jaw. *Bulletin of Scientific Research*, 4, 68–70.
7. Nahirniy, Ya. P. (2008) Optimization ways of reparative osteogenesis in patients with traumatic fractures of mandible. *Ternopil*, 298.
8. Bouchard, C., Mansouri, M. (2017). Open Reduction with Internal Fixation of Mandibular Angle Fractures: A Retrospective Study. *Journal of the Canadian Dental Association*, 83 (3), 1–6.
9. Snäll, J., Apajalahti, S., Suominen, A. L., Törnwall, J., Thoren, H. (2015). Influence of perioperative dexamethasone on delayed union in mandibular fractures: A clinical and radiological study. *Medicina Oral Patología Oral y Cirugía Bucal*, 20 (5), 621–626. doi: <http://doi.org/10.4317/medoral.20553>
10. Malanchuk, V. A., Kopchak, A. V., Gordiychuk, M. A., Mamonov, R. O., Rybachuk, A. V., Kravchuk, M. G. (2015). Traumatic fractures of mandible in 1995 to 2009 (materials of the departments clinic). *Visnyk stomatologiy*, 1, 69–73.
11. Dusupov, K. B., Kenbaev, V. O. (2012). Retrospective analysis of patients with mandibular fractures and methods of assessment of treatment outcomes. *Vestnik KazNMU*, 2, 157–160.

Received date 17.09.2019

Accepted date 15.10.2019

Published date 30.10.2019

© The Author(s) 2019

This is an open access article under the CC BY license

(<http://creativecommons.org/licenses/by/4.0>).