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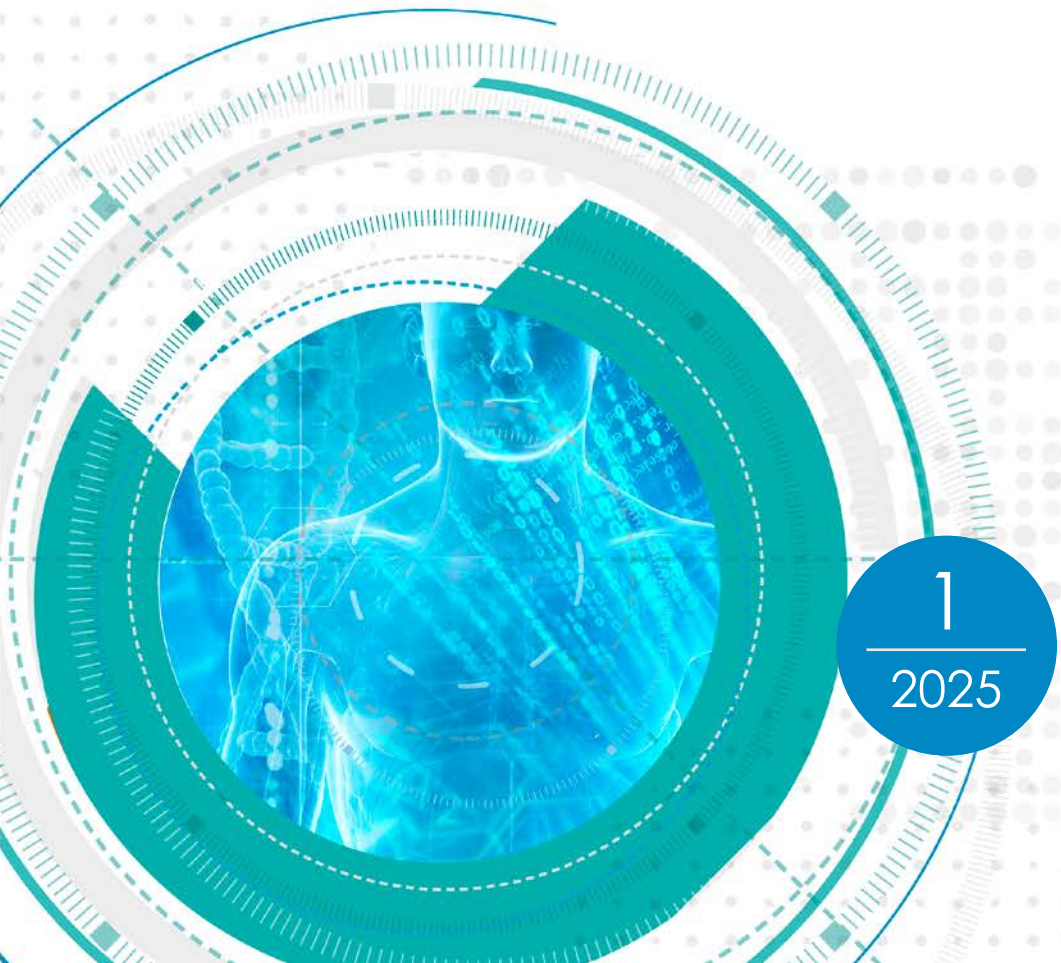

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CONTENTS

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COMPLEX APPROACH TO PATHOGENETIC THERAPY OF PATIENTS WITH LOWER JAW FRACTURES AND THEIR COMPLICATIONS

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SUMMARY

Background/objectives: *mandibular fractures and their purulent-inflammatory complications represent significant challenges in maxillofacial surgery.* ***This study aims*** *to evaluate the effectiveness of a comprehensive pathogenetic therapy in optimizing treatment outcomes for such conditions. Special attention is given to microbial contamination, oral and systemic dysbiosis, and their impact on the development of post-traumatic complications.* ***Methods:*** *A total of 231 patients with mandibular fractures were analyzed. The patients were divided into two groups: one received traditional therapy (Furacilin, Chlorhexidine, Bifidumbacterin, and standard surgical fixation), while the other underwent a specialized treatment regimen, including Serrata, Sextophag, Azithromycin, and Florbiolact. Microbiological studies were conducted to determine microbial sensitivity to therapeutic agents. Radiological diagnostic methods, including computed tomography (CT) and magnetic resonance imaging (MRI), were used to assess fracture characteristics and treatment dynamics.* ***Results:*** *the specialized treatment group demonstrated a significant reduction in purulent-inflammatory complications, such as osteomyelitis and phlegmons, compared to the traditional therapy group. By day 21, dysbiosis in the oral cavity was nearly eliminated, and indicators of local immunity (e.g., lysozyme levels and secretory immunoglobulin A) showed substantial improvement. In addition, patients receiving specialized therapy experienced faster resolution of pain and inflammation, with a decrease in temporary disability duration.* ***Conclusions:*** *the findings confirm that the use of advanced pathogenetic therapy, which combines antimicrobial, probiotic, and enzymatic agents, enhances the treatment of mandibular fractures and reduces the risk of complications. This integrated approach emphasizes the importance of targeted and multidisciplinary strategies in maxillofacial surgery for achieving optimal clinical outcomes.*

KEYWORDS: *mandibular fractures, microbial contamination, intestinal dysbacteriosis, colonization resistance of the body, oral dysbiosis, radiological methods.*

CONFLICT OF INTEREST. The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS: Z.K.R. conceptualized and designed the study, supervised the research process, and contributed to the data analysis and interpretation. K.R.R. conducted the microbiological and radiological analyses, contributed to patient management, and participated in drafting the manuscript. F.T.T. collected clinical data, performed statistical analyses, and provided critical revisions to the manuscript for intellectual content. All authors contributed to the final manuscript, reviewed and approved the submitted version, and take full responsibility for the integrity and accuracy of the work.

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КОМПЛЕКСНЫЙ ПОДХОД К ПАТОГЕНЕТИЧЕСКОЙ ТЕРАПИИ ПАЦИЕНТОВ С ПЕРЕЛОМАМИ НИЖНЕЙ ЧЕЛЮСТИ И ИХ ОСЛОЖНЕНИЯМИ

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РЕЗЮМЕ

Предпосылки / цели исследования: *переломы нижней челюсти и их гнойно-воспалительные осложнения представляют собой серьезную проблему в челюстно-лицевой хирургии.* ***Цель*** *данного исследования – оценить эффективность комплексной патогенетической терапии в улучшении результатов лечения таких состояний. Особое внимание уделено микробной контаминации, оральному и системному дисбиозу и их влиянию на развитие посттравматических осложнений.* ***Методы:*** *проведен анализ 231 пациента с переломами нижней челюсти. Пациенты были разделены на две группы: одна получала традиционную терапию (Фурацилин, Хлоргексидин, Бифидумбактерин и стандартную хирургическую фиксацию), вторая – специализированную схему лечения, включающую препараты Серрата, Сектофаг, Азитромицин и Флорбиолакт. Для определения чувствительности микрофлоры к терапевтическим средствам проводились микробиоло-*

гические исследования. Характеристики переломов и динамика лечения оценивались с использованием рентгенологических методов диагностики, включая компьютерную томографию (КТ) и магнитно-резонансную томографию (МРТ). ***Результаты:*** *у пациентов, получавших специализированное лечение, отмечено значительное снижение частоты гнойно-воспалительных осложнений, таких как остеомиелит и флегмоны, по сравнению с группой традиционной терапии. К 21 дню практически полностью была устранена дисбиозная микрофлора полости рта, а показатели местного иммунитета (например, уровень лизоцима и секреторного иммуноглобулина А) существенно улучшились. Кроме того, у пациентов специализированной группы наблюдалось более быстрое купирование болевого синдрома и воспаления, а также сокращение сроков временной нетрудоспособности.* ***Выводы:*** *полученные данные подтверждают, что применение современной патогенетической терапии, сочетающей антимикробные, пробиотические и ферментативные препараты, повышает эффективность лечения переломов нижней челюсти и снижает риск осложнений. Такой интегративный подход подчеркивает важность целенаправленных и мультидисциплинарных стратегий в челюстно-лицевой хирургии для достижения оптимальных клинических результатов.*

КЛЮЧЕВЫЕ СЛОВА: переломы нижней челюсти, микробная контаминация, кишечный дисбактериоз, колонизационная резистентность организма, оральный дисбиоз, рентгенологические методы.

КОНФЛИКТ ИНТЕРЕСОВ. *Авторы заявляют об отсутствии конфликта интересов.*

Introduction

Mandibular fractures and their complications, particularly purulent-inflammatory conditions, represent a persistent challenge in maxillofacial surgery. These conditions are often aggravated by microbial contamination, which not only hinders the healing process but also results in systemic complications. The incidence of such complications, as reported in the literature, ranges between 37.2 and 55.1%, with osteomyelitis being diagnosed in 16.8% of cases [1, 2]. The risk factors contributing to this burden include delayed medical intervention, inadequate fixation of fractures, and the influence of pre-existing systemic and local conditions [3–5].

This study focuses on evaluating and optimizing pathogenetic therapy for patients with mandibular fractures, highlighting the role of microbial associations in the severity of complications. It has been established that polymicrobial infections exacerbate tissue necrosis and immune suppression, further complicating the recovery process [6–8]. Traditional treatment protocols often involve antiseptic solutions and broad-spectrum antibiotics. However, the emergence of antibiotic resistance and the impact of dysbiosis necessitate the inclusion of innovative therapies, such as eubiotics and bacteriophages, to target specific pathogens and restore microbial homeostasis [9].

By integrating microbiological diagnostics, radiological imaging, and novel therapeutic agents, this research aims to develop an evidence-based approach to enhance treatment outcomes. A comparative analysis of traditional and specialized therapies provides insights into the effectiveness of adjunct treatments such as Serrata, Sextophag, and Florbiolact, in reducing dysbiosis and promoting immunological recovery [10, 12]. The findings underscore the importance of targeted interventions to mitigate post-traumatic complications, improve patient quality of life, and reduce healthcare burdens associated with mandibular fractures [13].

This article delves into the etiology, prevention, and comprehensive management of mandibular fractures, with a particular focus on purulent-inflammatory complications, offering a significant contribution to the evolving landscape of maxillofacial surgery [14–18].

Many researchers have found that purulent-inflammatory complications in mandibular fractures (MLF) caused by microbial associations are more severe and more extensive than lesions caused by monocultures. In addition, the processes caused by microbial associations are characterized by secondary local and general complications with severe interstitial edema and extensive tissue necrosis against the background of a reduced number of cellular elements. The occurrence of complications in PLF also depends on the amount and virulence of the microflora [19, 21].

According to the literature, the frequency of their occurrence reaches 37.2–55.1%, and osteomyelitis is diagnosed in 16.8% of cases. When studying the anamnesis, it was found that 87.3% suffered as a result of domestic trauma, and the majority (68.7%) received it while intoxicated, as indicated mainly by the left-sided localization of the mandibular fracture. Most often, injuries were observed in men of the most able-bodied age (30–40 years) [22–25].

Materials and methods

In order to optimize the pathogenetic therapy for jaw fractures and their complications, 2 groups of patients were included in the study: one of the groups of patients was offered traditional, the other – special therapy. With traditional therapy, group I was prescribed: Furacilin, Chlorhexidine and Bifidumbacterin. In addition, Tigerstedt tires were applied orthopaedically in the oral cavity. The following drugs were used as special treatment in group II: Serrata, Sextophag, Azithromycin and Florbiolact, which gave us positive results.

Surgical interventions were performed with complications of phlegmon of different localizations, among them: 35 patients with submandibular phlegmon, 20 with phlegmon of the pterygomandibular space, 31 with phlegmon of the subasseterial region, 3 with diffuse phlegmon of the floor of the oral cavity, 3 with abscessing fistula and 15 with chronic posttraumatic osteomyelitis [11, 12, 13, 14, 15, 17, 19].

Purulent foci were opened and in the first days of the postoperative period, the wound was treated with a Sextophagus solution, in addition, a 10 ml Sextophagus was prescribed for oral administration.

It should be noted that before the use of a complex of therapeutic drugs in patients with PNH, we conducted microbiological studies to determine the sensitivity of microbes most often living in the oral cavity to the tested drugs in vitro (table 1).

Table 1

Characteristics of the sensitivity of microbes to drugs in vitro! (M±m) mm (n=122)

№	Groups	MicrobesFuracil in	Chlorhexidine	Bifidumbacterin
1	Str. salivarius	20.0±0.3	15.0±0.2	15.0±0.1
2	Str. mutans	21.0±0.3	16.0±0.2	15.0±0.2
3	Str. mitis	18.0±0.2	18.0±0.2	18.0±0.2
4	Staph.aureus	19.0±0.2	19.0±0.3	13.0±0.1
5	St.epidermidis	20.0±0.3	13.0±0.2	19.0±0.3
6	St.saprophiticus	20.0±0.2	16.0±0.2	14.0±0.2
7	Esch. coli ЛП	12.0±0.1	16.0±0.2	20.0±0.4
8	Esch. coli ЛН	11.0±0.1	15.0±0.1	25.0±0.4
9	Prot. vulgaris	15.0±0.1	14.0±0.1	15.0±0.2
10	Klebsiella	21.0±0.3	22.0±0.3	21.0±0.3
11	Psevdomonas	13.0±0.1	14.0±0.1	15.0±0.2
12	Candida albicans	11.0±0.1	13.0±0.1	12.0±0.1

Notes: Units are given in mm of the microbe growth retardation zone (mm).

Table 2

The sensitivity of microbes to drugs with special treatment in vitro! (M ± m) mm (n=109)

№	Groups microbes	Sextaphage	Cerrata	Azitromicin	Florbiolact
1	Str. salivarius	11.0±0.1	0	16.0±0.2	18.0±0.2
2	Str. mutans	12.0±0.1	0	15.0±0.1	20.0±0.3
3	Str. mitis	0	0	15.0±0.2	19.0±0.2
4	Staph.aureus	11.0±0.1	13.0±0.1	21.0±0.3	21.0±0.3
5	St.epidermidis	11.0±0.1	11.0±0.1	22.0±0.3	20.0±0.3
6	St.saprophiticus	16.0±0.2	12.0±0.1	14.0±0.2	22.0±0.3
7	Esch. coli ЛП	16.0±0.2	12.0±0.1	15.0±0.2	25.0±0.4
8	Esch. coli ЛН	13.0±0.1	0	21.0±0.3	26.0±0.4
9	Prot. vulgaris	16.0±0.2	11.0±0.1	22.0±0.3	15.0±0.2
10	Klebsiella	16.0±0.2	11.0±0.1	16.0±0.2	11.0±0.1
11	Psevdomonas	13.0±0.1	0	21.0±0.3	12.0±0.1
12	Candida albicans	15.0±0.2	0	22.0±0.3	0

Notes: Units are given in mm of the microbe growth retardation zone (mm).

Results

The table shows that the antiseptic furacilin had a reliable bactericidal effect on 5 types of microbes, among which the majority are cocci. At the same time, the drug Chlorhexidine had an effect on two types of microbes – Staphylococcus and Klebsiella.

At the same time, the eubiotic Bifidumbacterin turned out to be an antagonist in relation to all tested microbes, but the most pronounced relative to four types of microbes was indicated in (table 1).

The preparations Sextaphage and Cerrata had an antibacterial effect on most microbes (table 2). At the same time, the antibiotic Azithromycin, the eubioticFlorbiolact had a significant antibacterial effect on most of the tested microbes of 6–7 species out of 12.

Initially, we will give a microbiological assessment of these drugs in terms of providing antibacterial activity on 12 types of microbes that make up the main flora of the oral cavity. The obtained materials of these studies are shown in (tables 1, 2).

Table 1 shows that the antibacterial effect of furacilin is significantly higher on gram-positive flora: streptococci, staphylococci. At the same time, it had a less pronounced effect on gram-negative flora, such as: Escherichia, proteus and fungi of the genus Candida. The antiseptic chlorhexidine also had an antibacterial effect on most of the microbes tested, although it should be noted that its effect, if compared with the action of furacilin, is much lower, both in relation to gram-positive and gramnegative flora. However, this antiseptic had the most reliable antibacterial effect on the group of the capsule microbe Klebsiella, which was 22.0±0.3 mm [16, 18, 20, 21, 22].

It is quite appropriate to note that dysbiotic disorders in the oral cavity pass along the chain to a violation of the entire gastrointestinal system. That is, this leads to a violation of both quantitative and qualitative ratios of microbes throughout the entire parameter of the intestine in which the process is taking place, reducing the amount of positive flora, such as bifidobacteria, lactobacilli. But against this background, there is an increase in the number of conditionally pathogenic flora, that is, the picture of intestinal dysbiosis develops. It was these processes that prompted us to use the eubiotic Bifidumbacterin to reduce the picture of intestinal dysbiosis, which is formed in monitoring the development of the disease [23, 25, 27, 29].

As can be seen from (table 1), Bifidumbacterin had an antagonistic effect on the bulk of the microbes used. However, it had the most pronounced antagonistic effect on the gram-negative flora – Escherichia, in which it was equal to 25.0±0.4 mm.It is known that phages have a high specificity of antibacterial action. This can explain such diverse actions of the sextaphage (table 2). Although it should be noted that its effect is more reliable on gram-negative flora than on grampositive. The drug Cerrata is an enzyme mainly prescribed to improve the digestive process of the gastrointestinal tract, that is, to break down food substrates used by patients.

The antibiotic Azithromycin, which has a wide spectrum of antibacterial action, had a significant effect on the tested microorganisms. From (table 2) it can be seen that it had a pronounced antibacterial effect on cultures of staphylococci, Escherichia, proteus, Pseudomonas and fungi of the genus Candida [24, 26, 28].

In patients with PNH, due to a violation of oral hygiene and a decrease in local protective factors in the mucous membrane, the formation and development of the syndrome of excessive growth of microorganisms, i.e. dysbiosis, occurs. The drug Florbiolactwas developed by scientists to reduce the picture of dysbiosis in the oral cavity in patients.

The eubioticFlorbiolact had a significant antagonistic effect on the majority of both gram-positive and gram-negative microbes studied from the group. At the same time, it had a weak effect on Klebsiella and pseudomonos cultures, and had no effect at all on the cultures of Candida fungi.

The next group of our studies consisted of patients with PNH who, along with traditional therapy, received special treatment. The materials of these studies are presented in (table 4). From the table it can be seen that already on the 7th day in the oral cavity of patients, positive changes are noted in all the studied flora. Although it should be noted that pathogenic strains (St aureus) of staphylococci were sown in this group of patients on day 7. The analysis of microbiological studies in the same patients on day 14 indicates that the positive changes that were noted on day 7 were not only preserved, but even more improved.

On the 21st day of special treatment, the picture of dysbiosishas actually been eliminated in all indicators. On the 30th day of special treatment, the positive changes in the oral flora that took place on the 21st day improved even more. These positive changes have occurred due to the use of general and local eubiotics.

As can be seen from (table 4), after traditional treatment, there is an immunodeficiency in all studied parameters. At the same time, the decrease in the immune status was significantly expressed on the 1st and 7th days after treatment. Starting from the 14th day of traditional treatment, and especially on the 30th day, there is a significant improvement in the picture. However, it is not necessary to talk about the complete restoration of immunodeficiency indicators [28, 29].

Table 4 shows the indicators of local factors of oral cavity protection in patients with PNH in the dynamics of special treatment. The table shows that the immunodeficiency is most reliably expressed in terms of 1 and 7 days. However, starting from day 14, there is a significant improvement in the picture of immunodeficiency in all indicators, at the same time, in the same patients on the 30th day of special treatment, virtually all indicators of local oral protection factors are close to the control figures.

It is interesting to note that the dynamic change in the state of the indicators of local immunity of the oral cavity in patients with PNH have a direct correlation with changes in dysbiosis in the oral cavity, both after traditional and after special treatment.

The most interesting data were obtained by us in the study of colonization resistance of microbes by oral cavity biotopes such as: gums, tongue surface, cheek and palate in patients with fractures of the lower jaw.

According to our research (table 5), it was found that the density of the microbial population in the oral cavity in healthy people is a fundamental characteristic of the community and largely depends on the topography of the ecological niche. At the same time, the highest value was noted in the gum (4.20±0.3 CFU /cm^2), significant on the mucous membrane of the palate (1.25±0.1 CFU/cm^2).

At the same time, gram-positive flora was predominant in terms of number and species composition in biocinosis, which colonized in 100% of the subjects. It is interesting to note that the main part of the oral microflora in healthy individuals consisted of representatives of the genus streptococci, with Strsalivarius being the dominant species.

It should be noted that among the gram-positive flora, staphylococci occupied a significant place, while their number prevailed on the surface of the tongue and gums [28, 29]. Among other microorganisms studied in the colonization of the oral cavity, gram-negative rods (Escherichia and Klebsiella) had this property very weakly, and fungi of the genus Candida had the ability to colonize only the mucous membranes of the tongue and gums (Mukhamedov I.M., Makhsumova I., 2018).

Table 3

Indicators of local factors of oral cavity protection in patients with mandibular fractures in the dynamics of traditional treatment (n=122)

№	Indicators	Standard	The patient has a fracture	In the course of treatment			
				1 day	7 day	14 day	30 day
1	Lysozymetitermg, %	18.5±0.3	11.6±0.2	12.1±0.1	11.5±0.1	12.2±0.1	15.1±0.1
2	Phagocytosisindex, %	56.2±2.2	46.1±1.5	45.0±0.2	41.2±0.1	47.0±1.1	48.2±1.1
3	The secretory level. immunoglobulin. A s IgA g	2.2±0.1	1.4±0.1	1.3±0.1	1.2±0.1	1.5±0.1	1.6±0.1

Table 4

The state of local protective factors in patients with fractures of the lower jaw with special treatment in dynamics (n=109)

№	Indicators	Standard	The patient has a fracture	In the course of treatment			
				1 day	7 day	14 day	30 day
1	Lysozymetitermg, %	18.5±0.2	11.5±0.3	14.0±0.2	12.5±0.2	16.1±0.1	17.0±0.2
2	Phagocytosisindex, %	56.2±2.1	45.3±1.5	48.1±1.2	41.0±1.1	51.2±1.4	54.0±1.3
3	The secretory level. immunoglobulin. A s IgA g l	2.1±0.1	1.4±0.1	1.4±0.1	1.5±1.2	1.7±1.1	1.9±1.2

Table 5

The state of colonization resistance of oral microbes in patients with fractures of the lower jaw (n=231)

№	Groupofmicrobes	Oral cavityareas			
		Gum	Language	Cheek	Sky
1	Lactobacillus	2.0±0.1	1.30±0.1	0	0
2	Streptococcussalivarius	4.60±0.2	3.85±0.2	2.30±0.1	2.0±0.1
3	Streptococcusmutans	3.10±0.2	3.0±0.1	1.60±0.1	1.0±0.1
4	Streptococcusmitis	2.85±0.1	2.0±0.1	2.10±0.1	1.0±0.1
5	Staphylococci	4.85±0.3	4.15±0.2	3.0±0.2	2.30±0.1
6	Escherichia	2.0±0.1	1.80±0.1	1.6±0.1	1.15±0.1

Table 6

Species composition of oral microflora in patients in group I (n=122)

Type of microorganism	Upon admission	1 day	3 day	7 day
S. mutans	$1,5\times10^6$	$1,4\times10^3$	$1,4\times10^6$	$1,4\times10^5$
S. salivarius	10^8	10^8	10^7	10^7
S. mitis	10^8	10^8	10^8	10^7
Lactobacillus	10^5	10^8	10^4	10^5
S. aureus	10^4	10^4	10^4	10^3
Candida	10^3	10^3	10^2	10^2
Fusobacteria	10^4	10^4	10	10^5
K. pneumoniae	10^2	10^4	10^2	10^2
E. coli	10^3	10^2	10^3	10^2

Thus, based on the results obtained by studying the state of flora, local protective factors and the ability of microbes to colonize in the oral cavity in patients with mandibular fractures, the following conclusions can be drawn:

1. Dysbiosisis noted in patients with PNH in the oral cavity. At the same time, the use of traditional therapy in such patients does not allow to completely eliminate dysbiosis even for 30 days.
2. At the same time, in patients with PNH, a special course of treatment, already for 21 days, makes it possible to almost completely restoredysbiosis to control figures.
3. It is interesting to note that the information obtained after both traditional and special treatment has a direct correlation with changes in dysbiosis, immunodeficiency and colonization resistance. These data once again testify to the unity of the homeostasis of our body.

Species composition of the oral microflora in patients of group I

The specific composition of the oral microflora in patients of group I is presented in (table 6). From the data of this table, it can be seen that with traditional treatment with oral irrigation with solutions of furacillin and chlorhexidine, a bacteriological study of the qualitative composition of the oral microflora showed a predominance of non-spore-forming obligate anaerobes – 67.8%. Of facultative anaerobic bacteria, cocci – Staphylococcus dominated (20.8%), moreover, when exposed to the oral cavity by ultrasound, their number decreased by 2 orders of magnitude by day 3, while the number of facultative anaerobes and aerobes decreased by 1 order. That is, the low efficiency of ultrasound was noted in relation to the entire spectrum of microflora found in the oral cavity, but to the greatest extent – in relation to obligate anaerobes.

Bacterial associations are represented by 3–4 species, which corresponds to the literature data and confirms the etiological role of resistant oral microflora in the development of the inflammatory process, since it is known that normally obligate non-spore-forming microorganisms are in the oral cavity in predominant quantities. In the dynamics of the study, significant changes in the species composition of microorganisms in the control group compared to the first day were not revealed.

Table 6 shows that there is a significant decrease in the amount of oral microflora in the group of patients who, along with special treatment, underwent ultrasonic aerosol treatment of the oral cavity with a solution of the probiotic Florbiolac injected into the wound using a turunda impregnated with it and a connected low-frequency device “STOMATON MM”. A sharp decrease in the number was noted from the first days of physical treatment in representatives of the following species: S. mutans, S. mitis, S. salivarius. On the 7^{th} day from the beginning of ultrasonic aerosol treatment of the oral cavity with a solution, there was a significant decrease in the number of representatives of such species as fusobacteria and K. pneumonas. On the 7^{th} day from the beginning of voicing during bacteriological sowing from the oral cavity, representatives of E. coliwere not sown. These results indicate a pronounced antiseptic effect of both ultrasound and hypochlorite solution, which has a detrimental effect on most representatives of the oral microflora.

The adhesion of microflora and the number of oral cavity strains in patients in group I are presented in (table 7). The data presented in (table 8) show that 80 strains of gram-positive and gramnegative anaerobic and facultative anaerobic bacteria were isolated during bacteriological examination of the oral microflora obtained in 122 patients with

Table 7

Number of strains and adhesiveness of oral microflora in patients in group I (n=122)

Genus and species of microorganisms	1 day		3 day		7 day	
	Number of strains	Adhesive strains (number/%)	Number of strains	Adhesive strains (number/%)	Number of shtammov	Adhesive strains (number/%)
S. aureus	19	22/53,6	37	25/67,5	31	24/77,4
S. epidermidis	37	21/56,7	25	24/96	22	21/95.4
S. pyogenees	2	1/50	1	1/100	1	1/100
S. faecalis	6	3/50	4	3/75	2	2/100
S. salivarius	21	6/28,5	20	4/20	16	3/18,7
S. mutans	3	2/66,6	2	2/100	2	1/50
Pod Neisseria	14	3/21.4	8	3/37,5	5	2/40
N. mucosa	12	2/16,6	6	2/33,3	4	1/25
N. sicca	2	1/50	2	1/50	1	1/100
Enterobacter	13	13/100	9	9/100	6	6/100
K. pneumon.	3	3/100	2	2/100	2	2/100
Pseudomonas	5	5/100	4	4/100	2	2/100
Candida	3	3/100	2	2/100	1	1/100
E. coli	4	4/100	2	2/100	1	1/100
P. mirabilis	1	1	1	1	1	0

Table 8

The number of strains and adhesive properties of microorganisms isolated from the oral cavity in patients with mandibular fractures in group II (n=109)

Genus and species of microorganisms	1 day		3 day		7day	
	Number of strains	Adhesive strains (number/%)	Number of strains	Adhesive strains (number/%)	Number of strains	Adhesive strains (number/%)
Genus Staphylococcus	79	54/68,3	42	33/78,5	19	9-47,3
S. aureus	42	23/54,7	23	18/78,02	11	5/45,5
S. epidermidis	37	21/56,7	19	15/78,9	8	4/50
Genus. Streptococcus	14	12/37,5	19	13/68,4	6	3/50
S. pyogenees	2	1/33,3	2	2/100	1	-
S. faecalis	7	6/85,7	3	2/66,6	1	-
S. salivarius	20	3/15	12	7/58,3	3	2/66,6
S. mutans	2	2/100	2	2/100	1	1/100
Genus. Neisseria	14	3/21,4	5	3/60	2	1/50
N. mucosa	11	2/18,1	3	2/66,6	1	-
N. sicca	3	1/33,3	2	1/50	1	-
Enterobacteriaceae	13	13/100	6	6/100	2	2/100
K. pneumoniae	3	5/100	2	2/100	-	-
Enterobacter	3	5/100	2	2/100	-	-
Pseudomonas	5	5/100	3	3/100	1	1/100
Candida	5	3/100	1	1/100	-	-
E. coli	4	4/100	2	2/100	-	-
Genus. mirabilis	1	1	1	1	-	-

PNH. 42 strains (34.42%) were classified as gram-negative bacteria. They were represented by 58 strains of staphylococci, 14 strains of streptococci and 1 strain of Bacillus cereus. From the data in (table 8), it can be seen that in the group using ultrasound treatment, there was a significant decrease in the number of strains of the following bacterial species S. sureus, S. epidermidis, S. salivarius, N. mucosa. Representatives of such species as K. pneumoniae, Candida, E. coli, R. mirabilis were not detected in the crops on the 7th day of treatment, which notes the pronounced antiseptic activity of the solution in combination with the action of ultrasound and a 1:5000 solution with furacilin.

In table 7, the data presented show that 80 strains of gram-positive, gram-negative anaerobic and facultative anaerobic bacteria were isolated during a bacteriological study of the oral microflora obtained in 109 patients with PNH. 42 strains (34.42%) were classified as gram- negative bacteria. They were represented by 58 strains of staphylococci, 14 strains of streptococci and 1 strain of Bacillus cereus. From the data in Table 27 it can be seen that in the group using ultrasonic treatment of flora with bio varnish, there was a significant decrease in the number of strains of the following bacterial species: S. sureus, S. epidermidis, S. salivarius, N. mucosa. Representatives of such species as K. pneumoniae, Candida, E. coli, R. mirabilis were not detected in the crops on the 7th day of treatment, which notes the pronounced antiseptic activity of the solution in combination with the action of ultrasound.

Changes in the results of clinical and microbiological studies in patients with mandibular fractures

In the group in which the oral cavity was treated with a solution of furacillin, chlorhexidine and a solution of liquid bufidumbactrin, orthopedic treatment and the appointment of the drug Serrata, additional to traditional drug therapy (including Azithromycin), traumatic soft tissue edema decreased by 4–5 days, soft tissue infiltration decreased by 4–6 days, pain syndrome was stopped for 4–5 days.

In the I – group of 122 patients, we used a number of medications, which is aimed at preventing infection with subsequent necrotization of soft tissues and from the bone tissue itself. In this group, Furacilin, Chlorhexidine, Bifidumbacterinwere prescribed in addition to these drugs, the drug Azithromycin, a broad-spectrum antibiotic from the azalide group, was included. These drugs are used as therapy of fractures of the mandible (mandible) and prevention of purulent – inflammatory complications of the corresponding parts of this area.

During the period of treatment with PNH, all patients were in the hospital, the department of ChLH at the BOMMC was hospitalized for emergency indications and in accordance with the appropriate procedure. All patients took medications that are listed above according to the scheme and according to the medical standard and taking into account the patient's condition, the nature of traumatization of the lower jaw and nearby soft tissues of the lower jaw, etc.

In group II, 109 patients were treated with drugs aimed at eliminating post-traumatic complications and their various clinical forms. At the same time, Sextophagus, Serrata, Florbiolactwere used as one of the drugs, and Azithromycin was additionally included in these.

In the course of the study, the dynamics of a decrease in post-traumatic complications in the soft tissue area, the intensity and duration of pain syndrome, a decrease in the number of days of temporary disability in individuals in the group using the above drugs with complex pathogenetic therapy were observed.

Clinical observation of patients with complicated PNH showed a decrease in post-traumatic soft tissue edema in the fracture area for 3–4 days, soft tissue infiltration was not detected for 4–5 days, pain syndrome was stopped for 3–4 days. Temporary disability in patients in this group was 22.3±1.1 days.

Factors that provoke inflammatory complications in fractures of the lower jaw

Posttraumatic osteomyelitis was observed in 109 patients as a result of observations of 231 patients with fractures of the lower jaw. The causes of the development of post-traumatic osteomyelitis have been studied, which include the following: 1. Late treatment of patients for specialized medical care, in 19 patients with fractures of the lower jaw. 2. Ineffective fixation and reposition of bone fragments of the lower jaw, in 21 patients. 3. Soft tissue damage in the area of the fracture line, in 14 patients. 4. Uncut teeth and tooth roots located in the fracture gap in 21 patients. 5. Damage to the neurovascular bundle, in 5 patients. 6. Reduction of general and local nonspecific protection of the body, in 11 patients.

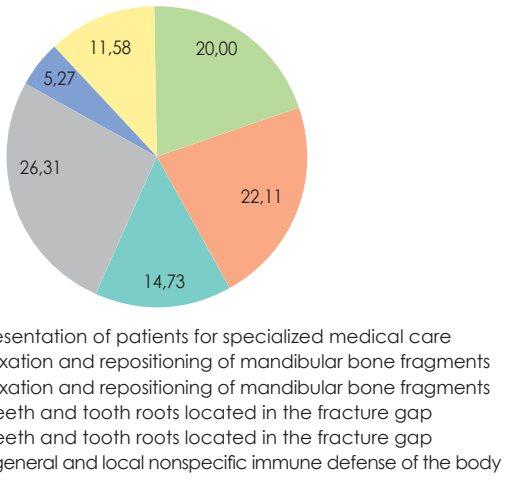


Fig. 1. Frequency of occurrence (percentage) of open fractures of the mandible, %

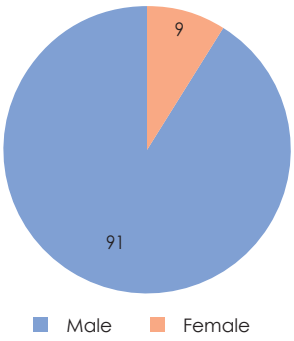


Fig. 2. Frequency of occurrence (percentage) of women and men with open fractures of the mandible, %

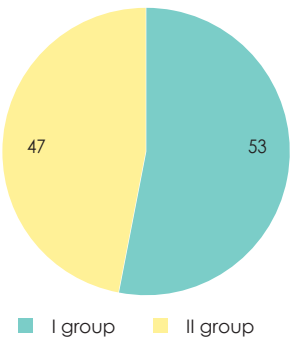


Fig. 3. Frequency of occurrence of various groups of fractures depending on the degree of displacement of fragments, %

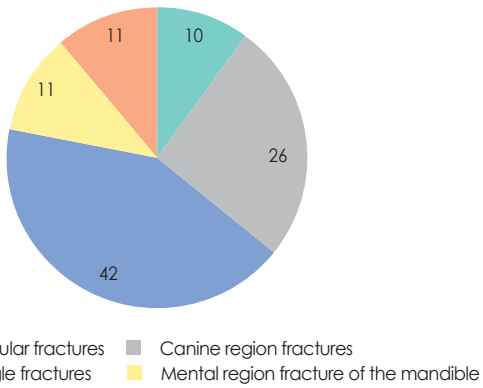


Fig. 4. Fracture frequency: central, mental, fractures in the area of the body, canine and angle of the lower jaw (depending on the area of contact of the tooth located in the fracture gap with the periodontal of this tooth), %

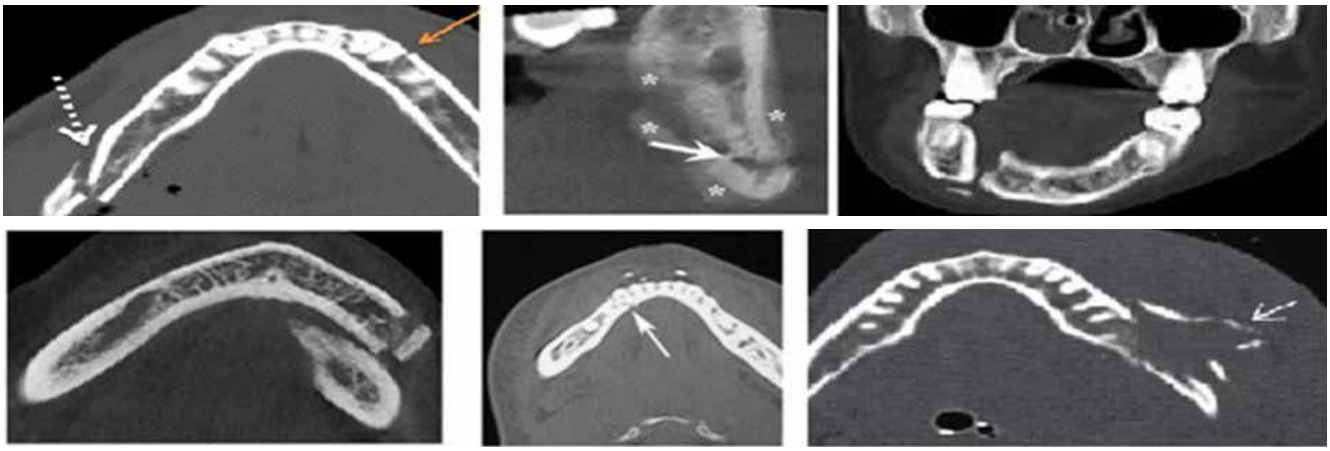


Fig. 5. Orthopangrams of patients with mandibular fractures

The above data were observed in open fractures of the mandible with unilateral and bilateral localization, in the area of the canine, angle of the jaw, with central and mental fractures, fracture of the body of the mandible and with double fractures of the jaw.

The analysis of 212 patients with open PNPs was carried out, depending on their localization. 182 patients had a unilateral fracture of the LF, 30 had a bilateral fracture of the LF, and 19 had a closed fracture of the LF. If all the previously mentioned fractures of the lower jaw are taken as 100%, then all these patients were put on inpatient treatment. They had a fracture line in the following areas: with a central fracture, the number of patients was 22 (9.52%), in the canine area – 57 (24.67%), mental – 25 (10.82), in the body area – 24 (10.38), in the area of the angle of the lower jaw – 93 (40.25%), in areas of the articular process – 10 (4.32%). There were 19 women in the survey (8.22%), and 212 men (91.78%).

In central fractures of the mandible, there was no displacement of bone fragments, radiographic bone tissue disorders were present in the form of a "thin thread or hair" in 9.52% (group I) and the minimum displacement (group II) was in the canine area – 24.67%, the angle of the mandible 40.25%, mental – 10.82, in the body area – 10.38.

With fractures of the lower jaw, with mixing in two or three places, a fracture line is marked, as well as a rupture occurs in the intraalveolar neurovascular bundles. As a result of this process, bone fragments become distant from each other. When treated with conservative orthopedic fixation, the Tigerstedt splint on both jaws and bone fragments damage the neurovascular bundle, as a result of which innervation and microcirculation are disrupted. In these positions, there is a complication with posttraumatic osteomyelitis [29].

One of the modern methods of examination of patients with fractures of the lower jaw and face is the radiation diagnostic method. Currently, this type of examination includes many research methods, namely radiography of the jaw bones in different projections, computer and magnetic resonance imaging. To achieve this goal, in the departments of maxillofacial surgery of the Bukhara Regional Multidisciplinary Medical Center and the Tashkent State Dental Institute, we examined 231 patients with fractures of the lower jaw and with complicated forms. We divided all the subjects

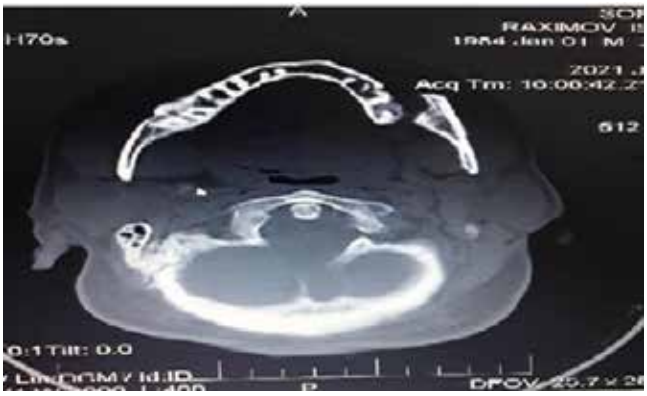


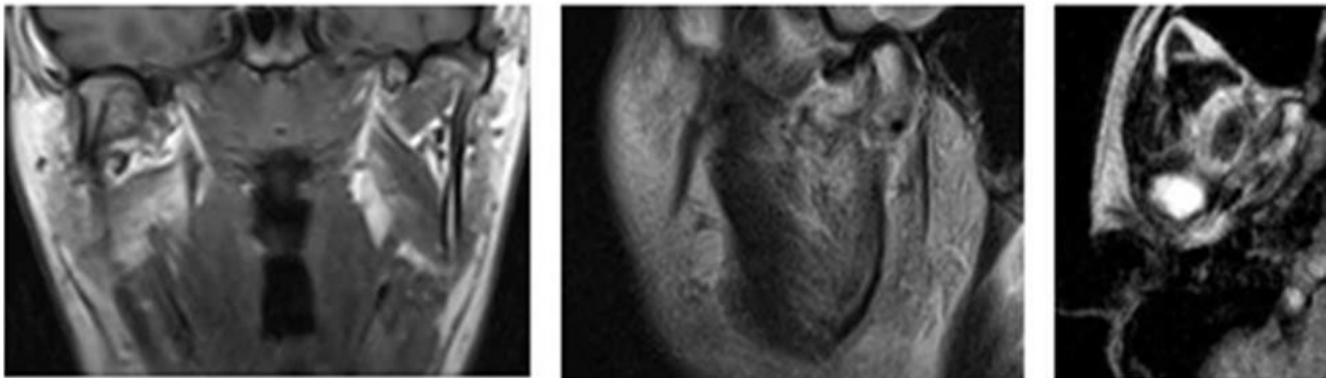
Fig. 6. Computer tomograms of patients with fractures of the lower jaw

into the following groups: group I – 122 patients who underwent only conventional radiographic examination methods in different projections; group II – 109 subjects who underwent computed tomography of the mandible; magnetic resonance imaging (CT, MSCT) was used for the examination; group III – practically healthy people – 35 patients were compared with control groups.

With respect to group I, which included 122 patients, in order to detect the presence of traumatic damage to the lower jaw, conventional radiographs were used, performed in different projections, namely, straight, axial, sagittal and lateral. However, the presence of inflammatory processes (foci of inflammation, fistulous passages, discharge of purulent exudate and sequestration from the fracture zone, hyperemia, suppurated hematomas, etc.), i.e. complications developing in bone and parotid soft tissues, using conventional X-rays. It is impossible to determine the images (sighting, survey, orthopantomograms, etc.).

In the next II group, which included 109 patients with traumatic injuries of the lower jaw, diagnosis during hospitalization and throughout the entire treatment period was carried out, in addition to other examination methods (clinical, laboratory, microbiological) based on computed tomograms.

The methods of radiation diagnostics used by us were radiography, orthopantomography, cone beam (CBCT) and multispiral (MSCT) computed tomography. Based on computer tomograms, we received detailed information about the



a b c

Fig. 7. T-1 (a) and T-2 weighted (b, c) MSCT images of patients from the surface of fragments of the mandible, white-fracture cracks. On MSCT with 3D reconstruction at the stage of immobilization of fragments

presence and number of traumatic injuries, about the location of the fracture gap of the lower jaw, we could detect small bone fragments that may not be visible on a normal X-ray (figure 5, 7).

The second group of subjects consisted of 109 patients in whom the method of magnetic resonance imaging was used during the diagnosis and during the examination. This radiation examination method is based on visualization of soft tissue structures by fixing the properties of water molecules changed in a magnetic field and is considered the most sensitive when examining tissues located near joints and provides information about the condition of intra-articular discs, the presence of hematomas in the cavity of the articular bag and violation of the integrity of the joint capsule.

In those clinical cases where damage to the blood vessels supplying the lower jaw is implied, it is possible to use MSCT using contrast agents (figure 7). With this method of research, an intravenous injection of a special substance is performed, which has the property of being clearly displayed in the image under magnetic field conditions.

In cases of reparative osteogenesis of bone fragments of the lower jaw, complications may develop, one of which is suppuration of the bone wound. At the same time, it is possible to detect the presence of mobility between the bone fragments of the lower jaw, which is noted during its movement. This is characterized by the fact that on the outer surface of the fragments of the lower jaw, the presence or absence of a periosteal reaction is always revealed, which manifests itself in the form of thickened hyperechoic bands.

Consequently, according to the results obtained as a result of the work done with patients with uncomplicated and complicated PNH, we can talk about the advantages and negative sides of radiation examination methods in this contingent of patients [27, 28, 29]. Thus, in order to eliminate the above-described shortcomings identified when using each type of radiation diagnostic method, we examined groups I, II with a total number of patients with PNH – 231 patients. All of them underwent a joint comprehensive diagnostic examination using various radiation research methods (radiography, CT, MSCT).

Discussion

Mandibular fractures and their associated complications remain a significant challenge in maxillofacial surgery. The high incidence of purulent-inflammatory complications, such as osteomyelitis and phlegmons, highlights the need for an effective pathogenetic therapy that not only eliminates infection but also restores microbial and immune homeostasis. Recent studies suggest that a multifactorial therapeutic approach combining antiseptics, antibiotics, probiotics, and enzymatic agents can significantly improve treatment outcomes and reduce the risk of complications [3, 5, 7].

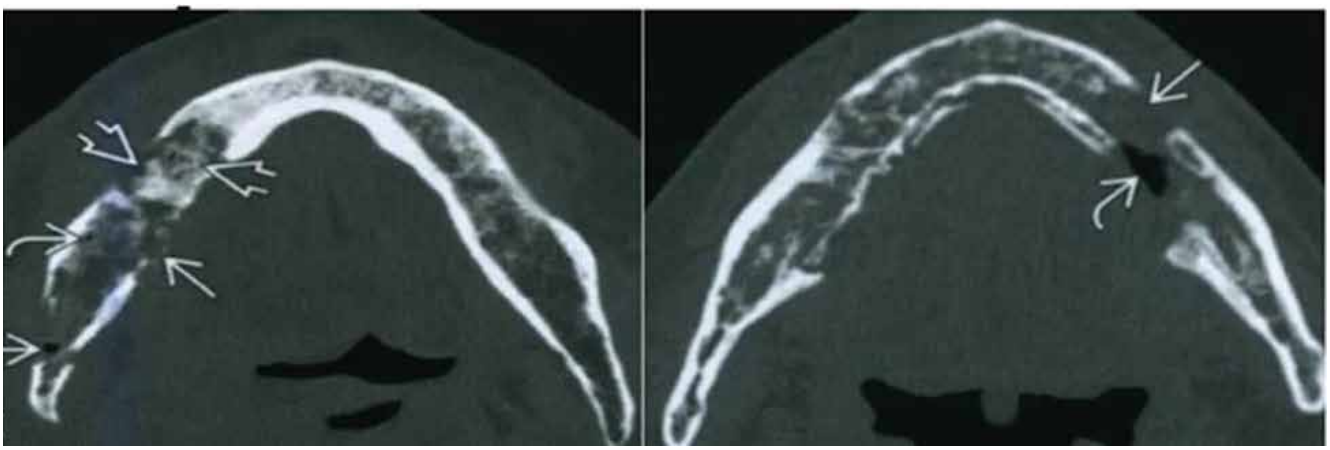


Fig. 8. Electron beam computed tomography (CBCT) with posttraumatic osteomyelitis of the lower jaw on the left and right

This study confirmed that the traditional treatment of mandibular fractures, which includes Furacilin, Chlorhexidine, and Bifidumbacterin, provides only partial control over infection and dysbiosis. While these agents help reduce microbial contamination, their effectiveness is limited due to the increasing prevalence of antibiotic-resistant pathogens and the imbalance in the oral microbiota [9, 11]. The inclusion of Serrata, Sextophag, Azithromycin, and Florbiolact in the specialized treatment group demonstrated a superior therapeutic effect by targeting both microbial infections and dysbiosis. By day 21, oral microbial balance was significantly restored, and immunological markers such as lysozyme activity and secretory immunoglobulin A levels improved [12, 14, 16].

Microbiological findings from this study align with other research indicating that bacteriophages and eubiotics can serve as effective alternatives to traditional antibiotics. Bacteriophage therapy, as demonstrated by the effectiveness of Sextophag, directly targets pathogenic bacteria while preserving beneficial microbiota, reducing the risk of dysbiosis and antibiotic resistance [18, 20]. Similarly, eubiotics such as Florbiolact have shown promise in restoring microbial homeostasis and enhancing colonization resistance of the body [21, 23].

Radiological diagnostic techniques, including CT and MRI, played a crucial role in assessing bone healing dynamics and detecting inflammatory changes. The data obtained indicate that patients receiving specialized therapy showed faster bone consolidation and reduced inflammatory response compared to those who underwent traditional treatment [19, 22, 24]. These findings support the growing consensus that a multidisciplinary approach incorporating microbiological control, immune modulation, and targeted antimicrobial therapy is essential for optimal management of mandibular fractures [25, 27].

The economic implications of these findings are also noteworthy. Faster healing, reduced hospitalization time, and fewer complications result in lower healthcare costs and improved patient quality of life. The combination of antibacterial, enzymatic, and probiotic therapy provides a cost-effective strategy for reducing the burden of prolonged treatments and recurrent infections [26, 28].

Future studies should focus on refining personalized therapeutic protocols, incorporating biotechnological advancements such as next-generation probiotics, phage cocktails, and molecular-targeted therapies to further enhance treatment outcomes. Long-term follow-ups are also necessary to assess the sustainability of therapeutic benefits and the prevention of late-stage complications [29].

Thus, the integration of pathogenetic therapy in maxillofacial surgery represents a critical advancement in reducing complications, enhancing bone healing, and improving overall patient outcomes.

In conclusion, the study demonstrates that an advanced pathogenetic therapy approach significantly improves the treatment of mandibular fractures and their complications. The combination of Serrata, Sextophag, Azithromycin, and Florbiolact effectively reduces purulent-inflammatory complications, accelerates pain relief, and shortens recovery time. By day 21, oral dysbiosis was nearly eliminated, and immune function markers showed significant improvement. Microbiological analysis confirmed the role of bacteriophages and eubiotics in restoring microbial balance and reducing antibiotic resistance risks. Radiological diagnostics (CT, MRI) provided objective evidence of better bone healing and reduced inflammation. Thus, the integration of antimicrobial, probiotic, and enzymatic agents enhances clinical outcomes, minimizes complications, and reduces hospitalization time. Further research should focus on optimizing personalized therapy protocols and assessing their long-term effectiveness.

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DIABETIC NEUROPATHY: INNOVATIVE APPROACHES TO DIAGNOSIS AND TREATMENT AUTHORS

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SUMMARY
Diabetic neuropathy is one of the most severe complications of diabetes mellitus, significantly impairing patients' quality of life. This article presents current approaches to the diagnosis and treatment of this condition, including the application of innovative technologies such as gene and cell therapy, nanotechnology, and artificial intelligence. Special emphasis is placed on prevention and the interdisciplinary approach aimed at improving patient outcomes.

KEYWORDS: *diabetic neuropathy, diagnosis, treatment, prevention, gene therapy, cell therapy, nanotechnology, artificial intelligence.*

CONFLICT OF INTEREST. The authors declare no conflict of interest.

ДИАБЕТИЧЕСКАЯ НЕЙРОПАТИЯ: НОВЫЕ ПОДХОДЫ К ДИАГНОСТИКЕ И ЛЕЧЕНИЮ

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РЕЗЮМЕ
Диабетическая нейропатия – одно из наиболее тяжёлых осложнений сахарного диабета, существенно ухудшающее качество жизни пациентов. В статье представлены современные подходы к диагностике и лечению этого состояния, включая использование инновационных технологий, таких как генная и клеточная терапия, нанотехнологии и искусственный интеллект. Особое внимание уделено профилактике и междисциплинарному подходу, направленному на улучшение прогнозов пациентов.

КЛЮЧЕВЫЕ СЛОВА: *диабетическая нейропатия, диагностика, лечение, профилактика, генная терапия, клеточная терапия, нанотехнологии, искусственный интеллект.*

КОНФЛИКТ ИНТЕРЕСОВ. *Авторы заявляют об отсутствии конфликта интересов.*

Introduction

Diabetic neuropathy (DN) is one of the most common and severe complications of diabetes mellitus (DM). It affects approximately 50% of patients with long-standing DM and may develop in both type 1 and type 2 diabetes. The diversity of clinical manifestations, including sensory, motor, and autonomic disturbances, makes DN not only a medical but also a social problem that significantly impairs patients' quality of life [1, 2].

According to the World Health Organization (WHO), about 422 million people worldwide are affected by diabetes, and this number continues to rise. Considering that the risk of developing DN correlates with the duration of the disease and the level of glycemic control, the problem of early diagnosis and effective treatment becomes especially urgent. Diabetic neuropathy is associated with increased disability rates, decreased work capacity, and a growing financial burden on healthcare systems, particularly in developing countries.

Existing diagnostic methods often rely on subjective assessment of symptoms and do not always allow for detection of the disease at early stages. As a result, interest is growing in new instrumental and molecular techniques, including the use of biomarkers and modern imaging technologies. Significant changes are also taking place in the field of treatment: new pharmacological agents and innovative approaches are emerging, aimed at neural tissue repair and reduction of pain symptoms [3–6].

The purpose of this article is to provide a comprehensive overview of current approaches to the diagnosis and treatment of diabetic neuropathy, including promising methods that may change patient management in the near future. Attention will be paid to pathogenetic aspects, innovative technologies, and preventive measures aimed at reducing the prevalence of this complication.

Etiopathogenesis of Diabetic Neuropathy

Diabetic neuropathy (DN) has a complex and multifactorial pathogenesis based on metabolic, vascular, and immune mechanisms. Chronic hyperglycemia is considered the key trigger initiating a cascade of pathological changes in nerve tissue. It activates several processes, including the polyol metabolic pathway, which leads to the accumulation of sorbitol and a decrease in the level of myo-inositol – both essential for the normal functioning of nerve fibers. As a result, electrolyte balance and ion transport across neuronal membranes are disrupted, further exacerbating the pathological changes. In addition, chronic hyperglycemia contributes to the formation of advanced glycation end-products (AGEs), which trigger inflammatory reactions and enhance oxidative stress, exerting a toxic effect on nerve tissue [7–9].

The Role of Oxidative Stress and Inflammation

One of the central mechanisms in the pathogenesis of diabetic neuropathy is oxidative stress, initiated by the excessive production of reactive oxygen species (ROS). These highly reactive molecules cause damage to cell membranes through lipid peroxidation and also modify protein and DNA structures, thereby initiating apoptotic signaling cascades in neurons. Such changes lead to the activation of inflammatory pathways, including the synthesis of proinflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α). These mediators exacerbate neural damage, increase vascular permeability, and promote hypoxia progression. Thus, oxidative stress not only induces primary axonal injury but also creates a chronic environment that impairs the regeneration of nerve fibers [10].

Microvascular Ischemia and Hypoxia

Diabetic microangiopathy, affecting the blood vessels that supply nerves, leads to ischemia and hypoxia of the nerve fibers. The persistent reduction in oxygen levels directly damages nerve endings and worsens the pathological process. This impairment in nutrient and oxygen transport to nerve cells creates a foundation for further progression of neuropathy [11].

Pathogenetic Classification

Diabetic neuropathy is classified into several forms depending on clinical presentation.

- Sensory neuropathy is characterized by altered sensation, including paresthesia and pain. These manifestations are often underestimated by patients in the early stages.
- Motor neuropathy presents with muscle weakness and atrophy, significantly reducing patients' physical activity and overall condition.
- Autonomic neuropathy affects internal organ function, causing disturbances such as orthostatic hypotension, gastroparesis, and erectile dysfunction.

Modern understanding of the pathogenesis of diabetic neuropathy opens new perspectives for its diagnosis and treatment. The following section will examine innovative approaches to detecting this condition.

Current Approaches to Diagnosis

Modern diagnostic strategies for diabetic neuropathy are based on the integration of clinical, instrumental, and molecular approaches, which significantly enhance the accuracy of early detection.

Instrumental Methods

One of the key instrumental techniques is electromyography (EMG), which evaluates the functional state of peripheral nerves and detects alterations in nerve conduction velocity. However, despite its widespread use, this method requires highly qualified medical personnel and access to specialized equipment.

Another important diagnostic tool is skin biopsy, employed to assess the density of small nerve fibers and identify their degeneration. This method provides unique insights into the condition of neural structures that cannot be obtained through other diagnostic modalities.

Additionally, ultrasound and magnetic resonance neurography (MRN) enable visualization of peripheral nerve structures, detecting pathological changes that may remain unnoticed with standard diagnostic methods [12, 13].

Clinical Tests

Clinical tests remain an essential component of DN diagnosis. The most commonly used include:

- Vibration perception test using a tuning fork – a convenient method for rapid, non-invasive screening of sensory disturbances, particularly in early disease stages.
- Semmes – Weinstein monofilament test – evaluates tactile sensitivity. Its simplicity and accessibility make it a valuable tool in clinical practice.
- Quality of life questionnaires, such as DN4 (Douleur Neuropathique 4), aid in assessing the presence and severity of pain syndrome, as well as in planning subsequent treatment strategies.

Liquid Biopsy

Liquid biopsy is an emerging diagnostic approach based on the analysis of biological fluids for the identification of specific biomarkers. For instance, neurofilaments, glycoproteins, and proinflammatory cytokines can be used to evaluate the extent of nerve tissue damage and the activity of inflammatory processes. These markers not only support disease diagnosis but also enable monitoring of disease progression and treatment efficacy [14, 15].

New Approaches to Treatment

Pharmacological Therapy

Modern pharmacological agents used in the treatment of diabetic neuropathy aim to target the underlying pathogenic mechanisms and alleviate symptoms. Among them:

- Antioxidants: Alpha-lipoic acid has demonstrated efficacy in randomized clinical trials, showing its ability to reduce sensory symptoms and slow the progression of neuropathy [16].
- Metabolic agents: Polyol pathway inhibitors, such as epalrestat and isodibutine, reduce sorbitol accumulation in nerve tissue, thereby limiting neuronal damage [17].

Neuroprotective Agents

To promote nerve repair, the following are actively utilized:

- Agents that stimulate nerve fiber growth, such as cerebrolysin, which show beneficial effects on regeneration and function of the peripheral nervous system.
- Poly(ADP-ribose) polymerase (PARP) inhibitors, which help reduce oxidative stress and prevent DNA damage, playing a role in halting neuropathy progression.

Pain Management

Pain is one of the cardinal symptoms of diabetic neuropathy. Management strategies include:

- First-line drugs: Duloxetine and amitriptyline, which reduce pain intensity by acting centrally on neuropathic mechanisms.
- Antiepileptic agents: Gabapentin and pregabalin, which are the standard pharmacologic treatments for neuropathic pain.
- Innovative therapies: Botulinum toxin for localized pain relief and cannabinoids, which have shown efficacy in chronic pain syndromes.

Therapeutic Prospects

Gene Therapy

Recent advances in genetic engineering have opened new horizons for diabetic neuropathy treatment:

- Use of viral vectors to deliver growth factors such as NGF and BDNF aids in regenerating damaged nerve fibers. These factors are key in neuronal regeneration and intercellular communication, which are essential for restoring peripheral nervous system function [18].
- CRISPR-Cas9 technology allows gene modification involved in neuropathy pathogenesis, facilitating both prevention and treatment. For example, research explores correcting mutations that increase neuronal sensitivity to hyperglycemia [19].
- Gene therapy is also being investigated to improve microcirculation in nerve tissue by upregulating genes responsible for angiogenesis, potentially reducing ischemic injury.

Cell Therapy

Cell-based technologies offer novel options for nerve tissue regeneration:

- Mesenchymal stem cells (MSCs) possess regenerative potential and support remyelination of damaged axons. Their secretion of neurotrophic factors makes them a promising tool for DN treatment. Moreover, MSCs can suppress inflammatory responses exacerbating nerve damage.
- Schwann cell transplantation is being studied as a method to enhance nerve regeneration. These cells restore the myelin sheath and create favorable conditions for axonal growth.
- Combined approaches, integrating cellular therapies with biomaterials such as hydrogels, are also under investigation to improve transplantation efficacy and promote sustained tissue repair.

Nanotechnology

Nanotechnology provides unique solutions for targeted drug delivery:

- Nanoparticles enable site-specific delivery of antioxidants and anti-inflammatory agents. Due to their small size, they can reach otherwise inaccessible regions of nerve tissue, minimizing systemic side effects.
- Liposomes offer sustained drug release, reducing dosing frequency and enhancing treatment effectiveness. They can also carry combination therapies, improving overall efficacy.
- Magnetic nanoparticles, guided by external magnetic fields, allow localized drug delivery, minimizing collateral tissue damage.

The Role of Prevention in DN Management

Preventive strategies are crucial for reducing the prevalence of diabetic neuropathy:

- Maintaining target glycemic levels in accordance with modern clinical guidelines remains the cornerstone of neuropathy prevention. This includes the use of real-time glucose monitoring systems, allowing patients to promptly adjust glucose levels [20].
- A healthy lifestyle, incorporating regular physical activity, a balanced diet, and avoidance of harmful habits, reduces the risk of complications. For instance, aerobic exercise improves microcirculation and reduces inflammation [21].
- Screening programs facilitate early detection and timely intervention before irreversible changes develop. Mobile clinic-based initiatives have proven effective in rural settings where access to healthcare is limited [22].

Clinical Trials and Current Challenges

Clinical trials dedicated to diabetic neuropathy aim to enhance understanding of its pathogenesis, develop novel diagnostic tools, and implement innovative treatment strategies. In recent years, several large-scale studies have clarified the efficacy of various therapeutic approaches. For example, research has shown that alpha-lipoic acid and polyol pathway inhibitors significantly reduce neuropathic symptoms, including pain and sensory dysfunction.

Other studies have focused on evaluating the effectiveness of combination therapies. The synergistic effect of antioxidants with neuroprotective agents such as cerebrolysin promotes nerve tissue regeneration. Furthermore, clinical trials are investigating the utility of novel biomarkers that may aid early diagnosis and serve as indicators of therapeutic success [23, 24].

However, current diagnostic and treatment methods have limitations. Tools such as biomarkers and skin biopsies require specialized equipment and trained personnel, restricting their use in primary care settings. Moreover, pharmacological treatments often have side effects and do not ensure full neural restoration. For example, while duloxetine reduces pain, it does not address the core pathogenic mechanisms of neuropathy.

The economic burden of diabetic neuropathy also poses a significant challenge. The high cost of medications and diagnostics renders them inaccessible for many patients, particularly in developing countries. The lack of insurance coverage for modern diagnostic and therapeutic options further exacerbates the problem. These issues highlight the need to develop cost-effective diagnostic and therapeutic methods accessible to a broader patient population. Mass screening programs for early-stage neuropathy represent a promising approach to reducing the cost of late-stage treatment.

Conclusion

Diabetic neuropathy remains one of the most complex challenges in modern medicine, requiring a multifaceted approach. The development of innovative diagnostic and treatment strategies is critical for improving patients' quality of life and minimizing the socioeconomic impact of this condition. Promising technologies, including gene and cell therapies, nanotechnology, and personalized medicine, offer unique opportunities for individualized treatment – especially important given the chronic nature of diabetic neuropathy.

Preventive measures warrant special attention, as early intervention can significantly delay disease progression. For example, improving glycemic control and implementing new monitoring tools – such as wearable devices for peripheral nerve assessment – can markedly enhance preventive strategies. Furthermore, combining traditional methods with advanced technologies like artificial intelligence for patient data analysis opens avenues for developing personalized treatment plans tailored to individual needs.

The integration of interdisciplinary approaches, uniting expertise from endocrinology, neurology, and bioengineering, is essential for creating more effective therapeutic strategies. This collaboration may not only improve treatment outcomes but also lead to the establishment of new standards of care, alleviating the healthcare system's burden. Finally, the implementation of educational programs for healthcare professionals and patients will enhance awareness and adherence to treatment, ensuring broader success in combating diabetic neuropathy.

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