Review Article

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Mechanisms of monoclonal antibodies affecting healing in the oral cavity

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Abstract

This article reviews the mechanisms of monoclonal antibodies affecting wound healing in the oral cavity and the maxillofacial region. The analysis focuses on key targets, including TNFα, IL4/IL13, TSLP, IgE, RANKL-RANK, and VEGF/VEGFR, and their impact on inflammation, angiogenesis, epithelialization, and bone remodeling. Particular attention is given to anti-TNF agents (infliximab), Th2-targeted therapies (dupilumab, tezepelumab, omalizumab), anti-RANKL therapy (denosumab), and anti-VEGF/VEGFR agents (ramucirumab), and their association with medicationrelated osteonecrosis of the jaw (MRONJ) and other oral complications. The article emphasizes the need for a interdisciplinary approach in dental and maxillofacial surgical practice to minimize complications and improve outcomes in patients receiving monoclonal antibodybased targeted therapy.

Keywords: monoclonal antibodies, wound healing, oral mucosa, MRONJ, medicationrelated osteonecrosis of the jaw, infliximab, dupilumab, tezepelumab, omalizumab, denosumab, ramucirumab

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Механизмы моноклональных антител, влияющих на заживление в полости рта

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Резюме

В статье представлен обзор механизмов действия моноклональных антител, влияющих на процессы заживления тканей полости рта и челюстнолицевой области. Анализируются ключевые мишени, такие как TNFα, IL4/IL13, TSLP, IgE, RANKL-RANK и VEGF/VEGFR, а также их влияние на воспаление, ангиогенез, эпителиализацию и костное ремоделирование. Особое внимание уделяется препаратам антиTNF (инфликсимаб), Th2-таргетной терапии (дупилумаб, тезепелумаб, омализумаб), анти-RANKL (деносумаб) и анти-VEGF/VEGFR (рамуцирумаб), их роли в развитии медикаментассоциированного остеонекроза челюстей (MRONJ) и других оральных осложнений. Подчеркивается необходимость междисциплинарного подхода в стоматологической и челюстнолицевой хирургии для снижения риска осложнений и улучшения исходов лечения пациентов, получающих таргетную терапию моноклональными антителами.

Ключевые слова: моноклональные антитела, заживление ран, слизистая оболочка полости рта, медикаментассоциированный остеонекроз челюстей, инфликсимаб, дупилумаб, тезепелумаб, омализумаб, деносумаб, рамуцирумаб

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INTRODUCTION

Healing of oral and bone of the maxillofacial region's wounds is multiphase process dental and maxillofacial's outcomes depend of [1; 2].

Nowadays monoclonal antibodies (MAB) became potent tool in medicine because of opportunity to impact on molecular targets participating in tissue regeneration [1; 3; 4]. MAB are widely used in oncology, chronic inflammatory and allergic processes, therefore dental care is provided in the context of general therapy [5; 6]. Targeted changing of key mediators of inflammation, angiogenesis and remodelling can change infection complication's risk, lead to disruption of epithelization [1; 2; 7].

AIM

Generalizing of clinical data of MAB's main classes impact on healing of oral and maxillofacial wounds and presenting quantitative assessment of the risk of complications with the use of targeted therapy based on data from published meta-analyses of randomized trials.

MATERIALS AND METHODS

This review was conducted in accordance with the principles of a systematic literature search. The search was conducted in November 2025 in two databases: PubMed and eLIBRARY.RU. Key words and their combinations used in PubMed searching are of the following: "monoclonal antibodies", "wound healing", "oral mucosa", "MRONJ", "medication-related osteonecrosis of the jaw", "denosumab", "infliximab", "dupilumab", "Tezepelumab", "omalizumab", "ramucirumab", "anti-RANKL", "anti-TNF", "anti-VEGF", "oral complications", "targeted therapy". Additional words used in eLIBRARY.RU searching: monoclonal antibodies, adverse effects, wounds healing, osteonecrosis of jaw, targeted therapy, complications of oral mucosa. Besides scientific publications official instructions were used to taking following medications: infliximab, dupilumab, tezepelumab, omalizumab, denosumab, ramucirumab.

RESULTS

A search of the PubMed database yielded a significant number of publications for each keyword. Sources were manually selected based on their relevance to the review topic: publications on the mechanisms of action of monoclonal antibodies, their impact on oral and maxillofacial tissue healing, and clinical complications of targeted therapy in dental practice were included. Duplicate publications and sources that did not meet the inclusion criteria were excluded. The final list included 46 sources: 35 English-language publications, primarily identified through PubMed, and 11 Russian-language sources from eLIBRARY.RU.

MAB as targeting and potent points of impact on healing phases

MAB realise their action due to binding with inflammation mediators, cytokines, receptors or lygands of signal paths which let selectively transform inflammation and next regeneration stages [1; 8; 9].

Pro-inflammatory cytokines (like TNF-α), regulators Th2-inflammation (IL-4/IL-13, TSLP, IgE), RANKL-RANK and signal path, determining angiogenesis and epithelial regeneration (VEGF/VEGFR и EGFR-addicted processes) [1; 2; 6; 10–13].

Clinical significance of these targets is participating in microinflammation' control, vascular reaction, epithelization and bone regeneration which may increase complications' risk after invasive treatments [2; 7; 14; 15].

Anti-TNF-therapy and risks for oral surgery

Anti-TNF-therapy is widely used in autoimmune diseases and may be associated with periodont health changing and risks of complications related to dental practice [5; 16]. **Infliximab** is a monoclonal antibody to TNF-α which decreases pro-inflammatory reactions including a secondary reduction in the production of other cytokines and inflammatory response molecules [1; 17; 18]. General complications of MAB-therapy are increased infectious risks and immunologic adverse events which are important in planning of invasive treatment in oral cavity [19–24].

Infusion reactions of infliximab have been systematically reviewed in other systematic review highliting the need to consider tolerability of therapy in preoperative period [19]. Researchs of significant complications after intervention with infliximab including infection cases and osteomyelitis of the lower jaw after extraction of teeth are presented in literature [25].Infectious complications associated with infliximab have also been described in other areas which supports clinical awareness regarding infectious risk in some patients [26].

Practic aspects of management

The recommendations call for the need to debride foci of chronic infection before planned interventions and interdisplinary coordination of therapy since outcomes depend on activity of underlying disease and the degree of immunosupression [5; 7].

In highly invasive procedures and bone surgeries, antibiotic prophylaxis and enhanced surveillance for high-risk patients should be considered, based on a clinical study on the impact of modern antitumor therapy on bone complications [7; 27].

Th-2 targeted therapy in dental practice

Dupilumab – simultaneously blocks IL-4Rα and decreases signalling IL-4/IL-13, which reduces Th2-mediated inflammation and IgE-related effects [6]. Adverse effects of dupilumab include conjunctivitis, eosinophilia and reactions in the area of injection, adverse effects of skin [6; 28]. Clinical case of successful preoperative use of dupilumab in high-risk operation demontrates opportunity of continuation of the therapy in individual risk assessment and interdisplinary management [29].

For the patients taking dupilumab, monitoring of inflammatory manifestations is clinically significant (since it is necessary to take into account the state of barrier tissues in the perioral area), which requires more careful monitoring in the postoperative period [6; 28].

Tezepelumab – the antibody to TSLP, targets an upstream epithelial cytokine activating dendritic cells and then Th2-response [11]. Its efficacy in severe uncontrolled asthma is demonstrated in randomized trials and united analyses and in the safety profile, upper respiratory tract infections and local reactions are more frequently noted [10; 30]. Nowadays, there is no evidence of increased MRONJ or severe oral infections with tezepelumab. Considering mechanism (targeting on epithelial cytokine, rather than total immunosupression) risk of severe surgical complications is minimal theoretically. However, trials are still ongoing [10; 11]. In severe asthma treated with tezepelumab, it is necessary to ensure stable disease control before anesthesia and intervention [10; 11].

Omalizumab binds free IgE, reducing FcεRI-mediated mast cell and basophil activation. It is clinically effective for chronic urticaria and asthma [31–33]. Clinical data and systematic reviews confirm the efficacy and high safety profile of omalizumab, although clinical discussions emphasize the increased risk of anaphylaxis and the importance of post-injection monitoring [34]. Long-term observations in selected patient groups also support good tolerability of therapy while maintaining standard precautions [22; 35]. Routine discontinuation before most dental procedures is unnecessary, but detailed allergy history and emergency preparedness are recommended [32; 33].

Immune-mediated adverse events in oncologic targeted therapy and oral lesions

Immune-mediated complications of antitumor therapy may include oral mucosa pathologies and be accompanied by the need of systemic immunosupression, which increases risk of infections and impaired healing [8]. Oral complications of targeted antitumor therapy have been described as a clinically significant group of conditions, including inflammatory lesions of the oral mucosa, xerostomia, secondary infection [2]. Combination of antitumor therapy with anti-RANKL may be associated with MRONJ, as reported by case reports and reviews [7; 15; 23].

Clinical trials of PD-1-inhibitor therapy in domestic practice highlight the need of interdisplinary approach and adverse effects control [36].

Practical aspects of managing

Prior to antitumor therapy sanation of the oral cavity and minimization of future traumatic invasions are of high importance, since adverse events of the oral mucosa and bone worsen the quality of life and can complicate treatment [2; 7]. During the therapy if ulcers/erosions appear differential diagnosis between toxic muxositis, infectious complications and immuno-mediated damage is carried out [2; 8].

Anti-RANKL-therapy and MRONJ: meta-analysis

Denosumab – fully human antibody that binds with high affinity to RANKL (Receptor Activator of Nuclear Factor Kappa-B Ligand), which blocks RANKL-RANK interaction and supresses formation and activity of osteoclasts, resulting in a significant reduction [12; 24]. Denosumab is also associated with high risk of hypocalcyemia, which what is important for perioperative safety and patient monitoring [12].

MRONJ (Medication-related osteonecrosis of the jaw) – is a clinically significant complication of anti-resorptive therapy and has direct implications for dentistry due to its association with invasive procedures and inflammatory diseases of the oral cavity [14; 37–40]. Pathogenetic aspects of MRONJ include immune disturbances and changes in bone remodeling, as reflected in reviews on immune dysfunction in MRONJ [38; 41].

Risk factors and prevention

Invasive dental intervention, low level of the oral hygiene and inflammatory diseases of periodontium may increase the risk of MRONJ [14; 37; 38; 40]. Clinical guidelines indicate the need for oral sanitation before starting anti-resorptive therapy and the use of standardized protocols for managing patients at risk [12; 40; 42].

Antiangiogenic therapy and impair of healing

Ramucirumab – fully human monoclonal antibody to IgG1. Ramucirumab is an antibody to VEGFR-2 and inhibits angiogenesis which can pathogenetically impair the vascular phase of healing [13]. Randomized trials in solid tumors confirm clinically significant adverse events of antiangiogenic therapy such as arterial hypertension and bleeding [16; 43–45].

Dental management of anti-VEGF/anti-VEGFR approaches should take into account the potential risk of impaired healing and hemorrhagic complications, especially in extensive interventions [13; 44].

Targeted therapy and oral toxicity (EGFR-related effects)

Oral complications of target antitumor therapy described as often and clinically significant problem, including mucositis, stomatitis, xerostomia and secondary infections of the oral mucosa [2; 46]. Impaired epithelial regeneration with targeted therapy impact on signal paths (including EGFR-related effects) can prolong the epithelization time and increase the risk of complications after dental procedures [2]. Practical measures include prevention and treatment of mucositis, pain control and hygiene, and monitoring for secondary infections. [2].

CONCLUSION

The combined data demonstrate that the effect of mAbs on oral healing outcomes is class-specific and is determined by the processes the drug affects: anti-infective defense, angiogenesis, epithelial repair, or bone remodeling. MABs can significally influence clinical outcomes in oral cavity which requires a interdisciplinary approach in dentistry and oral & maxillofacial surgery. Prevention of complications requires preoperative oral sanitation, risk assessment, timing of invasive procedures and adherence to MRONJ clinical guidelines.

This issue is understudied, and databases do not provide precise statistics on specific complications. Therefore, the topic is relevant for further research.

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