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THE USE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN THE PRACTICE OF THE DENTIST DEPENDING ON THE FEATURES OF THE PAIN SYNDROME

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A literature review was conducted on the results of clinical studies examining the characteristics of pain syndrome in dental practice for the selection of adequate pharmacotherapy using non-steroidal anti-inflammatory drugs. Retrospective review and analysis of domestic and foreign publications on the characteristics of pain syndrome, and determination of pain relief tactics with the use of nonsteroidal anti-inflammatory drugs were selected as research methods. The research results indicate that pain is the most prevalent symptom in dental practice. During the diagnostic process, it is essential to rule out non-dental causes of pain in the orofacial region. The results of the study show that pain is the most prevalent symptom in dental practice. During the diagnostic process, it is essential to exclude non-dental causes of pain in the orofacial area, while also considering the localization, duration, and nature of the pain, the stimuli that provoke it, and the results of auxiliary examinations. Acute pain requires adequate treatment to eliminate the risk of developing chronic pain syndrome. Nonspecific anti-inflammatory drugs are pathogenetically justified for the treatment of such patients, but it is necessary to individually select the dosage and duration of use, taking into account not only their effectiveness but also their safety.

Key words: pain, nonsteroidal anti-inflammatory drugs, dentistry.

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ВИКОРИСТАННЯ НЕСТЕРОЇДНИХ ПРОТИЗАПАЛЬНИХ ЗАСОБІВ В ПРАКТИЦІ ЛІКАРЯ-СТОМАТОЛОГА В ЗАЛЕЖНОСТІ ВІД ОСОБЛИВОСТЕЙ БОЛЬОВОГО СИНДРОМУ

Проведено огляд літератури щодо результатів клінічних досліджень особливостей больового синдрому в стоматологічній практиці для підбору адекватної фармакотерапії із застосуванням нестероїдних протизапальних засобів. Методами дослідження обрано ретроспективний огляд та аналіз вітчизняних та зарубіжних публікацій щодо характеристики больового синдрому, визначення тактики знеболення із застосуванням нестероїдних протизапальних засобів. Результати дослідження показують, що біль є домінуючим симптомом у практиці лікаря-стоматолога. У процесі діагностики необхідно виключити нестоматологічні причини болю в орофаціальній ділянці, а також звернути увагу на локалізацію, тривалість і характер болю, подразники, що провокують біль, результати допоміжних обстежень. Гострий біль потребує адекватного лікування для усунення ризику розвитку хронічного больового синдрому. Неспецифічні протизапальні засоби є патогенетично обґрунтованими препаратами для лікування таких пацієнтів, але необхідо індивідуально обирати дозування, тривалість застосування з урахуванням не тільки їх ефективності, а й безпеки.

Ключові слова: біль, нестероїдні протизапальні засоби, стоматологія.

The study is a fragment of the research projects "Substantiation of the choice of methods of treatmentof diseases of the oral cavity depending on their morphological and functional characteristics", state registration No. 0124U004553 and "The contribution of microRNA complex expression to the pathogenesis of chronic periodontitis for the development and evaluation of targeted treatment methods", state registration No. 0122U201709.

A significant number of dental diseases, as well as the postoperative period in dental practice, are accompanied by pain syndrome. The cause of pain is various algogenic factors that act from the outside or are formed as a result of pathological processes in the teeth (pulpitis, apical periodontitis), periodontal tissues, oral mucosa and after dental operations.

According to the definition of the International Association for the Study of Pain (IASP), "pain is an unpleasant feeling or emotional experience associated with actual or potential tissue damage and described in terms of this damage" [30].

According to the results of a survey of residents of Ukraine, 21% of patients with pain consulted a dentist-therapist, 28% consulted a dental surgeon. In the case of inflammatory processes in the maxillofacial area, which were accompanied by pain, 4% of patients visited a dentist-therapist, 15% of patients visited a dentist-surgeon. In cases of dental trauma and injuries of the maxillofacial region, accompanied by inflammation, swelling and pain, 17% of patients consulted a dentist-therapist, 20% consulted a dental surgeon. 70% of patients report about pain associated with surgical interventions in the maxillofacial region, and in 50% of cases it was moderate and severe. Severe and prolonged pain significantly disrupts the regulation of homeostasis and the activity of the autonomic nervous system, suppresses the psyche, causes stress, depression, in addition, it is the cause of immune deficiency, depletes physiological and emotional resources. Over time, pain turns into a damaging factor, promoting

development of new pathological processes and, acquiring the status of an independent disease, negatively affects the patient's quality of life, leads to material, social and moral losses.

Without a clear understanding of the nature of pain, the search for reliable methods of combating it will remain ineffective. The use of new methods of pain relief and adequate methods of combating pain syndrome requires clear concept about the physiological, biochemical and psychophysiological mechanisms of pain and the possibility of reducing or eliminating them. There is currently no universal drug that effectively eliminates pain of various origins (inflammatory, traumatic, neuralgic, etc.). According to the principles of pathogenetic therapy, the use of drugs that affect different links in the inflammatory process is justified; therefore, the drugs of first choice are nonsteroidal anti-inflammatory drugs (NSAIDs) [10].

The purpose of the study was to review the results of clinical studies of the features of pain syndrome in dental practice for the selection of adequate pharmacotherapy using nonsteroidal anti-inflammatory drugs.

Materials and methods. A retrospective review of domestic and foreign publications on the characteristics of pain syndrome, determination of pain relief tactics using nonsteroidal anti-inflammatory drugs was conducted.

Results of the study and their discussion. The main complaint of a dental patient is usually pain of various genesis, intensity, localization, duration. The function of pain is a preventive and protective action that causes a reflex reaction of the body, which minimizes the effects of a damaging stimulus [18].

Pain treatment in dentistry is subject to the principle of "3-D" – diagnosis of the pain syndrome, dental treatment and appropriate pharmacotherapy (drugs).

The first and most important step in the treatment of pain syndrome is the diagnosis of the condition that causes pain and the determination of what caused this condition.

Based on complaints, history of the disease and the results of an objective examination, toothache are defined as odontogenic or non-odontogenic.

Most often in dental practice, odontogenic pain is diagnosed, which occurs when teeth are damaged by caries, non-carious lesions, pulpitis, periodontitis, against the background of inflammatory processes of periodontal tissues, oral mucosa, difficult teething, neoplastic lesions, injuries of the maxillofacial region tissues [5, 16, 23]. Odontogenic pain is characterized by the fact that it decreases with treatment of the causative tooth and under the influence of analgesic drugs.

If the cause of pain is not identified and in case of discrepancy between objective and subjective examination of the nature of odontogenic pain, it is defined as non-odontogenic. Examples of such pain are: pain in the head and neck area as a manifestation of general somatic diseases (neurological diseases, viral infections, diabetes, systemic lupus erythematosus, etc.); pain caused by pathology of the maxillary sinus and nasal mucosa, myofascial pain, cardiac pain, psychogenic pain, vascular pain, neuropathic pain.

Depending on the leading pathogenetic mechanism underlying their development, pain syndromes (according to the classification developed by IASP experts) can be divided into three main groups [28]:

– somatogenic (nociceptive pain) – arise as a result of stimulation of superficial or deep tissue receptors (nociceptors) during trauma, inflammation, ischemia, tissue stretching;

– neurogenic (neuropathic pain) – is a direct consequence of damage or changes in the peripheral or central somatosensory nervous system;

– psychogenic (psychogenic pain) – appear regardless of somatic, visceral or neuronal damage and are determined by psychological and social factors.

As a rule, all types of pain participate in the formation of pain syndrome in one patient. In dental diseases, nociceptive pain is the priority, which occurs after tissue damage and the release of inflammatory mediators, usually has a favorable course and completely regresses after the healing of damaged tissues.

Perception of damaging stimuli is carried out by nociceptors – sensitive receptors that are responsible for the transmission and encoding of damaging stimuli. Nociceptors are unencapsulated endings of afferent nerve fibers that are located in all tissues and internal organs. Their greatest number is noted in tooth tissues: if there are about 200 receptors per 1 cm^2 of skin, then in dentin – 15000-30000, and at the enamel-dentin junction – 75000 receptors.

Nociceptor activation occurs under the influence of mechanical, thermal and chemical stimuli (inflammatory mediators). Inflammatory mediators are formed in the area of injury and include: tissue algogens – histamine, serotonin, arachidonic acid metabolites (leukotrienes, prostaglandins), interleukin-1, tumor necrosis factor, blood plasma algogens – bradykinin, kallidin and algogens released from peripheral nerve endings of C-nociceptors – substance P, neurokinin A. Algogens interact with nociceptors and increase their sensitivity to mechanical and damaging stimuli, forming primary hyperalgesia. The most

powerful algogenic modulator is bradykinin, which, acting through B2 receptors, stimulates the formation of arachidonic acid. In turn, arachidonic acid, with the participation of the enzyme cyclooxygenase (COX), is oxidized to prostaglandins, prostacyclins, thromboxanes and leukotrienes, which have a pronounced independent algogenic effect. Next, the impulse caused by irritation of nociceptors, C and A-delta fibers enters the Gasserian ganglion, and then into the caudal nucleus of the trigeminal nerve, rises to the thalamic nuclei of the opposite side and into the somatosensory area of the cerebral cortex. The use of NSAIDs is associated with their ability to inhibit the activity of COX – the main enzyme of the synthesis of prostaglandins and other metabolites of arachidonic acid, which sensitize nociceptors in damaged tissues, increase the permeability of the vascular wall, cause edema and inflammation.

According to the intensity, pain is divided into weak, moderate, strong/very strong (also referred to as “unbearable” pain), according to localization – unilateral and bilateral; according to subjective manifestations (by nature) – shooting, pulsating, cutting, constant or periodic.

To conduct a reliable clinical assessment of pain, it is necessary to carefully conduct a patient survey: take into account the individual description of pain, its localization, duration, character and severity, as well as assess the patient's reaction to pain and its impact on sleeping, mood, physical performance and quality of life [15].

Taking into account the etiological factor, the following types of orofascial pain are distinguished:

– pain in hyperesthesia of hard tissues of teeth: short-term, localized pain caused by mechanical, thermal and chemical stimuli, sometimes can radiate to neighboring teeth. It manifests itself at caries, wedge-shaped defects, teeth root necks exposure, periodontal diseases, pathological abrasion of teeth, progressive form of tooth erosion, after preparation of teeth for artificial crowns and inlays;

– pulpal pain: acute involuntary, paroxysmal, increases under the influence of stimuli and at night; irradiation of pain along the branches of the trigeminal nerve is possible;

– periapical pain: constant sharp throbbing, possibly radiating, increasing pain in the area of damaged tooth, feeling of "an extended" tooth. The pain intensifies when chewing, pressing on the tooth [12];

– pain in odontogenic sinusitis (sinusitis): unilateral facial pain, toothache in the projection of the maxilla, unilateral discharge from the nasal cavity, feeling of pressure, fullness, pain in the projection of the maxillary sinus, feeling of stuffiness in the ears, sore throat;

– postoperative pain: occurs during periodontal procedures (gingivoplasty), after tooth extraction (alveolitis – causes long-term constant pain that can radiate along the branches of the trigeminal nerve), after implantation;

– pain caused by inflammation of the facial or trigeminal nerve [13]. Inflammation of the facial nerve can cause phantom pain.

– pain in inflammation of the oral mucosa (as a result of a typical disease of the oral mucosa or a symptom of a general disease) [31];

– pain due to neoplastic lesions localized in the head and neck region;

– orthodontic pain that occurs in patients treated with a brace system;

– pain caused by inflammation of the temporomandibular joint;

– Munchausen syndrome, in which patients with mental disorders consult a dentist, describing symptoms of the disease (including pain), which are not actually present.

A thorough subjective examination allows us to identify certain mechanisms of pain formation: 1) causal pain (under the influence of mechanical, thermal and chemical stimuli), which passes after the end of their action; 2) causal pain (under the influence of mechanical, thermal and chemical stimuli), which after the removal of the stimulus persists for some time; 3) acute pain – severe, sharp pain that arose suddenly [11]; 4) primary pain – this is the first case of pain associated with a certain area or tooth [27]; 5) spontaneous pain – occurs without the participation of an external stimulus acting on the tooth and is the result of an inflammatory process occurring in the tooth pulp or in the periapical tissues; 6) night pain (at pulpitis); 7) radiating pain – spreads from the upper jaw teeth to the temple, supraspinal region, wing of the nose; from the lower jaw teeth – in the ear, back of the head, neck; 8) throbbing pain is characterized by a pulsation that coincides with the heart rate and indicates the purulent nature of inflammation in the tooth area; 9) permanent pain as a kind of chronic pain with periodic remissions.

The nature of the pain syndrome can be acute or chronic.

Acute pain is a new, recent pain, inextricably linked to tissue damage (pulpitis, trauma), disappears during healing, subsiding of the pathological process.

Chronic pain lasts for a long time and often acquires the status of an independent disease (chronic inflammatory diseases), it can be a manifestation of the patient's depressive state. Chronic pain is

characterized by a significant cognitive-behavioral aspect, lasts more than three months and persists after the completion of the normal healing process. It is generally accepted that chronic pain does not disappear 1 month after the intervention or lasts more than 3–6 months without a clear connection with the intervention. Thus, pulpectomy or tooth extraction can cause the formation of not only acute pain after the procedure, but also chronic neuropathic (phantom) tooth pain. Persistent pain after successful endodontic treatment occurs in 3–7% of cases, more often it occurs if the patient has a long history of preoperative pain [1].

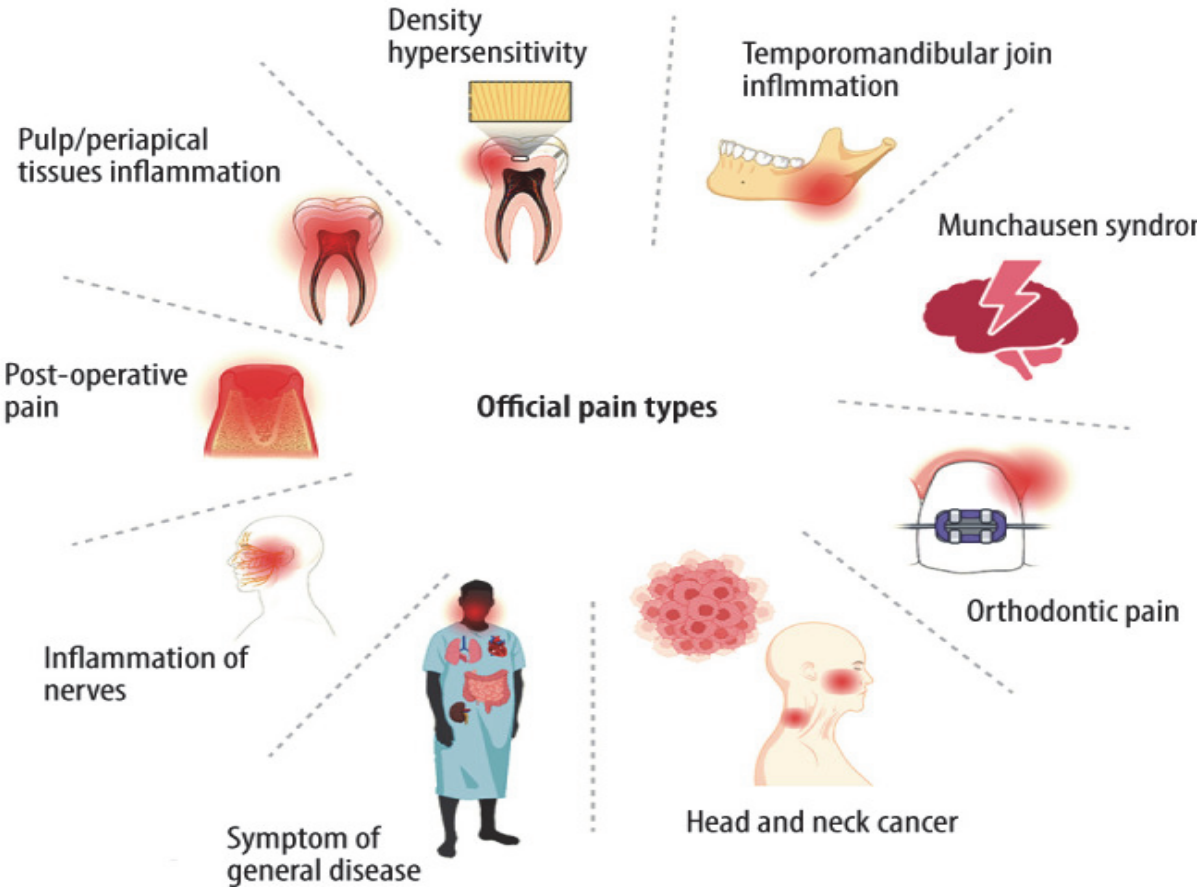

Fig.1. Main causes of orofacial pain [Kotowska-Rodziewicz A. et al., 2023].

Chronic orofacial pain is divided into 3 main types: musculoskeletal, neurovascular and neuropathic.

Prolonged pain not only significantly depletes physiological and emotional resources, but also contributes to the development of new pathological processes, disrupts the regulation of homeostasis, suppresses the psyche, causes depression, sleep disorders, is the cause of immune deficiency, turns into a harmful factor, often induces generalized processes that pose a danger to the body, and, acquiring the status of an independent disease (chronic inflammatory diseases), has a negative impact on the patient's quality of life. Certain anatomical and physiological features of the maxillofacial region model the mechanisms of the occurrence and passage of pain impulses and predetermine the pharmacokinetics of painkillers and, as a result, their clinical effect. The features of the maxillofacial region include:

– high degree of innervation and vascularization of the maxillofacial region;

– development of the inflammatory process in tissues of different structures (pulp, periodontium, gums, alveolar bone), possibly in a closed space;

– tissues of the oral mucosa, periodontium are constantly exposed to mechanical stress during eating, talking, etc.;

– density of microbial colonization of the oral cavity (1 ml of saliva contains from 4 million to 5 billion microorganisms; 1 g of dental plaque – 10–1000 billion. Bacteria prevail in the oral cavity, represented by a relatively stable group of aerobes and anaerobes, the spectrum of which can vary within 120–200 species).

For successful treatment of pain syndrome, it is necessary to:

– determine the causes of pain;

– determine the tactics of anesthesia – local with the use of local anesthetics and anti-inflammatory drugs to reduce pain or systemic use of analgesics;

– perform dental interventions aimed at reducing or eliminating pain;

– prescribe analgesic drugs (with systemic use) depending on the intensity of pain, effectiveness and safety of the drugs;

– apply systemic analgesic drugs until the end of the action of local anesthetics to increase the effectiveness of the postoperative pain syndrome treatment [2, 9].

– take into account the risk of adverse reactions according to the patient's history when prescribing an analgesic drug.

The next step in the 3–D principle is to provide appropriate dental treatment to address the underlying cause and reduce or eliminate pain. Medication is an essential part of dental treatment.

The primary treatment aim for pain management should be prevention of acute severe pain rather than rescuing as sensitization of the pain pathway leads to positive feedback loop and pathological changes at multiple sites of the pain pathway-peripheral, spinal and supra-spinal levels [28].

The principle of stepwise pain management is to prescribe the right medication at the right time and in the right dosage. This is especially important in dental practice, since pain of varying intensity may occur before treatment, in the process of performing diagnostic and therapeutic manipulations and after treatment.

Adequate pharmacotherapy of pain syndrome involves a differentiated approach to the selection of drugs for premedication, local anesthesia, systemic use of anti-inflammatory and analgesic agents, taking into account concomitant pathology.

Taking into account the pathogenesis of pain syndrome of an inflammatory and traumatic nature, for its prevention and treatment it is justified to use drugs that inhibit the synthesis and secretion of endogenous algogens and mediators that affect various links of the inflammatory process, in connection with which using of NSAIDs is pathogenetically justified.

According to WHO recommendations, non-narcotic analgesics and NSAIDs are used to treat mild and moderate pain, and for the treatment of severe pain, injections of NSAIDs and combinations of NSAIDs with narcotic analgesics are used. The method of administration of non-steroidal anti-inflammatory drugs does not have a significant effect on the effectiveness of the drug, so injections are used only to obtain a quick effect in case of intense pain.

Non-steroidal anti-inflammatory drugs contribute to:

1. Reducing pain during dental procedures and in the postoperative period. Reducing the severity of the inflammatory reaction in periodontal tissues and the oral mucosa [25, 26].

2. Preventing the formation of the main mediators of pain and inflammation – prostaglandins (PGs), prostacyclin and thromboxane. Blocking the synthesis of prostaglandin E2 in the gingival fluid under the influence of NSAIDs provides a decrease in vascular permeability, migration of polymorphonuclear neutrophils, manifestations of exudation, edema and inflammation.

3. Prevention of bone resorption. Under the influence of NSAIDs, the processes of differentiation of preosteoclasts into active osteoclasts and resorption of bone tissue of the alveolar process are slowed down.

4. Active influence on the clinical manifestations of the inflammatory-destructive process in periodontal tissues. NSAIDs have an anti-inflammatory effect, reduce edema, suppress the production of gingival fluid in periodontal pockets, which reduces the level of pro-inflammatory and pro-osteoporotic cytokines.

5. Antipyretic effect, which is manifested only at elevated body temperature. This is due to the inhibition of PG synthesis in the CNS and the elimination of their effect on the thermoregulation center (located in the hypothalamus), which increases heat loss. However, it is recommended to prescribe antipyretics only at body temperature above 38.5 ° C, since an increase in temperature allows you to increase the body's nonspecific protection against infection.

6. Impact on the patient's psychological health. Systemic administration of NSAIDs to patients with generalized periodontitis during the treatment period reduces pain, increases the threshold of pain sensitivity, and reduces the patient's unpleasant experiences associated with dental manipulations [32].

7. Suppression of uncontrolled proliferation of tumor cells due to inhibition of PG cell apoptosis. This fact is confirmed by data on the protective effect of NSAIDs on epithelial tumors and Alzheimer's disease.

Indications for the use of NSAIDs in dentistry are:

1. Inflammatory diseases of the maxillofacial region and the oral mucosa (pulpitis, apical periodontitis, periodontitis, arthrosis of the temporomandibular joint, bursitis).

2. Preventive analgesia. The use of NSAIDs before traumatic interventions makes it possible not only to suppress pain that has already arisen, but also to actively prevent its development, increases the activity of drugs used for local and general anesthesia, significantly reduces the level of inflammatory mediators in the tissues, reducing the severity of the postoperative inflammatory reaction and the intensity of pain, which allows to reduce the necessity in opioid analgesics.

3. Postoperative and post-traumatic inflammatory edema and pain.

4. Neuritis of the facial nerve.

5. Trigeminal neuralgia.

6. Myofascial pain syndrome of the maxillofacial region.

7. Hyperthermia.

Contraindications:

1. Hypersensitivity to drugs of this group.

2. Peptic ulcer of the stomach and duodenum, leukopenia, blood clotting disorders, severe renal and hepatic dysfunction.

3. Pregnancy, breastfeeding, childhood. The exception is ibuprofen, which can be used in children from 6 months of age.

4. It is prescribed with caution to patients with bronchial asthma, arterial hypertension and heart failure, who have a history of gastric bleeding, as well as to weakened and elderly patients. [7, 24].

Despite the fact that all nonsteroidal anti-inflammatory drugs have similar pharmacodynamics, when choosing drugs, one should take into account differences in the strength of action, the speed of onset of the effect, the duration and severity of individual effects, as well as the ability to cause side effects. Nonsteroidal anti-inflammatory drugs eliminate hyperalgesia in the area of inflammation and reduce the flow of pain impulses to the CNS, but do not affect the psychoemotional assessment of pain, therefore their analgesic effect is more pronounced in pain of mild and moderate intensity, especially caused by the inflammatory process.

In acute pain, it is advisable to start treatment with a high dose of a fast-acting NSAID that has pronounced analgesic activity, reducing the dose when the effect is achieved. In chronic pain, long-acting drugs are preferred, used 1–2 times a day.

The arsenal of nonsteroidal anti-inflammatory drugs used in dentistry is represented by both original drugs and a large number of generics: acetylsalicylic acid (aspirin), dexketoprofen (dexalgin), diclofenac sodium (voltaren, naclofen, ortofen), ibuprofen (brufen, dolgit, nurofen), indomethacin (metindol), ketoprofen (arthrosilen, artrum, arketal, bystrumgel, valusal, flamadex), ketorolac (adolor, dolak, ketalgin, ketanov, ketorol), lornoxicam (xefokam), meloxicam (movalis), nimesulide (naise, nimesil), naproxen (algezir, nalgesin), piroxicam (piroxifer, finalgel), etoricoxib (arkoxia). These drugs have different chemical structures and are available in various dosage forms for systemic and local use, and are also part of complex drugs for resorptive (pentalgin, solpadein, tempalgin, cofitsil, sedalgin, coldrex, advil) and local (cholisal, mundisal-gel) use. A significant number of drugs of this series are presented on the pharmaceutical market of Ukraine, and this dictates the need for more complete information for dentists about the pharmacological action, indications, contraindications, and features of the appointment of NSAIDs in dentistry [3].

Significant number of studies indicate that ibuprofen has the most pronounced analgesic efficiency in endodontic treatment. However, using of 500 mg of naproxen or 50 mg of ketoprofen for the elimination of post-endodontic pain in the first 6 hours is more effective than 600 mg of ibuprofen. The results of a survey of dentists indicate that during the treatment of complicated caries, they most often recommend the following non-steroidal anti-inflammatory drugs to patients: nimesulide, prescribed by 42.6% of dentists, ibuprofen – 34.4%, ketorol – 11.5%, meloxicam – 4.9%. The most popular non-steroidal anti-inflammatory drugs taken by patients in the pre-treatment period were nimesulide (29.7%), ibuprofen (25.0%), ketorol (25.0%). Patients associated their choice to media advertising of these drugs, over-the-counter options, and low cost [4]. The American Dental Association Institute of Clinical Practice Guidelines for the Pharmacological Treatment of Acute Toothache in Adolescents, Adults, and the Elderly recommends the use of a nonsteroidal anti-inflammatory drug (NSAID) as monotherapy (e.g., 400 mg ibuprofen or 440 mg naproxen sodium) or in combination with acetaminophen (e.g., 500 mg) as first-line therapy for acute toothache in adolescents, adults, and the elderly [6].

In the treatment of irreversible pulpitis in children, the combination of acetaminophen and ibuprofen has been shown to reduce pain intensity compared with acetaminophen and ibuprofen alone [21].

Advil Dual Action is the first product to receive the American Dental Association's Seal of Approval in a new category of short-term pain relievers. Advil Dual Action combines two analgesic

ingredients, acetaminophen (paracetamol) and ibuprofen. Clinical studies show that the combination of ingredients is stronger and longer-acting than ibuprofen and regular acetaminophen alone.

Nonsteroidal anti-inflammatory drugs are well absorbed when taken orally (80–100%), have high bioavailability (60–100%) and are well bound to blood plasma proteins (80–99%). However, with hypoalbuminemia, the concentration of free fractions of NSAIDs in the blood plasma becomes higher, which increases the activity and toxicity of the drugs. The maximum concentration in the blood is reached after 0.3–1.5 hours. Biotransformation of NSAIDs occurs in the liver, with the formation of inactive metabolites (exception – phenylbutazone and ketoprofen), which are excreted mainly by the kidneys. The half-life of a significant number of NSAIDs (acetylsalicylic acid, diclofenac sodium, ibuprofen, indomethacin, ketoprofen, ketorolac, nimesulide) is from 1 to 6 hours; in lornoxicam, celecoxib – 4–12 h, meloxicam 18–21 h, etoricoxib – 22 h. Liver and kidney dysfunction, as well as the patient's age, affect the pharmacokinetics of NSAIDs.

NSAIDs are widely used in anesthesiology for preoperative or preventive analgesia because they not only suppress the pain that has arisen, but also prevent its development by suppressing the activity of algogens, which are synthesized in response to tissue damage.

To relieve acute inflammatory pain in the postoperative period, it is advisable to start treatment with a high dose of short-acting highly effective analgesics, reducing it when the effect is achieved. The following drugs have such properties: dexketoprofen, ketorolac, ketoprofen, lornoxicam. When the dose is increased, the effectiveness of the drug increases, develops faster and persists longer [14].

Ketorolac has high analgesic activity. Therefore, it is used for moderate or severe pain after surgery in the maxillofacial region. However, it is not the drug of choice for preventive analgesia, since it has a moderate anti-inflammatory effect and gives a pronounced antiplatelet effect, which can provoke bleeding when used before surgery in the highly vascularized maxillofacial region. To relieve postoperative pain, ketorolac is prescribed 4 times a day for no more than 5 days, because it acts quickly, but briefly (4–6 hours) [8, 17]. NSAIDs that act mainly on cyclooxygenase-2 (COX–2) – nimesulide, celebrex, meloxicam do not affect platelet aggregation and do not increase bleeding during surgery. The scheme of use of NSAIDs depends on the pharmacokinetics of the drug.

Thus, ketorolac is used every 4–6 hours; ibuprofen, indomethacin, ketoprofen – 3–4 times a day; diclofenac, naproxen – 2–3 times a day; dexketoprofen – 1–3 times a day, lornoxicam – 2 times a day, nimesulide, celecoxib – 1–2 times a day, meloxicam, piroxicam, etoricoxib – 1 time a day.

According to studies by domestic scientists on the frequency of prescribing NSAIDs for various dental diseases, the following results were obtained: for acute and exacerbation of chronic pulpitis, NSAIDs were prescribed in 100% of cases, for chronic generalized catarrhal gingivitis – in 60%, for chronic generalized periodontitis – in 52%. According to the results of the survey, the most effective and widely used drugs in therapeutic dentistry are: ketoprofen, ketorolac, nimesulide. Of the listed drugs, the safest is nimesulide, but it is not effective enough in postoperative pain compared to ketorolac [2].

NSAIDs differ in their potency, speed of onset and duration of analgesic effect, and ability to cause side effects.

When choosing NSAIDs for the relief of inflammatory pain, it is necessary to take into account that the severity of the analgesic effect does not always coincide with their anti-inflammatory effect, and the speed of development of the anti-inflammatory effect lags behind the analgesic effect.

When planning a course of treatment, it should also be taken into account that analgesia occurs within 0.5–2 hours after a single use of nonsteroidal anti-inflammatory drugs, while the anti-inflammatory effect develops only after 3–4 days with regular use of the drug [29].

Taking NSAIDs can lead to complications from the gastrointestinal tract (GI): gastric and duodenal ulcers, bleeding and perforation of the upper GI tract, dyspepsia. To reduce the risk of complications, NSAIDs should be taken with meals, avoid prolonged use of NSAIDs, use them only during periods of increased pain, and take only one drug. Celecoxib is the “gold standard” of safety in gastrointestinal diseases.

All drugs from the NSAID group can cause liver dysfunction, but severe hepatotoxic reactions with acute liver failure are extremely rare. It is believed that the risk of their occurrence is higher in elderly patients who have liver disease and are taking hepatotoxic drugs in addition to NSAIDs.

Taking NSAIDs can negatively affect the cardiovascular system: heart rhythm disturbances (most often atrial fibrillation), the risk of vascular thrombosis, the risk of cardiovascular events. When studying the incidence of strokes in patients with hypertension, it was shown that ketorolac increases the incidence of ischemic and hemorrhagic strokes. It has been proven that naproxen and celecoxib contribute to the destabilization of arterial hypertension and heart failure to a lesser extent. Clinical trials have shown that

ibuprofen and naproxen can attenuate the antiplatelet effect of low-dose aspirin, which is used to prevent myocardial infarction and other cardiovascular diseases. The use of naproxen is not associated with a significant increase in the risk of cardiovascular complications [22].

It is believed that side effects develop only with prolonged use of NSAIDs, so it is not recommended to use these drugs for fever for more than 3 days, as an analgesic – for more than 10 days. However, numerous experimental studies have shown that changes in the gastric mucosa can appear after using one tablet, and after 3–4 days, ulcers may develop, including perforated ulcers, which are a factor in high mortality due to gastric bleeding. In most cases (up to 81% of cases), complications from the gastrointestinal tract are asymptomatic. To reduce complications when using NSAIDs, it is recommended to use them during meals (enterocoxib regardless of meals), use only one drug of this group (it is safe to prescribe together with paracetamol, metamizole sodium (analgin). However, 34 countries of the world have completely stopped or partially restricted the sale of analgin. In the USA, Norway, Great Britain, the Netherlands, Sweden, the use of analgin has been prohibited since the mid – 70s of the 20th century.

The correct choice of NSAIDs allows to adequately eliminate pain syndrome and inflammation, reduce the risk of postoperative complications, improve the quality of patients life, their working capacity and psychological state [19, 20].

Thus, an analysis of the literature on the study of the features of pain syndrome in dental practice for the selection of adequate pharmacotherapy indicates the need to use NSAIDs taking into account an individual approach to the selection of drugs of this group, effectiveness, dose, duration of use and safety for the patient.

Conclusions

1. Pain is the dominant symptom in the practice of a dentist.

2. Before treatment, non-dental causes of pain in the orofacial region should be excluded (myocardial infarction, migraine, trigeminal neuralgia, etc.).

3. In the differential diagnosis of pain syndromes, attention should be paid to the localization, duration and nature of pain, stimuli that provoke pain, the results of the survey and auxiliary examinations.

4. Acute pain requires adequate treatment to exclude the risk of developing chronic pain syndrome.

5. NSAIDs are pathogenetically based drugs for the treatment of patients with pain syndrome.

6. Planning a course of treatment with NSAIDs, should take into account not only the duration of the pain syndrome, but also the presence of inflammation that accompanies most diseases of the maxillofacial region (alveolitis, periostitis, pericoronitis, lymphadenitis, trigeminal neuropathy, etc.) and the postoperative period (tooth extraction, gingivectomy, etc.).

7. Analysis of the literature indicates the need for an individual approach to the choice of NSAIDs: dose, duration of using, taking into account not only their effectiveness, but also safety.

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