Review Article

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Chronopathophysiological justification of prevention and treatment of dental diseases in children

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Abstract

INTRODUCTION. This article is devoted to the chronophysiological aspects of the prevention and treatment of dental diseases in children. The influence of biorhythms on the development, course, and prevention of dental pathologies in the pediatric population is considered a promising direction in modern dentistry. In both domestic and international literature, this issue is insufficiently addressed, which underscores the relevance of further research in this area.

AIM. To deepen understanding of chronodiagnosis and chronotherapy of dental diseases in children, aiming to optimize the treatment process through early diagnosis and the timely implementation of personalized preventive and therapeutic interventions.

MATERIALS AND METHODS. Within the framework of this article, an analytical review of domestic and international publications addressing biorhythmological and chronophysiological aspects of dental diseases was conducted. The analysis included an evaluation of data on the influence of circadian rhythms on the condition of dental hard tissues, periodontium, and oral mucosa, as well as the particularities of their consideration in the implementation of preventive and therapeutic interventions in children.

RESULTS. The conducted analysis demonstrated that the influence of biorhythms on the dental health of children is systemic in nature. Taking chronophysiological patterns into account enables increased effectiveness of preventive measures, improved treatment outcomes, and a reduction in the incidence of complications.

CONCLUSIONS. The chronophysiological approach in pediatric dentistry represents a promising direction capable of significantly enhancing the quality of dental care. Deepening knowledge of biorhythms and their application in practice will contribute to the development of personalized dentistry and stimulate professional interest in further investigation of the biorhythmological foundations of diagnosis and therapy.

Keywords: children, biorhythms, chronotherapy, dental diseases.

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Хронопатофизиологическое обоснование профилактики и лечения стоматологических заболеваний у детей

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Резюме

ВВЕДЕНИЕ. Статья посвящена хронофизиологическим аспектам профилактики и лечения стоматологических заболеваний у детей. Вопросы влияния биоритмов на развитие, течение и профилактику стоматологических патологий у детского контингента рассматриваются как перспективное направле-

ние современной стоматологии. В литературе, как отечественной, так и зарубежной, данная проблема освещена крайне слабо, что обусловливает актуальность дальнейших исследований в этой области.
ЦЕЛЬ. Углубить представления о хронодиагностике и хронотерапии стоматологических заболеваний у детей для оптимизации лечебного процесса за счет ранней диагностики и своевременного проведения персонализированных профилактических и лечебных мероприятий.
МАТЕРИАЛЫ И МЕТОДЫ. В рамках статьи проведен аналитический обзор отечественных и зарубежных публикаций, посвященных биоритмологическим и хронофизиологическим аспектам стоматологических заболеваний. Анализ включал оценку данных о влиянии циркадных ритмов на состояние твердых тканей зубов, пародонта и слизистой оболочки полости рта, а также особенностей их учета при проведении профилактических и лечебных мероприятий у детей.
РЕЗУЛЬТАТЫ. Проведенный анализ показал, что влияние биоритмов на состояние стоматологического здоровья детей имеет системный характер. Учет хронофизиологических закономерностей позволяет повысить эффективность профилактических мероприятий, улучшить результаты лечения и снизить частоту осложнений.
ВЫВОДЫ. Хронофизиологический подход в детской стоматологии представляет собой перспективное направление, способное существенно повысить качество оказания стоматологической помощи. Углубление знаний о биоритмах и их применении в практике будет способствовать развитию персонализированной стоматологии и стимулировать интерес специалистов к дальнейшему изучению биоритмологических основ диагностики и терапии.

Ключевые слова: дети, биоритмы, хронотерапия, стоматологические заболевания.

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Introduction

The widespread prevalence of dental diseases in childhood has a significant impact on the physical and psycho-emotional development of children and on their quality of life [1]. The prevalence of dental caries varies depending on the country, social conditions, and age of children, ranging from 7% to 94% [2], while the prevalence of non-carious hard tissue diseases ranges from 1.5% to 72% [3]. In Russia, the prevalence of dental caries among 12-year-old children exceeds 83%, and the prevalence of periodontal disease is 22% [4].

RESULTS

According to epidemiological surveys of early and school-age children in Moscow, 28.2% of boys and 37.2% of girls require oral cavity treatment. The need for dental care increases with age [5; 6]. Dentists from Kazan Federal University [7] note that in preschool-aged children, the prevalence of dental caries and its complications reaches 70%, while the prevalence of craniofacial developmental anomalies and diseases of the oral mucosa and periodontium reaches 80%. Many dental diseases arise before the age of one. This is more frequently observed in restored families, which should be considered when planning preventive measures and monitoring children [7].

According to L.V. Sukhacheva and colleagues [8], dental caries in permanent teeth is diagnosed in 78% of 12-year-old children and in 88% of 15-year-olds. The prevalence of inflammatory periodontal diseases in 15-year-old children ranges from 40% to 50% [9]. Thus, the most common dental diseases in childhood are dental caries and inflammatory periodontal diseases, which, in turn, negatively affect the formation of dental health in adulthood[1] [10; 11].

It should be noted that there is a close pathogenetic relationship between dental diseases and chronic diseases of internal organs, particularly in systems such as the digestive, respiratory, and cardiovascular systems. This interrelation indicates that oral health care is integral to maintaining overall human health. Therefore, increased attention must be paid to the prevention of dental diseases, utilizing highly effective technological approaches [8; 12].

The core principles of specialized preventive measures are presented in detail in the Federal State Program for the Primary Prevention of Dental Diseases among the population of Russia, including children of various age groups, beginning from the neonatal period. The available medical literature includes numerous works – monographs, articles, methodological guidelines, and textbooks – that address this issue, expanding knowledge on the factors contributing to the development of dental diseases in children, as well as on methods for their prevention and treatment. Unfortunately, parents and their children have limited awareness of this problem. Physicians not specializing in dentistry also pay insufficient attention to it, despite its relevance to their professional practice.

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[1] Project of the Federal State Program for Primary Prevention of Dental Diseases among the Population of Russia (Program approved by the decision of the Council of the Russian Dental Association on April 26, 2011). Available at: https://e-stomatology.ru/star/work/2011/sovet_april/03_profil.htm (accessed: 27.12.2024).

Currently, the central ideology in medicine is an individualized (personalized) approach to the patient and their health issues. The primary goal of a personalized approach is disease prevention rather than treatment. To prevent dental diseases in children, it is necessary to determine the genetic predisposition to their development, diagnose preclinical metabolic disorders, and identify pathogenetically significant risk factors [13–18].

Life in living organisms is impossible without interaction with the environment. Under the influence of environmental factors, evolutionarily determined endogenous biorhythms have developed in organisms, associated with specific molecular-genetic mechanisms. Biological rhythmicity ensures the organism's adaptation to the external environment. Biorhythms are based on the alternating interaction of qualitatively distinct states: catabolism and anabolism, dissimilation and assimilation, excitation and inhibition. Through biorhythms, the development of the organism and the synchronization of its physiological functions with diverse changes in the external and internal environment are achieved via the rhythmic alternation of these processes. Determining biorhythms allows for the assessment of the functional state of the organism and its adaptive capabilities [19].

The alternation of light and dark periods during the day is an important environmental factor affecting 24-hour circadian rhythms. This stimulus, known as a zeitgeber (a technical term from German, meaning "timer"), is perceived by the retinal photoreceptors, which activate a complex photoperiodic system associated with all organs and systems of the body. The central elements of the photoperiodic system include the suprachiasmatic nucleus (SCN) of the hypothalamus, the pineal gland, and several other brain structures. Within these structural regions are the central circadian clocks, which generate neuronal and hormonal signals for the peripheral clocks.

Peripheral molecular clocks regulate the circadian rhythm, which is based on autonomous transcriptional and translational feedback loops among key components of the circadian clocks. These components include the heterodimeric protein complex CLOCK, encompassing the circadian locomotor cycle kaput, and BMAL1, which regulates the activity of transcriptional genes such as Per1, Per2, Per3, Cry1, and Cry2. The molecular genes are also regulated by their associated transcription factors, DEC1 and DEC2.

Circadian clocks in various tissues receive signals either from the central circadian clocks or directly from the time of day, thereby regulating the timing of physiological functions. Light and the daily cycle activate CLOCK and BMAL1, initiating the transcription of CRY and PER genes. When a certain level of mRNA is reached, the CRY and PER proteins form dimers that inhibit CLOCK and BMAL1 complexes in the cell nucleus, preventing new transcription. During the night, light degrades the dimers, allowing CLOCK and BMAL1 to become active and initiate a new transcriptional cycle.

Through this molecular mechanism, the circadian timing system controls various physiological processes. Central circadian clocks receive light or dark signals and transmit them to peripheral clocks. Central and peripheral circadian clocks interact with each other, ensuring the regular activity of biorhythms [20; 21].

Biorhythms, depending on the duration of their periods, are classified as low-, medium-, and high-frequency. Among low-frequency biorhythms, the most well-known are monthly, seasonal, and annual rhythms; among medium-frequency biorhythms are circadian (approximately 24-hour) rhythms; and among high-frequency biorhythms are those with periods shorter than 30 minutes, such as respiratory and heart rates. The circadian rhythm, associated with the alternation of day and night, plays the most important role among biorhythms.

All functions in a living organism are characterized by wave-like patterns and a rhythmic organization of alternating processes. The assessment of natural biorhythms forms the basis for diagnosing the early stages of pathological processes, which can be used to prevent their development.

The effectiveness of preventive and therapeutic interventions in all human diseases, including dental diseases in children, can be increased through a chronophysiological approach. Chronobiological research methods make it possible to predict disease development at a preclinical stage. The use of chronotherapy as a treatment method, based on the consideration of the organism's biorhythms – primarily circadian rhythms – is a promising direction in preventive and therapeutic care. However, unfortunately, this approach has not yet been fully developed [22].

Biorhythms are associated with all organs and systems of the body, where they participate in the regulation of physiological and metabolic processes. There is evidence of their influence on the development of teeth and oral tissues. It has been established that disruptions of the circadian rhythm may be associated with impaired formation of dental pulp, periodontal tissues, oral mucosa, enamel, and dentin, as well as the development of mandibular hypoplasia and the occurrence of oral cancer [20; 21; 23–25].

The causes of circadian rhythm disturbances in contemporary children are most often the following:

1) constant exposure to artificial light;

2) excessive screen time (frequent use of smartphones, tablets, and computers emitting blue light, which suppresses melatonin production);

3) relocation across time zones;

4) irregular daily routines (insufficient or excessive sleep with disrupted circadian rhythms);

5) stress, anxiety, or depression associated with lifestyle;

6) unbalanced nutrition, including high consumption of caffeine, other stimulants, and sugar.

If these disturbances occur repeatedly, they can provoke biorhythm disorders and shift sleep–wake cycles, which inevitably affects oral health [26; 27].

These and other disturbances become regular because children may wake up and go to bed at varying times, which disrupts their internal sleep–wake clocks. The repeated occurrence of these patterns causes them to become habitual for the body and may persist for a long time if no measures are taken to restore normal circadian rhythm. Parents, as a rule, pay little attention to these disturbances, and strict daily routines or restrictions on gadget use are often perceived as overly authoritarian in child-rearing.

Consequently, it can be stated that the proper functioning of the circadian timing system plays a key role in maintaining oral health. Understanding the circadian timing system can be applied for targeted treatment with consideration of the optimal timing of procedures, thereby achieving maximum efficacy and minimizing potential side effects.

Desynchronization of internal biorhythms, as well as misalignment between the body's biorhythms and external environmental rhythms, is one of the key causes of pathological disorders in the organism. In all pathological processes, signs of dysrhythmia are observed, the severity of which correlates with the extent of the disorder. In such cases, it becomes necessary to administer medications taking into account the rhythm of the body's sensitivity to them. This objective can be achieved using a chronopharmacological approach to disease treatment. This approach reflects the principle of individualized, more economical, and safer therapy for a specific patient. Chronopharmacology, which studies the effects of drugs on the biorhythms of pathological processes and the organism's sensitivity to them at different times of day, forms the basis of chronotherapy.

When implementing chronotherapy, multiple factors must be considered: the individual characteristics of patients, their age, the pathogenesis of the disease, the mechanisms of drug action, and the biorhythms of the organism's sensitivity to these drugs [19; 28; 29].

The dento-maxillary system is closely interconnected with almost all organs and systems of the body. It participates in the processes of digestion, speech, and respiration. Through sensory interactions, the dento-maxillary system influences auditory, visual, olfactory, gustatory, vestibular, motor, muscular, and pain functions [30; 31].

The foundations of chronodentology are based on evidence that the dental pulp, periodontal tissues, oral mucosa, enamel, dentin, and mandibular bone clearly exhibit peripheral clocks that regulate their key processes [20–23]. It has been established that clock genes, via melatonin receptors modulating mitochondrial functions, can influence the differentiation of osteoblasts, fibroblasts, and ameloblasts, as well as the development of connective tissues, oral tissues, craniofacial structures, and enamel.

An early sign of desynchronosis may be altered sensitivity of taste receptors. Normally, the tongue exhibits low taste sensitivity in the morning, which increases by 19:00–21:00. This should be taken into account during dental monitoring of a child. Disruption of the circadian rhythm leads to immune dysregulation and increased oxidative stress, contributing to the development of periodontitis. Under these conditions, there is a high risk of oral and craniofacial malformations, mandibular skeletal hypoplasia, and tumors, including malignant neoplasms such as carcinoma. In such cases, chronopharmacotherapy may serve as a reliable and effective method for personalized prevention and treatment of dental diseases [20; 22–25].

Unfortunately, the practice of applying chronodiagnosis and chronotherapy in pediatric dentistry in our country has not yet reached the required level of development. Modern dentistry is primarily based on standardized protocols familiar to most practitioners. While this ensures an adequate level of dental care, it limits progress in advancing the field. Among many contemporary clinicians, the use of chronotherapy for dental diseases – especially in children – faces notable resistance. They remain skeptical of this treatment method and require more convincing evidence of its efficacy.

The limited number of clinical studies on chronotherapy in pediatric dentistry complicates the establishment of a consistent practice for its use. The lack of empirical data primarily restricts its widespread adoption. At present, it is crucial to investigate the relationship between environmental circadian rhythms and the biorhythms of dental disease progression. This need is increasingly emphasized in calls for the development of personalized medicine, including within the dental specialty. Disruption of biorhythms indicates early signs of pathological processes; therefore, chronodiagnosis allows for the prediction of disease formation at a preclinical stage. Chronotherapy, as a treatment method based on the consideration of the organism's circadian rhythms, requires a deeper understanding of biological processes and the mechanisms through which time influences the body [27; 28].

The process of tooth development – including tissue mineralization and cell differentiation – as well as the formation of basal cells in the oral cavity, saliva production, and salivary secretion, is regulated by circadian clocks. Teeth play a crucial role in fulfilling the basic life needs of the human organism, primarily in food intake. Throughout human evolution, dietary changes prompted adaptive remodeling of teeth, including alterations in their morphology and genetics. These changes were possible only through synchronization with the rhythmically changing environmental conditions. This ability to synchronize with the environment is mediated by molecular clocks. Such knowledge is essential for justifying chronotherapeutic approaches in pediatric dentistry. Literature indicates that circadian fluctuations in salivary pH influence the structure of tooth enamel, as well as all oral tissues and the functioning of various organs and systems [18; 19; 21–23].

Saliva serves as an active protector of oral tissues. Disruption of circadian rhythms in patients may lead to hyposalivation, which can cause difficulties with swallowing and mastication, and in some cases, speech impairment, altered taste perception, and discomfort in the oral cavity, predominantly during nighttime. Compelling evidence demonstrates that the oral mucosa exhibits rhythmic circadian expression of Per1, Cry1, and BMAL1 in the evening and at night. Dysfunction of these genes leads to uncontrolled DNA damage and neoplastic growth, potentially resulting in malignant neoplasms, including oral, head, and neck cancers [21].

Consequently, saliva, as a relevant chronobiological object of the organism, can be reasonably utilized for the diagnosis of early (preclinical) stages of dental diseases, as well as for planning and implementing early chronotherapeutic interventions [22].

In addition to general etiological factors contributing to the development of early childhood caries, chronophysiological aspects must also be considered. It has been established that in children, salivary secretion slows down and salivary pH decreases at night, impairing the natural self-cleaning process of the oral cavity. This, in turn, promotes the formation of a cariogenic environment; therefore, it is recommended that young children avoid acidic juices, salt, and sugar before bedtime and during the night [2; 32; 33].

At present, there is a very low level of attention to chronophysiological aspects in dentistry, particularly in pediatric dentistry. To draw attention to chronodiagnostic and chronotherapeutic approaches, this article analyzes research findings not only in children but also in adults, which may positively influence the development of chronotherapy in pediatric dentistry.

Biological rhythms allow living organisms to adapt to environmental changes, such as day–night cycles and seasonal variations. The better this adaptation, the stronger the individual's health. Disease begins with a disruption of the biorhythms of organs and systems, with clinical symptoms appearing at later stages. Assessment of biorhythm characteristics enables the detection of pathological processes at a pre-disease stage.

Provision of dental care is inherently associated with pain responses. Consequently, many patients, especially children, are reluctant to visit dentists, which negatively impacts treatment outcomes. In such cases, a chronophysiological approach can help by providing data on individual circadian rhythms of pain sensitivity and identifying time intervals during which pain perception is reduced.

In a study by Efremova and Shemonaev [34], maximal levels of pain and tactile sensitivity in patients aged 19 to 39 were observed between 12:00 and 14:00, while minimal sensitivity occurred at 08:00 and from 18:00 to 20:00. Literature data indicate that dental pulp pain sensitivity largely depends on the daily concentration of melatonin in the body. Higher melatonin levels are associated with reduced pain sensitivity [35]. Consequently, administering analgesics in the afternoon, especially in the evening, produces more profound and prolonged local and systemic anesthesia compared with morning administration [36]. The maximal analgesic effect of lidocaine for dental pain occurs at 14:00–15:00, while that of meperidine and morphine occurs at 21:00 [31; 37; 38].

In dental practice, consideration of circadian rhythms extends to drugs with various mechanisms of action. For example, in cases of oral pemphigus vulgaris, prednisolone is recommended to be administered at 06:00. Nonsteroidal anti-inflammatory drugs (NSAIDs) following dental surgery should be given in the afternoon, as their analgesic and anti-inflammatory effects are enhanced during this period. Chronoradiotherapy for head and neck cancers is most effective when administered in the morning, particularly during winter, as this timing reduces the risk of radiotherapy-related side effects and severe oral mucositis [36].

A 2023 literature review conducted by an international team led by Abusamak [39] demonstrated that the use of chronoradiotherapy and chronochemotherapy in oncology patients with dental conditions significantly improves treatment outcomes and increases survival rates. Administration of analgesic drugs in the evening can achieve deeper and more prolonged local anesthesia. Animal studies have shown that tooth movement and periodontal tissue responses to orthodontic forces also follow circadian rhythms, which can influence bone metabolism. The peak of bone tissue turnover occurs in the late morning and early evening [36]. These findings may inform the timing of dental implant placement.

Platinum-based chemotherapeutic agents (cisplatin, carboplatin, oxaliplatin) and fluorouracil are recommended in the evening (peak efficacy at 16:00), coinciding with circadian peaks in their antioxidant activity, which helps prevent cellular damage. Despite the relatively small number of studies conducted, the review authors concluded that the application of chronotherapy in dentistry yields positive outcomes, particularly in the treatment of head and neck cancers.

When monitoring children with dental diseases, it is also necessary to consider the influence of seasonal biorhythms. According to Khubetsova [40], tooth extraction in dental patients induces a state of acute desynchronosis, accompanied by oxidative stress and complicated by coagulopathy. In patients with alveolitis, this manifests as hypercoagulation, whereas in patients with socket bleeding, it presents as hypocoagulation. Hypercoagulation in alveolitis patients is more frequently observed during the summer–autumn period, while hypercoagulation with socket bleeding and associated microcirculatory disturbances occurs predominantly in the autumn–winter period.

Data from Razmakhina [41] indicate that the most unfavorable period of the year in terms of oral homeostasis (enamel resistance, calcium and phosphorus content in saliva, and salivary mineralizing potential) in children is winter. The most favorable periods for maintaining oral homeostasis are autumn and summer.

CONCLUSION

These findings motivate further research and exploration of new approaches in the chronotherapy of dental diseases. Continued studies in this field may lead to the development of innovative methods for the treatment and prevention of dental diseases in children, taking into account their biological rhythms. Overall, chronodentistry as a specialized area of scientific research and practical knowledge is still in its nascent stage. It is hoped that increased interest in the chronophysiological aspects of pediatric dental diseases among researchers and practicing pediatric dentists, together with governmental support, will undoubtedly stimulate the development and eventual establishment of chronodentistry as a full-fledged branch of medical science.

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