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MONITORING OF NITROXIDERGIC SYSTEM INDICATORS IN THE TREATMENT OF ACUTE AND CHRONIC PURULENT RHINOSINUSITIS

Faizullaev Dilshod Shodievich
Samarkand State Medical University, Republic of Uzbekistan, Samarkand

ЎТКИР ВА СУРУНКАЛИ ЙИРИНГЛИ РИНОСИНУСИТЛАРНИ ДАВОЛАШДА НИТРОКСИДЕРГИК ТИЗИМ КЎРСАТКИЧЛАРИНИ КУЗАТИШ

Файзуллаев Дилшод Шодиевич
Самарқанд давлат тиббиёт университети, Ўзбекистон Республикаси, Самарқанд ш.

МОНИТОРИНГ ПОКАЗАТЕЛЕЙ НИТРОКСИДЕРГИЧЕСКОЙ СИСТЕМЫ ПРИ ЛЕЧЕНИИ ОСТРЫХ И ХРОНИЧЕСКИХ ГНОЙНЫХ РИНОСИНУСИТОВ

Файзуллаев Дилшод Шодиевич
Самаркандский государственный медицинский университет, Республика Узбекистан, г. Самарканд

e-mail: dilshod.fayzullaev@sammi.uz

Резюме. *Ўткир ва сурункали йиринли риносинуситлар катта тиббий-ижтимоий муаммо бўлиб, катталарнинг 5-15% ва болаларнинг 5% ни зарарлайди. Ташхислаш ва даволашдаги ютуқларга қарамай, ушбу касалликлар патогенезида нитроксидергик тизимнинг роли етарлича ўрганилмаган. Тадқиқот мақсади - риносинуситларнинг кечишини аниқлаш ва даволаш самарадорлигини ошириш учун нитроксидергик тизимнинг функционал ҳолатини ўрганиш. Ушбу проспектив рандомизирланган тадқиқотда 120 нафар ўткир ва сурункали йиринли риносинуситли беморлар ва 25 нафар соғлом кўнгиллилар иштирок этди. Риносинуситларда нитроксидергик тизим кўрсаткичларининг сезиларли бузилиши ва уларнинг коррекцияси даволаш натижаларини яхшилаши кўрсатилди.*

Калит сўзлар: *Ўткир риносинусит, сурункали риносинусит, нитроксидергик тизим, азот оксиди, мукоцилиар клиренс, ҳаёт сифати, комплекс даволаш.*

Abstract. *Acute and chronic purulent rhinosinusitis represent a significant medical and social problem, affecting 5-15% of the adult population and 5% of children. Despite advances in diagnosis and treatment, the role of the nitroxidergic system in the pathogenesis of these diseases remains poorly understood. The aim of this study was to evaluate the functional state of the nitroxidergic system to determine the course of rhinosinusitis and improve treatment effectiveness. This prospective, randomized study involved 120 patients with acute and chronic purulent rhinosinusitis and 25 healthy volunteers. Significant impairment of nitroxidergic system parameters was demonstrated in rhinosinusitis, and its correction improves treatment outcomes.*

Keywords: *Acute rhinosinusitis, chronic rhinosinusitis, nitric oxide system, nitric oxide, mucociliary clearance, quality of life, complex treatment.*

Introduction. Acute and chronic purulent rhinosinusitis represent one of the most prevalent conditions in otorhinolaryngology, affecting 5-15% of adults and approximately 5% of children globally. The socioeconomic burden of these conditions is substantial, with rhinosinusitis being the leading cause of antibiotic prescriptions (20% of all prescriptions) and generating healthcare costs exceeding $11 billion annually in the United States alone. In Europe, the prevalence ranges from 6.9% to 27.1%, while in Korea it reaches 8.4%, and in China approximately 8% [5, 9, 13, 14].

The pathogenesis of rhinosinusitis involves complex interactions between anatomical factors, mucociliary dysfunction, and inflammatory mediators. Recent research has highlighted the crucial role of the nitric oxide (NO) system in the pathophysiology of sinonasal diseases. NO, synthesized from L-arginine by nitric oxide synthase (NOS), plays multiple roles in respiratory tract physiology, including vasodilation, antimicrobial activity, and regulation of ciliary function [2, 7, 10, 12].

In healthy paranasal sinuses, NO is produced at high concentrations by the epithelium and serves as a natural antimicrobial agent, maintaining sterile condi-

tions within the sinuses. The discovery of NO production by sinonasal mucosa has provided new insights into the functional significance of paranasal sinuses, which were previously considered "functionless air-filled cavities" [1, 6, 11, 12].

However, during inflammatory processes, the NO system undergoes significant alterations. Studies have shown that patients with acute and chronic rhinosinusitis exhibit decreased nasal NO levels, impaired mucociliary transport, and accumulation of stable NO metabolites (nitrites and nitrates) in sinus secretions. These changes contribute to perpetuation of the inflammatory process and development of complications [2, 5, 8, 9].

Despite advances in surgical techniques and antimicrobial therapy, the management of rhinosinusitis remains challenging, with recurrence rates remaining high. Current treatment approaches often fail to address the underlying pathophysiological mechanisms involving NO system dysfunction. Understanding these mechanisms could lead to more targeted therapeutic interventions and improved patient outcomes [12, 13].

This study aims to evaluate the functional state of the nitroксидергic system in patients with acute and chronic purulent rhinosinusitis and develop optimized treatment approaches based on correction of NO system parameters.

Research Objective. To study the functional state of the nitric oxide system in determining the course of rhinosinusitis and improving treatment effectiveness.

Materials and Methods. This prospective, randomized, comparative study was conducted at the Department of Otorhinolaryngology, Samarkand State Medical University, from January 2020 to May 2022. The study population consisted of 120 patients diagnosed with acute and chronic purulent rhinosinusitis and 25 healthy volunteers who served as controls. Patients were allocated into two study groups and one control group. The main group included 62 patients who received treatment based on normalization of the nitric oxide (NO) system according to a developed algorithm. The comparison group consisted of 58 patients who received conventional treatment. The control group comprised 25 healthy volunteers without clinical signs of rhinosinusitis or systemic pathology.

Patients were eligible for inclusion if they presented with clinical signs of acute or chronic rhinosinusitis and were aged 18 years or older. Exclusion criteria were established to minimize confounding factors and included a history of corticosteroid or antihistamine use, acute asthma episodes, cystic fibrosis, vasomotor rhinitis, odontogenic rhinosinusitis, previous endoscopic sinus surgery, chronic systemic diseases, oncological conditions, and pregnancy.

The demographic composition of the study population included 69 women (57.5%) and 51 men (42.5%). The mean age in the main group was 37.08 ± 16.92 years, in the comparison group 37.43 ± 16.57 years, and 36.68 ± 17.32 years in the control group. The majority of patients in both study groups (64–66%) were in the age range of 36 to 54 years.

All participants underwent comprehensive clinical evaluation, which included standard otorhinolaryngological examination and assessment of quality of life using the visual analog scale (VAS). Endoscopic evaluation was performed using a 4 mm, 0° nasal endoscope to assess the anatomical and pathological state of the nasal cavity and paranasal sinuses. Computed tomography (CT) of the paranasal sinuses was performed for all patients, and findings were graded according to the Lund-Mackay scoring system to quantify the extent of sinus involvement. Functional assessment included measurement of mucociliary transport time using the saccharin test to evaluate the physiological clearance function of the nasal mucosa.

Assessment of the nitric oxide system involved quantitative measurement of nasal NO concentrations using an electrochemical analyzer, as well as evaluation of NO metabolites in blood and urine by enzyme-linked immunosorbent assay (ELISA). Microbiological analysis was conducted through culture of nasal discharge and sinus aspirates to identify the causative pathogens. In addition, nasal secretion pH was measured using pH-metry to evaluate the local biochemical environment of the nasal mucosa.

All procedures were performed following standard operating protocols to ensure reliability and reproducibility of the results. The combination of clinical, endoscopic, imaging, functional, biochemical, and microbiological assessments allowed for comprehensive characterization of the disease status, evaluation of treatment efficacy, and the role of the NO system in the pathophysiology of acute and chronic purulent rhinosinusitis.

The study design was prospective and randomized, with patients assigned to the main or comparison group based on a random allocation protocol to minimize selection bias. Both groups were followed longitudinally to evaluate the effects of the interventions on clinical, functional, and biochemical parameters over the study period. All patients provided written informed consent prior to inclusion, and the study protocol was approved by the local ethics committee of Samarkand State Medical University, in accordance with the principles of the Declaration of Helsinki.

Treatment in the main group was guided by the normalization of NO system parameters according to the algorithm developed by the research team. This approach integrated both pharmacological and non-pharmacological interventions targeting the restora-

tion of NO homeostasis and modulation of local inflammatory responses. Patients in the comparison group received conventional treatment for acute and chronic purulent rhinosinusitis, which included standard antibiotic therapy, decongestants, and symptomatic management according to existing clinical guidelines. Healthy volunteers in the control group did not receive any interventions but underwent the same set of assessments for comparative analysis.

Outcome measures included changes in clinical symptoms as quantified by VAS scores, endoscopic findings, CT Lund-Mackay scores, mucociliary transport time, nasal NO concentration, NO metabolite levels in blood and urine, microbiological profile of nasal and sinus secretions, and nasal pH values. The integration of these multidimensional assessments allowed for the correlation of local and systemic NO status with disease severity, functional impairment, and microbial colonization, as well as the evaluation of the effectiveness of the proposed treatment algorithm.

All data were collected and recorded systematically using standardized forms. To ensure reproducibility and accuracy, all measurements were performed by trained clinicians and laboratory personnel blinded to group allocation wherever feasible. This methodological approach provided a robust framework for assessing both the pathophysiological mechanisms underlying purulent rhinosinusitis and the clinical efficacy of NO system-targeted interventions compared to conventional therapy.

Results. The clinical assessment revealed significant differences between the study groups in terms of symptom severity and treatment outcomes. Patients in the main group, who received therapy targeting the normalization of the nitric oxide (NO) system, demonstrated significantly lower symptom severity scores compared to those receiving conventional treatment, indicating the potential effectiveness of the optimized intervention approach ($p<0.05$).

Analysis of NO system parameters demonstrated marked alterations in patients with both acute and chronic purulent rhinosinusitis. Nasal NO concentrations in healthy volunteers averaged 426.76 ± 143.27 ppb, whereas patients with acute rhinosinusitis exhibited significantly reduced levels of 187.3 ± 58.4 ppb ($p<0.001$) and those with chronic rhinosinusitis demonstrated even lower concentrations of 156.8 ± 62.1 ppb ($p<0.001$). Conversely, systemic NO metabolites measured in blood were elevated in the patient groups, with healthy controls showing 18.7 ± 3.2 μmol/L, acute rhinosinusitis patients 31.4 ± 8.7 μmol/L ($p<0.001$), and chronic rhinosinusitis patients 38.9 ± 11.2 μmol/L ($p<0.001$). Functional evaluation using the saccharin test revealed a significant impairment of mucociliary transport in affected patients. The control group exhibited a mean transport time of 8.2 ± 2.1 minutes, whereas acute rhinosinusitis patients required 19.2 ± 5.8 minutes ($p<0.001$) and chronic rhinosinusitis patients 24.7 ± 7.3 minutes ($p<0.001$). These findings indicate a clear relationship between rhinosinusitis severity, NO system dysfunction, and impaired mucociliary clearance.

Treatment outcomes further highlighted the superiority of the NO system-targeted approach. Complete symptom resolution at one month was observed in 87.1% of patients in the main group, compared to 65.5% in the comparison group receiving conventional therapy ($p<0.01$). Mucociliary transport improved significantly in the main group, with transport time decreasing from 22.4 ± 6.8 minutes at baseline to 11.3 ± 3.2 minutes after treatment. In contrast, the comparison group showed a reduction from 21.8 ± 7.1 to 16.7 ± 4.8 minutes ($p<0.05$). Patient-reported quality of life, measured by the visual analog scale (VAS), improved from 7.8 ± 1.4 to 2.1 ± 0.8 points in the main group, whereas the comparison group improved from 7.6 ± 1.6 to 4.3 ± 1.2 points ($p<0.001$), indicating a more pronounced subjective benefit of the NO-targeted intervention.

Microbiological analysis revealed that the most frequently isolated pathogens in patients with purulent rhinosinusitis were Streptococcus pneumoniae (28.3%), Haemophilus influenzae (21.7%), Staphylococcus aureus (19.2%), and mixed flora in 30.8% of cases. The treatment protocol for the main group incorporated L-arginine supplementation at a dose of 3 grams per day to provide substrate for NO synthesis, combined mucolytic and antimicrobial therapy using Fluimucil-antibiotic, and Sinuforte, a herbal preparation aimed at enhancing sinus drainage. Conventional therapy, including antibiotics, nasal decongestants, and saline irrigation, was administered to both groups as indicated.

A representative clinical case illustrates the effectiveness of the optimized approach. A 42-year-old male patient presented with chronic rhinosinusitis lasting eight months. Initial assessment demonstrated nasal NO of 142 ppb, mucociliary transport of 28 minutes, a VAS score of 8.2 points, and a CT Lund-Mackay score of 18/24. Following four weeks of the NO system-targeted treatment, nasal NO increased to 298 ppb, mucociliary transport improved to 12 minutes, the VAS score decreased to 2.1 points, and complete symptom resolution was achieved.

Statistical analysis was performed using SPSS version 23.0. Non-parametric comparisons between groups were conducted using the Mann-Whitney U test, and Spearman correlation analysis was applied to assess associations between variables. Statistical significance was set at $p<0.05$. The results collectively demonstrate that NO system dysfunction is closely associated with disease severity, impaired mucociliary clearance, and symptom burden, while targeted correction of the NO system provides signif-

icant clinical, functional, and quality-of-life benefits compared to conventional treatment.

Discussion. The findings of this study highlight the critical role of the nitric oxide system in the pathophysiology of both acute and chronic purulent rhinosinusitis. Significant reductions in nasal NO concentrations observed in affected patients, accompanied by elevated systemic NO metabolites, suggest a dysregulation of local and systemic NO homeostasis. This imbalance appears to correlate closely with disease severity, impaired mucociliary transport, and clinical symptom burden. The saccharin test results further confirmed functional impairment of mucociliary clearance, which is a key protective mechanism of the nasal mucosa against microbial invasion and inflammation.

Patients treated with the NO system-targeted approach demonstrated more pronounced improvements across all measured parameters compared to conventional therapy. The accelerated normalization of mucociliary transport, higher rates of symptom resolution, and significant improvement in patient-reported quality of life underscore the clinical relevance of NO modulation. The integration of L-arginine supplementation provided a substrate for endogenous NO synthesis, while the combined use of mucolytic and antimicrobial therapy, along with herbal sinus drainage support, appears to enhance both biochemical and functional recovery. These findings are consistent with current evidence suggesting that interventions aimed at restoring NO homeostasis can improve mucosal defense mechanisms, reduce local inflammation, and promote more effective resolution of infection.

Microbiological analysis indicated a predominance of Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus, and mixed bacterial flora, reflecting the typical microbial spectrum associated with purulent rhinosinusitis. The observed reduction in bacterial load and improvement in clinical outcomes following the optimized treatment protocol suggest that NO system normalization may enhance the efficacy of conventional antimicrobial therapy, potentially through modulation of local immune responses and improvement of mucociliary clearance.

The case example presented in this study illustrates the practical implications of these findings. Rapid improvement in NO levels, mucociliary transport, symptom scores, and CT findings following the NO-targeted treatment demonstrates the translational potential of this approach for routine clinical practice. The results also support the hypothesis that local NO deficiency contributes to chronicity and functional impairment in rhinosinusitis, and that correction of this imbalance can accelerate recovery and reduce the risk of complications.

Overall, this study provides strong evidence for the inclusion of NO system evaluation and targeted correction in the comprehensive management of purulent rhinosinusitis. The combined use of biochemical, functional, and clinical assessments allows for a more precise understanding of disease mechanisms and the development of personalized therapeutic strategies. Future research should aim to further elucidate the molecular mechanisms linking NO dysregulation, mucociliary dysfunction, and microbial colonization, as well as to assess the long-term benefits of NO-targeted therapy in diverse patient populations.

Conclusions. The findings of this study provide compelling evidence that patients with both acute and chronic purulent rhinosinusitis exhibit significant dysfunction of the nitric oxide system, characterized by decreased local nasal NO production and elevated systemic NO metabolites. This dysregulation is closely associated with increased symptom severity, impaired mucociliary clearance, and deterioration in patient-reported quality of life, indicating a central role of the NO system in the pathogenesis and progression of rhinosinusitis. Targeted correction of NO system parameters through a structured therapeutic protocol resulted in markedly improved clinical outcomes compared to conventional treatment. Patients receiving the NO-targeted therapy demonstrated higher rates of complete symptom resolution, accelerated restoration of mucociliary transport, and greater improvements in quality-of-life measures, confirming the clinical relevance of this approach.

The optimized treatment regimen, which incorporated L-arginine supplementation to provide substrate for endogenous NO synthesis, Fluimucil-antibiotic therapy to combine mucolytic and antimicrobial effects, and Sinuforte to enhance sinus drainage, proved to be safe, effective, and superior to standard care. These results support the implementation of NO system evaluation and targeted correction as a routine component of comprehensive management for patients with purulent rhinosinusitis.

Furthermore, the study emphasizes the potential of NO-targeted therapy as a novel and mechanism-based treatment strategy, capable of addressing both the biochemical and functional aspects of the disease. Monitoring NO system parameters not only facilitates individualized treatment planning but also offers an objective method for assessing therapeutic response. Future research should focus on refining dosing regimens, exploring long-term outcomes, and identifying specific patient subgroups most likely to benefit from NO-based interventions. Overall, the integration of NO system modulation into clinical practice represents a promising advancement in the management of acute and chronic purulent rhinosinusitis, with the potential to improve both clinical outcomes and patient quality of life.

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МОНИТОРИНГ ПОКАЗАТЕЛЕЙ НИТРОКСИДЕРГИЧЕСКОЙ СИСТЕМЫ ПРИ ЛЕЧЕНИИ ОСТРЫХ И ХРОНИЧЕСКИХ ГНОЙНЫХ РИНОСИНУСИТОВ

Файзуллаев Д.Ш.

Резюме. *Острые и хронические гнойные риносинуситы представляют значительную медико-социальную проблему, поражая 5-15% взрослого населения и 5% детей. Несмотря на прогресс в диагностике и лечении, роль нитроксидергической системы в патогенезе данных заболеваний остается недостаточно изученной. Цель исследования - изучить функциональное состояние нитроксидергической системы для определения течения риносинуситов и повышения эффективности лечения. В данном проспективном рандомизированном исследовании приняли участие 120 пациентов с острыми и хроническими гнойными риносинуситами и 25 здоровых добровольцев. Показано значительное нарушение показателей нитроксидергической системы при риносинуситах, коррекция которых улучшает результаты лечения.*

Ключевые слова: *Острый риносинусит, хронический риносинусит, нитроксидергическая система, оксид азота, мукоцилиарный клиренс, качество жизни, комплексное лечение.*