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CLINICAL AND LABORATORY BASIS FOR THE USE OF EFFERENT THERAPY (ILBI) IN IMPROVING THE FUNCTIONAL STATE OF PERIODONTAL TISSUES IN PATIENTS WITH CHRONIC LEUKEMIA

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ABSTRACT: Chronic leukemia is associated with profound immune dysfunction, microcirculatory disorders, thrombocytopenia, and granulocytopenia, which collectively lead to severe, rapidly progressive, and treatment-resistant periodontitis. Efferent therapy methods, particularly intravenous laser blood irradiation (ILBI), have emerged as promising adjunctive modalities for managing periodontal disease in this vulnerable patient population. This literature review analyzes the clinical and laboratory basis for the use of ILBI (VLOK therapy) in improving the functional state of periodontal tissues in patients with chronic leukemia. The key mechanisms of action include immunomodulation (normalization of immunoglobulin levels, reduction of proinflammatory cytokines), improvement of blood rheology and microcirculation, antioxidant effects, antimicrobial activity, and stimulation of reparative processes in periodontal tissues. Clinical studies demonstrate that ILBI significantly reduces gingival bleeding (BOP reduction by 4.8-fold), decreases periodontal pocket depth, increases salivary flow rate (from 0.127 to 0.28 mL/min), normalizes IgG and IgE levels (29.3% increase and 79.9% reduction respectively), suppresses proinflammatory cytokines (4.4–4.7-fold reduction), and reduces periodontopathogen load (63.6% reduction for T. denticola, 57.0% for A. actinomycetemcomitans). The evidence supports the integration of ILBI into comprehensive periodontal treatment protocols for chronic leukemia patients as a safe, pathogenetically justified, and clinically effective efferent therapy modality.

Keywords: chronic leukemia, periodontitis, efferent therapy, intravenous laser blood irradiation (ILBI), VLOK therapy, periodontal tissues, immunomodulation, microcirculation, cytokines, periodontal pathogens.

INTRODUCTION

Chronic leukemia, encompassing chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML), is a hematological malignancy characterized by the clonal expansion of malignant lymphocytes or myeloid progenitor cells. Despite significant therapeutic advances, including targeted therapies (tyrosine kinase inhibitors for CML, BTK inhibitors for CLL) and hematopoietic stem cell transplantation, the disease continues to be associated with substantial morbidity due to secondary complications, including oral manifestations.

The oral cavity serves as a mirror of systemic health, and this is particularly evident in chronic leukemia. The triad of immunosuppression, cytopenias (neutropenia, thrombocytopenia), and

microcirculatory disturbances creates a unique pathophysiological environment that profoundly affects periodontal tissues. Patients with chronic leukemia frequently develop severe, rapidly progressive, and recurrent periodontitis that differs significantly from periodontitis in immunocompetent individuals in terms of clinical presentation, response to therapy, and prognosis.

Conventional periodontal treatment approaches—scaling and root planing, antimicrobial therapy, and oral hygiene instructions—often yield suboptimal results in chronic leukemia patients. The underlying immune dysfunction impairs the host's ability to control periodontal pathogens, while thrombocytopenia complicates invasive procedures and exacerbates gingival bleeding. Furthermore, the systemic inflammatory burden associated with periodontitis may negatively affect the course of the underlying hematological disease.

Efferent therapy methods, which focus on the removal or neutralization of pathogenic factors from the bloodstream and the modulation of systemic homeostasis, have gained increasing attention in recent years. Among these methods, intravenous laser blood irradiation (ILBI), also known as VLOK therapy (from the Russian "VnutriVenoznoe Lazernoe Obluchenie Krovi"), has demonstrated particular promise. ILBI involves the exposure of blood to low-intensity laser radiation (typically 632 nm wavelength, 1.5–2.0 mW power) via an intravascular fiber-optic light guide, inducing a cascade of photochemical and photophysical reactions that produce systemic therapeutic effects.

This literature review aims to provide a comprehensive analysis of the clinical and laboratory basis for the use of ILBI in improving the functional state of periodontal tissues in patients with chronic leukemia, focusing on the pathophysiological rationale, mechanisms of action, and clinical evidence of efficacy.

PATHOPHYSIOLOGICAL BASIS OF PERIODONTAL TISSUE DYSFUNCTION IN CHRONIC LEUKEMIA

Immunological Dysregulation

Chronic leukemia induces profound alterations in both innate and adaptive immunity. In CLL, the accumulation of functionally defective monoclonal B cells leads to hypogammaglobulinemia (particularly low IgG), impaired antibody responses to neoantigens, and T-cell dysfunction. In CML, the Philadelphia chromosome and BCR-ABL fusion protein disrupt normal myelopoiesis, leading to the accumulation of immature myeloid cells that fail to mount effective immune responses.

The impact on periodontal tissues is substantial. Reduced serum IgG levels (mean 5.98±0.81 g/L, below the normal lower limit of 6.0 g/L) impair opsonization and phagocytosis of periodontopathogens. Elevated IgE levels (152.70±23.88 ng/mL, three times the normal upper limit of 50 ng/mL) reflect systemic allergic and inflammatory dysregulation. Proinflammatory cytokines—IL-1β, IL-6, and TNF-α—are markedly elevated (6–14 times above normal), driving local and systemic inflammation and promoting tissue destruction.

Microcirculatory Disturbances

Hyperviscosity syndrome, leukostasis (accumulation of leukemic cells in small vessels), and thrombocytopenia contribute to impaired blood flow in the microvasculature of periodontal tissues. Reduced capillary perfusion leads to local hypoxia, accumulation of metabolic waste products, and delayed clearance of inflammatory mediators. The result is a vicious cycle of ischemia, inflammation, and tissue damage that is poorly responsive to conventional therapy.

Salivary Gland Dysfunction

Hyposalivation is a common finding in chronic leukemia patients, with salivary flow rates reduced by 2.5–3.5-fold below normal (0.127±0.078 mL/min versus 0.45±0.10 mL/min in healthy controls). This reduction compromises the natural protective functions of saliva: mechanical cleansing, buffering, maintenance of oral pH, antimicrobial activity (mediated by lysozyme, lactoferrin, histatins, and secretory IgA), and tissue repair. The acidic shift in oral pH (6.81±0.22 versus 7.02±0.15 in controls) further promotes the growth of aciduric and periodontopathogenic bacteria.

Periodontal Tissue Destruction

The net effect of immunological, microcirculatory, and salivary dysfunction is accelerated periodontal tissue destruction. Increased RANKL/OPG ratio promotes osteoclast activation and alveolar bone resorption. Matrix metalloproteinases (MMPs), particularly MMP-1, MMP-8, and MMP-13, degrade collagen and other extracellular matrix components. The result is deepening of periodontal pockets, progressive attachment loss, tooth mobility, and ultimately tooth loss.

Rationale for Efferent Therapy

Given the multifactorial nature of periodontal tissue dysfunction in chronic leukemia, therapeutic strategies must address multiple pathogenetic pathways simultaneously. Efferent therapy methods, which focus on systemic modulation of the internal environment, are theoretically well-suited to this challenge. By removing or neutralizing pathogenic factors in the blood and restoring homeostatic balance, efferent therapies can potentially improve periodontal outcomes even when local factors alone are addressed.

ILBI, as a particularly well-studied efferent modality, offers several advantages: it is minimally invasive, has a favorable safety profile, can be administered in outpatient settings, and does not interfere with ongoing anti-leukemic therapy. The remainder of this review focuses on the clinical and laboratory evidence supporting its use.

MECHANISMS OF ACTION OF ILBI IN PERIODONTAL TISSUE FUNCTION

Immunomodulatory Effects

ILBI exerts profound effects on the immune system, which constitute the primary mechanism underlying its efficacy in chronic leukemia-associated periodontitis.

Reduction of proinflammatory cytokines. Low-intensity laser irradiation suppresses the production of IL-1β, IL-6, and TNF-α by activated monocytes and macrophages. Studies have documented reductions of 4.4–4.7-fold following a course of ILBI, approaching the upper limits of normal ranges. This cytokine suppression dampens the inflammatory response in periodontal tissues, reducing edema, hyperemia, and pain.

Normalization of immunoglobulin profile. ILBI increases serum IgG levels by 29.3% (from 5.98±0.81 to 7.73±1.36 g/L), restoring humoral immune competence and improving opsonization of periodontopathogens. Concomitantly, IgE levels decrease by 79.9% (from 152.70±23.88 to 30.64±10.55 ng/mL), reducing the allergic/inflammatory component of the disease.

Enhancement of local immunity. Salivary secretory IgA levels increase following ILBI, improving the mucosal barrier function of the oral epithelium and reducing bacterial adhesion.

Induction of anti-inflammatory cytokines. Photons from the laser induce the synthesis of IL-10 and transforming growth factor-beta (TGF-β), which suppress proinflammatory responses and promote tissue repair respectively.

Effects on Blood Rheology and Microcirculation

ILBI significantly improves the rheological properties of blood through multiple mechanisms:

Reduced blood viscosity. Laser irradiation decreases plasma viscosity and whole blood viscosity, improving flow characteristics.

Decreased erythrocyte aggregation. The deformability of erythrocytes increases, allowing them to pass more easily through narrow capillaries. Erythrocyte aggregation—a major determinant of blood viscosity—is significantly reduced.

Reduced platelet aggregation. ILBI decreases platelet aggregation tendency, reducing the risk of microthrombus formation in the microvasculature of periodontal tissues.

Improved microcirculation. The combined rheological effects lead to enhanced capillary blood flow in periodontal tissues, improving oxygen delivery, nutrient supply, and clearance of metabolic waste products. Restoration of microcirculation is critical for periodontal tissue health, as even mild hypoxia impairs fibroblast function and collagen synthesis.

Antioxidant Effects

Oxidative stress, resulting from overproduction of reactive oxygen species (ROS) by activated neutrophils and macrophages, plays a significant role in periodontal tissue destruction. ILBI activates the enzymatic antioxidant defense system:

Increased superoxide dismutase (SOD) activity. SOD catalyzes the dismutation of superoxide anion to hydrogen peroxide, reducing direct oxidative damage.

Increased catalase activity. Catalase converts hydrogen peroxide to water and molecular oxygen, completing the detoxification pathway.

Increased glutathione peroxidase activity. This enzyme reduces lipid hydroperoxides and hydrogen peroxide using reduced glutathione as a substrate.

Reduced lipid peroxidation products. Concentrations of malondialdehyde (MDA) and diene conjugates—markers of oxidative membrane damage—decrease significantly following ILBI.

By reducing oxidative stress, ILBI protects periodontal cells (fibroblasts, osteoblasts, epithelial cells) from ROS-mediated damage and preserves their functional capacity.

Antimicrobial and Bactericidal Effects

ILBI has direct and indirect antimicrobial effects that are particularly relevant to periodontitis management:

Direct bactericidal action. Low-intensity laser radiation exerts direct lethal effects on microorganisms, particularly Gram-negative anaerobes that dominate the periodontopathic flora. The bactericidal effect is mediated by the generation of singlet oxygen and other ROS within bacterial cells.

Enhanced phagocytosis. ILBI activates neutrophil and macrophage phagocytic function, improving the clearance of periodontopathogens from periodontal pockets.

Reduced periodontopathogen load. Clinical studies have documented significant reductions in the detection rates of key periodontopathogens following ILBI: T. denticola by 63.6%, A. actinomycetemcomitans by 57.0%, P. intermedia by 49.5%, P. gingivalis by 40.6%, and T. forsythia by 32.0%.

Reparative and Regenerative Effects

ILBI stimulates the processes of tissue repair and regeneration in the periodontium:

Fibroblast proliferation and differentiation. Laser irradiation stimulates the proliferation of gingival fibroblasts and periodontal ligament fibroblasts, increasing the cellular population available for tissue repair.

Increased collagen synthesis. Fibroblasts increase their production of type I and type III collagen, the major structural proteins of the periodontal extracellular matrix.

Enhanced angiogenesis. ILBI promotes the formation of new capillaries (angiogenesis) in inflamed and damaged periodontal tissues, improving vascular supply and supporting tissue regeneration.

Accelerated epithelialization. Re-epithelialization of the gingival margin is accelerated following ILBI, restoring the epithelial barrier and reducing the risk of recurrent inflammation.

Neuromodulatory Effects

ILBI influences the autonomic nervous system, reducing sympathetic tone and increasing parasympathetic activity. This shift has several beneficial effects on periodontal tissues: reduced vasospasm with improved blood flow, relaxation of masticatory muscles with reduction of trauma to inflamed periodontal tissues, and reduced pain perception through modulation of nociceptive pathways.

CLINICAL EVIDENCE FOR ILBI IN PERIODONTITIS ASSOCIATED WITH CHRONIC LEUKEMIA

Effects on Clinical Periodontal Parameters

Clinical studies have consistently demonstrated significant improvements in all major periodontal indices following ILBI therapy (typically administered as 5 sessions of 15–20 minutes each, 632 nm wavelength, 1.5–2.0 mW power):

Bleeding on probing (BOP). ILBI reduces BOP by 4.8-fold (from 87.7% to 18.4%), compared to a 2.5-fold reduction with standard treatment alone (from 86.8% to 34.2%). The difference between groups is statistically significant ($p<0.01$).

Periodontal pocket depth. Mean pocket depth decreases by 2.1–2.8 mm following ILBI, with the greatest reductions observed in initially deep (≥6 mm) pockets.

Tooth mobility. ILBI reduces tooth mobility in 71.4% of initially affected patients, with improvement by at least one grade on the Miller scale.

Oral hygiene index (OHI-S). While ILBI does not directly remove plaque, the improvement in salivary flow and reduction in inflammation facilitates better oral hygiene maintenance by patients.

Effects on Salivary Function

ILBI significantly improves salivary gland function in chronic leukemia patients:

Salivary flow rate. Mean salivary flow increases from 0.127±0.078 mL/min (severe hyposalivation) to 0.28±0.09 mL/min (approaching the lower limit of normal, 0.31 mL/min). In contrast, patients receiving standard treatment alone show only minimal improvement (0.19±0.07 mL/min). The difference between groups is statistically significant ($p<0.05$).

Oral pH. The acidic shift in oral pH (from 7.02±0.15 in controls to 6.81±0.22 at baseline) partially normalizes following ILBI, with mean pH increasing to 6.95±0.18.

Salivary gland functional activity. The compensatory increase in salivary gland functional activity (from a normal range of 1.0–3.9 to 4.15±0.03 absolute units at baseline) decreases toward normal following ILBI, indicating reduced compensatory demand as gland function improves.

Effects on Immunological Parameters

ILBI produces significant improvements in immunological markers that correlate with clinical outcomes:

IgG. Levels increase by 29.3% (from 5.98±0.81 to 7.73±1.36 g/L, $p<0.001$), entering the normal range (6.0–15.0 g/L). This restoration of humoral immune competence is associated with improved clinical outcomes and reduced infection rates.

IgE. Levels decrease by 79.9% (from 152.70±23.88 to 30.64±10.55 ng/mL, $p<0.001$), normalizing values that were previously three times the upper limit of normal. The reduction in IgE correlates with reduced gingival inflammation and bleeding.

IgM. Levels decrease by 25.7% (from 1.71±0.35 to 1.27±0.29 g/L, $p<0.001$), reflecting resolution of the acute inflammatory component.

IgA. A non-significant trend toward reduction (1.75±0.60 to 1.54±1.24 g/L, $p=0.187$) is observed, with considerable individual variability.

Proinflammatory cytokines. IL-1β decreases by 4.6-fold (from 68.7±12.9 to 14.9±5.1 pg/mL, $p<0.001$), IL-6 by 4.7-fold (from 45.6±9.9 to 9.8±3.4 pg/mL, $p<0.001$), and TNF-α by 4.4-fold (from 53.3±11.6 to 12.1±4.2 pg/mL, $p<0.001$). These reductions are significantly greater than those achieved with standard treatment alone (2.2-fold, 1.8-fold, and 2.0-fold respectively; $p<0.01$–0.001).

Effects on Microbiological Parameters

ILBI produces significant reductions in the prevalence and load of periodontopathogens:

Pathogen Pre-ILBI (%) Post-ILBI (%) Reduction p-value

Treponema denticola 67.41±0.30 24.52±0.33 63.6% <0.001

Aggregatibacter actinomycetemcomitans 52.48±0.35 22.56±0.47 57.0% <0.001

Prevotella intermedia 60.50±0.32 30.57±0.39 49.5% <0.001

Porphyromonas gingivalis 61.46±0.26 36.51±0.35 40.6% <0.001

Tannerella forsythia 51.46±0.29 34.97±4.19 32.0% <0.001

Complete elimination of all periodontopathogens is rarely achieved due to persisting immunosuppression from the underlying leukemia. However, the substantial reductions achieved with ILBI significantly reduce the risk of periodontitis exacerbation and prolong relapse-free intervals.

Long-term Outcomes

Studies with follow-up periods of 6–12 months demonstrate that the beneficial effects of ILBI are sustained:

Prolonged remission. The median relapse-free interval following combined treatment (standard periodontal therapy + ILBI) is 8.5 months, compared to 4.2 months for standard therapy alone.

Reduced frequency of exacerbations. Patients receiving ILBI experience 1.2 exacerbations per year on average, compared to 2.8 exacerbations per year for those receiving standard therapy alone.

Improved quality of life. Disease-specific oral health-related quality of life measures (OHIP-14, OHIP-49) show significant improvement following ILBI, with particular benefits in the domains of physical pain, psychological discomfort, and functional limitation.

SAFETY AND TOLERABILITY OF ILBI IN CHRONIC LEUKEMIA

ILBI has an excellent safety profile when properly administered:

No exacerbation of underlying leukemia. Multiple studies have confirmed that ILBI does not stimulate leukemic cell proliferation or worsen hematological parameters. The therapy can be safely administered during both active disease and remission phases.

Minimal adverse effects. The most common adverse effect is mild local discomfort at the venipuncture site, which resolves spontaneously. No systemic adverse effects have been reported in the literature.

Compatibility with anti-leukemic therapy. ILBI does not interfere with the efficacy of chemotherapy, targeted therapy (tyrosine kinase inhibitors, BTK inhibitors), or supportive care medications (growth factors, transfusions).

Precautions. As with any intravenous procedure, strict aseptic technique is essential to prevent catheter-related infections. Patients with severe thrombocytopenia (platelet count <20–30×10⁹/L) may require platelet transfusion before venipuncture. In practice, these precautions are routinely implemented in the management of chronic leukemia patients.

CONCLUSION

The functional state of periodontal tissues in patients with chronic leukemia is severely compromised by the combined effects of immunological dysregulation, microcirculatory disturbances, salivary gland dysfunction, and persistent periodontopathogen colonization. Conventional periodontal treatment often yields suboptimal results in this population, highlighting the need for adjunctive therapeutic modalities that address the systemic determinants of periodontal health.

Efferent therapy using intravenous laser blood irradiation (ILBI, VLOK therapy) has a strong clinical and laboratory basis for improving periodontal tissue function in chronic leukemia patients. The therapy exerts multiple beneficial effects that target key pathogenetic pathways:

· Immunomodulation (reduction of proinflammatory cytokines, normalization of IgG and IgE, enhancement of local immunity)

· Improved blood rheology and microcirculation (reduced viscosity, decreased cell aggregation)

· Antioxidant effects (activation of enzymatic defenses, reduction of lipid peroxidation)

· Antimicrobial activity (direct bactericidal effects, enhanced phagocytosis, reduced pathogen load)

· Reparative and regenerative effects (fibroblast proliferation, collagen synthesis, angiogenesis, epithelialization)

· Neuromodulatory effects (reduced sympathetic tone, improved vascular regulation)

Clinical studies have demonstrated that ILBI significantly reduces gingival bleeding (BOP reduction by 4.8-fold), decreases periodontal pocket depth, increases salivary flow rate (normalizing previously severe hyposalivation), restores normal immunoglobulin profiles (29.3% increase in IgG, 79.9% reduction in IgE), suppresses proinflammatory cytokines (4.4–4.7-fold reduction), and reduces periodontopathogen load (up to 63.6% reduction for T. denticola). These improvements translate into prolonged relapse-free intervals, reduced frequency of periodontitis exacerbations, and improved oral health-related quality of life.

The safety profile of ILBI is favorable, with no evidence of exacerbation of the underlying leukemia and minimal adverse effects. The therapy is compatible with anti-leukemic medications and can be administered in outpatient settings.

In conclusion, the integration of ILBI into comprehensive periodontal treatment protocols for chronic leukemia patients is strongly supported by clinical and laboratory evidence. As an efferent therapy modality that addresses the systemic determinants of periodontal disease, ILBI represents a significant advance in the management of this challenging patient population. Future research should focus on optimizing treatment protocols (dose, duration, frequency), identifying predictors of response, and evaluating long-term outcomes in larger multicenter trials.

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