INFLAMMATORY PATHOGENIC FACTORS AND THEIR CONTRIBUTION TO GLYCOLYTIC AND MITOCHONDRIAL METABOLIC DYSFUNCTION IN OSTEOARTHRITIS

Rejabboyeva N. L.
Tashkent State Medical University
Xadjimetov A.A.
Tashkent State Medical University
nafisarezabboeva@gmail.com.

Annotation. *Osteoarthritis (OA) is among the most common chronic joint diseases, characterized by progressive degeneration of articular cartilage, accompanied by synovial inflammation, structural changes in the subchondral bone, and a gradual decline in joint function. Interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) stimulate the expression of catabolic genes in chondrocytes and consequently accelerate extracellular matrix breakdown. Impaired mitochondrial function can further contribute to excessive reactive oxygen species (ROS) generation, diminished ATP production, alterations in mitochondrial membrane potential, and deterioration of chondrocyte function.The reciprocal relationship between inflammatory signaling and glycolytic activity has therefore emerged as an important area of research for elucidating the metabolic mechanisms underlying OA pathogenesis.*

Keywords: *osteoarthritis (OA), chondrocytes, glycolysis, mitochondria, IL-1β, TNF-α, ATP.*

Annotatsiya. *Osteoartrit (OA) eng ko‘p uchraydigan surunkali bo‘g‘im kasalliklari qatoriga kirib, bo‘g‘im tog‘ayining progressiv degeneratsiyasi, sinovial yallig‘lanish, subxondral suyak tuzilishining o‘zgarishi va bo‘g‘im funksiyasining asta-sekin pasayishi bilan kechadi. Interleykin-1β (IL-1β) va o‘sma nekrozi omili-α (O‘NO-α) xondrotsitlarda katabolik genlar ekspressiyasini rag‘batlantiradi va natijada hujayradan tashqari matriksning parchalanishini tezlashtiradi. Mitoxondriya funksiyasining buzilishi qo‘shimcha ravishda reaktiv kislorod turlarining (ROS) haddan tashqari ko‘p hosil bo‘lishiga, ATF ishlab chiqarishning pasayishiga, mitoxondriya membranasi potensialining o‘zgarishiga va xondrotsitlar funksiyasining yomonlashishiga olib kelishi mumkin. Shu sababli, yallig‘lanish signalizatsiyasi va*

glikolitik faollik o‘rtasidagi o‘zaro bog‘liqlik OA patogenezi asosida yotuvchi metabolik mexanizmlarni aniqlash uchun muhim tadqiqot yo‘nalishi sifatida namoyon bo‘ldi.

Kalit so‘zlar: *osteoartrit (OA), xondrotsitlar, glikoliz, mitoxondriyalar, IL-1β, TNF-α, ATF.*

Аннотация. *Остеоартрит (ОА) относится к наиболее распространенным хроническим заболеваниям суставов, характеризующимся прогрессирующей дегенерацией суставного хряща, сопровождающейся воспалением синовиальной оболочки, структурными изменениями подхондриальной кости и постепенным снижением функции суставов. Интерлейкин-1β (IL-1β) и фактор некроза опухоли-α (ФНО-α) стимулируют экспрессию катаболических генов в хондроцитах и, следовательно, ускоряют разрушение внеклеточного матрикса. Нарушение функции митохондрий может в дальнейшем способствовать избыточной генерации реактивных видов кислорода (РСК), снижению выработки АТФ, изменению потенциала мембран митохондрий и ухудшению функции хондроцитов. Поэтому взаимосвязь между воспалительной сигнализацией и гликолитической активностью стала важным направлением исследований для выяснения метаболических механизмов, лежащих в основе патогенеза ОА.*

Ключевые слова: *остеоартроз (ОА), хондроциты, гликолиз, митохондрии, ИЛ-1β, ФНО-α, АТФ.*

MATERIALS AND METHODS

1. Isolation and Culture of Primary Human Hip Joint Chondrocytes

Tissue source: Primary human hip joint chondrocytes were isolated from cartilage tissue obtained from donors undergoing total hip arthroplasty. Tissue collection was performed following informed patient consent and approval by the institutional Bioethics Committee. Enzymatic isolation: Cartilage samples were mechanically minced under sterile conditions and subjected to sequential enzymatic digestion. Initially, the tissue was treated with 0.25% trypsin-EDTA for 30 minutes at 37 °C, followed by incubation with 0.1–0.2% type II collagenase (Collagenase Type II, *Sigma-Aldrich*) at 37 °C for 12–16 hours.

2. Treatment with Inflammatory Mediators

Once the cultured chondrocytes reached approximately 70–80% surface coverage, corresponding to a sub-confluent state, the cells were allocated to the respective experimental groups. **Control group:** Chondrocytes maintained in culture medium

without recombinant cytokines. **IL-1β group:** Cells were exposed to recombinant human IL-1β (*Recombinant Human IL-1β, R&D Systems*) at a concentration of 10 ng/mL for 24 hours. **TNF-α group:** Cells were treated with recombinant human TNF-α (*Recombinant Human TNF-α, R&D Systems*) at a concentration of 20 ng/mL for 24 hours. Assessment of reactive oxygen species (ROS) production: Intracellular ROS levels were determined using the fluorescent DCFH-DA probe (2′,7′-dichlorofluorescein diacetate) at a final concentration of 10 μM. Statistical analysis and data processing All experiments were performed in at least three independent replicates (n = 3) [3].

RESULTS

Analysis of the experimental findings demonstrated that inflammatory mediators, particularly IL-1β and TNF-α, exert a significant influence on both glycolytic activity and mitochondrial metabolism in chondrocytes under osteoarthritic conditions. These findings indicate that mitochondrial dysfunction is associated with enhanced ROS generation and decreased ATP synthesis.

Table 1. Effects of inflammatory mediators on chondrocyte metabolism

Pathogenic factor	Main metabolic alteration	Potential biological consequence
IL-1β	Glycolysis ↑; mitochondrial ATP ↓	Energy imbalance and extracellular matrix degradation
TNF-α	Glycolytic metabolic reprogramming	Disruption of chondrocyte metabolic homeostasis
· ROS — Reactive Oxygen Species (ROS)	Mitochondrial damage ↑	Oxidative stress and decreased ATP production

DISCUSSION

The findings of the present study demonstrate a close relationship between inflammatory processes and metabolic disturbances in the pathogenesis of osteoarthritis (OA). IL-1β and TNF-α appear to be among the principal inflammatory mediators involved in these processes [2]. Another important consequence of mitochondrial dysfunction is excessive generation of reactive oxygen species (ROS). Elevated ROS levels can impair mitochondrial membrane integrity and interfere with the function of the electron transport chain, ultimately contributing to reduced ATP production [1].

CONCLUSION

1. In osteoarthritis, inflammatory processes and metabolic dysfunction are closely interconnected and contribute jointly to disease progression.
2. IL-1β and TNF-α alter the metabolic phenotype of chondrocytes and affect the balance between glycolytic metabolism and mitochondrial energy production.
3. Mitochondrial dysfunction is associated with increased ROS generation, reduced ATP synthesis, and enhanced oxidative stress.

REFERENCES

1. Li K, Yang T, Chen F, et al. **MOTS-c attenuates mitochondrial dysfunction induces pyroptosis and cartilage degradation in osteoarthritis via an Nrf2-dependent mechanism.** *Free Radical Biology and Medicine.* 2025;241:717–731.
2. Lin S, Wu B, Hu X, Lu H. **Sirtuin 4 downregulation contributes to chondrocyte senescence and osteoarthritis via mediating mitochondrial dysfunction.** *International Journal of Biological Sciences.* 2024;20(4):1256–1278.
3. Arra M, Abu-Amer Y. **Cross-talk of inflammation and chondrocyte intracellular metabolism in osteoarthritis.** *Osteoarthritis and Cartilage.* 2023;31(8):1012–1021. doi:10.1016/j.joca.2023.04.003.