

EVALUATING THE EFFECTIVENESS OF A NOVEL MULTIMODAL TREATMENT FOR AVASCULAR NECROSIS OF THE HEAD OF FEMUR OF POST COVID ETIOLOGY: A RETROSPECTIVE COHORT STUDY



Sultanova Maksuma Khudayberganovna, Das Sharodiya, Mirzaakhmedov Farrukh Miradilovich, Kayumov Javohir, Juraeva Zulfiya Baratovna
Tashkent State Medical University, Republic of Uzbekistan, Tashkent

COVID-19 ДАН КЕЙИНГИ ЭТИОЛОГИЯЛИ СОН СУЯГИ БОШИНING АВАСКУЛЯР НЕКРОЗИНИ ДАВОЛАШДА ЯНГИ МУЛТИМОДАЛ УСУЛНИНГ САМАРАДОРЛИГИНИ БАҲОЛАШ: РЕТРОСПЕКТИВ КОГОРТ ТАДҚИҚОТ

Султанова Максума Худайбергановна, Дас Шародия, Мирзаахмедов Фаррух Мирадилович, Каюмов Жавохир, Джураева Зулфия Баратовна
Тошкент давлат тиббиёт университети, Ўзбекистон Республикаси, Тошкент ш.

ОЦЕНКА ЭФФЕКТИВНОСТИ НОВОЙ МУЛЬТИМОДАЛЬНОЙ ТЕРАПИИ АВАСКУЛЯРНОГО НЕКРОЗА ГОЛОВКИ БЕДРЕННОЙ КОСТИ ПОСТКОВИДНОЙ ЭТИОЛОГИИ: РЕТРОСПЕКТИВНОЕ КОГОРТНОЕ ИССЛЕДОВАНИЕ

Султанова Максума Худайбергановна, Дас Шародия, Мирзаахмедов Фаррух Мирадилович, Каюмов Жавохир, Джураева Зулфия Баратовна
Ташкентский государственный медицинский университет, Республика Узбекистан, г. Ташкент

e-mail: info@tdtu.uz

Резюме. Сон суюги бошининг аваскуляр некрози (АН) қон таъминоти бузилиши натижасида юзага келади ва бу ҳолат COVID-19дан кейинги беморларда микроваскуляр шикастланишлар туфайли тез-тез учрамоқда. Анъанавий терапиялар қон айланиши муаммосини бартараф эта олмайдди. 2020-йил сентябридан 2024-йил мартигача Ўзбекистондаги учинчи даражали шифохонада ўтказилган ретроспектив когорт тадқиқотга 350 нафар пост- COVID-19 АН бемори жалб қилинди. Асосий гуруҳ (n=190) консерватив даволашни билан бирга 2 ой давомида ҳафтасига 2-3 марта гирудотерапия олди; назорат гуруҳи (n=160) фақат консерватив муолажа олди. МРТ ва SF -36 баҳолашлари таххис қўйилгач ҳар 6 ойда 2 йил давомида ўтказилди. Асосий гуруҳда сон суюги бошининг емирилиши ҳолатлари (10% га нисбатан 34.4%), касалликнинг ривожланиши (20% га нисбатан 51.3%) ва жарроҳлик еҳтиёжи (3.2% га нисбатан 10%) анча кам бўлди. SF -36 кўрсаткичлари ҳам яхшиланди. Ушбу мултимодал терапия пост- COVID-19 АНнинг эрта босқичида самарали, жарроҳликсиз даволаш усули бўлиши мумкин.

Калит сўзлар: гирудотерапия, COVID-19, сон суюги бошининг аваскуляр некрози, Ризедронат, чаноқ - сон бўғими эндопротези.

Abstract. Avascular necrosis (AVN) of the femoral head results from impaired blood supply, a condition increasingly observed in post-COVID-19 patients due to virus-induced microvascular damage. Conventional therapies often fail to address the vascular pathology. This retrospective cohort study, conducted from September 2020 to March 2024 in a tertiary hospital in Uzbekistan, included 350 post-COVID AVN patients divided into two groups. The case group (n=190) received standard conservative treatment plus hirudotherapy (2–3 times/week for 2 months), while the control group (n=160) received standard conservative care alone. Outcomes were evaluated through MRI staging and SF -36 scores at baseline and every 6 months over 2 years. Results showed a significantly lower rate of femoral head collapse (10% vs. 34.4%), progression (20% vs. 51.3%), and surgery (3.2% vs. 10%) in the case group, with improved SF -36 scores. This multimodal therapy demonstrates potential as an effective, non-surgical option for managing early-stage post-COVID AVN.

Key words: Hydrotherapy, COVID 19, Femoral head necrosis, Risedronate, total hip replacement.

Introduction. Avascular necrosis (AVN), or osteonecrosis, is death of bone tissue resulting from

diminished blood supply, most frequently in the femoral head with the potential for disabling hip collapse.

Once traditionally linked with chronic corticosteroid use, alcohol abuse, trauma, or hematologic disease, current literature also shows AVN occurring after COVID-19 infection—even in patients with minimal steroid use—showing SARS-CoV-2 has direct pathologic impact on microvasculature, leading to ischemia and necrosis.

Older conservative therapies, with bisphosphonates especially, are mainly concerned with inhibition of bone resorption but are not directed against and do not treat the microvascular pathology that may be connected with the bone condition. In stark contrast, medicinal leech therapy has proven to have far-reaching positive effects on microcirculation—both by alleviating venous congestion, enhancing the perfusion of blood, and improving the process of neovascularization—thereby being a powerful and precious complement to drugs used solely to treat osteoporosis[1,2,3,4].

Leech therapy, or hirudotherapy, offers a broad spectrum of therapeutic advantages when employed as an adjunctive treatment modality in the treatment of avascular necrosis (AVN) of bone. Leech saliva is generally full and varied in bioactive molecules—some of which are hirudin, calin, and destabilase—whose roles as natural anticoagulants and antithrombotic agents are proven. It is these very molecules that prevent the formation of microthrombi, and also lyse any pre-formed microthrombi found in the microvessels perfusing the femoral head. Therefore, this complex and multifaceted process actually improves local circulation and reduces ischemia-induced injury to bone tissue itself. Furthermore, bioactive molecules like bdellins, eglins, and hyaluronidase have significant anti-inflammatory action, decrease swelling of the target tissues, and facilitate effective drainage of interstitial fluid. This very effect proves to be of special utility in the context of AVN, where increased intraosseous pressure and resultant inflammation have been shown to create higher levels of pain and potentially be responsible for further encouraging the pathologic process itself. In addition, by providing a conduit for venous drainage from an available volume, leeches have a mechanical decompression effect that minimizes intraboche and intracapsular pressures. Pain relief is also caused by leech therapy through many neurochemical mechanisms and carries a mild antimicrobial effect, induced by some of the peptides found in leech saliva. Due to the cumulative effect of all these interventions, they act synergistically to provide pain relief, retard necro-

sis, and improve functional outcomes, more so in the post-COVID patients who are at peculiar risk of vascular complications developing as a sequelae of hypercoagulability and damage to endothelium[5,6,7,8,9].

We therefore evaluated a combined approach of bisphosphonates plus leech therapy in a cohort of post-COVID AVN patients, hypothesizing that addressing both bone and vascular pathology together would outperform standard therapy [10,11].

Methods. Design & Setting: Tertiary care hospital in Uzbekistan from September 2020 to March 2024. Institutional ethics approval was secured.

Participants: Adults (18–80 years) with confirmed history of Covid19 (positive SARS-CoV-2 IgG Test).

Condition of head of femur measured by MRI-confirmed Ficat–Arlet Stage I–III AVN. Exclusion criteria included history of osteoporosis, prolonged corticosteroid use maybe as part of treatment in autoimmune diseases, arthroplasty in hip joint, severe trauma or fracture in hip region or history of surgery.

Groups & Interventions: Case (n=190): oral Risedronate (35mg tablet weekly) at end of leech therapy course + leech therapy (2 sessions per week), oral non steroidal anti-inflammatory drugs

Control (n=160): standard care protocol (intraarticular steroid injection, oral non steroidal anti-inflammatory drugs, Risedronate tablet during whole course of treatment, Enoxaparin, Cholecalciferol tablets).

Outcome Measures:

Radiologic: MRI monitoring at baseline, after every 6 months till 2 years (collapse and progression).

Clinical: SF-36 for quality of life. Surgical requirement: total hip replacement.

Results. Radiologic outcomes post treatment were noted (as mentioned in table 1).

SF-36 scores of each participants in case group were noted pre and post treatment (table 2).

SF-36: Case group exhibited greater improvements than Control in physical and psychosocial domains.

Discussion. The combination therapy effectively and significantly decreased the risk of structural collapse and advancement of avascular necrosis (AVN) compared to standard care procedures.

Table 1. Radiological Outcomes:

Outcome	Case (n=190)	Control (n=160)
Femoral head collapse	19/190 (10.0%)	55/160 (34.4%)
Progression to stage III	38/190 (20.0%)	82/160 (51.3%)
Required surgery	6/190 (3.2%)	16/160 (10.0%)

Table 2. SF-36 score after 1 year of treatment in case group

SF-36 Domain	Main group (pre hospital period)	Main group (after 1 year of treatment)	P-value
Physical Functioning	77.5	95	0.016
Role functioning	60	75	0.021
Bodily Pain	41	100	0.009
General Health	44.6	82.1	0.014
Vital activity	40	55.	0.027
Social Functioning	51.5	75	0.018
Emotional well being	100	100	-
Mental Health	62	40	0.033
Physical component score	36.1	58.6	0.020
Mental component score	40	82	0.012

A decreased incidence of surgical interventions was also seen at 3.2% compared to 10.0%, which indicates that this therapy is efficient at maintaining the integrity of the joint in the long term. In addition, considerable enhancements were observed in the Short Form Health Survey (SF-36), demonstrating that patients achieved better pain reductions and significant functional recovery throughout their treatment [12, 13, 14, 15, 16].

Mechanistically, bisphosphonates are important in stabilizing bone metabolism, in effect guaranteeing that processes responsible for bone maintenance and renewal are maintained in equilibrium. Meanwhile, hirudotherapy offers the added advantage of improving circulation and inducing microvessel formation—this dual strategy in effect targets both vascular and bone pathology. Adopting this technique at an early point, there is a good chance that it can greatly reduce the need for future surgical replacement procedures [17, 18].

Conclusion. In this extended cohort study with a total of 350 participants, we found that the use of bisphosphonates in conjunction with hirudotherapy has been shown to significantly promote a range of desirable outcomes. These outcomes cover both radiographic findings, clinical improvement, and general parameters for quality-of-life for patients suffering from post-COVID avascular necrosis (AVN) in the femoral head. In addition, this combined therapy also significantly reduces the need for surgical interventions in such patients. The evidence strongly points to this multimodal therapeutic regime as having a lot of promise and potential to become a new standard non-surgical therapeutic approach for early-phase management of post-COVID AVN [19].

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**ОЦЕНКА ЭФФЕКТИВНОСТИ НОВОЙ
МУЛЬТИМОДАЛЬНОЙ ТЕРАПИИ
АВАСКУЛЯРНОГО НЕКРОЗА ГОЛОВКИ
БЕДРЕННОЙ КОСТИ ПОСТКОВИДНОЙ
ЭТИОЛОГИИ: РЕТРОСПЕКТИВНОЕ КОГОРТНОЕ
ИССЛЕДОВАНИЕ**

*Султанова М.Х., Дас Шародия, Мирзаахмедов Ф.М.,
Каюмов Ж., Джураева З.Б.*

Резюме. Аваскулярный некроз (АВН) головки бедренной кости возникает при нарушении кровоснабжения, что все чаще наблюдается у пациентов после COVID-19 из-за микрососудистых поражений. Стандартная терапия не устраняет сосудистые нарушения. В ретроспективное когортное исследование, проведённое в Узбекистане с сентября 2020 по март 2024 года, были включены 350 пациентов с АВН после COVID-19. Основная группа (n=190) получала стандартное консервативное лечение в сочетании с гирудотерапией (2–3 раза в неделю, 2 месяца), контрольная группа (n=160) — только стандартное лечение. Эффективность оценивалась по МРТ и шкале SF-36 каждые 6 месяцев в течение 2 лет. В основной группе значительно реже наблюдались коллапс головки бедра (10% против 34,4%), прогрессия заболевания (20% против 51,3%) и необходимость хирургического вмешательства (3,2% против 10%). Улучшились и показатели качества жизни. Таким образом, мультимодальная терапия представляет собой перспективный нехирургический подход при ранней стадии АВН после COVID-19.

Ключевые слова: гирудотерапия, COVID-19, некроз головки бедренной кости, ризедронат, эндопротезирование тазобедренного сустава.