

# COVID etiologiyali son suyagi boshchasi avaskulyar nekrozini erta bosqichlarda tashxislash va davolash

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**Annotatsiya:** Butun dunyoni qamrab olgan COVID-19 (SARS-CoV-2) pandemiyasining yomon oqibati sifatida suyaklarning avaskulyar nekrozi (osteonekroz) rivojlandi. COVID-19 o'g'ir turi bilan kasallangan bemorlarning 5-58% ida suyaklar avaskulyar nekrozi bilan zararlangan. SARS-CoV-2 bilan kasallangan bemorlarning 39 % ida son suyagi boshchasi avaskulyar nekrozi atipik pnevmoniyadan keyin bir necha oy ichida rivojlangan. Avaskulyar nekroz ko'pincha mehnatga layoqatli yoshdagilarda (o'rtacha yosh ko'rsatkichi 33-45 yosh) rivojlanadigan va ma'lum bir sohadagi suyak to'qimasining nobud bo'lishi bilan bog'liq bo'lgan og'ir nogironlikka olib keluvchi kasallikdir. Postkovid avaskulyar nekrozning patogenezi, uni erta bosqichlarda tashxislash va davolash imkoniyatlari haqida munozaralar faol muhokamalarga sabab bo'lmoqda. COVID-19 infeksiyasi yoshlar va mehnatga layoqatli yoshdagilar orasida keng tarqalganligini hisobga olib, osteonekrozning ushbu shaklini erta tashxislash va davolash katta ijtimoiy va iqtisodiy ahamiyatga ega.

**Kalit so'zlar:** COVID-19 etiologiyali son suyagi boshchasi avaskulyar nekrozi, glyukokortikoidlar, tashxislash, konservativ va xirurgik davolash.

## Diagnosis and treatment of avascular necrosis of the femoral head of COVID etiology in the early stages

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**Abstract:** Avascular bone necrosis (osteonecrosis) developed as a bad consequence of the COVID-19 pandemic (SARS-CoV-2) that swept the whole world. In 5-58% of patients with severe type COVID-19, the bones are affected by avascular necrosis. In 39% of patients with SARS-CoV-2, avascular necrosis of the femoral head developed within a few months after atypical pneumonia. Avascular necrosis is a disease that most often develops in people of working age (the average age is 33-45 years) and leads to severe disability associated with the death of bone tissue in a certain area. Discussions about the pathogenesis of postcovid avascular necrosis, the possibilities of its diagnosis and treatment at early stages cause active discussions. Given that COVID-19 infection is widespread among young people and people of working age, early diagnosis and treatment of this form of osteonecrosis are of great social and economic importance.

**Keywords:** avascular necrosis of the femoral head with the etiology of COVID-19, glucocorticoids, diagnosis, conservative and surgical treatment

#### Muammoning dolzarbligi

Yangi koronavirus SARS-CoV-2 va uni keltirib chiqaradigan infeksiya JSST tomonidan COVID-19 deb nomlanib, pandemiyani yuzaga keltirdi. Koronavirus allaqachon 7,2 milliondan ortiq odamning hayotiga zomin bo'ldi [1]. Ko'p bemorlarda uzoq muddat davom etgan COVID-19 asoratlari nafaqat charchoq, nafas siqishi, xavotir va depressiya, o'ychanlik yoki diqqatni jamlay olmaslik, taxikardiya, ko'krak qafasidagi og'riqlar, juda kam uchraydigan Giyena-Barre sindromi, o'pka fibrozi, o'pka tromboemboliyasi, kardiomiopatiya, hissiy disfunktsiya va insult [2], shuningdek, avaskulyar nekrozga hos bo'lgan mushak va bo'g'imlardagi og'riqlarni keltirib chiqardi [3, 4].

Turli manba'larga ko'ra, avaskulyar nekroz COVID-19 og'ir turi bilan kasallangan bemorlarning 5-58% da kuzatiladi [5, 6]. de Vlas S.J. ma'lumotlariga ko'ra, SARS-CoV-2 bilan kasallangan bemorlarning 39% da son suyagi boshchasining avaskulyar nekroz atipik pnevmoniyadan keyin bir necha oy ichida rivojlangan [7]. Avaskulyar nekroz ko'pincha mehnatga layoqatli yoshdagi kishilarda (o'rtacha yosh ko'rsatkichi 33-45 ni tashkil qildi) rivojlangan. Bu esa ma'lum bir sohadagi suyak to'qimalarining nobud bo'lishi bilan bog'liq bo'lgan og'ir nogironlikka olib keluvchi kasallik sifatida namoyon bo'ldi [8]. Osteonekroz o'choqlari son va katta boldir suyaklari do'mboqchalarida, yelka suyagi boshchasida, oshiq va tovon suyagida, hamda skeletning boshqa sohalarida ham aniqlangan [5].

Adabiyot ma'lumotlarida, COVID-19 infeksiyasidan keyingi avaskulyar nekroz rivojlanish patogenezida ikkita mumkin bo'lgan mexanizm: virusning suyak to'qimasi qon tomirlariga zarar etkazishi va infeksiyani davolash maqsadida qo'llanilgan glyukokortikoidlarning suyak to'qimasiga salbiy ta'sir ko'rsatishi muhokama qilinmoqda (Agarwala S.R., Hong N., Vlas S.J. va boshqalar).

Yangi koronavirus infeksiyasidan so'ng avaskulyar nekrozni dastlabki bosqichlarda tashxislash usullari va uning rivojlanishi uchun xavf omillarini izlash davom etmoqda. Keltirilgan adabiyotlar ma'lumotida, avaskulyar nekrozning 3-4 bosqichlarida (Ficat, 1964 y.) jarrohlik yo'li bilan davolash ko'rsatilgan bo'lsa, dastlabki bosqichlarida esa (1-2 bosqichlar) konservativ davolash texnologiyalari yetarli darajada ishlab chiqilmagan.

#### Materiallar va usullar

PubMed, Scopus va Google Scholar ma'lumotlar bazalaridan quyidagi kalit so'zlardan foydalangan holda maqolalar qidirildi: COVID-19, avaskulyar nekroz, diagnostika, jarrohlik va konservativ davolash. Qidiruv muddati oxirgi 4 yil. Yuklab olingan 90 ta maqoladan 75 tasi tanlab olindi. COVID-19 infeksiyasidan keyingi avaskulyar nekrozni erta tashxislash va davolash bilan bog'liq nashrlar tanlab olindi.

#### Asosiy qism

##### *COVID-19 asorati sifatida yuzaga kelgan avaskulyar nekrozning patogenezini.*

COVID-19 davrida SARS-CoV-2 virusi angiotenzinni o'zgartiruvchi ferment-2 (AO'F2) orqali qon tomir endoteliy hujayralariga to'g'ridan-to'g'ri kirib boradi. Bu endoteliy hujayralari nafaqat o'pkada, balki boshqa ko'plab a'zolar va to'qimalarda ham koagulopatiya va tarqoq yallig'lanish sindromi rivojlanishi orqali qon tomirlarining shikastlanishiga olib keladi [9]. R. Escher va boshqa mualliflarning kuzatishlari bo'yicha, COVID-19 infeksiyasi bilan kasallangan bemorlarda Villebrand omili sezilarli darajada oshadi, bu esa qon tomir endoteliysining to'liq zararlanganligini tasdiqlaydi [10]. Bundan tashqari, SARS-CoV yuqtirgan bemorda, tomirlarning silliq mushak hujayralarida TRIM55 ubiquitin ligaza E3 genining ekspressiyasini keltirib chiqaradi, bu esa o'z navbatida, tomir devorining yallig'lanishiga va leykotsitlarning to'planishiga olib keladi [11]. Arterial obstruksiya joyidan distal sohada giperkoagulyatsiya bilan birgalikda mikrotromboz va suyak osteonekrozi rivojlanish ehtimoli oshadi [12].

Virusning qon tomir endoteliysiga to'g'ridan-to'g'ri kirib borishi bilan bir qatorda, SARS-CoV-2 shuningdek, SARS-CoV-1 [13] suyak to'qimasini, umumiy yallig'lanishini va sitokin bo'ronini o'z ichiga olgan zararlanish jarayonini kuchaytiradi. Yallig'lanishga qarshi sitokinlar: interferon gamma (IFN- $\gamma$ ), o'sima nekroz omili (TFN), interleykin-1 (IL-1), interleykin-6 (IL-6) [14] va immun javobdan kelib chiqqan yallig'lanish joyiga T-limfotsitlarning xemotaksisi kuzatiladi

[15]. Bunday holatda mikrotromboz va qon tomirlarning virus tomonidan bevosita zararlanishi avaskulyar nekroz rivojlanishiga olib kelishi mumkin [16].

Biroq, bu COVID-19 dan keyin osteonekroz rivojlanishining yagona mexanizmi emas. Glyukokortikoidlardan foydalanish COVID-19 da avaskulyar nekroz rivojlanish xavfiga ko'proq ta'sir qiladi [17]. Ularning COVID-19 da qo'llanilishi IL-1, IL-2, IL-6, TNF kabi yallig'lanishga qarshi sitokinlarning ekspressiyasini kamaytiradi. Bu orqali to'qimalarning immunopatologik shikastlanishini va yallig'lanishga qarshi erta javob reaksiyasini kamaytirish bo'yicha boshqa dorilarga nisbatan potensial ustunligiga asoslanadi [18]. Shu bilan birga, bir qator mualliflar glyukokortikoidlarning potensial zararini, jumladan, virus ekskretsiyasining kechikishi, diabet, psixoz, suyaklarda tizimli osteoporoz va avaskulyar nekroz kabi nojo'ya ta'sirlarning mavjudligini qayd etadilar [19, 20, 21].

Organizmning glyukokortikosteroid (GKS)larni qabul qilgandagi salbiy reaksiyasi bemor COVID-19 dan tuzalganidan keyin tez orada paydo bo'ladi. Shunday qilib, atipik pnevmoniya bilan og'rigan bemorlar sog'aygandan keyin tekshirilganda, suyak to'qimasi mineral zichligi (SMZ) ning pasayishi ehtimoli aniqlandi.

Suyak to'qimasi mineral zichligini yo'qolish darajasi ko'p jihatdan kortikosteroidlarning dozasi va davomiyligiga bog'liq. GKSlar boshlang'ich infitsirlanish, keyingi rehabilitatsiya hamda, dastlabki tiklanish davrida yallig'lanishni kamaytirishga qaratilgan terapiyaning asosiy komponenti bo'ldi [22].

COVID-19 bilan og'rigan bemorlarda glyukokortikoidlarni qo'llash ehtimoli turli tibbiyot muassasalarida 28% dan 70% gachani tashkil qiladi [23]. Glyukokortikoidlarning COVID-19 infeksiyasida keng qo'llanilishi SARS-Co-V epidemiyasi davrida atipik pnevmoniya bilan kasallangan bemorlarda ulardan foydalanish bo'yicha ijobiy tajribaga asoslanadi. Tadqiqotlar shuni ko'rsatdiki, deksametazonning erta muddatlarda qo'llanilishi o'tkir respirator distress sindromi (O'RDS) bo'lgan bemorlarda mexanik ventilyatsiya davomiyligini va umumiy o'lim ko'rsatkichini kamaytirishi mumkin [24]. COVID-19 ni davolashda RECOVERY klinik sinovi natijalariga ko'ra, ushbu preparat COVID-19 og'ir turi bilan og'rigan sun'iy o'pka ventilyatsiyasida bo'lgan yoki kislorod qabul qiluvchi bemorlarda o'lim xavfini 20% ga kamaytiradi [25]. Shu bilan birga, kortikosteroidlar suyakka to'g'ridan-to'g'ri va bilvosita salbiy ta'sir ko'rsatadigan, avaskulyar nekroz rivojlanishiga moyillik qiluvchi omil hisoblanadi [26]. Avvalo, ular mezenximal hujayralarning ko'payishiga ta'sir qiladi: RUNX2 ni bloklaydi, preosteoblastlarning shakllanishiga, osteoblastlarga transformatsiyasiga to'sqinlik qiladi. Bu esa yetuk osteoblastlar sonini kamaytiradi va metabolizmni mezenxima hujayralaridan adipotsitlar hosil bo'lishiga olib keladi [27, 28]. Glyukokortikoidlar ta'sirida

osteoblastlar va osteotsitlarning apoptozi kuchayadi, osteoklastlar RANKL va DKK-1 signalizatsiya oqsillari tizimiga ta'siri tufayli faollashadi [29].

Glyukokortikoidlarning suyak to'qimalariga salbiy ta'siri ularning lipidlar almashinuviga ta'siri orqali ham namoyon bo'ladi. Past zichlikdagi lipoproteinlar (PZLP) ning to'planishi, yog'li emboliyalarning paydo bo'lishi, o'z navbatida, periferik qon tomirlarning tromboziga va natijada suyak to'qimalarining ishemik nekroziga olib keladi. Yog' emboliyalari gidrolizlanishi jarayonida hosil bo'lgan erkin yog' kislotalari kapillyarlarning endoteliy hujayralarini shikastlab, diffuz vaskulit va tomir ichidagi koagulyatsiyani keltirib chiqaradi, bu esa suyak to'qimalarining ishemik nekrozini kuchaytiradi [30].

Glyukokortikoidlarning suyak to'qimalariga salbiy ta'sirining yana bir ko'rinishi mahalliy qon oqimining regulyatori sifatida ishlaydigan glyukokortikoidlar tomirlarning endotelin-1, norepinefrin va bradikinin kabi vazoaaktiv moddalarga sezgirligini o'zgartiradi. Bu esa son suyagi boshchasida vazokonstriksiyaga olib keladi, o'z navbatida esa suyak ishemiyasini kuchaytiradi. GKSlarning yuqori dozalari to'qimalarning plazminogen aktivlashtiruvchisi (t-PA) faolligini pasaytiradi va plazmadagi plazminogen aktivator inhibitori-1 (PAI-1) antigen darajasini oshiradi, bu plazma prokoagulyant potentsialini va giperkoagulyatsion holatini oshiradi [31].

Yuqorida ta'kidlab o'tilganidek, osteonekrozning rivojlanishiga glyukokortikoidlarning dozasi ham, davolash davomiyligi ham ta'sir qiladi. 2003-yilda Xitoyda SARS epidemiyasidan olingan saboqlar shuni ko'rsatdiki, 3-5 kunlik qisqa kursda 1-2 mg/kg dan kam dozadagi metilprednizolon COVID-19 uchun yordamchi davolash sifatida tavsiya etiladi [32].

Ushbu qo'llash usuli, kuchli yallig'lanish reaksiyasi va kasallikning o'tkir rivojlanishi (o'pka kompyuter tomografiyasi bo'yicha) bo'lgan bemorlarda ijobiy davo ta'siri ko'rsatishi bilan birga, suyaklarda osteonekroz rivojlanishiga olib kelmaydi [33]. Shu bilan birga, yuqori kumulyativ dozalarda steroidlar bilan uzoqroq davolanish osteonekrozning rivojlanishiga olib keladi [34]. Ba'zi tadqiqotchilarning fikriga ko'ra, glyukokortikoidlarning maksimal sutkalik dozasi va son suyagi boshchasining osteonekrozi o'rtasida bog'liqlik mavjud bo'lib, bu yetarli nazoratni talab qiladi [35].

G.Motomura va boshqalarning quyonlar ustida o'tkazgan tajribalari xulosasiga ko'ra, 1 mg/kg, 5 mg/kg, 20 mg/kg va 40 mg/kg metilprednizoloni guruhlarda qo'llanganda, osteonekroz rivojlanish ehtimoli, mos ravishda 0%, 42%, 70% va 96% ni tashkil qiladi [36].

Metilprednizoloni kuniga 5 mg/kg dozada klinik qo'llash tajribasi shuni ko'rsatdiki, bu har beshinchi bemorda osteonekroz rivojlanishiga olib keladi, kuniga 1 mg/kg dozada qabul qilingan bemorlarda nazorat guruhidan farqli o'laroq kasallik

rivojlanmagan [37]. Prednizolon dozasini har 10 mg ga ko'paytirish osteonekroz bilan kasallanish xavfini 3,6% ga oshiradi [38].

GKSlarning kumulyativ dozasiga alohida ahamiyat beriladi. O'tkir respirator sindromi (O'RS) bo'lgan 539 bemorni o'z ichiga olgan retrospektiv tadqiqotda osteonekroz rivojlanish tezligi preparatning umumiy dozasini oshirish bilan bog'liq bo'ldi [39].

Metilprednizolonning umumiy dozasi 5g dan kam bo'lsa, osteonekroz rivojlanish xavfi nisbatan kamroq bo'ldi. Ammo, umumiy doza 5g dan 10g gacha ko'tarilganligi sababli, xavf keskin oshdi (R.Zhao va boshqa avtorlar).

J.Rademaker va boshqalar prednizolonning 700 mg dozasida son suyagi boshchasi nekrozining boshlanishi uchun chegara ekanligini ko'rsatdi [40]. M.H.M.Chan va boshqalar 2000 mg dan ortiq metilprednizolon yoki 1900 mg dan ortiq gidrokortizonning kumulyativ dozalari osteonekrozning prognozi ekanligini ta'kidladilar [41].

Davolash davomiyligi osteonekrozning rivojlanishiga ham ta'sir qiladi. Atipik pnevmoniya bilan og'rikan 1137 bemorni o'rganish shuni ko'rsatdiki, davolanishning har 10-kunida osteonekrozning ehtimoli 1,29 (95% CI 1,09-1,53;  $p = 0,003$ ) ni tashkil qiladi, mualliflarning fikriga ko'ra bu, osteonekroz xavfini kamaytirish uchun steroidlarni qo'llash muddatini qisqartirish muhimligini ko'rsatadi [38]. Glyukokortikoidlarni haftalik qabul qilish: agar per oral qabul qilingan metilprednizolonning dozasi 300 mg dan oshsa, ya'ni 5 kun davomida og'irligi 60 kg bo'lgan bemorda kuniga taxminan 1 mg/kg dan oshsa, osteonekroz rivojlanish xavfi yuqori bo'lishi mumkin degan fikr mavjud. Ushbu ma'lumotlarga asoslanib, mualliflar e'tiborni COVID-19 bilan kasallanganidan keyin avaskulyar nekrozni erta aniqlash uchun yuqoridagi xavfi bo'lgan bemorlarni tekshirishga qaratdilar [42].

*COVID-19 o'tkazgan bemorlarda son suyagi boshchasi avaskulyar nekrozi diagnostikasi*

Son suyagi boshchasi aseptik nekrozi diagnostikasida standart usul xisoblang rentgenologik tekshiruv usuli, postkovid avaskulyar nekroz diagnostikasida ham o'zining ahamiyatini yo'qotmagan.

F.S.Zhao va boshqalarning so'zlariga ko'ra, glyukokortikoidlarni qabul qilish tugaganidan keyin 3, 6 va 12 oylarda MRT tavsiya etiladi [43].

COVID-19 dan keyin bemorlarning retrospektiv tadqiqotida 3 oydan keyin MRT yordamida 23 bemorning 21 tasida davolanish tugagandan so'ng osteonekroz aniqlangan [44].

Magnit-rezonans spektroskopiya (MRS) tekshiruv usulini son suyagi boshchasi avaskulyar nekrozida qo'llanilishi ishemiya natijasida yuzaga keladigan zaralangan sohadagi kimyoviy moddalar o'zaro nisbatining o'zgarishini to'liq o'rganish imkonini beradi.

MRT diagnostikasi bilan bir qatorda, kasallikning yangi prognozlarini laborator usullar yordamida ham doimiy ravishda qidirib kelinmoqda. Qon plazmasida plazminogen aktivator ingibitori-1 (PAI-1) ni kamayishi osteonekroz xavfi yuqori bo'lgan bemorlarni tekshirish uchun yuqori sezgir usul ekanligi ko'rsatilgan [45]. B. Vey va V. Vey biomarker sifatida mikroRNK 423-5p dan foydalanishni taklif qildilar, uning darajasi glyukokortikosteroidlar qo'zg'atadigan osteonekrozli bemorlarda qonda sezilarli darajada oshadi. Shu bilan birga, ko'p hollarda koagulogramma ko'rsatkichlari normal qiymatlar ko'rinishida qolishi qayd etilgan [46].

*O'tkazilgan COVID-19 infeksiyasi bilan bog'liq son suyagi boshchasi avaskulyar nekrozini davolash*

COVID-19 asorati sifatida avaskulyar nekrozni o'z vaqtida aniqlash va uni glyukokortikoidlar bilan davolash kasallikning faol bosqichi rivojlanish xavfini kamaytirishi mumkin, lekin bu muqarrar ravishda kelajakda bo'g'imlarning artroplastikasiga olib keladi. Shu bilan birga, agar osteonekroz tashxisi erta bosqichda (I yoki II) aniqlansa, bemorlarning 92-97%i jarrohlik aralashuviga muhtoj bo'lmaydi [47] va konservativ davo muolajalari yordamida tiklanishga olib kelishi mumkin [48].

Idiopatik osteonekroz yoki COVID-19 bilan bog'liq bo'lmagan ikkilamchi osteonekroz kabi kasalliklarning dastlabki bosqichida davolashning asosiy maqsadi og'riqni kamaytirish, kasallikning rivojlanishini sekinlashtirish, subxondral suyaklarning impressiyasini oldini olish va bo'g'imlar faoliyatini tiklashdir. COVID-19 dan keyingi avaskulyar nekrozning dastlabki bosqichlarida konservativ davolash, yosh va o'rta yoshdagi bemorlarda aseptik beqarorlik rivojlanish xavfi yuqori bo'lganligi uchun bo'g'imlarni total endoprotezlash amaliyotidan uzoqlashtiradi.

Hozirgi vaqtda COVID-19 dan keyingi osteonekrozning dastlabki bosqichini davolash uchun standartlashtirilgan protokol mavjud emas. Klinik amaliyotda farmakoterapiya va bo'g'imlarga dekompressiya berish kombinatsiyasi qo'llaniladi va u o'zining samaradorligini ko'rsatdi, shu jumladan steroidlar keltirib chiqaradigan osteonekrozda ham [49]. Bo'g'imlarga dekompressiya berish kamida 3 oy davomida amalga oshiriladi. Son suyagining boshcha qismidagi osteonekrozni qo'ltiq tayoqlar yordamida, skeletning boshqa lokalizatsiyalarida nekroz aniqlanganida esa qo'ltiq tayoqdan tashqari tayoqcha va ortezlardan foydalanish mumkin [50].

Kattalardagi glyukokortikoidlar bilan bog'liq ikkilamchi osteonekrozni dastlabki bosqichlarda davolash uchun antirezorbtiv dori-darmonlarni muvaffaqiyatli qo'llash S. Agarvala va boshqalar [51] tomonidan ta'kidlab o'tilgan. Antirezorbtiv preparatlarning kasallik rivojlanishini sekinlashtirish va jarrohlik aralashuvga bo'lgan ehtiyojni kamaytirish qobiliyati isbotlangan. Amerika Qo'shma Shtatlari Amerika Ortoped Jarrohlari Akademiyasi (AAHKS) ma'umotlariga ko'ra, son suyagi boshchasi osteonekrozini davolashda bisfosfonatlarning ulushi 10%ni tashkil qiladi

[52]. Ulardan foydalanish osteonekroz sohasida rezorbsiya intensivligini kamaytirishga qaratilgan bo'lib, bu subxondral suyakning [53] va uning atrofidagi suyak to'qimalarining [54] impressiya bo'lish xavfini kamaytiradi. Alendron kislotasi aseptik nekrozli bemorlarni davolashning butun davri uchun mumkin bo'lgan bisfosfonat sifatida ko'rib chiqiladi - 70 mg haftada bir marta [55]. Biroq, peroral qo'llaniladigan bisfosfonatlarining kamchiliklari ularning past muvofiqligidir. Shu munosabat bilan vena ichiga qo'llaniladigan shakllarini, birinchi navbatda zoledronik kislotani 5 mg dozada qo'llash, qabul qilish chastotasini hisobga olgan holda (yiliga bir marta) istiqbolli deb hisoblanadi [56].

To'g'ridan-to'g'ri antirezorbtiv ta'siriga qo'shimcha ravishda suyak to'qimalarining shishini kamaytiradi [57], shuningdek tomir ichiga yuboriladigan bisfosfonatlar sezilarli og'riq qoldiruvchi ta'sirga ega, bu esa bemorlarning hayot sifatini yaxshilaydi [58].

Buyraklar orqali azot qoldiqlari ajralishi buzilgan bemorlarda bifosfonatlarni qo'llash mumkin emas [59]. Bunday hollarda avaskulyar nekroz uchun antirezorbtiv dori sifatida yiliga ikki marta 60 mg dozadan denosumabni qo'llash tajribasi mavjud [60].

Antirezorbtiv dorilarni qo'llash kalsiy preparatlarini bir vaqtning o'zida kuniga 500-1000 mg/sut dozada va xolekalsiferolni kamida 1000 IU/sut dozada yoki kuniga kamida 0,5-0,75 mkg/sut dozada al fakalsidolni qo'llashni talab qiladi [61].

Pandemiya davrida xolekalsiferolni buyurish, birinchi navbatda, COVID-19 ning kechishiga ta'sir qilish uchun tavsiya etiladi. Bunday holda, infeksiya kursining og'irligi pasayadi va omon qolish darajasi oshadi [62, 63]. Ushbu ta'sirlar virus replikasi tezligining sekinlashishi va yallig'lanishga qarshi sitokinlar kontsentratsiyasining oshishi bilan izohlanadi [64]. Biroq, xolekalsiferolning ushbu ta'sir mexanizmi zaif dalillar bazasiga ega, chunki D vitamini ta'siri va u bilan bog'liq bo'lgan nafas yo'llari infeksiyalari xavfi bo'yicha o'tkazilgan kuzatuv va klinik tadqiqotlar qarama-qarshidir: ba'zilar xavfning pasayishi haqida xabar berishadi, boshqalari esa yo'q [65, 66]. Ushbu qarama-qarshi natijalar bemorlar populyatsiyasining geterogenligi va D vitamini dozasi bilan bog'liq deb taxmin qilinadi. Shuning uchun D vitaminining yaxshi ishlab chiqilgan sinovlari natijalarini ularning organizmga mumkin bo'lgan ta'siri haqida xulosa chiqarishdan oldin kutish kerak.

Xolekalsiferolni buyurish uchun yana bir dalil osteonekroz rivojlanishi va suyaklar mineral zichligi pasayishi o'rtasidagi bog'liqlik xisoblanadi [67]. Xolekalsiferolni kalsiy preparatlari bilan birgalikda qo'llash hozirgi vaqtda birlamchi va ikkilamchi osteoporoz fonida suyak metabolizmini sekinlashishi hamda suyaklar mineral zichligini saqlash uchun asosiy davo usuli hisoblanadi [68].



Osteonekroz va mikrosirkulyatsiya buzilishi o'rtasidagi qayd etilgan munosabatni hisobga olgan holda, osteonekroz tashxisi qo'yilgandan keyingi birinchi kunlardan boshlab (trombotsitlar agregatsiyasi ingibitori va angioprotektiv vosita sifatida) dipiridamol 25 mg dozadan kuniga 3 mahal per oral qo'llaniladi, 3 hafta davomida. [69]. Suyak ichi bosimini pasaytirish va mikrosirkulyatsiya holatini yaxshilash maqsadida Iloprostni buyurish mumkin. Ushbu preparatning osteonekrozni davolashda samaradorligi haqida ilgari ham qayd etilgan [70]. Iloprost infuziya qilinganida qon bosimini keskin pasaytirish xavfi bo'lganligi tufayli uni statsionar sharoitda intensiv terapiya bo'limlarida shifokor nazoratida olgan maqsadga muvofiqdir [71].

Son suyagi boshchasi postkovid etiologiyali avaskulyar nekrozi bilan og'rikan bemorlarda giperkoagulyatsiya yoki gipofibrinolizni kasallikning 1-2 rivojlanish bosqichlarida (ARCO klassifikatsiyasi bo'yicha) kompleks terapiya sifatida antikoagulyantlar tavsiya etiladi. Xususan, Enoksiparin-Natriy kuniga 4000 IU (0,4 ml) dan 6000 IU (0,6 ml) gacha dozadan teri ostiga ineksiya buyuriladi 2 haftadan 12 haftagacha davomiylikda. [72]. Shunisi aniqki, COVID-19 ni davolashda tabletka ko'rinishidagi antikoagulyantlar ham teri ostiga yuboriladigan preparatlardan kam ta'sir ko'rsatmaydi, masalan, apiksabanni 2,5 mg dozadan kuniga 2 mahal 12 hafta davomida qo'llash [73].

Son suyagi boshchasi avaskulyar nekroziga chalingan bemorlarda antikoagulyant terapiyani mahalliy qo'llanilishi ya'ni girudoterapiya bilan davolash kompleksi ishlab chiqilmagan. Ishemiya natijasida yuzaga kelgan son suyagi boshchasi avaskulyar nekrozini erta bosqichlarda girudoterapiya yordamida kompleks-konservativ davolash haqida ko'p izlanish va o'rganish zarur.

Ba'zi hollarda simptomatik fizioterapiya usuli og'riqni qoldirish imkonini beradi [74]. Shu munosabat bilan avaskulyar nekrozni kompleks davolashda impulsi elektromagnit terapiya, giperbarik oksigenatsiya, ozonoterapiya, ekstrakorporal zarba-to'lqinli terapiyasini qo'llash mumkin. Biroq, COVID-19 dan keyingi osteonekrozni davolashda ularning samaradorligini baholash uchun qo'shimcha tadqiqotlar o'tkazish talab qilinadi.

Dastlabki bosqichlarda og'riqni kamaytirish va qon ta'minotini yaxshilash maqsadida, ilgari buyurilgan konservativ terapiyadan so'ng son suyagi boshchasining zararlangan joyini tunnel qilish (dekompressiya berish) mumkin [75].

#### Xulosa

Maqolamiz so'ngida, SARS-CoV-2 dan keyin yuzaga kelgan son suyagi boshchasi avaskulyar nekrozini erta muddatlarda diagnostika qilishda Magnit rezonans spektroskopiya usuli kelajakda katta avzalliklarga ega bo'ladi. U orqali bemorlarda kasallikning erta muddatlarida davolashning aynan qaysi turini (konservativ/jarrohlik) aniq tanlash imkoniyati paydo bo'ladi. Kasallik

diagnostikasida qo'shimcha ravishda oyoq qon-tomirlarini Ultra tovushli dupleks skanerlash usuli ham kasallik istiqbolini prognozlashda va davolash usulini tanlashda muhim ahamiyat kasb etadi. Hozirgi vaqtda mavjud nashrlarga ko'ra, COVID-19dan keyin avaskulyar nekroz rivojlanishining ikkita alohida mexanizmlari muhokama qilinmoqda: infeksiyani davolash uchun ishlatiladigan glyukokortikoidlarning ta'siri va suyak metabolizmi buzilishiga COVID-19 virusining o'zining hissasi. Ikkinchi holatda, osteonekroz rivojlanishi qon tomirlarga virus tomonidan to'g'ridan-to'g'ri zarar etkazilishi yoki qon tomir devori endoteliy qavati yallig'lanishining rivojlanishi fonida mikrotromboz va suyak to'qimalari qon ta'minoti buzilishi tufayli yallig'lanishga qarshi sitokinlar ta'siri ostida qon ivishining kuchayishi hamda infeksiyaga qarshi immun javob ortishi bilan bog'liq. Shuningdek kasallikni erta muddatlarda ya'ni, 1-2 bosqichlarda kompleks-konservativ davolashda mahalliy girudoterapiyaning o'rni alohida qayd etiladi. Mahalliy mikrosirkulyatsiyani yaxshilash va trombolizis terapiya zararlangan soha vena qon tomirlarida venoz stazni bartaraf qilishda muhim ahamiyat kasb etadi. Biz taklif qilayotgan kompleks konservativ davolash usuli mavjud an'anaviy konservativ davolash usullaridan farqli o'laroq o'zining samaradorligi bilan ajralib turadi.

Xulosamiz so'ngida, COVID-19 ta'sirida rivojlangan son suyagi boshchasi avaskulyar nekroziga uchragan bemorlarda, kasallik oqibatlarini 6, 9, 12, 18 oy muddatlarda dinamik rentgenografiya, MRT, MCKT va UT-dupleks tekshiruvlari orqali baholash mumkin. Shuningdek qonning koagulyatsion tarkibini dinamikada taxlil qilib borish maqsadga muvofiq bo'ladi. Kasallikni erta bosqichlarida (I-II bosqich, Ficacat b'yicha) konservativ davolash orqali mahalliy qon aylanishini yaxshilashga qaratilgan davolash texnologiyalarini yaratish zarur bo'ladi.

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