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COVID-19 O'TKAZGAN REVMATOID ARTRITLI BEMORLARNI DAVOLASH.

Toshkent tibboyot akademiyasi

2 son ichki kasalliklar kafedrasasi assistenti

Sharapov Zafar Abdunayemovich

Annotasiya: Ko'plab revmatoid artritli bemorlarda COVID-19 pandemiyasidan so'ng kasallikni klinik kechishining aktivlashishi, yangi asoratlari va aksariyat bemorlarda koviddan keying holat kuzatildi. Ushbu maqolada COVID-19 pandemiyasidan so'ng 3 yil davomidagi xalqaro ilmiy izlanishlarda aniqlangan COVID-19 revmatoid artrit klinik kechishiga ta'siri va davolanishdagi natijalari o'rganiladi.

Kalit so'zlar: revmatoid artrit, bo'g'imlarning shikastlanishlari, interlyukin, COVID-19, gen injenerli biologik vositalar (GIBDV), interlyukin 6 ingibitori (irIL6) va yanus kinaza ingibitori (IYK),

Ko'plab olimlar ta'kidlashiga ko'ra immunyallig'lanishli revmatik kasalliklarda (IYRK) Covid-19 og'ir kechadi va o'lim xavfini 1,5 baravar oshiradi [1,2]. Dunyo bo'ylab 20 million kishi revmatoid artrit (RA) bilan yashaydi [3,4], ularning aksariyati kamida bir marta SARSCoV-2 bilan kasallangan yoki tez orada yuqtiradi.

COVID-19 pandemiyasi mutaxassislarning IYRK uchun terapiyaning xavfsizligi haqidagi tushunchalarini sezilarli darajada o'zgartirdi. Rossiyalik va xorijiy mualliflar pandemiya davrida IYRK davolash xususiyatlarini faol o'rganmoqda, shuningdek, yangi koronavirus infeksiyasining yanada og'ir kechishini belgilovchi omillarni tahlil qilmoqda [5].

Biroq, COVID-19 patogenezi haqida haligacha ham aniq tushuntirish yo'q. Hozirgi vaqtda sitokin regulyatsiyasining buzilishi va yuqori yallig'lanish ushbu kasallikning asosiy klinik ko'rinishlari va asoratlari uchun mas'ul ekanligiga ishoniladi, ular sitokinlar xujumi deb ataladi. SARS-CoV-2 infeksiyasidan so'ng o'pkada ko'p miqdordagi signal reaksiyalari paydo bo'ladi, so'ngra IL-1b, IL-6, IL-8, CXCL10 va TNF-a kabi sitokinlar va kimyokinlar chiqariladi va yallig'lanish hujayralarini infeksiyalangan joylarga jalb qilish, bu ko'pincha o'tkir respirator distress sindromi, ko'p organ etishmovchiligi va hatto o'limga olib keladi [6].

RA li bemorlarda COVID-19 infeksiyasiga beriluvchanlikka va uning asoratlari sabab bo'luvchi bir necha asosiy xavf omillari mavjud. Bular o'zgargan asosiy o'zgartirilgan immunitet, vaksinalar va infeksiyalarga immun javobni susaytiradigan immunomodulyatsiya qiluvchi dori vositalari [3] va interstitsial

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o'pka kasalligi (IO'K) va yurak-qon tomir kasalliklari COVID-19 ni og'ir kechishiga sabab buluvchi xavf omillari bo'lib, odatda o'lim xavfini oshiradi va kasalxonada yotib davolanishga ko'rsatma bo'lib hisoblanadi.[7]

SARS-CoV-2 keltirib chiqaradigan infeksiyalar, birinchi navbatda, nafas olish tomchilari orqali yuqadi, ular patogenligi yuquvchanligi juda yuqori. [8]

SARS-CoV-2 sabab bo'lgan COVID-19 nafas yo'llarining og'ir kasalligi bo'lib, u ko'plab populyatsiyalarga, ayniqsa qariyalarga ta'sir qiladi va butun dunyo bo'ylab tez tarqalib, odamlar uchun jiddiy xavf tug'diradi. Jahon sog'liqni saqlash tashkiloti (JSST) statistik ma'lumotlariga ko'ra (<https://covid19.who.int/>), shu paytgacha dunyo bo'ylab 760 milliondan ortiq tasdiqlangan holatlar qayd etilgan, 6,8 millionga yaqin kishi vafot etgan.

Shunisi e'tiborga loyiqki, COVID-19 bilan kasallangan bemorlarda sitokin va immun faollashuv RA bilan og'rigan bemorlarga o'xshaydi [9]. RA bilan og'rigan bemorlarning mahalliy yallig'lanish uchoqlarida immun hujayralar va yallig'lanishga qarshi sitokinlar, shu jumladan IL-1b, IL-6, IL-17 va TNF-a autoimmun yallig'lanish patogenezda hal qiluvchi rol o'ynaydi.

RA bilan og'rigan bemorlarda immun tizimining potentsial disfunktsiyasi, komorbid kasalliklar va uzoq muddatli immunosuppressiv dorilar tufayli infeksiyaga qarshi qobiliyat umumiy aholinikidan past bo'lishi mumkin [10,11].

Oldingi ba'zi tadqiqotlarga ko'ra, COVID-19 RA bilan og'rigan bemorlarda ko'proq uchraydi va klinik kechishi umumiy populyatsiyadagiga qaraganda og'irroqdir [12].

Tadqiqotlar shuni ko'rsatdiki, yuqumli kasalliklar RA bemorlarida erta o'limning asosiy sababidir.[13,14,15]. Buyuk Britaniyada o'tkazilgan prospektiv kohort tadqiqotiga ko'ra, RA bilan og'rigan bemorlarda infeksiya xavfi umumiy aholiga qaraganda 3,5 baravar yuqori [16].

Bundan tashqari, to'g'ridan-to'g'ri RA yoki davolashning bilvosita ta'siri tufayli yuzaga keladigan immunitet o'zgarishlari COVID-19 uchun yomon prognozga olib kelishi mumkin.[17]. Oqibatda, SARS-CoV-2 bilan kasallanishning yuqori ehtimoli va COVID-19 ning salbiy oqibatlari, shubhasiz, RA bemorlarini davolashda jiddiy to'siq bo'ladi [18].

COVID-19 bo'yicha umumlashtirilgan tadqiqotlar shuni ko'rsatadiki, RAni davolash uchun ishlatiladigan ba'zi dorilar ham COVID-19 ga ta'sir qilishi mumkin [19].

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RA bilan og'rigan bemorlarda timus disfunktsiyasi, periferik T hujayralarining yangilanishi va qon T hujayralarining disfunktsiyasi kuchayadi, bu ularni virusli infeksiyalarga nisbatan zaifroq qiladi [20].

So'nggi yillarda RAni davolashda sezilarli yutuqlarga erishildi. Zamonaviy asosiy antirevmatik dorilar (MT, LF va boshqalar) va ayniqsa gen injenerli biologic vositalar (*GIBDV*) (masalan, TNF ga monoklonal antitanalar – Remicade, ИЛ-6 ингибитори— тоцилизумаб) yordamida ko'plab bemorlar kasallik faolligini sezilarli 70% ga pasayishiga erishishlari mumkin.

Revmatoid artrit va koronavirus infeksiyasi (COVID-19) kabi etiologiyasi va patogenezi jihatidan farq qiluvchi kasalliklarning asosiy rivojlanish mexanizmlarini ko'rib chiqilganda, ikkala nozologiyada ham yallig'lanishga qarshi sitokinlarning sintezi kuchayishi aniqlangan va biologik faol preparatlarni qo'llash bo'yicha amaldagi klinik tavsiyalarni hisobga olgan holda ushbu holatlarda *GIBDV* qullash maqsadga muvofiqdir[21].

D. Galarza-Delgado va boshqalarga ko'ra. [22], biologik faol dorilar bilan davolash paytida IYRK bo'lgan bemorlar COVID-19, odatda, rituksimab (RTM) olgan bemorlar bundan mustasno, koronavirus infeksiyasining og'ir kechishi kuzatilmagan. J. Loarce-Martos va boshqalar. RTM dan foydalanganda kasallik og'irroq kechishi ham tasvirlangan bunda ikki tomonlama o'pka shikastlanishi va o'lim xavfi yuqori bo'lgan.[23]

Jahon sog'liqni saqlash tashkilotining (JSST) farmakologik nazorat bo'yicha hisobotiga ko'ra interleykin 6 ingibitori (irIL6) va yanus kinaza ingibitori (IYK) [12] bilan davolash havfsizroq va samaradorligi yuqoriligini ko'rsatadi[24]

Bir qator tadqiqotlarga ko'ra, biologik faol dori-darmonlarni, ayniqsa TNF-a inhibitorlarini olgan bemorlar kasalxonada yotib davolanishi kamroq kuzatilgan. [25].

COVID-19 o'tkazgan RA bemorlarning kasallikning dastlabki bosqichi, ayniqsa kasallikning boshlanishidan boshlab dastlabki 3 oy, samarali davo uchun eng qulay hisoblanadi. Bemorlarni davolashning asosi davolashning etarililigini diqqat bilan kuzatish (kamida 3 oyda bir marta), agar kerak bo'lsa, davoni keyinchalik tuzatishdir. COVID-19 o'tkazgan RA davolash uchun zamonaviy talablar quyidagilarni o'z ichiga oladi: 3 oy ichida klinik belgilar boshlanganidan keyin yallig'lanishga qarshi nosteroid vositalar (YAQNV) larni tashxis qo'yilgandan so'ng darhol buyurish, har bir bemorda imkon qadar tezroq remissiya yoki past kasallik faolligiga erishish, agar bu maqsadga erishilmasa, tez-tez va to'g'ridan-to'g'ri nazorat qilish orqali davoni tanlash kerakligi (har 1-3 oyda), RA faollik

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ko'rsatkichlari dinamikasini diqqat bilan kuzatib borish va davoni o'z vaqtida tuzatish.

RA bilan og'riqan bemorlarni davolash bo'yicha ACR (2021) ning so'nggi tavsiyalari dori-darmonlarni buyurishda e'tiborga olinishi kerak bo'lgan asosiy parametrlarni islab chiqqan:

1. Erta RA (kasallik davomiyligi <6 oy), oraliq (kasallik davomiyligi 6-24 oy) va o'rnatilgan (uzoq davom etgan simptomlar 24 oydan ortiq vaqt davomida mavjud) ga bo'lingan RA davomiyligi;

2. Turli indekslar (Disease Activity Score-28 (DAS-28) va boshqalar) yordamida bo'linadigan kasallik faolligi aniqlash;

3. Prognostik jihatdan noqulay belgilarning mavjudligi: kasallik faolli (ko'p sonli og'riqli va shishgan bo'g'inlar), erta bosqichda eroziya mavjudligi, revma factor(RF) yoki siklik sitrullinlangan peptidlarga antitanalar(SSPA) ning oshishi, eritrotsitlar cho'kish tezligi (ECHT), S-reaktiv oqsil(SRO) ning oshishi, YAQNV bilan erta davo rentgenologik rivojlanish tezligini pasaytiradi, uzoq muddatli remissiyalar (bemorlarning 65% gacha) chastotasini oshiradi, jiddiy funktsional buzilishlarning oldini oladi va bemorlarning o'limini kamaytiradi. YAQNV lar RA boshlanganidan boshlab 3 oydan kechiktirmay, optimal ta'sirga erishish uchun dozani tez oshirib yuborish kerak (DAS-28<2,4), so'ngra samarasiz bo'lsa, 2-4 oy ichida preparatni almashtirish kerak YAQNV davosi kasallik faolligi pasayganda va remissiyaga erishilganda ham davom ettirilishi kerak.

YAQNV qo'llash fonida kasallik faolligi dinamikasi DAS-28 indeksi bo'yicha baholanadi, bu asosiy davoni tanlashni individuallashtirishga va uning samaradorligini sezilarli darajada oshirishga yordam beradi.

EULAR tavsiyalariga ko'ra, COVID-19 o'tkazgan RAni kasallikni MT preparati bilan davolash maqsadiga erishilmagan bo'lsa, davolanishga biologik dori vositalarini qo'shilishi kerakligi tavsiya etdilar.

COVID-19 bilan kasallangan bemorlarda interleykin-6 miqdoriy ko'rsatkichi balandligining qayt etilishi va kasallik og'irlik darajasi ishonchli korrelyatsion bog'liqligi qayt etilgan. Sitokinlar xujumi vaqtida IL-6 ning ko'p miqdorda hosil bo'lishi kuzatiladi va kasallik og'ir kechishida asosiy rol o'ynaydi.[26]

Revmatologiyada GIBDV maqsadli davoga o'xshash joyni egallaydi. GIBDV klinik amaliyotga kiritilgandan so'ng, kasallik belgilarini to'xtatish bilan bir qatorda, bo'g'imlarda eroziv jarayonni kamaytirishi, bemorning funktsional holati va hayot sifatini yaxshilashiga olib keldi .

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RA bilan og'rigan bemorlar odatda o'z kasalliklarini davolash uchun DMARDlardan foydalanadilar.[27]

Ba'zi DMARDlar immunosupressiv dorilar sinfiga mansub bo'lib, ular organizmda immunosupressiyaga olib kelishi mumkin. Bu RA bemorlarida immun disfunktsiyasi va komorbid kasalliklar tufayli COVID-19 infeksiyasini davolashda ayniqsa tashvishlidir [28].

Immunosupressantlar TNF, IL-1, IL-6 va interferon tomonidan qo'zg'atiladigan sitokinlar hujuminini kamaytiradi, bu COVID-19 bemorlarida organlarning kuchli shikastlanishini kamaytiradi [29], ular shuningdek, autoimmun reaksiyaning pasayishi tufayli infeksiyalar xavfini oshiradi.

Tadqiqotlar shuni ko'rsatdiki, immunosupressant terapiyasi sitokin inhibitori terapiyasini olgan bemorlarga nisbatan COVID-19 natijalarini yomonlashtirishi mumkin [30]. Bundan tashqari, RAli bemorlarda immunosupressantlarning yatrogen ta'siri tufayli infeksiya yomonlashishi mumkin [31].

Glyukokortikoidlar (GC) RA davolashda keng tarqalgan immunosupressiv dorilar bo'lib, og'ir COVID-19 holatlarida yuqori yallig'lanish holatini yumshatib, o'lim va kasalxonaga yotqizish vaqtini kamaytiradi [32].

Biroq, GK lardan ortiqcha foydalanish immunitetni susaytirishi va virusni tozalashni kechiktirishi mumkin. Revmatizm bilan og'rigan bemorlarda GK (kuniga ≥ 10 mg prednizon) qo'llagan holda, og'ir COVID-19 [33] tufayli kasalxonaga yotqizish ehtimoli yuqori.

Bundan tashqari, GK lardan foydalanish COVID-19 bemorlarida, ayniqsa osteoporozga ko'proq moyil bo'lgan keksa bemorlarda suyak yo'qotilishini tezlashtirishi mumkin [34].

Klinik tadqiqotlar past dozali GKlar qabul qilgan surunkali artrit bilan og'rigan bemorlarda COVID-19 [35] ning ko'payishini kursatadi .

Bundan tashqari tadqiqotlar, biologik kasallikni o'zgartiruvchi revmatik dori (bDMARD)larni qabul qilgan RA bilan og'rigan bemorlarda an'anaviy sintetik kasallikni o'zgartiruvchi revmatik dori (csDMARD) [116] qabul qilganlarga qaraganda COVID-19 rivojlanish ehtimoli ko'proq va vaqt o'tishi bilan bu xavf ortib bormoqda [36].

Xulosa qilib aytganda, RA bemorlarida COVID-19 ni davolashda immunosupressantlardan foydalanish ikki qirrali qilichni ko'rsatadi. Klinisestlar har bir bemorning o'ziga xos holatiga qarab yallig'lanishga qarshi foydani yuzaga kelishi mumkin bo'lgan nojo'ya ta'sirlar bilan solishtirishlari kerak. [37]

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COVID-19 ning rivojlanish xususiyatlari va klinik kechishini o'rganish natijasida olingan to'plangan ma'lumotlar bizga COVID-19 va autoimmun kasalliklarning patogenezi asosan o'xshash degan xulosaga kelish imkonini beradi. COVID-19 da qo'zg'atilgan yallig'lanishga qarshi sitokinlar spektri RA dagiga o'xshaydi [38].

Bu holat COVID-19 asoratlarini davolash uchun bir qator biologik faol dori vositalaridan muvaffaqiyatli foydalanish imkonini beradi va pandemiya davrida IYRK terapiyasini davom ettirishni tavsiya qilish imkonini beradi.

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