

БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

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ANNOTATION

A regular increase in arterial pressure above normal levels, manifesting as arterial hypertension (AH) syndrome, occurs alongside cardiovascular diseases as well as other conditions. According to World Health Organization (WHO) analyses, AH is observed in 27% of the population over the age of 20. By 2025, this figure reached 29%. Among the population of Uzbekistan aged 40-60, AH was observed in 30.4% of cases. In this regard, there are numerous types of antihypertensive drugs used for AH, which are recommended to patients based on the mechanisms of blood pressure elevation and specific indications. This text examines the primary mechanisms of action of drugs belonging to the class of Angiotensin II receptor antagonists (ARAs), primarily telmisartan.

Keywords. Arterial hypertension (AH), arterial blood pressure (ABP), hypotensive agents, sartans, ARA, telmisartan.

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ANTIGIPERTENZIV DORI PREPARATLARIDAN SARTANLAR GURUHIGA MANSUB TELMISARTANNING GIPOTENZIV VA ORGANOPROTEKTORLIK XUSUSIYATLARI

ANNOTATSIYA

Arterial bosimning muntazam me'yordan balandligi arterial gipertenziya (AG) sindromi ko'rinishida yurak-qon tomir kasalliklari bilan bir qatorda boshqa kasalliklarda ham uchraydi. Jahon Sog'liqni Saqlash Tashkiloti (JSST) tahlillariga ko'ra 20 yoshdan oshgan aholining 27% da AG kuzatiladi. 2025 yilga kelib bu ko'rsatgich 29% ni tashkil etgan. O'zbekistonning 40-60 yosh oralig'idagi

aholisida esa AG 30,4% hollarda kuzatilgan. Ushbu tadqiqotimizda Angiotenzin II retseptor antagonistlari (ARA) sinfiga mansub preparatlardan, asosan telmisartanning asosiy ta'sir mexanizmlari ko'rib chiqiladi.

Kalit so'zlar. Arterial gipertenziya (AG), arterial qon bosimi (AQB), gipotenziv vositalar, sartanlar, ARA, telmisartan.

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ГИПОТЕНЗИВНЫЕ И ОРГАНОПРОТЕКТОРНЫЕ СВОЙСТВА ТЕЛМИСАРТАНА — ПРЕДСТАВИТЕЛЯ ГРУППЫ САРТАНОВ СРЕДИ АНТИГИПЕРТЕНЗИВНЫХ ПРЕПАРАТОВ

АННОТАЦИЯ

Регулярное превышение нормы артериального давления в виде синдрома артериальной гипертензии (АГ) встречается как при сердечно-сосудистых, так и при других заболеваниях. Согласно анализу Всемирной организации здравоохранения (ВОЗ), АГ наблюдается у 27% населения старше 20 лет. К 2025 году этот показатель составил 29%. Среди населения Узбекистана в возрасте 40–60 лет АГ наблюдалась в 30,4% случаев. В связи с этим существует множество видов антигипертензивных лекарственных средств, применяемых при АГ, которые рекомендуются пациентам на основании механизмов повышения АД и определенных показаний. В данной работе рассматриваются основные механизмы действия препаратов, принадлежащих к классу антагонистов рецепторов ангиотензина II (АРА), в основном телмисартана.

Ключевые слова. Артериальная гипертензия (АГ), артериальное давление (АД), гипотензивные средства, сартаны, АРА, телмисартан.

Bugungi kunda arterial gipertenziya (AG) nafaqat jahon miqyosida, balki O'zbekiston va Markaziy Osiyo mamlakatlari uchun ham eng dolzarb tibbiy-ijtimoiy muammolardan biri hisoblanadi. Mintaqada yurak-qon tomir kasalliklari umumiy o'lim sabablarining yetakchi o'rinlarini egallab kelmoqda va ushbu kasalliklarning rivojlanishida arterial gipertenziya asosiy xavf omillaridan biri sifatida e'tirof etiladi. Arterial gipertenziya bilan og'rikan bemorlarning sezilarli qismida vaqt o'tishi bilan chap qorincha miokardi gipertrofiyasi, buyrak funksiyasi buzilishi va miya-qon aylanishining surunkali yetishmovchiligi kabi nishon a'zolar shikastlanishi kuzatiladi. Markaziy Osiyo mamlakatlarida, jumladan O'zbekistonda, qandli diabet va semizlikning keng tarqalishi arterial gipertenziya bilan kechuvchi holatlarni yanada og'irlashtirmoqda. Kuzatuvlarga ko'ra, AG va qandli diabet birga uchraydigan bemorlarda buyrak asoratlari va yurak-qon tomir hodisalari xavfi keskin oshadi. Shu sababli, arterial gipertenziyani nafaqat simptomatik nazorat qilish, balki uning patogenetik mexanizmlariga ta'sir etuvchi dori vositalarini qo'llash alohida ahamiyat kasb etadi. Arterial gipertenziya patogenezida simpato-adrenal tizim va renin–angiotenzin–aldosteron tizimi (RAAT) ning faollashuvi muhim o'rin tutadi. RAATning ortiqcha faolligi qon tomirlar tonusining oshishiga, periferik qarshilikning kuchayishiga, natriy va suvning organizmda ushlanib qolishiga olib keladi. Shu sababli RAAT bo'g'inlariga yo'naltirilgan dori vositalari arterial gipertenziyani davolashda yetakchi o'rin egallaydi. So'nggi yillarda angiotenzin II retseptorlari antagonistlari (ARA), ya'ni sartanlar, yuqori samaradorligi, uzoq davom etuvchi gipotenziv ta'siri va nisbatan kam nojo'ya ta'sirlari bilan klinik amaliyotda keng qo'llanilmoqda. Ushbu guruh vakillaridan biri bo'lgan telmisartan arterial qon bosimini barqaror pasaytirish bilan bir qatorda, yurak, buyrak va miya kabi nishon a'zolarga nisbatan ifodalangan organoprotektiv xususiyatlarga ega ekanligi bilan ajralib turadi. Shu bois telmisartanning antigipertenziv va organoprotektiv ta'sirlarini o'rganish va tahlil qilish hozirgi zamon tibbiyotining dolzarb yo'nalishlaridan biri hisoblanadi.

MAVZUNING DOLZARBLIGI VA TAHLILI. Arterial qon bosimi oshishida bir qancha mexanizmlar ishga tushishi va gemodinamik o'zgarishlar kuzatiladi. Bu ko'rsatkichlar quyidagilar:

- Yurakning qon otib berish hajmi
- Aylanib yuruvchi qon hajmi
- Periferik qon tomirlar tonusi
- Qon ivuvchanligi

Bundan tashqari bu ko'rsatkichlar oldingi yuklama (preload)[1] va keyingi yuklama (afterload)[2] ning o'zgarishiga bog'liq. Chap bo'lmachaga keladigan umumiy qon hajmi ortishi hisobiga oldingi yuklama oshadi. Bu esa o'z navbatida chap qorinchaning sistoladan oldin katta qon hajmi bilan to'lishini ko'rsatadi. Keyingi yuklamaning oshishi esa aortaga chiqadigan qon hajmining hamda mos ravishda bosimning oshishiga olib keladi. AG patogenezida uni boshqaruvchi omillardan bir qanchasini ko'rib chiqish mumkin. Asosiy omillardan biri bo'lgan SAT (simpato-adrenal tizim) faollashib, α -, va β -adrenoretseptorlarni ishga tushiradi. Bu o'z navbatida arteriyalar silliq mushak tolalaridagi α -adrenoretseptorlarning presinaptik yorig'idan ajralib chiqadigan noradrenalin sekretsiyasi oshishiga olib keladi. Natijada tomirlar tonusi oshadi, periferik tomirlar qarshiligi ortadi. β -adrenoretseptorlar orqali esa buyrakning yukstaglomerulyar apparati qo'zg'alib RAAT (renin angiotenzin aldosteron tizimi) ishga tushadi. Buyraklardan bir qancha mexanizmlar faollashuvi bilan renin ko'p miqdorda ishlab chiqariladi, natijada qon zardobida aylanib yurgan renindan angiotenzinogen oqsil tabiatga ega bo'lgan biologik faol modda angiotenzin-I (AI) hosil bo'ladi. Angiotenzin-I o'z navbatida, asosan o'pka va buyraklarda sintezlanuvchi AAF (angiotenzin aylantiruvchi ferment) ta'siri bilan angiotenzin-II (AII) ga aylanadi. Angiotenzin-II renin-angiotenzin tizimining asosiy bo'g'ini bo'lib, maxsus 1- va 2-tur retseptorlar (AT1 va AT2) orqali ko'plab a'zo va to'qimalarga ta'sir ko'rsatadi. Angiotenzin-II ning bevosita effektlariga miokard qisqarishining kuchayishi, arteriya va arteriolalar vazokonstriksiyasi (tomirlar torayishi), aldosteron sintezi va buyrak usti bezlari tomonidan katexolaminlar (adrenalin va noradrenalin) ajralishining kuchayishi, buyraklarda natriy va suv reabsorbsiyasining ortishi, simpatik nerv oxirlari tomonidan noradrenalin ajralishining stimulyatsiyasi kiradi. Aynan yuqorida ta'kidlangan mexanizmlar ta'sirida kelib chiqqan AG ni davolashda Angiotenzin II retseptor antagonistlari (ARA) hozirda keng qo'llaniladi, ular boshqacha sartanlar ham deyiladi. Ular angiotenzin retseptorlarini ma'lum darajada bloklay qon bosimini pasaytiradi. ARAlar boshqa gipotenziv preparatlar samara bermaganda hamda AAFi ning nojo'ya ta'sirlari kuzatilganda qo'llanilishi mumkin. Quyida ushbu guruhga mansub asosan telmisartanning o'ziga xos xususiyatlarini ko'rib chiqamiz. Telmisartan o'ziga xos farmakokinetik profilga ega. Unga eng uzoq yarim yemirilish davri (24 soat) xos, ertalabki qon bosimining ko'tarilishini adekvat nazorat qilishda boshqa preparatlarga qaraganda afzalroq bo'lib, natijada yurak-qon tomir kasalliklari asoratlari xavfini kamaytiradi [3]. Shu tufayli telmisartanni SYB bor bemorlarga tavsiya qilishimiz mumkin. Bundan tashqari, preparat tez ta'sir qiladi, qabul qilinganidan keyin taxminan 0,5-1,0 soat o'tgach ta'siri namoyon bo'ladi va so'rilishi ovqat qabul qilish vaqti bilan bog'liq emas [4]. Bundan tashqari telmisartan eng yuqori qoldiq gipotenziv ta'sirga ega yoki qoldiqning maksimal faollikka nisbati deyarli 100%. Kuniga bir marta qo'llanganda, qoldiq qon bosimining klinik jihatdan sezilarli pasayishi kuzatilgan [5]. Bu xususiyatlari telmisartanni dori qabul qilishni ko'p unutilib qo'yadigan bemorlar uchun tanlov preparatiga aylantiradi. Telmisartan eng lipofil sartan bo'lib, eng katta tarqalish hajmiga (500 L) ega, u to'qimalarga osonlik bilan kirib boradi va nafaqat plazma, balki to'qimalarning RAATni ham bloklaydi va nishon a'zolarni himoya qiladi [6]. Telmisartanning organoprotektiv xususiyatlari eng keng ko'lamda tasdiqlangan. U nishon a'zolarning shikastlanishiga sezilarli ta'sir ko'rsatadi. Masalan, ONTARGET tadqiqotida telmisartan chap qorincha miokardi gipertrofiyasining (CHQMG) sezilarli darajada orqaga qaytishiga (regressiga) olib keldi [7]. Telmisartan CHQMGni boshqa gipotenziv preparatlardan ramipril va karvedilolga qaraganda ko'proq darajada kamaytirishi haqida ma'lumotlar mavjud [8]. Bundan tashqari telmisartan yaqqol ifodalangan nefroprotektiv xususiyatlarga ega. Preparatning 1% dan kamrog'i siydik bilan chiqariladi, bu esa buyraklarda zo'riqishni kamaytiradi, shu sabab biz uni buyrak funksiyasi buzilgan hamda diabetic nefropatiya asorati bor bemorlarga tavsiya berishimiz mumkin. Qandli diabet (QD) bilan kasallangan ko'p sonli bemorlar ishtirok etgan 20 ta RKT

(randomizatsiyalangan klinik tadqiqotlar) metatahlili ma'lumotlariga ko'ra, telmisartan proteinuriyani kamaytirish va profilaktika qilishda samaradorlik ko'rsatgan. Telmisartan albuminuriyani hamda siydikdagi albumin/kreatinin nisbatini boshqa ARA (angiotenzin retseptorlari antagonistlari), AAFi (angiotenzin aylantiruvchi ferment ingibitorlari) va boshqa antigipertenziv preparatlarga qaraganda ko'proq darajada kamaytirgan [9]. Nefroprotektiv effekt hatto arterial bosimi me'yorda bo'lgan QD bilan kasallangan bemorlarda ham kuzatilgan [10]. Telmisartan arterial gipertenziya (AG) va QD bo'lgan bemorlarda demensiya rivojlanish xavfini boshqa ARA'larga qaraganda ko'proq kamaytirishi haqida ham ma'lumotlar mavjud [11].

XULOSA. Arterial gipertenziya (AG) hozirgi kunda keng tarqalgan, surunkali kechuvchi va doimiy dinamik kuzatuv hamda muntazam davolashni talab qiladigan kasallik hisoblanadi. AG ning uzoq muddat davomida nazoratsiz kechishi yurak-qon tomir, buyrak va miya kabi nishon a'zolarining shikastlanishiga olib keladi hamda og'ir klinik asoratlar xavfini sezilarli darajada oshiradi. Shu sababli antigipertenziv terapiyada nafaqat arterial qon bosimini pasaytirish, balki nishon a'zolari himoyalashga qaratilgan yondashuv alohida ahamiyat kasb etadi. Antigipertenziv preparatlarning barcha guruhlari qon bosimini pasaytirishga qaratilgan bo'lsa-da, klinik amaliyotda har bir bemor uchun individual yondashuv asosida to'g'ri preparat tanlash va optimal dozlash muhim hisoblanadi. Ushbu jihatdan telmisartan o'zining uzoq davom etuvchi gipotenziv ta'siri, yuqori qoldiq samaradorligi hamda yaqqol ifodalangan organoprotektiv xususiyatlari bilan boshqa gipotenziv preparatlardan ajralib turadi. Preparatning AAF ingibitorlariga nisbatan nojo'ya ta'sirlarining kamligi ham uning klinik qo'llanilishini kengaytiradi. Yuqoridagilarni inobatga olgan holda quyidagi takliflarni ilgari surish mumkin:

1. AG bilan kasallangan bemorlarda dori tanlashda nafaqat qon bosimini pasaytirish darajasi, balki preparatning yurak, buyrak va miya kabi nishon a'zolarga ko'rsatadigan organoprotektiv ta'siri ham inobatga olinishi lozim.

2. RAAT faolligi ustun bo'lgan bemorlarda, ayniqsa qandli diabet, surunkali yurak yetishmovchiligi (SYY) va surunkali buyrak yetishmovchiligi (SBY) mavjud holatlarda telmisartanni tanlov preparati sifatida qo'llash maqsadga muvofiqdir.

3. Dori qabuliga rioya qilinishi past bo'lgan bemorlarda (kunlik dori ichishni tez-tez unutadigan shaxslarda) telmisartanning uzoq yarim yemirilish davri va kuniga bir marta qabul qilinishi klinik jihatdan ustunlik beradi.

4. AAF ingibitorlarini qabul qila olmaydigan yoki nojo'ya ta'sirlari kuzatilgan bemorlarda telmisartanni muqobil va samarali preparat sifatida qo'llash tavsiya etiladi.

5. AG bilan birga kechuvchi diabetik nefropatiya va albuminuriya holatlarida telmisartanning nefroprotektiv ta'siridan keng foydalanish maqsadga muvofiq hisoblanadi.

Xulosa qilib aytganda, telmisartan arterial gipertenziyani davolashda nafaqat samarali gipotenziv vosita, balki yurak-qon tomir va buyrak asoratlari xavfini kamaytiruvchi muhim organoprotektiv preparat sifatida klinik amaliyotda keng qo'llashga loyiqdir.

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