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MODERN DIAGNOSTIC METHODS OF TUBERCULOSIS

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ABSTRACT

This article reviews modern diagnostic approaches to the study of tuberculosis (TB) infections and their clinical and epidemiological significance. The article analyzes the possibilities of detecting Mycobacterium tuberculosis using molecular-genetic methods, in particular polymerase chain reaction (PCR), multiplex PCR, nucleic acid amplification tests (NAAT), GeneXpert and LAMP technologies, along with traditional bacteriological methods. The sensitivity and specificity of these methods, their diagnostic efficiency based on various clinical samples, and their role in determining drug resistance are also discussed. It is emphasized that molecular diagnostic methods play an important role in early detection of TB, differential diagnosis and selection of treatment strategies. In addition, the article analyzes the global epidemiological situation of TB, the problem of co-infection with HIV, and the negative impact of the disease on life expectancy. These approaches are an important tool in optimizing preventive measures aimed at early detection of TB, increasing treatment effectiveness and reducing the burden of the disease. The results of the article serve to improve modern diagnostic and treatment strategies.

Keywords: Mycobacterium tuberculosis, molecular diagnostics, polymerase chain reaction (PCR), multiplex PCR, nucleic acid amplification tests (NAAT), GeneXpert, LAMP

TUBERKULYOZ KASALLIGINING ZAMONAVIY DIAGNOSTIK USULLARI

ANNOTATSIYA

Ushbu maqola sil kasalligi (tuberkulyoz) bilan bog'liq infeksiyalarni o'rganishning zamonaviy diagnostik yondashuvlarini hamda ularning klinik va epidemiologik ahamiyatini ko'rib chiqadi. Maqolada an'anaviy bakteriologik usullar bilan bir qatorda molekulyar-genetik metodlar, xususan polimeraza zanjir reaksiyasi (PCR), multipleks PCR, nuklein kislota amplifikatsiya testlari (NAAT), GeneXpert va LAMP texnologiyalari orqali Mycobacterium tuberculosis ni aniqlash imkoniyatlari tahlil qilinadi. Shuningdek, ushbu usullarning sezgirligi va o'ziga xosligi, turli klinik namunalar asosida diagnostik samaradorligi hamda dori vositalariga chidamlilikni aniqlashdagi roli yoritilgan. Molekulyar diagnostika usullari sil kasalligini erta aniqlash, differensial tashxis qo'yish va davolash strategiyasini tanlashda muhim ahamiyat kasb etishi ta'kidlanadi. Bundan tashqari, maqolada sil kasalligining global epidemiologik holati, OIV bilan qo'shma infeksiya muammosi hamda kasallikning umr davomiyligiga salbiy ta'siri tahlil qilingan. Ushbu yondashuvlar sil

kasalligini erta aniqlash, davolash samaradorligini oshirish va kasallik yukini kamaytirishga qaratilgan profilaktik choralarni optimallashtirishda muhim vosita hisoblanadi. Maqola natijalari zamonaviy diagnostika va davolash strategiyalarini takomillashtirishga xizmat qiladi.

Kalit so'zlar: Mycobacterium tuberculosis, molekulyar diagnostika, polimeraza zanjir reaksiyasi (PCR), multipleks PCR, nuklein kislota amplifikatsiya testlari (NAAT), GeneXpert, LAMP

АННОТАЦИЯ

СОВРЕМЕННЫЕ МЕТОДЫ ДИАГНОСТИКИ ТУБЕРКУЛЕЗА

В данной статье представлены современные диагностические подходы к изучению инфекций, связанных с туберкулезом, и их клинико-эпидемиологическое значение. В статье анализируются возможности выявления Mycobacterium tuberculosis с использованием молекулярно-генетических методов, в частности полимеразной цепной реакции (ПЦР), мультиплексной ПЦР, тестов амплификации нуклеиновых кислот (NAAT), технологий GeneXpert и LAMP, наряду с традиционными бактериологическими методами. Также обсуждаются чувствительность и специфичность этих методов, их диагностическая эффективность на основе различных клинических образцов и их роль в определении лекарственной устойчивости. Подчеркивается, что молекулярно-диагностические методы играют важную роль в раннем выявлении туберкулеза, дифференциальной диагностике и выборе стратегий лечения. Кроме того, в статье анализируется глобальная эпидемиологическая ситуация с туберкулезом, проблема коинфекции с ВИЧ и негативное влияние заболевания на продолжительность жизни. Эти подходы являются важным инструментом для оптимизации профилактических мер, направленных на раннее выявление туберкулеза, повышение эффективности лечения и снижение бремени заболевания. Результаты статьи способствуют совершенствованию современных диагностических и лечебных стратегий.

Ключевые слова: Mycobacterium tuberculosis, молекулярная диагностика, полимеразная цепная реакция (ПЦР), мультиплексная ПЦР, тесты амплификации нуклеиновых кислот (NAAT), GeneXpert, LAMP

Sil kasalligi (TB) tashxis qo'yish, davolash va oldini olish qiyin bo'lgan keng tarqalgan kasallikka oid ulkan mavzuni qamrab oladi. Tarix davomida sil kasalligi boshqa har qanday yuqumli kasalliklarga qaraganda ko'proq inson hayotining yo'qolishiga sabab bo'lgan [21]. Jahon sog'liqni saqlash tashkiloti 2015 va 2035 yillar oralig'ida kasallanishni 90% ga kamaytirish maqsadini qat'iy belgilab qo'ygan [17]. 2017-yilda qayd etilgan 1127 ta sil kasalligi holatidan 1105 tasi (98%) OIVga tekshirildi, bu esa sil/OIV qo'shma infeksiya darajasini 32,0% ga yetkazdi. Yakuniy tahlilga faqat OIV bilan tekshirilgan holatlar (n=1105) kiritildi. Ularning aksariyati erkaklar (69,3%), 25-34 yoshdagilar (29,2%) va o'pka sili bilan kasallanganlar (96,3%) edi. Davolash natijalari quyidagicha edi: 29,0% davolangan, 29,0% yakunlangan, 0,5% davolash muvaffaqiyatsiz bo'lgan, 24,2% kuzatuvdan o'tgan, 12,8% boshqa joyga o'tkazilgan tekshirilmagan va 4,5% vafot etgan. O'limning aksariyati (80,0%, 40/50) sil kasalligini davolash boshlanganidan keyin 2 oy ichida sodir bo'lgan. 65 yosh va undan katta yosh (moslashtirilgan ehtimollik nisbati 3.48, 95% ishonch oralig'i 1.15-10.56; p=0.027) va OIV-musbat holati (moslashtirilgan ehtimollik nisbati 3.50, 95% ishonch oralig'i 1.72-7.12; p=0.001) o'limning mustaqil bashorat qiluvchi omillari bo'lgan [12]. 2023-yilda global miqyosda sil kasalligi bilan kasallanish darajasi 10,8 millionga yetdi (har 100 000 kishiga 134 ta holat) va 2022-yildagi 10,7 milliondan 0,9% ga oshdi. Sil kasalligidan o'lim holatlari 5,3% ga kamaydi va o'tgan yilgi 1,32 milliondan 1,25 millionga tushdi

[13]. 12-noyabr Jahon sog'liqni saqlash tashkiloti hisobotiga ko'ra, yuqumli kasallikni tashxislash va davolashdagi uzilishlar tufayli ketma-ket uch yil davomida o'sishdan so'ng, global sil kasalligi darajasi 2024-yilda o'tgan yilga nisbatan taxminan 2% ga kamaydi. 2024-yilda 1,23 million kishi sil kasalligidan vafot etdi, bu 2015-yilga nisbatan 29 foizga kam. Sog'liqni saqlash agentligining ta'kidlashicha, bu 2025-yilga kelib 75 foizga va 2030-yilga kelib 90 foizga kamaytirish maqsadlaridan ancha uzoq [10]. Sil kasalligini davolash kamida 6 oylik ko'p dorili terapiya dasturini o'z ichiga oladi, afzalroq dastlabki 2 oy davomida to'g'ridan-to'g'ri kuzatuv bilan. Bemorlarga ko'rsatmalar, maslahatlar va maslahatlar kerak va sil kasalligini davolash odatda klinika, sog'liqni saqlash markazi yoki kasalxonada boshlanadi [18].

Ko'p dori-darmonlarga chidamli sil kasalligi (KDT-TB) bilan og'rigan bemorlarning o'rtacha umr ko'rish davomiyligi 1,9-7,6 yilni tashkil etdi (tashxis qo'yilgandan boshlab indekslangan), keng dori-darmonlarga chidamli sil kasalligi (KDT-TB) uchun bu ko'rsatkich 2,9-6,5 yil va KDT-TB bo'lmagan sil kasalligi uchun 2-8 yil. O'rtacha umr ko'rish bo'yicha hisob-kitoblar shuni ko'rsatdiki, sil/OIV bilan birgalikda yuqtirish 30 yoshdagi umr ko'rish davomiyligini 4,2 dan 21,6 yilgacha qisqartirdi, bu OIV bilan og'rigan, ammo sil kasalligi bo'lmagan odamlarda 35,0 yildan ortiq vaqtni tashkil etdi. Potensial hayot yo'qotish yillari tahlillari shuni ko'rsatdiki, faol sil kasalligi bilan og'rigan bemorlar potentsial hayotni 4,9-15,8 yilga yo'qotdilar, yashirin sil kasalligi (LTBI) bilan og'riganlar uchun esa 1-3 yil. Sil - OIV qo'shma infeksiyasi bu yukni yanada kuchaytirdi, yo'qotishlar 16 yoshgacha yetdi. 69 yoshdagi belgilangan yosh chegarasidan foydalangan holda, sil bilan og'rigan bemorlar o'rtacha 39,1 yillik umr ko'rishni yo'qotishdi, sil kasalligi bo'lmagan nazorat guruhidagi bemorlar esa 24,5 yilni yo'qotishdi [15]. 2024-yil avgust holatiga ko'ra, sil kasalligini davolash bo'yicha sinovlarni kuzatuvchi I, II yoki III bosqich sinovlarida sil kasalligini davolash uchun 29 ta dori vositasi mavjudligini ko'rsatadi, bu 2023-yildagi 28 ta va 2015-yildagi sakkiztadan ko'p. Bu o'sish bir nechta moliyachilarning investitsiyalari va bir nechta platformalar va konsorsiumlarning sa'y-harakatlari ortib borishi ortidan sil kasalligiga qarshi dorilarni ishlab chiqish sur'atining tezlashishini ko'rsatadi. Bu shuningdek, sil kasalligini davolash va boshqarishni yaxshilash uchun tez orada yanada samarali va xilma-xil terapevtik variantlar paydo bo'lishi mumkinligini ko'rsatadi [24].

M. tuberculosis ni aniq aniqlash , asosan o'pkaga ta'sir qiluvchi nafas yo'llari orqali yuqadigan kasallik bo'lgan sil kasalligini tashxislash uchun juda muhimdir. Bundan tashqari, sil infektsiyasi to'qimalarning shikastlanishiga olib kelishi mumkin, ayniqsa yosh bolalar va o'smirlarda, ularda sil kasalligi kattalarga qaraganda ko'proq uchraydi [9]. Nobel mukofotiga sazovor bo'lgan (1993) polimeraza zanjiri reaksiyasi (PCR) kashfiyoti 1983-yilda Kari Mullis tomonidan amalga oshirildi. Ushbu PCR texnologiyasi 1980-yillarning boshlarida tibbiyot fanlari uchun katta yutuqlarga erishdi va bu texnologiya 1990-yillarning boshlaridan beri sil kasalligini tashxislashda qo'llanilmoqda [19]. So'nggi yillarda PCRning turli shakllari, jumladan, bitta naychada jins va turga xos amplikonlarni aniqlay oladigan multipleks PCR (mPCR) ishlab chiqildi [8]. An'anaviy PCR kuchaytirilgan mahsulotlarni aniqlash uchun agaroza gelini talab qildi va bu cheklov real vaqt rejimida PCR (RT-PCR) ishlab chiqilishi bilan bartaraf etildi, bunda PCR real vaqt rejimida ishlayotganida DNK kuchaytirish reaksiyasini yorug'lik chiqaradigan diod (LED) ekranida kuzatish mumkin edi [6]. Mycobacterium jinsini , eng keng tarqalgan Mycobacterium tuberculosis (MTB) turlarini va Mycobacterium avium hujayra ichidagi kompleksini aniqlash va aniqlashga qodir multipleks polimeraza zanjiri reaksiyasi. Yuqori 441 tayanch juftligi (bp) tasmasi namunalarda mikobakteriya turlarining mavjudligini ko'rsatadi, ikkinchi va uchinchi 192 va 145 bp tasmasi esa turning MTB, M. avium kompleksi (MAC) yoki ikkalasi ham ekanligini ko'rsatadi. Agar 441 bp ning faqat

birinchi tasmasi ijobiy bo'lsa, lekin qolgan ikkitasining hech biri musbat bo'lmasa, bu boshqa sil kasalligiga chalinmagan va MAC bo'lmagan mikobakteriya turlarini ko'rsatadi [7].

GeneXpert o'pka ichidagi va o'pkadan tashqari sil kasalligini aniqlashda samaradorligini oshirdi. Biroq, Xpertning sezgirligi tahlil uchun ishlatiladigan namunalarga, ya'ni balg'am, najas, bronxo alveolyar lavaj suyuqligi (BALF), me'da shirasining, interstitsial suyuqlik va biopsiyalarga qarab o'zgarishi aniqlandi. Xpertning barcha namunalar orasida taxminiy o'ziga xosligi odatda 98% dan yuqori [11]. GeneXpertning ushbu versiyasi 10 rangli GeneXpert® texnologiyasi yordamida kuchaytirilgan multiplekslash yordamida TB DST ni soddalashtiradi. 2020-yilda ishga tushirilgan GeneXpert MTB/XDR tezroq molekulyar DST imkonini beradi. GeneXpert MTB/XDR bitta sinov jarayonida RIF, izoniazid (INH), ftorxinolonlar (FLQs), ikkinchi qator in'ektsiya dorisi (amikasin, kanamitsin va kapreomitsin) va etionamid (ETH) ga qarshilik ko'rsatish uchun javobgar deb hisoblangan mutatsiyalarni aniqlash orqali yangi standartlarni o'rnatadi. Yaqinda ikkita joyda 100 ta balg'am namunalari va 214 ta klinik izolatlar bilan o'tkazilgan tadqiqotda, uning ketma-ketlik bilan solishtirganda samaradorligi ETHdan tashqari barcha dorilar uchun 94%–100% sezgirlik va 100% o'ziga xoslikni ko'rsatdi [2].

Loop vositachiligidagi izotermik kuchaytirish (LAMP) molekulyar diagnostika usuli hisoblanadi. Bu usul DNKning izotermik kuchaytirilishiga asoslangan. U joriy etilganidan beri LAMP sil kasalligini tashxislash uchun qimmatli vositaga aylandi va JSST tomonidan ma'qullangan [1]. LAMP usuli Yaponiyadagi Eiken Chemical Company tomonidan yaratilgan innovatsion LAMP platformasiga asoslangan . Ushbu texnologiya maqsadli DNKni taxminan 65°C doimiy haroratda kuchaytiradi va klinik namunalardan DNKni <2 soat ichida, minimal asboblar yordamida va vizual aniqlash tizimidan foydalangan holda to'g'ridan-to'g'ri aniqlash uchun mo'ljallangan [23] .

Sil kasalligining an'anaviy bakteriologik tashxisi bir nechta cheklovlarga ega bo'lgani uchun, NAAT potentsial alternativ sifatida paydo bo'ldi [16]. Ko'pgina NAAT tahlillari MTB kompleks organizmlarini aniqlash uchun mikobakterial qo'shilish elementi IS6110 ni aniqlaydi [22]. NAAT MTB ribosomal RNK yoki DNKni to'g'ridan-to'g'ri balg'am namunalaridan, ham kislotaga chidamli tayoqchalar (AFB) smear-musbat, ham AFB smear-manfiy bo'lgan holda aniqlaydi [20] . NAAT balg'am smear-musbat bemorlarda juda yuqori sezgirlikni va smear-manfiy balg'amli bemorlarda taxminan 61 dan 76% gacha sezgirlikni ko'rsatdi. [14]

Yuqori mikobakterial yuklamaga ega bo'lgan ko'p bakteriyali kasalliklarda, NAAT musbat bo'lgan AFB surtmasi faol sil kasalligini ko'rsatadi, ingibitorlar bo'lmagan taqdirda esa NAAT manfiy bo'lgan AFB surtmasi esa sil kasalligi bo'lmagan mikobakterial (NTM) kasallikni ko'rsatadi [5]. Bundan tashqari, agar NAAT natijasi musbat bo'lsa, lekin AFB surtmasi natijasi manfiy bo'lsa, silga qarshi davolanishni boshlash to'g'risidagi qaror bemor natijalarini kutayotganda klinik xulosaga asoslanadi [4]. Kasalliklarni nazorat qilish markazlari (CDC) ma'lumotlariga ko'ra, agar balg'am surtmasi manfiy bo'lsa va NAAT ham manfiy bo'lsa, qo'shimcha namunani NAAT bilan tekshirish kerak. Biroq, agar bemor natijalari MTB bakteriyalarining o'sishini aniqlasa, bemorni o'pka sil kasalligi bakteriologik jihatdan tasdiqlangan deb ham tasniflash mumkin. Nihoyat, agar AFB smear, NAAT va MTB kulturasi salbiy natijalarni ko'rsatsa, shifokor bemorlarni klinik jihatdan tashxis qo'yilgan sil kasalligi holati sifatida tasniflashi yoki boshqa tashxisni ko'rib chiqishi mumkin [3].

Sil kasalligi hozirgi kunda ham global sog‘liqni saqlash tizimi oldida turgan eng dolzarb muammolardan biri bo‘lib qolmoqda. Ushbu kasallikning keng tarqalganligi, OIV bilan qo‘shma infeksiyaning yuqori darajasi hamda dori vositalariga chidamli shakllarning ortib borishi uning tashxislash va davolash jarayonlarini yanada murakkablashtirmoqda. Maqolada ko‘rib chiqilgan

zamonaviy diagnostik yondashuvlar — xususan molekulyar-genetik usullar (PCR, NAAT, GeneXpert, LAMP) — sil kasalligini erta va aniq aniqlash, shuningdek dori vositalariga chidamlilikni tezkor baholash imkonini berishi bilan alohida ahamiyat kasb etadi. Ushbu texnologiyalar an'anaviy usullarning cheklovlarini bartaraf etib, klinik qaror qabul qilish jarayonini sezilarli darajada takomillashtiradi. Shu bilan birga, samarali davolash strategiyalarini to'g'ri tashkil etish, bemorlarni uzluksiz kuzatish va profilaktik choralarni kuchaytirish sil kasalligi bilan bog'liq o'lim va nogironlik ko'rsatkichlarini kamaytirishda muhim omil hisoblanadi. Umuman olganda, sil kasalligiga qarshi kurashda zamonaviy diagnostika usullarini keng joriy etish, innovatsion davolash yondashuvlarini rivojlantirish va global sog'liqni saqlash dasturlarini kuchaytirish orqali kasallik yukini sezilarli darajada kamaytirish mumkin.

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