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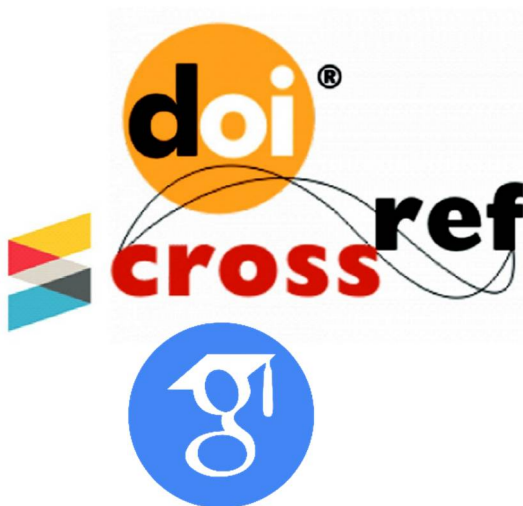
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БИМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

ЖУРНАЛ БИМЕДИЦИНЫ И ПРАКТИКИ | JOURNAL OF BIOMEDICINE AND PRACTICE

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ANNOTATION

Atopic dermatitis is a common chronic skin disease, the pathogenesis of which is largely associated with a congenital or acquired deficiency of the filaggrin protein. In recent years, a lot of data has been obtained on the causes of the flag green shortage. The structure and functions of this protein have been described, which opens up new possibilities for the benefits of treating atopic dermatitis.

Keywords: atopic dermatitis, skin barrier, filagrin, emollients, filagrinol

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АТОПИК ДЕРМАТИТДА ФИЛАГГРИН НУҚСОНИ ВА КОРРЕКСИЯЛАШНИНГ ЗАМОНАВИЙ УСУЛЛАРИ

ANNOTATSIYA

Atopik dermatit - terining keng tarqalgan surunkali kasalligi bo'lib, uning patogenezi ko'p jihatdan filaggrin oqsilining tug'ma yoki orttirilgan tanqisligi bilan bog'liq. So'nggi yillarda filaggrin tanqisligi sabablari to'g'risidagi juda ko'p ma'lumotlar olindi. Ushbu oqsilning tuzilishi va funksiyalari tavsiflangan, bu esa atopik dermatitni davolashning afzalliklari uchun yangi imkoniyatlarni ochadi.

Kalit so'zlar: atopik dermatit, teri baryeri, filaggrin, emolentlar, filagrinol

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ДЕФЕКТ ФИЛАГГРИНА ПРИ АТОПИЧЕСКОМ ДЕРМАТИТЕ И СОВРЕМЕННЫЕ МЕТОДЫ КОРРЕКЦИИ

АННОТАЦИЯ

Атопический дерматит-распространенное хроническое заболевание кожи, патогенез которого во многом связан с врожденным или приобретенным дефицитом белка филаггрина. В последние годы было получено много данных о причинах дефицита флагагрина. Структура и функции этого белка были описаны, что открывает новые возможности для преимуществ лечения атопического дерматита.

Ключевые слова: атопический дерматит, кожный барьер, филаггрин, эомоленты, филаггринол

KIRISH. Atopik dermatit (AtD) - surunkali teri kasalligi bo'lib, kasallik Rossiyada 20%gacha bolalarni va 3%gacha kattalarda uchraydi, bu ularning hayot sifatiga sezilarli ta'sir qiladi [1]. Kasallik patogenezing transepidermal suv yo'qotish (teri baryerini buzilishi), qichishish, immun disregulyatsiyada flaggrin tanqisligi muhim o'rin tutadi [1]. Qichishish tufayli teri shikastlanishini og'irlashtirishi mumkin va ikkilamchi infeksiya yuqishiga olib keladi. Quruq teri epidermal nerv tolalarini zichligini ortishi xisobiga qichishishni stimullaydi [3]. Qichishish pruritogenlarga o'xshab (yangi paydo bo'lgan qichishish manbalari), "aylanma yo'l" ni yopilishiga ta'sir qiladigan Th2 sitokinlari, eozinofillar va timus stromal limfopoetini intensiv ishlab chiqarilishiga olib keladi[4].

TA'RIF. Flaggrin muhim epidermal oqsil hisoblanadi, keratin filamentlarining agregatsiyasida ishtirok etadi [5].U proepidermisning donador qatlamida aniqlanadigan filaggrin, u tuzilishiga ko'ra takroriy- qo'zg'aluvchan filaggrin birliklarida takrorlanuvchi zanjir tuzilishidan hosil bo'lib, profilaggrinning o'tmishdosh molekulasidan -epidermisning donador qavatidan ajraladi [6]. Keratositlarni differentsirlash jarayonida donadorlikdan muguzulanuvchi proflaggrin filaggrinning monomerlar manbai bo'lib hisoblanadi [6]. Flaggrinning keratin filamentlari bilan agregatsiyasi keratinotsitlarning zichlashishiga yordam beradi [5]. Bundan tashqari, flaggrin, shuningdek uning parchalangan mahsulotlari epidermal gomeostazda asosiy komponentlari hisoblanadi [7]. Flaggrin va uning mahsulotlari miqdori bolalarda turli anatomik qismlardagi degradatsiyalar bir xil emas. Chunonchi, yonoqlar sohasida flaggrin miqdori chaqaloqlarda burun uchi yoki tirsak bo'g'imi sohasida terisiga nisbatan sezilarli darajada past AtDning dastlabki ko'rinishlarining lokalizatsiyasi bilan bog'liq bo'lishi kerak. Filaggrinning tarqalish xususiyatlari quyidagilarni ko'rsatadi: aynan shu sohalarda transkutan sensibilizatsiya amalga oshiriladi [8].AtD bilan og'rigan bemorlarda flaggrin yetishmovchiligining oqibatlari xilma-xil. Bu va esa muguz qatlamining baryer funksiyasi, suv-lipid muvozanatining buzilishi, transepidermal suv yo'qotilishining oshishi, allergenlar uchun epidermis o'tkazuvchanligining oshishi, toksinlar, mikroorganizmlar, mikroob keyinchalik boshqa atopik holatlarni rivojlanishiga olib keladi [4, 9, 10]. So'nggi yillarda sabablarni, oqibatlarni tushunishdagi muhim muvaffaqiyatlarga shuningdek, AtD da filaggrin yetishmovchiligi belgilarini o'rganishga erishildi. Masalan, flaggrin genining ba'zi variantlari, 21-xromosomaning qisqa yelkasida epidermal qiyoslash gen kompleksida joylashgan (profilaggrin, xornein, filaggrina 2, repetin, kornulin, trixogialin)ning nafaqat AtD bilan balki, vulgar ixtioz rivojlanishi bilan ham bog'liq [11]. Bemorlarning hammasida ham AtD mavjud emas va epidermal filaggrin yetishmovchiligining bu oqsil genining patologik variantlari bor. Epidermisdagi flaggrin ekspressiyasiga yallig'lanishga qarshi sitokinlar, shuningdek atrof-muhitning ifloslanishi (masalan havo), terining mexanik shikastlanishi ta'sir qilishi mumkin [11]. Shuni ta'kidlash kerakki, flaggrin genning patologik variantlari AtDni kechishiga ko'p darajada ta'sir qiladi [12]. Bundan tashqari, bronxial astma rivojlanish xavfi bo'lgan allergik astma, allergik rinit [9]variantlari o'rtasidagi bog'liqlikni o'rganishda olingan oziq-ovqat allergiyasiga ega filaggrin geni filaggrin genining ba'zi variantlari assotsiatsiyasi ko'rsatilgan [10]. Ta'kidlash kerakki, flaggrin genining patogen variantlarining tarqalishi (60 ga yaqin) turli irqiy guruhlarda bir xil emas [13]. AtD kechishi patogen filaggrin geni varianti mavjudligida klinik jihatdan oyoq kafti terisida giperchiziqliligi bilan follikulyar keratoz belgilari namoyon bo'ladi. Bunday hollarda kasallik erta boshlanadi va og'ir kechadi. Allergenlarga polivalent sensibilizatsiya nisbatan yuqori daraja aniqlanadi, kasallik yuqish

xavfi ortadi. Odatda, oilaviy anamnezni yig'ishda filaggrin genining patogen varianti AtD bilan og'riqan qarindoshlarda aniqlanadi [13]. Filaggrin ekspressiyaga sitokinlar asosiy ta'sir ko'rsatadi. Ma'lumki ular Th2 sitokini filaggrin ekspressiyasini ingibirlaydi (interlekinlar IL-4, IL-13, IL-17, IL-22, IL-31) [14], IL-33, IL-25 va timus stromal limfopoetini [15, 16], epidermisning pH ni ortishiga va buning natijasida terining epidermisini mikroblarga qarshi rezistentlikni kamaytirishga olib keladi [15-16]. Bundan tashqari, IL-4, IL-13 va IL-25 boshqa filaggringa o'xshash masalan xorerin va filaggrin 2 kabi oqsillarni ingibirlaydi [17]. Filaggrin ekspressiyasiga aks ta'sir etuvchi janus-kinaza (Janus kinases; JAK) va tirozinkinaza, qaysiki JAK-STAT va - STAT3 (signal transducer and activator of transcription proteins - oqsillar transkripsiyasini faollashtiruvchisi) IL-4/IL-13 ingibitorlari faolligini bloklash orqali ta'sir ko'rsatadi. Natijada sintezlanadigan filaggrin va tabiiy namlantiruvchi omil ortadi [18]. Shu sababli janus-kinaz [18] ingibitorlari, shuningdek filaggrin va uning epidermisda parchalanish mahsulotlariga [7] flaggrin sintezi uchun ta'sir ko'rsatishining istiqbolli usullari sifatida qaraladi.

FILAGRIN VA ATOPIK MARSH

Atopik marsh - epidemiologik hodisa bo'lib, u patogenetik aloqadorlik bilan tavsiflanadi bir nechta atopik kasalliklar, shu jumladan AtD, allergik rinit, bronxial astma va ovqat allergiyasini o'z ichiga oladi. Bu atama bir allergik kasallikni ikkinchisiga yoshdan yoshga o'tishni anglatib, AtD esa bu jarayonning "boshlang'ich nuqtasi" hisoblanadi [19]. Atopik marshlar tabiatning ko'plab tadqiqotlari AtD erta bolalikda flaggrin tanqisligi fonida atopik kasalliklarning rivojlanishiga terining baryer faoliyati buzilishiga olib keladi [20].

TERI BARYERINI TIKLASH

AtD ni davolash asosida uning sonini cheklamagan holda kasallik og'irlik darajasidan qat'i nazar doimiy ravishda emolentlarni qo'llash yotadi [19]. Teri to'sig'ini tiklash transkutan sensibilizatsiya, ayniqsa yanoq terisida kamayishi uchun muhimdir. Atopik marsh xavfini, xavf guruhidagi chaqaloqlarda tug'ilishdan boshlab - AtD rivojlanish xavfiga qadar rivojlanishini kamaytirishga emolentlardan muntazam foydalanish remissiya boshlanishini tezlashtirish, uni uzaytirish uchun zarur [19]. Bundan tashqari, emolentlar steroidlarni tejaydigan ta'siri bilan AtD ni davolashda qo'llash tarkibida glyukokortikosteroidlar saqlaydigan topik moddalarning miqdorini kamaytirishga imkon beradi [19]. Biroq, yallig'lanishning o'tkir davrida faqat emolentlarni qo'llash maqsadga muvofiq emas odatda tarkibida steroid bo'lgan topik birikmalar yoki kalsinevrin bilan birikishi mumkin. Preparatlarni qo'llashdan avval birinchi o'rinda yengil dori shakli applikasiyasini qilish zarurligini inobatga olinadi. Bunda preparatlarning surtish oralig'i kamida 15 minutni tashkil etishi kerak. Vannani qabul qilishda namlantiruvchi moylardan foydalanish so'ngra terini sochiq bilan quritish va emolentlar surtish tavsiya etiladi [21]. Emolentlar o'z tarkibida okklyuzivlar, xumektantlar va yumshatuvchi vositalar saqlaydi. Okklyuzivlar nofiziologik lipidlar: vazelin, lanolin, parafin, mum, silikonlarni saqlaydi. Vositaning bunday tarkibi transepidermal suv yo'qotilishni kamaytiruvchi teri yuzasida parda hosil qilish imkonini beradi. Xumektanlarga- aminokislotalar, glitserin, mochevina, gialuron kislotasi kiradi. Sanab o'tilgan moddalar gigroskopik molekularlar bilan epidermisdagi suv molekularidan iborat. Yumshatuvchi vositalar fiziologik lipidlarni seramidlar xolesterin, erkin yog' kislotalari, ba'zi spirtlar (setil, stearil va oleil)ni o'z ichiga oladi. Ular keratinotsitlararo oraliqlarni to'ldirish, terining lipid tarkibini me'yoriylashtirish xususiyatiga ega. Zamonaviy emolentlar turli xil moddalar kombinatsiyasini saqlaydi. Bunga innovation- faol emolentlar kompleksini o'z ichiga olgan Admer emolenti komponentlari: filagrinol - 5%, seramid PC104, niatsinamid, 18-beta-glitsirretin kislotasi, glitserol, ta'biy moylar (shi, kakao, mango, aloe) misol bo'ladi. Krem intensiv namlash, lipid muvozanatining tiklanishiga, transepidermal suv yo'qotishning kamayishigasezgir terining ko'p pog'onali himoyasini ushlab turishga yordam beradi. Ba'zi komponentlar (18-beta-glitsirretin kislotasi) qo'shimcha yallig'lanishga va qichishga qarshi ta'sir ko'rsatadi.

Filagrinol faol modda bo'lib, u o'simlik moylarining sovunlanmaydigan (zaytun, soya, bug'doy murtagi moylari) va lipidli entomofil chang fraksiyalaridan iborat. Ko'rsatilganki filagrinol epitelial hujayralar yuzasidagi retseptorlar vositasida va filagringa mos ravishda keratinning agregatsiyalanishi va tabiiy namlantiruvchi omil sintezini kuchaytiradi [22]. Yaqin kunlarda ilmiy

kashfiyotlar ko‘plab lipid yadrolari retseptorlarini kodlovchi 48 ta genlarni aniqladi. Unga "yadroviy lipidli yetim retseptorlar" deb nomlangan katta guruhi steroidlar va yog‘da eriydigan vitaminlar uchun gormonlarning klassik retseptorlari kiradi. Ular orasida PPAR (peroxisome proliferator-activated receptor - peroksisoma bilan proliferator tomonidan faollashtiriladigan retseptor), u differentsirlanishini stimullaydi keratinotsitlar proliferatsiyasini epidermal lipidlar sintezi va nihoyat teri yallig‘lanishini kamaytiradi [23] Bu retseptor yog‘ kislotalari, prostaglandinlar, eykohanoidlar va boshqa lipid metabolitlaridan faollashadi [24]. Yana bir filagrinolning ta’sir mexanizmi shundaki, adenozintrifosfat fermentining faolligini oshirib, tarkibida proflaggrin molekulalarini saqlagan adenozintrifosfat molekulasini ajralishining ortishiga bog‘liq [24]. Yuqorida aytib o‘tilgan kremni qichishish izlari va yaqqol ikkilamchi infitsirlanish sohasidan tashqari, shuningdek, butun terining remissiya davrida, topik yallig‘lanishga qarshi vositalar bilan birga AtDning qo‘zish davrida qo‘llash mumkin. Shuningdek AtD bo‘yicha uni xavf guruhidagi bolalarda parvarishlash vositasi sifatida transkutan sensibilizatsiyani kamaytirish uchun qo‘llash maqsadga muvofiqdir masalan, go‘daklik davrida bolani ovqatlantirishdan oldin yonoqlar sohasiga qo‘llash mumkin. Shunday qilib, filagrinolli krem- filagrin xususiy oqsilining sintezi modulyatori AtDda parvarishlashni ta’minlaydi, ulardan asosiy sabablardan biri rivojlanishidagi ta’sir qiladi, shuningdek, bir qator emolentlar ajralib chiqishiga olib keladi.

XULOSA

Flaggrin tanqisligi AtD patogeneza markaziy bo‘g‘in hisoblanadi. Ehtimol, bu tanqislik holat AtDning boshqa atopik holatlar rivojlanish xavfi bilan bog‘liqligini ham belgilaydi. Shu munosabat bilan bu oqsil ekspressiyasining modulyatsiyasiga yo‘naltirilgan yangi terapevtik imkoniyatlar dolzarb bo‘lib qolmoqda. Bemorlar uchun filaggrin yetishmovchiligining klinik ko‘rinishlari bilan, teri to‘sig‘ining buzilishiga olib keladigan ekspress- filaggrinni o‘z ichiga olgan vositalar hisobiga. Filagrin etishmovchiligining klinik ko‘rinishlari bilan kuzatilgan bemorlarda, teri to‘sig‘ining buzilishiga olib keladigan, filagrin va filagrinolning ekspressiyasini tiklash imkoniyatini o‘rganishdan iborat

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