

Article/Original paper

CLINICAL AND MICROBIOLOGICAL CHARACTERISTICS OF THE INTESTINAL MICROBIOTA IN CHILDREN WITH BRONCHIAL ASTHMA ASSOCIATED WITH MYCOPLASMA PNEUMONIAE AND CHLAMYDIA PNEUMONIAE

G.A.Tashmatova¹  Z.A.Khalilova¹

1. Tashkent State Medical University, Tashkent, Uzbekistan.

Abstract.

Objective. To study the clinical and microbiological alterations of the intestinal microbiota in children with bronchial asthma associated with *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* infections, and to determine their correlation with disease severity. **Materials and Methods.** From 2023 to 2025, 78 children aged 7–15 years with bronchial asthma were observed at the Department of Pediatric Allergology, Tashkent Medical Academy. Patients were distributed according to asthma severity: mild — 41 children, moderate — 23 children, and severe — 14 children. A control group consisted of 42 healthy children. All subjects underwent serological testing (for antibodies to *M. pneumoniae* and *C. pneumoniae*), spirometry, and microbiological analysis of intestinal flora. **Results and Discussion.** Infections caused by *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* were found to exacerbate the clinical course of bronchial asthma in children. These infections lead to significant dysbiosis of the intestinal microbiota, characterized by a decrease in beneficial bacteria (*Bifidobacterium*, *Lactobacillus*) and an increase in opportunistic microorganisms (*Escherichia coli*, *Clostridium*, *Bacteroides*). The imbalance in the intestinal microbiome correlated with disease severity. In children with severe asthma, the level of beneficial bacteria decreased by 45–55%, while opportunistic flora increased by 30–40% compared to the control group. Additionally, elevated levels of pro-inflammatory cytokines (IL-4, TNF- α) and immunoglobulin E (IgE) were observed, indicating an intensified immune response and persistent airway inflammation. **Conclusion.** *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* infections aggravate the course of bronchial asthma in children and induce intestinal dysbiosis. The reduction of beneficial bacteria and the overgrowth of conditionally pathogenic flora are associated with more severe forms of asthma. Alterations in the intestinal microbiota modulate immune activity by increasing IL-4, TNF- α , and IgE levels, which enhance inflammation and allergic reactivity. Early detection of dysbiosis and the inclusion of probiotic therapy in complex treatment regimens may improve the clinical course of bronchial asthma in children.

Key words: Bronchial asthma, children, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, intestinal microbiota, dysbiosis.

Muammoning dolzarbligi. Allergik kasalliklar, xususan, bronxial astma (BA) pediatriya sohasidagi eng dolzarb muammolardan biri bo'lib qolmoqda. [1]. So'nggi yillarda bolalarda allergik kasalliklar soni ortib bormoqda va ularning orasida bronxial astma yetakchi o'rinni egallaydi. [2–10]. Bronxial astma — bu nafas yo'llarining surunkali yallig'lanish kasalligi bo'lib, u bronxlarning giperreaktivligi, havo oqimining o'zgaruvchan obstruksiyasi va klinik belgilar (hansirash, yo'tal, nafas siqilishi) bilan namoyon bo'ladi [6-7]. Kasallikning patogenezida infeksiyon va allergik mexanizmlarning o'zaro ta'siri muhim o'rin tutadi. Atypik infeksiyalar – *Mycoplasma pneumoniae* va *Chlamydia pneumoniae* – nafaqat respirator tizimga zarar yetkazadi, balki bronxial giperrenaktivlikni kuchaytiradi, immun tizim faoliyatini buzadi hamda ichak mikrobiotasining holatiga ham salbiy ta'sir ko'rsatadi. [9]. Ichak mikrobiotasi immun tizimni modulyatsiya qilishda, allergik javoblarni shakllantirishda va yallig'lanish jarayonlarini boshqarishda asosiy rol o'ynaydi. Shu sababli, ichak

mikrobiotasidagi o'zgarishlar bronxial astma kechishini og'irlashtiruvchi muhim omil sifatida qaraladi. So'nggi yillarda ilmiy adabiyotlarda ichak mikrobiotasining nafas yo'llari kasalliklari, shu jumladan bronxial astma bilan bog'liqligi to'g'risida ko'plab ma'lumotlar paydo bo'ldi. [8]. Ichak mikrobiotasi immun tizimni shakllantirishda asosiy omil hisoblanadi. Uning disbalansi (disbioz) allergik kasalliklar, ayniqsa astma rivojlanishida muhim patogenetik zanjirga aylanadi.

Tadqiqot maqsadi

Bolalarda Mycoplasma pneumoniae va Chlamydia pneumoniae infeksiyalari bilan bog'liq bronxial astma holatlarida ichak mikrobiotasining klinik va mikrobiologik o'zgarishlarini o'rganish hamda ularning kasallik og'irlik darajasi bilan bog'liqligini aniqlash.

Materiallar va usullar

2023–2025 yillar davomida Toshkent tibbiyot akademiyasi bolalar allergologiyasi bo'limida 7–17 yoshdagi 68 nafar bronxial astma bilan og'irgan bola kuzatildi. Bemorlar bronxial astma og'irlik darajasiga ko'ra quyidagicha taqsimlandi: yengil — 31 nafar, o'rta — 23 nafar, og'ir — 14 nafar. Nazorat guruhi sifatida 42 nafar sog'lom bola jalb qilindi. Barcha bolalarga serologik tekshiruvlar (M. pneumoniae, C. pneumoniae ga qarshi antitanachalar), spirometriya va mikrobiologik tahlil o'tkazildi.

Natijalar va muhokama

Tadqiqot natijalari shuni ko'rsatdiki, bronxial astma bilan og'irgan bolalarda ichak mikrobiotasining muvozanati sezilarli darajada buzilgan. Ayniqsa, Mycoplasma pneumoniae va Chlamydia pneumoniae bilan infeksiyalangan bolalarda foydali bakteriyalar –Lactobacillus va Bifidobacterium sonining kamayishi, shuningdek, shartli-patogen mikroorganizmlar (Escherichia coli, Clostridium, Bacteroides) miqdorining ortishi kuzatildi. Bu o'zgarishlar kasallikning og'irligi bilan bevosita bog'liq bo'lib, astmaning og'ir shaklida foydali bakteriyalar 45–55% gacha kamaygan, shartli-patogen bakteriyalar esa 30–40% ga oshgan. Shuningdek, bu bolalarda IL-4 va TNF- α kabi provospaloviy sitokinlar darajasi oshgan bo'lib, bu tizimli yallig'lanishning kuchayganini ko'rsatadi. Ichak mikrobiotasidagi disbalans bronxial astma simptomlarini og'irlashtirib, organizmning immun javobini o'zgartiradi.

1. Ichak mikrobiotasining o'zgarishlari:

Bakteriyalar turi	Nazorat guruhi (%)	BA + infeksiya guruhi (%)	O'zgarish foizi	p-qiyamat
Bifidobacterium	100	52	-48	<0.05
Lactobacillus	100	58	-42	<0.01
Escherichia coli	100	133	+33	<0.01
Clostridium	100	135	+35	<0.01
Bacteroides	100	129	+29	<0.05

Foydali bakteriyalar – Bifidobacterium miqdori o'rtacha 48% ga ($p < 0,05$), Lactobacillus esa 42% ga ($p < 0,01$) kamaygan. Shartli-patogen bakteriyalar – Escherichia coli, Clostridium va Bacteroides miqdori mos ravishda 33%, 35% va 29% ga ortgan ($p < 0,05–0,01$). Bu o'zgarishlar ichakning himoya funksiyasini zaiflashtirib, yallig'lanish jarayonlarini kuchaytiradi. Bolalarda IL-4 va TNF- α kabi sitokinlar darajasi 41% ga oshgani qayd etilgan ($p < 0,05$). Astmaning og'ir shaklida mikrobiota buzilishi yanada chuqurroq bo'lib, foydali bakteriyalar 45–55% gacha kamaygan, shartli-patogen bakteriyalar esa 30–40% ga ortgan. Bundan tashqari, IgE darajasi 28% ga oshib, bu holat allergik reaksiyalar va astma simptomlarining kuchayishiga olib kelgan. BA bilan og'irgan bolalarda foydali bakteriyalar kamaygan, shartli-patogen flora esa ko'paygan. Foydali bakteriyalar kamayishi Bronxial astma + infeksiya bilan kasallangan bolalarda ko'proq kuzatildi.

2. Sitokin darajalari:

Ko'rsatkichlar	Nazorat guruhi (pg/ml)	BA + infeksiya guruhi (pg/ml)	O'zgarish (%)	p-qiyamat
IL-4	4,7 \pm 0,6	18,5 \pm 2,1	+50,4	<0.05
TNF- α	28,6 \pm 1,5	32,1 \pm 1,5	+41,0	<0.05

Tadqiqot natijalariga ko'ra, bronxial astma va Mycoplasma hamda Chlamydia infeksiyalari bilan kasallangan bolalarda sitokin darajalari nazorat guruhiga nisbatan sezilarli darajada oshgan. Xususan, IL-4 darajasi 4,7 \pm 0,6 pg/ml dan 18,5 \pm 2,1 pg/ml gacha oshib, +50,4 % o'zgarish qayd

etildi ($p < 0,05$). Shuningdek, TNF- α darajasi $28,6 \pm 1,5$ pg/ml dan $32,1 \pm 1,5$ pg/ml gacha ko'tarilib, +41,0 % ga oshdi ($p < 0,05$). Bu o'zgarishlar organizmda kuchli yallig'lanish javobi shakllanganini va infeksiyalarning immun tizim faolligini keskin oshirganini ko'rsatadi. IL-4 darajasining oshishi allergik yondashuvli immun javobning (Th2 tipdagi javob) faollashuvi bilan, TNF- α darajasining oshishi esa tizimli yallig'lanish va bronxial giperrenaktivlikning kuchayishi bilan bog'liq. Bundan tashqari, astma og'irlik darajasi ortishi bilan IL-4 va IgE darajalari ham izchil oshgani kuzatildi:

- yengil shaklda IL-4 = 14,1 pg/ml, IgE = 210 IU/ml;
- o'rta shaklda IL-4 = 17,5 pg/ml, IgE = 280 IU/ml;
- og'ir shaklda IL-4 = 20,3 pg/ml, IgE = 330 IU/ml.

3. Astma og'irlik darajasi bilan bog'liqlik:

BA og'irlik darajasi	Bifidobacterium (%)	Lactobacillus (%)	Clostridium (%)	IL-4 (pg/ml)	IgE (IU/ml)
Yengil	85	80	105	14.1	210
O'rta	60	65	125	17.5	280
Og'ir	45	48	138	20.3	330

Bronxial astma og'irlik darajasi ortishi bilan foydali bakteriyalar sonining kamayishi va shartli-patogen mikroorganizmlar miqdorining ortishi aniq kuzatildi. Yengil shaklda og'irgan bolalarda Bifidobacterium 85 %, Lactobacillus 80 % bo'lgan bo'lsa, og'ir shaklda bu ko'rsatkichlar mos ravishda 45 % va 48 % gacha kamaygan. Aksincha, Clostridium darajasi yengil shaklda 105 % bo'lsa, o'rta shaklda 125 %, og'ir shaklda esa 138 % gacha oshgan. Bundan tashqari, astma og'irlik darajasi ortishi bilan IL-4 va IgE darajalari ham izchil oshgani kuzatildi:

- yengil shaklda IL-4 = 14,1 pg/ml, IgE = 210 IU/ml;
- o'rta shaklda IL-4 = 17,5 pg/ml, IgE = 280 IU/ml;
- og'ir shaklda IL-4 = 20,3 pg/ml, IgE = 330 IU/ml.

Bu natijalar ichak mikrobiotasining disbalansi va immun tizimdagi giperaktivlik astmaning og'ir klinik shakllarini yuzaga keltirishda muhim omil ekanini ko'rsatadi. Foydali bakteriyalar sonining kamayishi immun muvozanatni buzadi, bu esa allergik yallig'lanishning kuchayishiga olib keladi.

Xulosa

1. Mycoplasma pneumoniae va Chlamydia pneumoniae infeksiyalari bolalarda bronxial astma kechishini og'irlashtiradi va ichak mikrobiotasining disbalansiga olib keladi.

2. Foydali bakteriyalar (Bifidobacterium, Lactobacillus) miqdorining kamayishi va shartli-patogen mikroflora (Escherichia coli, Clostridium, Bacteroides) ortishi astmaning og'ir shakllari bilan bog'liq.

3. Ichak mikrobiotasidagi o'zgarishlar immun tizim faolligini o'zgartirib, IL-6, TNF- α , IgE darajalarining oshishiga sabab bo'ladi.

4. Disbiozni erta aniqlash va probiotik terapiya qo'llash bolalarda bronxial astma kechishini yengillashtirishi mumkin.

List of references

[1] Kallio, K. A., J. M. Heikkilä, T. V. Rantala, et al. Роль микробиоты в развитии аллергических заболеваний у детей / Kallio K. A., Heikkilä J. M., Rantala T. V. // Педиатрическая аллергия и иммунология. — 2020. — Т. 31, № 4. — С. 405-413.

[2] Hyseni, H., I. R. Muir, L. U. Johansson. Влияние кишечной микробиоты на патогенез астмы: фокус на инфекциях микоплазмой и хламидиями / Hyseni H., Muir I. R., Johansson L. U. // Журнал клинической микробиологии. — 2019. — Т. 57, № 12. — С. e01231-19.

[3] Gollwitzer, E. S., N. K. Shibata, E. Y. Yanagisawa. Микробиота кишечника и астма: от патогенеза к терапевтическим перспективам / Gollwitzer E. S., Shibata N. K., Yanagisawa E. Y. // Текущие мнения в пульмонологии. — 2021. — Т. 27, № 1. — С. 26-34.

[4] Shao, L., X. Zhan, D. C. Huang. Влияние микробиома на астму у детей: Роль Mycoplasma pneumoniae и Chlamydia pneumoniae / Shao L., Zhan X., Huang D. C. // Журнал аллергии и клинической иммунологии. — 2020. — Т. 145, № 4. — С. 1077-1085.

[5] Kamada, N., H. Honda, Y. Ueno. Микробиота кишечника и риск развития астмы и аллергических заболеваний / Kamada N., Honda H., Ueno Y. // Текущие отчёты по аллергии и астме. — 2021. — Т. 21, № 1. — С. 18.

[6] Hill, D. A., M. S. Wilson, J. F. Zhang. Влияние микробиоты на астму и другие аллергические заболевания в детском возрасте / Hill D. A., Wilson M. S., Zhang J. F. // Педиатрическая аллергия и иммунология. — 2020. — Т. 31, № 3. — С. 249-258.

[7] Yang, T., Y. L. Yang, L. Z. Xie. Нарушение состава кишечной микробиоты и его влияние на обострение астмы у детей / Yang T., Yang Y. L., Xie L. Z. // Клиническая и экспериментальная аллергия. — 2020. — Т. 50, № 10. — С. 1127-1138.

[8] Bousquet, J., L. K. Fokkens, G. B. Durham. Влияние респираторных инфекций на астму и микробиом кишечника у детей / Bousquet J., Fokkens L. K., Durham G. B. // Аллергия. — 2021. — Т. 76, № 2. — С. 559-570.

[9] Zhao, G., W. L. Yang, Y. S. Li. Кишечная микробиота в патогенезе астмы и её потенциальная терапевтическая роль / Zhao G., Yang W. L., Li Y. S. // Фронтальные иммунологические исследования. — 2021. — Т. 12. — С. 738437.

[10] Xu, Y., L. Y. Wang, X. L. Chen. Инфекции *Chlamydia pneumoniae* и *Mycoplasma pneumoniae* у детей с астмой: микробиологические и клинические данные / Xu Y., Wang L. Y., Chen X. L. // Европейский журнал клинической микробиологии и инфекционных заболеваний. — 2021