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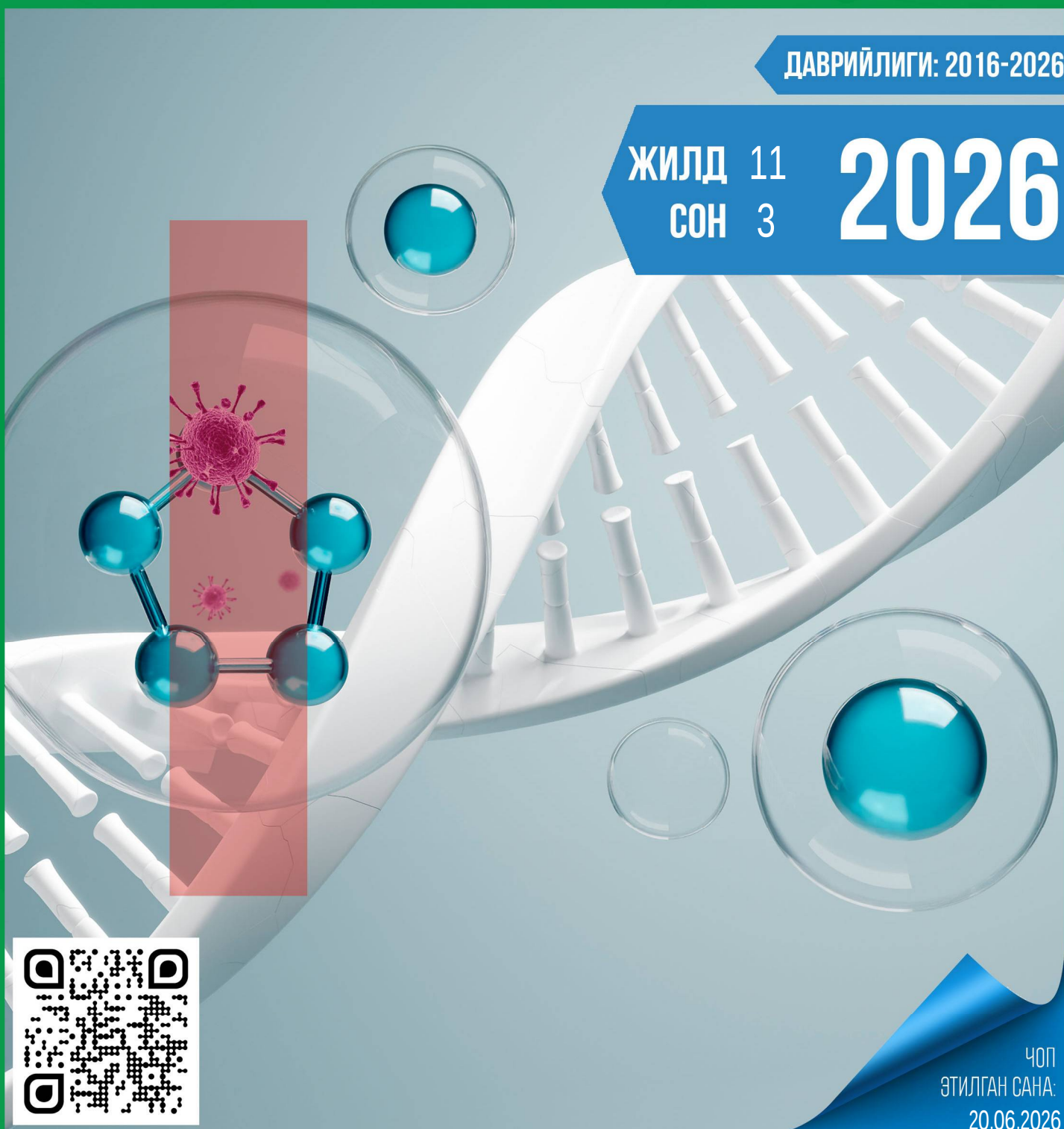
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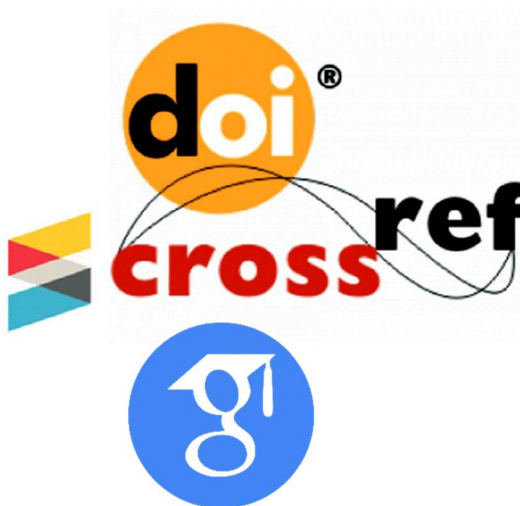
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ORCID ID: 0000-0002-6142-7054

Ответственный за публикацию:

Шаханова Шахноза Шавкатовна
DSc, доцент кафедры онкологии Самаркандского
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хирургии Самаркандского государственного медицинского
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ORCID ID: 0000-0002-9313-4918

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<https://orcid.org/0000-0003-3553-8727>

Шавази Наргиз Нуралиевна
DSc, доцент, заведующая кафедрой
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<https://orcid.org/0000-0001-7859-9955>

Юлдашев Равшан Захидович
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<https://orcid.org/0009-0002-7165-5373>

Алимов Жалолиддин Усмон угли
PhD, Доцент Чирчикского филиала Ташкентского
Государственного медицинского университета, ORCID
ID: 0009-0009-3959-9878

Саидов Садаммир Абборович
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ORCID ID: 0000-0002-6616-5428

Бабаджанов Ойбек Абдужаббарович
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ORCID ID: 0000-0002-3022-916X

Теребаев Билим Алдамуратович
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ORCID ID: 0000-0002-5409-4327

Юлдашев Ботир Ахматович
доктор медицинских наук, доцент кафедры Педиатрии,
неонатологии и протекции детских болезней №2
Самаркандского государственного медицинского университета
ORCID ID: 0000-0003-2442-1523

Ибрагимова Малика Худайбергеновна
доктор медицинских наук, профессор
Ташкентский государственный
медицинский университет
ORCID ID: 0000-0002-9235-1742

Рахимов Нодир Махамматкулович
доктор медицинских наук, профессор кафедры
онкологии Самаркандского государственного
медицинского университета
ORCID ID: 0000-0001-5272-5503

Даминов Феруз Асадуллаевич
Декан лечебного факультета №2 Самаркандского
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Ташкентский государственный медицинский университет.
ORCID: 0009-0004-7661-9253.

Сайфутдинов Зайниддин Асамутдинович
PHD, Республиканский специализированный научно-
практический медицинский центр педиатрии ORCID ID: 0009-
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Medical University, Docent the Department of
Dermatovenerology, pediatric dermatovenerology
and AIDS, ORCID ID: 0000-0002-3022-916X*

Terebaev Bilim Aldamuratovich

*Doctor of Medical Sciences, Associate Professor,
Tashkent Pediatric Medical Institute,
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ORCID ID: 0000-0002-5409-4327.*

Yuldashev Botir Akhmatovich

*Doctor of Medical Sciences, Associate Professor of
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Samarkand State Medical University No. 2.
ORCID ID: 0000-0003-2442-1523*

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*Doctor of Medical Sciences, Professor,
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ORCID ID: 0000-0002-9235-1742*

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*Doctor of Medical Sciences, Associate Professor
of Surgery Department, Tashkent State Medical University
ORCID: 0009-0004-7661-9253.*

Sayfutdinov Zayniddin Asamutdinovich

*PHD, Republican Specialized Scientific and Practical Medical
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БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ

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NASRETDINOVA Makhzuna

Doctor of Medical Sciences, Professor

DUSTBOBOEV Dilshod

Samarkand State Medical Institute

OPTIMIZATION OF CONSERVATIVE TREATMENT FOR EXUDATIVE OTITIS MEDIA IN CHILDREN: THE SYNERGISTIC EFFECT OF PILN, TOPICAL IMMUNOCORRECTION, AND PLAY AUTOINSUFFLATION

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ABSTRACT

Objective: To conduct a comparative evaluation of the clinical and biochemical efficacy of an optimized three-component treatment regimen for the secretory phase of exudative otitis media (EOM) in children aged 1–5 years, comprising low-intensity laser therapy (LILT), topical immunocorrection, and playful autoinsufflation, compared with standard treatment. **Methods:** 172 children (ages 1–5 years) were examined: subgroup A (n=40) — LI + lysates + autoinsufflation; subgroup B (n=37) — standard treatment; comparison group (n=60); control group (n=35). Salivary biomarkers (transferrin, ceruloplasmin, sIgA, myeloperoxidase), tympanometry data, OEA, and CSVP were assessed every 5 days. **Results:** In group A, by day 14, the transferrin level decreased 3.2-fold (to 3.8 ± 0.5 mg/L), while sIgA increased 2.3-fold (to 0.28 ± 0.03 g/L; $p < 0.001$). By day 30, type A tympanogram was restored in 92.5% of children in group A (OR = 7.8; 95% CI 1.9–31.6; $p < 0.05$) and in 62.2% in group B. The need for adenotomy in Group A decreased by a factor of 4.9 (5% vs. 24.3%). During the 6-month follow-up, recurrence rates were 2.5% in Group A and 18.9% in Group B ($p < 0.05$). **Conclusion:** The three-component regimen combined with non-invasive monitoring of biomarkers is an effective non-surgical method for treating ESO. At the 6-month follow-up, the recurrence rate was 2.5% in Group A and 18.9% in Group B ($p < 0.05$).

Keywords: exudative otitis media, children, low-intensity laser radiation, autoinsufflation, topical immunomodulation, transferrin, ceruloplasmin, sIgA, noninvasive monitoring, OS, 95% CI.

NASRETDINOVA Maxzuna Taxsinovna

tibbiyot fanlari doktori, professor

DUSTBOBOEV Dilshod Sadullaevich

Samarqand davlat tibbiyot universiteti

BOLALARDA EKSSUDATIV O'RTA OTITNI KONSERVATIV DAVOLASHNI OPTIMALLASHTIRISH: PILN, TOPIK IMMUNOKORREKSIYA VA

O'YIN AUTOINSUFFLYATSIIYASINING SINERGIK SAMARASI

ANNOTATSIYA

Maqsad: 1–5 yoshli bolalarda ekssudativ o'rta otit (EO'O) sekretli bosqichida past intensivlikli lazer nurlanishi (PILN), topik immunokorreksiya va o'yin autoinsufflyatsiyasidan iborat optimallashtirilgan uch komponentli davolash sxemasining klinik va biokimyoviy samaradorligini standart davolash bilan taqqoslab baholash. **Usul:** 172 bola (1–5 yosh) tekshirildi: A kichik guruhi (n=40) — PILN + lizatlar + autoinsufflyatsiya; B kichik guruhi (n=37) — standart davolash; qiyosiy guruh (n=60); nazorat (n=35). **OBS biomarkerlari** (transferrin, seruloplazmin, sIgA, miyeloperoksidaza), timpanometriya, OAE, KLCHP har 5 kunda baholandi. **Natijalar:** A guruhida 14-kunga kelib transferrin 3,2 barobar kamaydi ($3,8 \pm 0,5$ mg/l), sIgA 2,3 barobar ko'tarildi ($0,28 \pm 0,03$ g/l; $p < 0,001$). 30-kunda timpanogramma A tipiga A guruhida 92,5% (OR=7,8; 95%DI 1,9–31,6; $p < 0,05$), B guruhida 62,2% bolada qaytdi. Adenotomiyaga ehtiyoj A guruhida 4,9 barobar kamaydi (5% vs 24,3%). 6 oylik kuzatuvda qaytalanish A guruhida 2,5%, B guruhida 18,9% ($p < 0,05$). **Xulosa:** uch komponentli sxema noinvaziv biomarker monitoring bilan birgalikda EO'Oning samarali va jarrohliksiz davolash usuli hisoblanadi.

Kalit so'zlar: ekssudativ o'rta otit, bolalar, past intensivlikli lazer, autoinsufflyatsiya, topik immunokorreksiya, transferrin, seruloplazmin, sIgA, noinvaziv monitoring, OR, 95% DI.

НАСРЕТДИНОВА Махзуна Тахсиновна

доктор медицинских наук, профессор

ДУСТБОБОВ Дилшод Садуллаевич

Самаркандский государственный медицинский университет

**ОПТИМИЗАЦИЯ КОНСЕРВАТИВНОГО ЛЕЧЕНИЯ ЭКССУДАТИВНОГО
СРЕДНЕГО ОТИТА У ДЕТЕЙ: СИНЕРГЕТИЧЕСКИЙ ЭФФЕКТ ПИЛН,
ТОПИЧЕСКОЙ ИММУНОКОРРЕКЦИИ И ИГРОВОЙ АУТОИНСУФФЛЯЦИИ**

АННОТАЦИЯ

Цель: сравнительная оценка клинической и биохимической эффективности оптимизированной трехкомпонентной схемы лечения секреторной стадии экссудативного среднего отита (ЭСО) у детей 1–5 лет, включающей низкоинтенсивное лазерное излучение (НИЛИ), топическую иммунокоррекцию и игровую аутоинсуффляцию, по сравнению со стандартным лечением. **Методы:** обследовано 172 ребенка (1–5 лет): подгруппа А (n=40) — НИЛИ + лизаты + аутоинсуффляция; подгруппа В (n=37) — стандартное лечение; группа сравнения (n=60); контрольная группа (n=35). Биомаркеры ротовой жидкости (трансферрин, церулоплазмин, sIgA, миелопероксидаза), данные тимпанометрии, ОАЭ и КСВП оценивались каждые 5 дней. **Результаты:** в группе А к 14-му дню уровень трансферрина снизился в 3,2 раза (до $3,8 \pm 0,5$ мг/л), а sIgA повысился в 2,3 раза (до $0,28 \pm 0,03$ г/л; $p < 0,001$). На 30-й день тимпанограмма типа А была восстановлена у 92,5% детей в группе А (ОШ=7,8; 95% ДИ 1,9–31,6; $p < 0,05$) и у 62,2% в группе В. Потребность в аденотомии в группе А снизилась в 4,9 раза (5% против 24,3%). В течение 6-месячного наблюдения рецидивы в группе А составили 2,5%, а в группе В — 18,9% ($p < 0,05$). **Заключение:** трехкомпонентная схема в сочетании с неинвазивным мониторингом биомаркеров является эффективным безоперационным методом лечения ЭСО. При 6-месячном наблюдении частота рецидива в группе А составила 2,5%, в группе В - 18,9% ($p < 0,05$).

Ключевые слова: экссудативный средний отит, дети, низкоинтенсивное лазерное излучение, аутоинсуффляция, топическая иммунокоррекция, трансферрин, церулоплазмин, sIgA, неинвазивный мониторинг, ОШ, 95% ДИ.

KIRISH Ekssudativ o'rta otit (EO'O) — bolalar otorinolaringologiyasining ijtimoiy ahamiyati jihatidan eng dolzarb muammolaridan biri bo'lib, 5 yoshgacha bo'lgan bolalarning 80–

90% kamida bir marta ushbu kasallikni boshidan kechiradi [1]. Kasallik cho'qqisi (30–35%) 1–5 yoshdagi nutq shakllanishining kritik davriga to'g'ri kelishi uni alohida klinik muhimlikka ega qiladi. Ikki tomonlama zararlanishning yuqori chastotasi (86% gacha), kasallikning asimptomli «soqov otit» tipida kechishi va qaytmas eshitish zaifligining shakllanish xavfi (25–30% holatlarda) ushbu muammoni yanada og'irlashtiradi [2, 3].

Zamonaviy klinik tibbiyotda EO'Oni davolashda uchta asosiy yondashuv qo'llaniladi: (1) kutish taktikasi («watchful waiting»), (2) antibiotikoterapiya va mukoaktiv preparatlar, (3) jarrohlik usullari — adenotomiya, timpanosentez, shuntlash. Biroq ushbu usullarning har biri o'z cheklovlariga ega: kutish taktikasida kasallikning mukoze shakliga («yopishqoq quloq», glue ear) o'tish xavfi saqlanib qoladi; jarrohlik aralashuvlari esa maktabgacha yoshdagi bolalarda umumiy anesteziya xavflari, psixoemosional stress va qaytalanish holatlari bilan birga keladi [4]. Bu holat patogenetik asoslangan, kamjarohatli konservativ davolash usullarini izlashni talab etadi.

So'nggi yillarda EO'O patogenezida uchta asosiy bo'g'in aniqlanmoqda: (1) eshituv nayi disfunktsiyasi — shilliq qavatning mexanik obstruksiyasi va sekretiyan buzilishi; (2) mukozal immunitet tanqisligi — shilliq qavatning sIgA tomonidan amalga oshiriladigan mahalliy himoya imkoniyatining pasayishi; (3) oksidativ stress — erkin radikallarning o'rta quloq eksudati qovushqoqlashuviga ta'siri [5, 6]. Ushbu uchta bo'g'inga bir vaqtning o'zida ta'sir etuvchi sinergetik davolash sxemasini ishlab chiqish tadqiqotimizning asosiy maqsadi bo'ldi.

Past intensivlikli lazer nurlanishi (PILN) so'nggi o'n yilliklarda otorinolaringologiya amaliyotida keng qo'llanilmoqda. Uning fotobiomodulasiya mexanizmi orqali ta'sir qilishi — mitoxondriyal elektron transport zanjirini faollashtirish, prostaglandinlar sintezini inhibe etish va kapillyar mikrosirkulatsiyani yaxshilash — yallig'lanish shishini samarali bartaraf etadi [7]. Topik bakterial lizatlar (IRS-19, Lizobakt) shilliq qavatning sIgA ishlab chiqarish imkoniyatini ragbatlantiradi va nazofarings mikroflorasini sanasiya qiladi [8]. O'yin autoinsufflyatsiyasi («Otovent» trenajoëri) eutaxtik bosim prinsipiga asoslanib, eshituv nayi boshqaladigan ochilishini ta'minlaydi va og'riq yoki kateterizatsiyasiz nog'ora bo'shlig'ini mexanik aerasiya qiladi [9].

Og'iz bo'shlig'i suyuqligi (OBS) nazofarinks va o'rta quloqning mukozal immunitet tizimining ob'ektiv «ko'zgusi» hisoblanadi. Tubotumpanal tizim va nazofarinks shilliq qavatlari yagona mukozal immunitet tizimining funktsional-struktura birligi sifatida harakat qilganligi sababli, OBSdagi transferrin (kapillyar o'tkazuvchanligi va yallig'lanish intensivligining markeri) hamda seruloplazmin (oksidativ stressning akut faza oqsili) darajalari o'rta quloqdagi patologik jarayonlarni invaziv muolajalarsiz aks ettira oladi [10]. Ushbu maqolada biz uch komponentli optimallashtirilgan sxemaning samaradorligini OBS biomarkerlari yordamida ob'ektiv monitoring qilish natijalarini taqdim etamiz.

MATERIAL VA METODLAR

2.1. Tadqiqot dizayni va bemorlar

Prospektiv randomizatsiyalangan koxort tadqiqot 2021–2024 yillarda Qashqadaryo viloyati Kitob shahar bolalar ko'p tarmoqli shifoxonasida o'tkazildi. Tadqiqot SamDTU etika qo'mitasi tomonidan tasdiqlandi (bayonnoma № 12, 15.09.2021). Barcha bolalarning ota-onalari yozma roziliklarini berdilar. Kuzatuvga 172 nafar 1–5 yoshli bola jalb etildi. Guruhlar taqsimoti 1-jadvalda keltirilgan.

1-jadval. Tekshirilgan bemorlar guruhlarining tarkibi va asosiy xarakteristikalar

Guruh	n	Erkak/ Ayol	O'rtacha yosh (yil)	Klinik xususiyat
A kichik guruhi (optimal davolash)	40	23/17	3,1±1,0	EO'O + adenoidit; PILN+lizatlar+autoinsufflyatsiya
B kichik guruhi (standart davolash)	37	21/16	3,3±1,1	EO'O + adenoidit; dekongestantlar+yuvish

Qiyosiy guruh	60	34/26	3,8±1,3	Adenoidit, EO'Osiz (timpanogramma A tipi)
Nazorat guruhi	35	20/15	3,5±1,0	LOR aъzolari sog'lom, I-II salomatlik guruhi
JAMI	172	98/74	3,4±1,1	

Izoh: Guruhlar yosh, jins va adenoidit darajasi bo'yicha gomogen ($p>0,05$). A va B kichik guruhlar EO'O asosiy guruhidan randomizatsiya usulida ajratilgan.

Kiritish mezonlari: yoshi 1–5 yil; EO'O sekretli bosqichi (timpanometriya B yoki C tipi); adenoid giperfiyasi II yoki III daraja; ota-onalarning yozma roziligi. Chiqarish mezonlari: o'tkir otit epizodi so'nggi 1 oy ichida; antibiotik qabuli so'nggi 2 hafta; immun tanqislik holatlari; oraliq omillari (palatin yorig'i, kraniofasial anomaliyalar).

2.2. Davolash protokollari

Asosiy guruh (n=77) ikkita kichik guruhga randomizirlandi (2-jadval):
2-jadval. A va B kichik guruhlarining davolash protokollari (bosqichli sxema)

Bosqich	Muddat	A kichik guruhi (optimal)	B kichik guruhi (standart)
I	1-3-kun	Topik sanasiya: bakterial lizatlar (Lizobakt yoki IRS-19) burun spreysi — 3 marta/kuniga. Maqsad: nazofarinks florasini sanasiya qilish va shilliq qavat immunitetini ragbatlantirish	Nasal dekongestantlar (oksimetazolin 0,025%) — 3 kun; izotonik eritmalar bilan yuvish
II	1-10-kun	PILN (fotobiomodulasiya): «Mustang-2000», $\lambda=0,89$ mkm, impuls rejimi, quvvat 5–10 mVt, ekspozitsiya 2 daqiqa × har bir tomon (jami 4 daqiqa), kuniga 1 seans, 10 seans	Kutish taktikasi. Zarur bo'lganda mukoaktiv preparatlar (karboksistein)
III	3-17-kun	O'yin autoinsufflyatsiyasi: «Otovent» boshli sharlar tizimi. Texnikasi: bola shar adapterini bir burun teshigiga qo'yib, 2-3 marta chuqur nafas chiqaradi; eutaxtik bosim ostida yutish harakati bilan eshituv nayi ochiladi. Kuniga 2-3 marta; PILNdan 20-30 daqiqa keyin.	—
Monitoring	0,5,10,14,30-kun; 6 oy	OBS biomarkerlari (transferrin, seruloplazmin, sIgA) + timpanometriya har 5 kunda	Timpanometriya 10 va 14-kunlarda

PILN — past intensivlikli lazer nurlanishi; DI — доверительный интервал; PILNdan 20–30 daqiqa keyin autoinsufflyatsiya o'tkazilishi lazerning antiishi effekti ch'qqisiga to'g'ri keladi.

PILN muolajasi uchun «Mustang-2000» yarim o'tkazgichli lazer apparati (Rossiya, $\lambda=0,89$ mkm, impuls rejimi, quvvat 5–10 mVt) nazal optik moslama bilan qo'llanilib, nurlanish eshituv nayi

teshikchalari proeksiyasiga qaratildi. Ekspozisiya har bir tomon uchun 2 daqiqa, jami 4 daqiqa; kursi 10 kunlik seans.

Autoinsufflyatsiya texnikasi: bola «Otovent» trenajoëridan boshli sharni burun teshigiga qo'yib, diametri 8–10 sm ga yetguncha bur-un orqali majburiy nafas chiqaradi (eutaxtik bosim fazasi). Maksimal nazofaringeal bosim paytida yutish harakati bajariladi (eshituv nayi ochilish fazasi). Har tomon uchun 2–3 marta; kuniga 2–3 marta amalga oshirilib, nazofaringeal sekresiyaning retrograd otilib chiqish xavfi istisno etiladi.

2.3. Laboratoriya usullari

OBS namunalari ertalab ovqatlanmasdan oldin, og'izni yuvmasdan, passiv oqish usulida steril polipropilen idishlarga (5 ml) yig'ildi. Namunalar 4°C da 3000 rpm, 30 daqiqa sentrifugalanib, supernatant –70°C da saqlandi.

Tahlil usullari: (1) Transferrin — immuno-turbidimetrik usul (Beckman Coulter, AQSh); referent qiymat <4,0 mg/l. (2) Seruloplazmin — Ravin usulining modifikatsiyasi; referent qiymat <2,0 mg/l. (3) sIgA — ELISA usuli (Orgentec Diagnostika, Germaniya); referent qiymat >0,25 g/l. (4) Miyeloperoksidaza faolligi — spektrofotometrik usul ($\lambda=460$ nm); referent qiymat <7,0 nmol/min·ml. Monitoring davomiyligi: 0 (boshida), 5, 10, 14, 30-kunlar va 6 oydan keyin.

2.4. Instrumental tekshiruv

Barcha bolalarga quyidagi tekshiruvlar o'tkazildi: (1) Videoendoskopiya — nazofarinks va eshituv nayi teshikchalari holati baholandi. (2) Timpanometriya — GSI TympStar Pro apparati (A, B, C tipi); ipsilateral akustik refleks aniqlandi. (3) Otoakustik emissiya (OAE) — «Pass» (o'tdi) yoki «Refer» (o'tmadi) natijasi. (4) Qisqa latentli chaqirilgan eshitish potentsiallar (KLCHP) — V cho'qqi qayd etish bo'sag'asi va I cho'qqi latensi baholandi.

2.5. Statistik usullar

Statistik tahlil SPSS v.26 (IBM, AQSh) dasturida amalga oshirildi. Taqsimotning normalligi Shapiro–Wilk testi orqali tekshirildi. Normal taqsimlangan ko'rsatkichlar (sIgA, transferrin) uchun Student t-testi qo'llanilib, natijalar $M \pm m$ shaklida keltirildi. Nonnormal taqsimlangan ko'rsatkichlar (seruloplazmin, miyeloperoksidaza) uchun Mann–Whitney U-testi qo'llanilib, Me [Q1–Q3] shaklida keltirildi. Kategoriya o'zgaruvchilari χ^2 Fisher aniq testi bilan baholandi; odds ratio (OR) va 95% ishonch oralig'i (DI) hisoblab chiqildi. Korrelyatsion tahlil Spirmen ρ koeffisienti yordamida amalga oshirildi. Farqlar $p < 0,05$ bo'lganda statistik ahamiyatli deb qabul qilindi.

TADQIQOT NATIJALARI

3.1. Guruhlarning dastlabki klinik xarakteristikasi

Asosiy guruhda ($n=77$) o'g'il bolalar 57,2% ni tashkil etdi. Adenoidlarning III darajali giperfiyasi 55,8% (43 bola), II darajali giperfiyasi esa 44,2% (34 bola) da aniqlandi. Barcha 77 bolada eshituv nayi teshikchalari sohasida yopishqoq sekresiya mavjudligi videoendoskopiya orqali tasdiqlandi (100%). Shikoyatlar tahlili ko'rsatkichi, audiologik shikoyatlar (qayta so'rash — 92%, ovoz balandligini ko'tarish — 78%) faqat asosiy guruhda ustunlik qilib, qiyosiy guruhdan statistik ahamiyatli farq qildi ($p < 0,001$), holbuki rinofaringeal shikoyatlar (og'iz orqali nafas olish, xurrak) ikki guruhda ham bir xil darajada kuzatildi.

3.2. Timpanometriya va audiologik tekshiruv natijalari

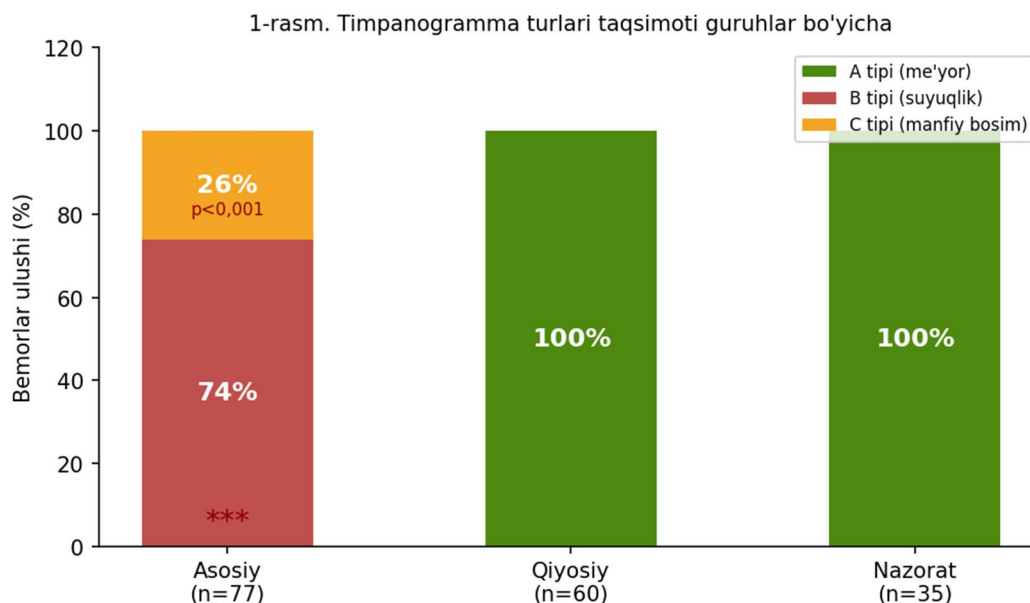
Asosiy guruhda timpanogramma B tipi (nog'ora bo'shlig'ida suyuqlik) 74% bolada, C tipi (eshituv nayi manfiy bosimi) 26% bolada aniqlandi. Akustik refleks 95% holatlarda qayd etilmadi. OAE «Refer» natijasi 92% bolada kuzatildi — bu kochlear buzilishlar bilan emas, balki eksudatning tovush o'tkazuvchi to'siq yaratishi bilan izohlanadi. KLCHP da V cho'qqi qayd etish bo'sag'asi $38,4 \pm 3,2$ dB ga ko'tarildi («mass-effekt»). Qiyosiy guruhda A tipi 100% da saqlandi (3-jadval).

3-jadval. Tekshirilayotgan guruhlar bo'yicha timpanometriya va audiologik ko'rsatkichlar

Ko'rsatkich	Asosiy guruh (n=77)	Qiyosiy (n=60)	Nazorat (n=35)	p
Timpanogramma B tipi	74% (57/77)	0%	0%	<0,001
Timpanogramma C tipi	26% (20/77)	0%	0%	<0,001

Akustik refleks yo'qligi	95% (73/77)	0%	0%	<0,001
OAE «Refer» (o'tkazilmagan)	92% (71/77)	0%	0%	<0,001
KLCHP V cho'qqi bo'sag'asi, dB	38,4±3,2†	18,1±2,5	15,8±2,0	<0,001
KLCHP I cho'qqi latensi, ms	1,92±0,14†	1,56±0,10	1,52±0,09	<0,001

Izoh: † — nazorat guruhi bilan solishtirganda $p < 0,001$. KLCHP — qisqa latentli chaqirilgan eshitish potentsiallar; OAE — otoakustik emissiya.



3.3. OBSning dastlabki immuno-biokimyoviy profili

A va B kichik guruhlar o'rtasida kuzatuvga qabul paytidagi barcha OBS biomarkerlari statistik ahamiyatli farq qilmadi ($p > 0,05$), bu randomizatsiyaning muvaffaqiyatli amalga oshirilganligini tasdiqlaydi. Asosiy guruhda transferrin darajasi ($12,4 \pm 1,1$ mg/l) nazorat qiymatidan 4 barobar yuqori bo'lib ($3,1 \pm 0,4$ mg/l; $p < 0,001$), o'rta quloq shilliq qavatidan plazma oqsillarining jadal transsudasiyasini ob'ektiv tasdiqlamoqda. Seruloplazmin konsentratsiyasi ($4,8 \pm 0,5$ mg/l) me'yordan 4 barobar yuqori bo'lib, faol oksidativ stressning ishonchli ko'rsatkichi hisoblanadi. sIgA darajasi $0,12 \pm 0,02$ g/l gacha kritik pasaydi — nazorat qiymatidan 2,7 barobar past. Transferrin/sIgA nisbati asosiy guruhda $105,0 \pm 12$ ni tashkil etdi, nazoratda esa $9,7 \pm 1,5$ ($p < 0,001$) — bu ikki biomarkerni birgalikda baholashning diagnostik qiymatini ko'rsatadi (4-jadval).

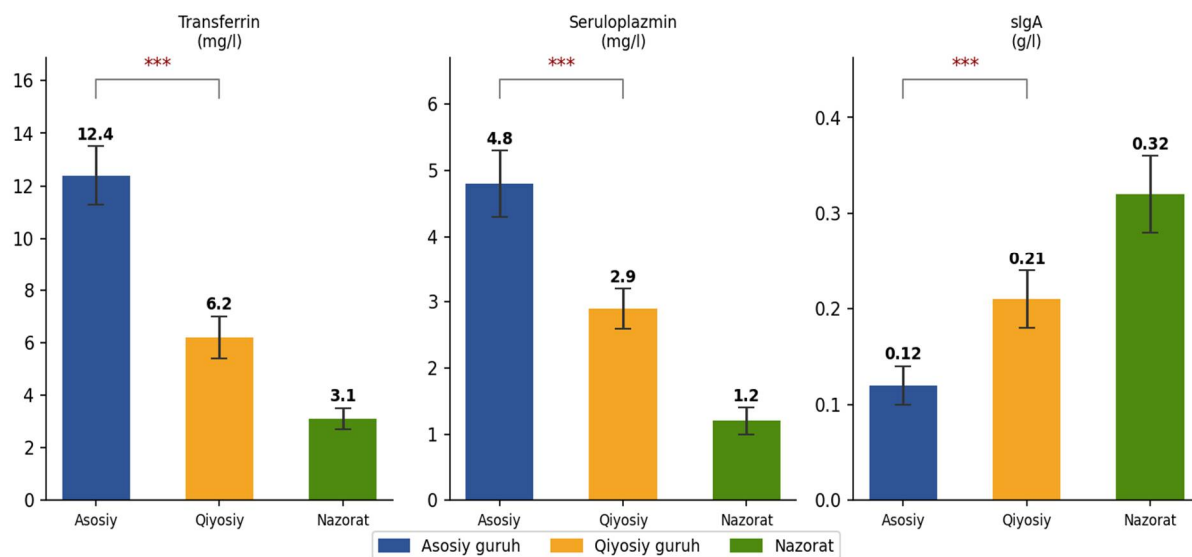
4-jadval. Tekshirilayotgan guruhlar bo'yicha OBSning dastlabki immuno-biokimyoviy ko'rsatkichlari ($M \pm m$)

Ko'rsatkich	A kichik guruhi (n=40)	B kichik guruhi (n=37)	Qiyosiy (n=60)	Nazorat (n=35)	p*
sIgA, g/l	$0,12 \pm 0,02 \dagger \#$	$0,11 \pm 0,02 \dagger \#$	$0,21 \pm 0,03 \dagger$	$0,32 \pm 0,04$	<0,001
Transferrin, mg/l	$12,6 \pm 1,2 \dagger \#$	$12,1 \pm 1,0 \dagger \#$	$6,2 \pm 0,8 \dagger$	$3,1 \pm 0,4$	<0,001
Seruloplazmin, mg/l	$4,9 \pm 0,6 \dagger \#$	$4,7 \pm 0,5 \dagger \#$	$2,9 \pm 0,3 \dagger$	$1,2 \pm 0,2$	<0,001
Miyeloperoksidaza, nmol/min·ml	$18,4 \pm 2,1 \dagger \#$	$18,1 \pm 2,0 \dagger \#$	$11,2 \pm 1,4 \dagger$	$5,8 \pm 0,9$	<0,001

Transferrin/sIgA nisbati	105,0±12	110,0±11	29,5±4	9,7±1,5	<0,001
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Izoh: † — nazorat guruhi bilan solishtirganda $p<0,001$; # — qiyosiy guruh bilan solishtirganda $p<0,001$.

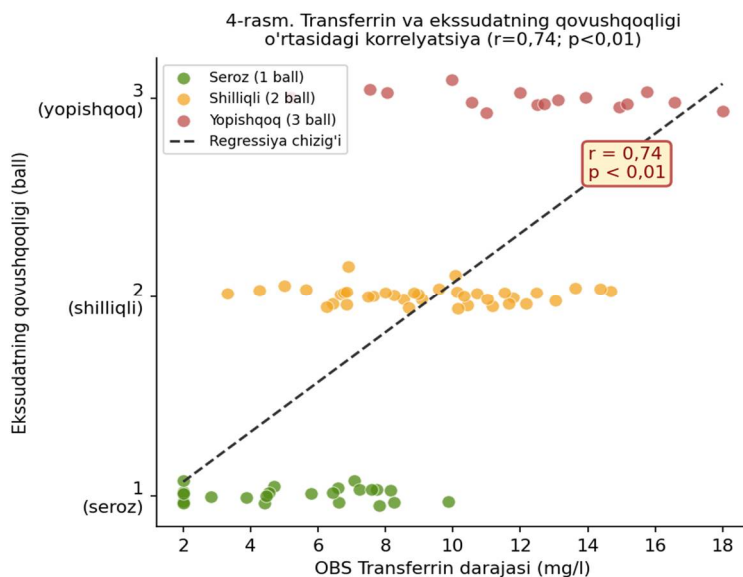
2-rasm. OBS dastlabki immuno-biokimyoviy ko'rsatkichlari ($M\pm m$)



3.4. Korrelyatsion tahlil va prognostik prediktor

Spirmen korrelyatsion tahlili OBSdagi transferrin darajasi va nog'ora bo'shlig'i eksudatining qovushqoligi o'rtasida kuchli to'g'ri statistik bog'liqlikni aniqladi ($p=0,74$; 95% DI 0,62–0,83; $p<0,01$). Eksudatning qovushqoligi ball tizimida raqamlashtirildi: 1 ball — seroz (past qovushqoq), 2 ball — shilliqli (o'rtacha), 3 ball — yopishqoq/gel-simon (yuqori). Ushbu korrelyatsion bog'liqlik 7-rasmda ko'rsatilgan.

Muhim prognostik topilma: transferrin >12 mg/l + sIgA $<0,12$ g/l kombinatsiyasi mavjud bo'lganda «yopishqoq quloq» rivojlanish xavfi 4,5 barobar ortadi ($p<0,01$). Bu kombinatsiya davolash taktikasini zudlik bilan faol patogenetik sxemaga o'tkazish uchun ob'ektiv indikator bo'lib xizmat qiladi. Miyeloperoksidaza faolligining ortishi ham eksudatning mukoze shakliga o'tishi bilan kuchli korrelyatsiyada ekanligi aniqlandi ($p=0,68$; $p<0,01$).



3.5. Klinik belgilarning yo'qolish dinamikasi

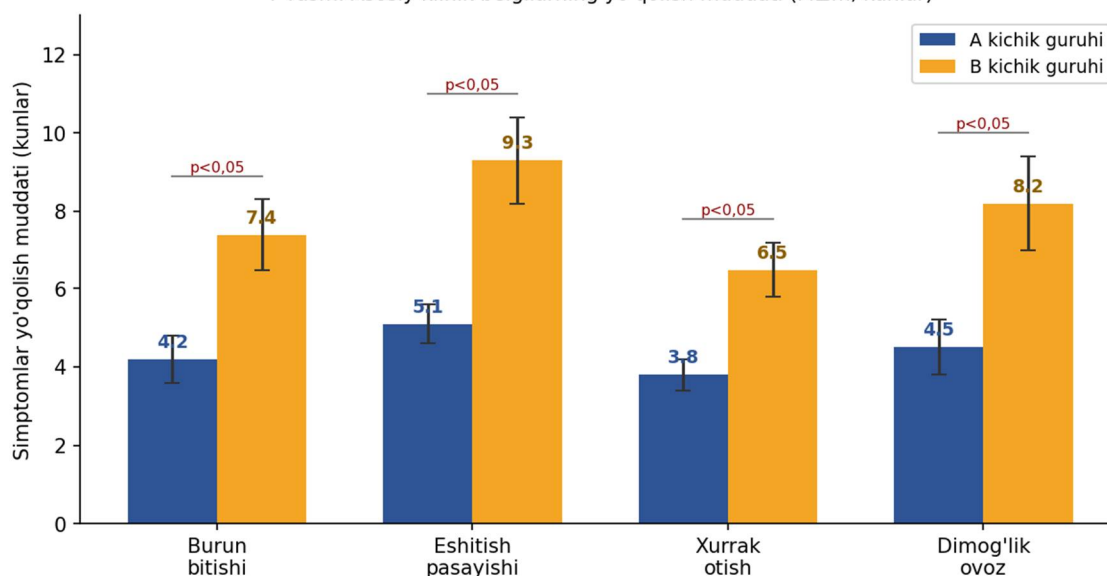
5-kunda A kichik guruhida tovush stimullariga adekvat javobning tiklanishi 72,5% bolalarda qayd etildi (B guruhida — 35,1%; $p<0,05$). Bu erta ijobiy natija PILNning eshituv nayi sohasidagi shishga qarshi tez ta'siri va autoinsufflyatsiyaning nog'ora bo'shlig'ini aerasiya qilish mexanizmi bilan izohlanadi. Barcha klinik belgilarning yo'qolish muddatlari A guruhida statistik jihatdan sezilari qisqa bo'ldi (5-jadval).

5-jadval. Asosiy klinik belgilarning yo'qolish muddatlari (kunlar, $M\pm m$)

Klinik belgi	A kichik guruhi $M\pm m$ (kun)	B kichik guruhi $M\pm m$ (kun)	Δ (kun)	P
Бурундан нафас олишнинг нормалланиши / Burundan nafas olish normallashishi	4,2 $\pm$ 0,6	7,4 $\pm$ 0,9	3,2	<0,05
Eshitish pasayishiga shikoyat yo'qolishi	5,1 $\pm$ 0,5	9,3 $\pm$ 1,1	4,2	<0,01
Xurrak otish va shovqinli nafas olishning to'xtashi	3,8 $\pm$ 0,4	6,5 $\pm$ 0,7	2,7	<0,05
Dimog'lik ovozning yo'qolishi (rinofoniya)	4,5 $\pm$ 0,7	8,2 $\pm$ 1,2	3,7	<0,05
Tovush stimullariga adekvat javobning tiklanishi	5-kun: 72,5%	5-kun: 35,1%	—	<0,05

Izoh: Δ — guruhlar orasidagi farq (kunlarda). Barqarorlik sinovnomasi: ota-onalar so'rovnomasi va bolaning hulq-atvorini kuzatish asosida.

7-rasm. Asosiy klinik belgilarning yo'qolish muddati ($M\pm m$, kunlar)



3.6. OBS biomarkerlari dinamikasi davolash davomida

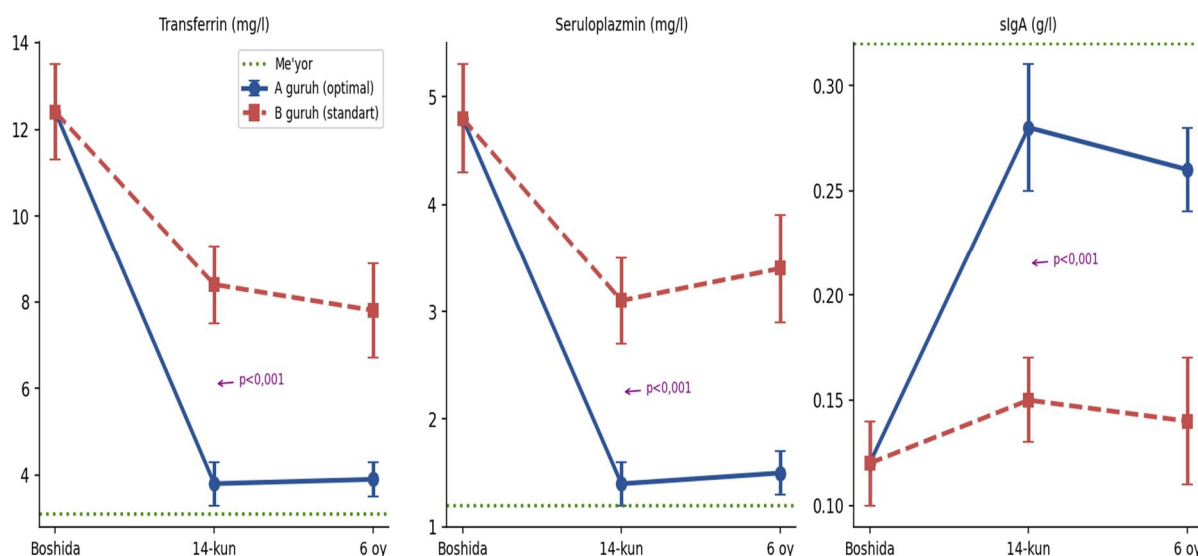
14-kunlik kurs yakunida A kichik guruhida transferrin 3,2 barobar kamaydi (3,8 $\pm$ 0,5 mg/l; 95% DI 2,8–4,8), seruloplazmin me'yorlashdi (1,4 $\pm$ 0,2 mg/l), sIgA 2,3 barobar ko'tarildi (0,28 $\pm$ 0,03 g/l) — bularning barchasi nazorat qiymatlariga yaqinlashgan. B kichik guruhida esa transferrin yuqori saqlanib qoldi (8,4 $\pm$ 0,9 mg/l; 95% DI 6,6–10,2) — bu kapillyar o'tkazuvchanligining persistensiyasini va qaytalanish xavfini ko'rsatmoqda (6-jadval).

6-jadval. Davolash yakunida (14-kun) OBS biokimyoviy ko'rsatkichlari dinamikasi (M±m)

Ko'rsatkich	A kichik guruh (n=40)	B kichik guruh (n=37)	Nazorat (n=35)	p (A vs B)
sIgA, g/l	0,28±0,03*	0,15±0,02	0,32±0,04	<0,05
Transferrin, mg/l	3,8±0,5*	8,4±0,9	3,1±0,4	<0,001
95% DI (transferrin, A)	2,8–4,8	6,6–10,2	—	
Seruloplazmin, mg/l	1,4±0,2*	3,1±0,4	1,2±0,2	<0,001
Miyeloperoksidaza, nmol/min·ml	6,5±0,8*	14,6±1,2	4,2±0,5	<0,01
Transferrin kamayish darajasi	3,2 barobar	1,4 barobar	—	<0,001
sIgA o'sish darajasi	2,3 barobar	1,4 barobar	—	<0,05

Izoh: * — dastlabki ko'rsatkichlar bilan solishtirganda $p < 0,05$; 95% DI — 95% ishonch oralig'i.

3-rasm. Davolash davomida OBS biomarkerlari dinamikasi (M±m)



3.7. 30 kunlik kuzatuv natijalari

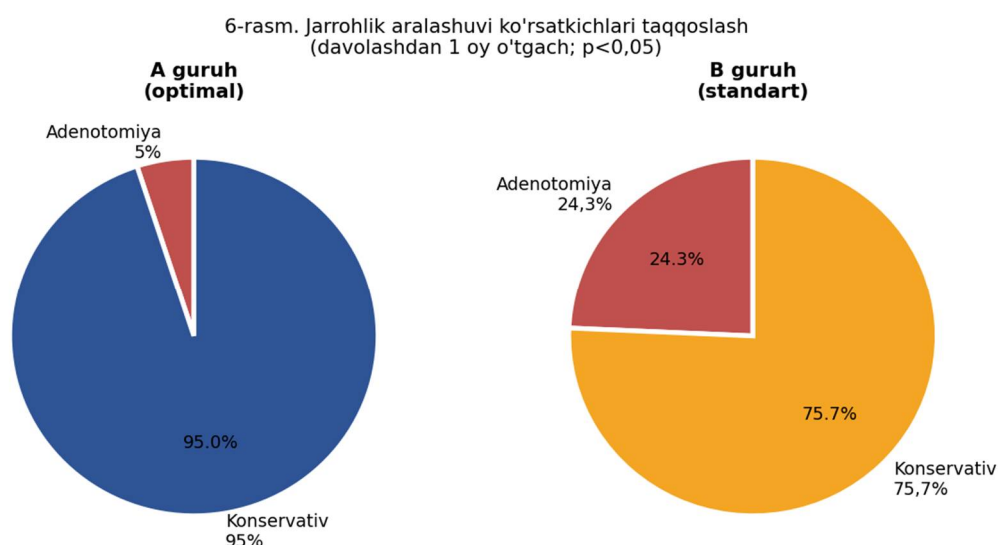
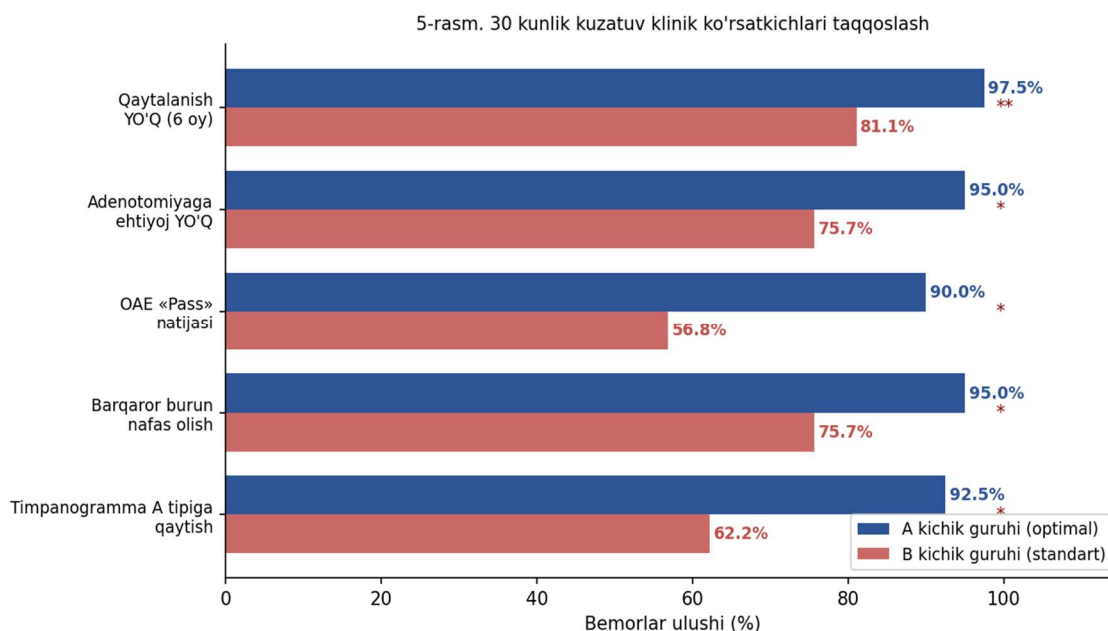
30-kunda timpanometrik tekshiruv A guruhida timpanogramma A tipiga 92,5% (37/40), B guruhida 62,2% (23/37) bolada qaytganligini ko'rsatdi (OR=7,8; 95% DI 1,9–31,6; $\chi^2=8,4$; $p < 0,05$). OAE «Pass» natijasiga A guruhida 90,0%, B guruhida 56,8% erishildi ($p < 0,05$). Adenotomiyaga ehtiyoj A guruhida 4,9 barobar kamaydi: 5% (2/40) vs 24,3% (9/37). Shuntlash (timpanostomiya) faqat B guruhida 5 bolaga (13,5%) bajarildi, A guruhida biror bola uchun talab qilinmadi (7-jadval).

7-jadval. 30 kunlik kuzatuv klinik natijalari: OR va 95% ishonch oralig'i bilan

Klinik ko'rsatkich (30 kundan keyin)	A guruh n(%)	B guruh n(%)	OR (95% DI)	p
Timpanogramma A tipiga qaytish	37 (92,5%)*	23 (62,2%)	7,8 (1,9–31,6)	<0,05
OAE «Pass» natijasiga erishish	36 (90,0%)*	21 (56,8%)	6,9 (2,0–23,4)	<0,05

Barqaror burun orqali nafas olish	38 (95,0%)*	28 (75,7%)	6,8 (1,5–31,2)	<0,05
Adenotomiyaga ehtiyoj YO'Q	38 (95,0%)*	28 (75,7%)	6,8 (1,5–31,2)	<0,05
Ekssudatsiya qaytalanishi YO'Q	39 (97,5%)*	30 (81,1%)	10,4 (1,2–89,4)	<0,05
Adenotomiya talab qilindi	2 (5,0%)*	9 (24,3%)	0,16 (0,03–0,82)	<0,05
Shuntlash (tympanostomiya) talab qilindi	0 (0%)*	5 (13,5%)	—	<0,05

Izoh: OR — odds ratio (nisbiy tavakkalchilik); 95% DI — 95% ishonch oralig'i; * — A vs B farqi statistik ahamiyatli ($p < 0,05$); χ^2 — Fisher aniq testi.



3.8. 6 oylik katamnestik kuzatuv natijalari

6 oy o'tgach laboratoriya monitoringi A kichik guruhida erishilgan natijalarning barqarorligini tasdiqladi: transferrin ($3,9 \pm 0,4$ mg/l) va seruloplazmin ($1,5 \pm 0,2$ mg/l) fiziologik me'yor doirasida saqlanib qoldi; sIgA ($0,26 \pm 0,02$ g/l) me'yor chegarasida turdi. B kichik guruhida esa yallig'lanish profiliga qaytish tendensiyasi kuzatildi: transferrin $7,8 \pm 1,1$ mg/l, seruloplazmin $3,4 \pm 0,5$ mg/l. EO'O qaytalanishi A guruhida 1 bolada (2,5%), B guruhida 7 bolada (18,9%) qayd etildi ($p < 0,05$). Adenotomiya 6 oy mobaynida A guruhida 2 bolaga (5%; obstruktiv uyqu apnoesi sababli), B guruhida 9 bolaga (24,3%) bajarildi (8-jadval).

8-jadval. 6 oylik katamnestik kuzatuv natijalari (OBS biomarkerlari va klinik ko'rsatkichlar)

Ko'rsatkich	A kichik guruhi	B kichik guruhi	Nazorat	p (A vs B)
sIgA, g/l	$0,26 \pm 0,02^*$	$0,14 \pm 0,03$	$0,32 \pm 0,04$	$< 0,05$
Transferrin, mg/l	$3,9 \pm 0,4^*$	$7,8 \pm 1,1$	$3,1 \pm 0,4$	$< 0,001$
Seruloplazmin, mg/l	$1,5 \pm 0,2^*$	$3,4 \pm 0,5$	$1,2 \pm 0,2$	$< 0,001$
Neyrofillar faolligi	Barqaror past	Ko'tarilgan/beqaror	Past	$< 0,05$
EO'O qaytalanishi	1/40 (2,5%)*	7/37 (18,9%)	—	$< 0,05$
Adenotomiya (6 oy ichida)	2/40 (5,0%)*	9/37 (24,3%)	—	$< 0,05$

Izoh: * — A vs B farqi statistik ahamiyatli ($p < 0,05$).

3.9. Statistik tahlil yig'indisi

Barcha asosiy statistik testlar natijalari 9-jadvalda keltirilgan. Shapiro–Wilk testi transferrin va seruloplazminning nonnormal taqsimlanganligini ko'rsatdi ($p < 0,05$), shuning uchun ular uchun Mann–Whitney U-testi qo'llanilib, Me [Q1–Q3] shaklida tasvirlandi. sIgA normal taqsimlangan edi ($W = 0,96$; $p > 0,05$), buning uchun parametrik t-test qo'llaniildi.

9-jadval. Asosiy statistik ko'rsatkichlar yig'indisi (test natijalari, OR, 95% DI)

Taqqoslash (biomarker)	Test	Statistik qiymat	95% DI	p
Asosiy vs Nazorat: Transferrin	Mann-Whitney U	U=112; Z=8,4	8,2–10,4	$< 0,001$
Asosiy vs Nazorat: Seruloplazmin	Mann-Whitney U	U=145; Z=7,9	3,0–4,2	$< 0,001$
Asosiy vs Nazorat: sIgA	Student t	t=14,6; df=110	-0,21 – -0,18	$< 0,001$
Transferrin ↔ Qovushqoqlik korrelyatsiyasi	Spirmen r	r=0,74	0,62–0,83	$< 0,01$
A vs B: Timpanogramma A (30-kun)	χ^2 Fisher	$\chi^2=8,4$	OR=7,8 (1,9–31,6)	$< 0,05$
A vs B: Adenotomiya (30-kun)	χ^2 Fisher	$\chi^2=5,9$	OR=0,16 (0,03–0,82)	$< 0,05$
A vs B: EO'O qaytalanishi (6 oy)	χ^2 Fisher	$\chi^2=6,2$	OR=0,11 (0,01–0,97)	$< 0,05$
Shapiro-Wilk normalligi (transferrin)	Shapiro-Wilk	W=0,89	—	$< 0,05$ (nonnorm.)

Izoh: DI — doberitel'nyy interval; OR — odds ratio; χ^2 — Fisher aniq testi; r — Spirmen korrelyatsiya koeffitsiyenti.

MUHOXAMA Ushbu tadqiqotda biz birinchi marta 1–5 yoshli bolalarda EO'O sekretli bosqichini davolashda uch komponentli sxema (PILN + topik immunokorreksiya + autoinsufflyatsiya) ning OBS biomarkerlari asosida ob'ektiv klinik-biokimyoviy samaradorligini ko'rsatdik. Olingan natijalar EO'O patogeneziidagi uchta asosiy buzilishga — kapillyar giperpermeabilitet, mukozal immunitet tanqisligi va oksidativ stress — maqsadli ta'sir ko'rsatishning klinisistlarga muhim ahamiyatli ekanligi g'oyasini tasdiqlaydi [6, 11].

OBSdagi transferrinning me'yordan 4 barobar ortishi (12,4 mg/l) o'rta quloq shilliq qavatidagi kapillyar giperpermeabilitetsiyani ob'ektiv aks ettiradi. Bu topilma Sirigu P. va boshqlar (2017) tomonidan o'rta quloq epiteliyida transferrin ekspressiyasining ko'rsatilishi bilan hamohangdir [12]. Seruloplazmining ortishi (4,8 mg/l) «o'tkir faza javobi» mexanizmi orqali tushuntiriladi: yallig'lanish mediatorlari (IL-1 β , IL-6, TNF- α) jigarda seruloplazmin sintezini faollashtirib, u mahalliy ravishda Fe²⁺ → Fe³⁺ oksidlanishi orqali Fenton reaksiyasini inhiye etadi va erkin radikallar hosil bo'lishiga to'sqinlik qiladi [13]. Seruloplazmining doimiy yuqori darajasi (B guruhida 6 oyda ham 3,4 mg/l) surunkali oksidativ stressning persistensiyasidan va kasallikning xronizatsiyasi xavfidan dalolat beradi.

Transferrin >12 mg/l + sIgA <0,12 g/l kombinatsiyasida «yopishqoq quloq» rivojlanish xavfining 4,5 barobar ortishi (p<0,01) klinisistlarga davolash taktikasini o'z vaqtida faol patogenetik sxemaga o'tkazish uchun ob'ektiv indikator beradi. Bu topilma Buzatto G. va boshqlar (2021) tomonidan nazofaringsdagi mediatorlar profili va otit kechishining og'irligi o'rtasida aniqlangan bog'liqlik bilan hamohangdir [5]. sIgA tanqisligi nazofarinks shilliq qavatining mahalliy himoya to'sig'ini zaiflashtirib, Haemophilus influenzae, Streptococcus pneumoniae va boshqa patogenlarning kolonizatsiyasiga yo'l ochadi, bu esa eksudatning mukoze shakliga o'tishini tezlashtiradi [14].

A kichik guruhida PILN + topik immunokorreksiya + autoinsufflyatsiya kombinatsiyasining statistik jihatdan tasdiqlangan ustunligi (OR=7,8; p<0,05) uch komponentning sinergizmiga asoslanadi. PILN eshituv nayi teshikchalari sohasidagi shishni maqsadli bartaraf etib, mikrotsirkulatsiyani yaxshilaydi va nayli ton oshadi [7]. Topik bakterial lizatlar (IRS-19) shilliq qavatda sIgA ishlab chiqarishni ragbatlantiradi — bizning tadqiqotimizda sIgA 2,3 barobar ko'tarildi (0,28 g/l), bu Bogomilskiy M.R. va boshqlar (2022) tomonidan immunomodulatorlar bilan davolashda sIgA ko'tarilishiga oid ma'lumotlar bilan hamohangdir [4]. Autoinsufflyatsiya esa nog'ora bo'shlig'ining mexanik aerasiyasini ta'minlab, eksudatning drenazhini jadallashtiradi; 92,5% bolada timpanogramma A tipiga qaytishi (B guruhiga nisbatan OR=7,8) bu mexanizmning klinik ahamiyatini isbotlaydi [9].

A guruhida 6 oylik kuzatuvda transferrin va seruloplazmining me'yor doirasida saqlanib qolishi (3,9 va 1,5 mg/l) mukozal homeostazning barqaror tiklanganligidan dalolat beradi. B guruhida esa yallig'lanish profilining tendension ortishi (transferrin 7,8 mg/l) surunkali bo'lishi mumkin bo'lgan oksidativ stress persistensiyasini ko'rsatmoqda. Bu ma'lumotlar standart davolashning kasallikni to'liq bostirmay, faqat vaqtincha remissiyani ta'minlashini ko'rsatadi.

Tadqiqotning asosiy afzalliklari: prospektiv dizayn, ob'ektiv instrumental monitoring (OBS biomarkerlari + timpanometriya + KLCHP), 6 oylik kuzatuv, OR va 95% DI hisobi. Cheklovlar: bir markazli dizayn; masking (ko'r usuli) amalga oshirilmagan. Kelajakda ko'p markazli, ko'r randomizatsiyalangan klinik sinovlar ushbu natijalarni tasdiqlashi lozim.

XULOSA

1. EO'O sekretli bosqichida OBSdagi transferrin (12,4 $\pm$ 1,1 mg/l) va seruloplazmin (4,8 $\pm$ 0,5 mg/l) me'yordan 4 barobar yuqori bo'lib, kapillyar giperpermeabilitet va faol oksidativ stressning ob'ektiv ko'rsatkichlari hisoblanadi (p<0,001; Mann-Whitney U).

2. Transferrin $\leftrightarrow$ eksudatning qovushqoqligi o'rtasida kuchli to'g'ri korrelyatsiya aniqlandi (ρ =0,74; 95% DI 0,62–0,83; p<0,01); transferrin >12 mg/l + sIgA <0,12 g/l kombinatsiyasi «yopishqoq quloq» xavfini 4,5 barobar oshiruvchi prognostik prediktor hisoblanadi.

3. Optimallashtirilgan uch komponentli sxema (PILN + topik immunokorreksiya + autoinsufflyatsiya) A kichik guruhida transferrinni 3,2 barobar kamaytirdi, sIgA ni 2,3 barobar

oshirdi, seruloplazmini me'yorlashtirdi — B standart guruhiga nisbatan statistik ahamiyatli afzallik ($p < 0,001$).

4. 30-kunda timpanogramma A tipiga A guruhida 92,5%, B guruhida 62,2% bolada qaytdi ($OR=7,8$; 95% DI 1,9–31,6; $p < 0,05$); adenotomiyaga ehtiyoj 4,9 barobar kamaydi (5% vs 24,3%); shuntlash A guruhida biror bolaga talab qilinmadi.

5. 6 oylik kuzatuvda A guruhida biomarkerlar fiziologik me'yor doirasida barqaror saqlanib qoldi; qaytalanish 7,5 barobar kamaydi (2,5% vs 18,9%; $p < 0,05$). OBSdagi transferrin va seruloplazminni noinvaziv monitoring mezoni sifatida klinik amaliyotga joriy etish tavsiya etiladi.

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