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THE CLINICAL-STAGE CLASSIFICATION OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONGENITAL SYSTEMIC-PULMONARY SHUNT IN CHILDREN

SUMMARY

Pulmonary arterial hypertension associated with congenital right-to-left shunt (APAH-CHD) has various clinical management issues. There are several classifications for adults and children with APAH-CHD [1-4].

Aim: to develop the clinical-stage classification of APAH-CHD for management of children with congenital left-to-right shunt based on our clinical experience.

Material and methods: retrospective analysis of 109 histories of children with APAH-CHD, in Scientific Centre of Paediatric and Paediatric surgery of Ministry of Health of Republic of Kazakhstan between 2012 and 2016. We analysed clinical status on admission, echocardiography (Echo), right heart catheterization (RHC), Acute vasoreactive test (AVRT), operation reports with early postoperative status.

Results: 104 children demonstrated APAH-CHD symptoms as dyspnoea, low weight, cyanosis, often-respiratory infections. Oxygen saturation (sO2) was <90% in 22 children, 90-94% in 54 patients and normal ranges in 33.

On Echo, mean systolic right ventricular pressure (SRVP) was 56.77 ± 15.51. Right to left ventricle ratio (RV/LV) was 0.54±0.51. Left-to-right shunt (LRS) was registered in 90 kids, right-to-left (RLS) in 8, and bidirectional (BDS) in 11 children. Left ventricle (LV) end diastolic index (EDI) showed LV dilation in 52 cases.

On RHC reports mean pulmonary arterial pressure (mPAP) was 49.19±22.87mmHg. The AVRT was positive in 27 children.

After operation 11 patients had complications with APAH-CHD progression. While 98 children did not present any signs of APAH-CHD after shunt correction. Based on our analysis and the outcome of the option we suggest the following criteria that may help in the clinical management:

1. PseudoPAH: sO2 97-100%, SRVP > 36mmHg., RV/LV 0.4 – 0.5, only LRS. No RHC needed, full operability, no specific medical treatment (SMT) needed;

2. Reversal APAH-CHD: sO2 91-97%, SRVP > 36mm.Hg., RV/LV 0.5 – 0.7, predominantly LRS. AVRT positive, full operability, no SMT needed or monotherapy for 3-6 months after operation;

3. Persistent APAH-CHD: sO2<95%, SRVP > 36mm.Hg., RV/LV>0.7, LRS or BDS. AVRT negative, no repair options, possible palliation, life-long SMT is indicated.

4. Irreversible APAH-CHD: Eisenmenger syndrome, no operability options, mandatory life-long SMT is required.

Conclusion: We believe that simplified clinical criteria described in results can help in guiding the clinical management of the APAH-CHD.

Key words: pulmonary hypertension, classification, management, strategy, children, left-to-right shunt

Pulmonary arterial hypertension associated with congenital right-to-left shunt (APAH-CHD) has various clinical management issues. There are several classifications for adults and children with APAH-CHD [1–4]. However, no one that would guide for management of children with APAH-CHD. Criteria for understanding of the tactic in every individual case. Left-to-right shunts are the most common amongst the congenital heart diseases. The adequate management of children with APAH-CHD on every stage is crucial for the long-term prognosis.

Aim: to develop the clinical-stage classification of APAH-CHD for management of children with congenital left-to-right shunt based on our clinical experience.

Material and methods: We analysed retrospective data of 104 medical records in Scientific Centre of Paediatric and Paediatric surgery of Ministry of Health of Republic of Kazakhstan between 2012 and 2016. All the patients were echocardiographically diagnosed APAH-CHD and confirmed it with direct invasive measurement of mean pulmonary arterial pressure (mPAP) on right heart catheterisation (RHC) of during the open-heart surgery. Inclusion criteria were age between 6 month and 16 years old, confirmed APAH-CHD diagnosis, one-month follow up data and signed parents / guardians informational consent for the procedures. We excluded patients under 6-month-old, with right ventricle outflow tract obstruction, pulmo-

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nary stenosis, left heart diseases, without the follow up data or with improper filling the protocols, without parent / guardian agreement for the procedures and operation.

The material for the study was the clinical status on admission (sO_2, heart rate, blood pressure, cyanosis), echocardiography (right ventricle systolic pressure (RVSP), secondary signs of pulmonary hypertension) and right heart catheterization (mean pulmonary arterial pressure) reports, acute vasoreactive test (AVRT) results, operation reports with early postoperative status, assessed by echocardiography.

During the clinical assessment, we were looking on the oxygen saturation, cyanosis presence, dyspnoea, heart rate, blood pressure, physical activity and tolerance. The physical tolerance in small children (6 months–3 years old) couldn't be evaluated by any tests, although we were collecting data of feeding and BMI [5].

For the Echocardiography investigation, we used Toshiba Artida and Phillips iE33 expert machines. The protocol included full paediatric segmental analysis in B-, M- and Doppler modes. For the calculations of RVSP, we measured tricuspid regurgitation (TR) velocity and summarised it with the right atrium pressure that was assessed by inferior vena cava collapsing. The diagnosis of APAH-CHD was considered if RVSP >36mmHg. [6]

Right heart catheterisation was performed on the Siemens Zee biplane angiograph. Standard protocol with acute vasoreactivity test was used. Inhalation of iloprost was the medication for selective pulmonary vasodilation.

Partly, CHD was repaired with the cardiac surgery, while other patients underwent transcatheter interventions.

Statistical analysis was performed with R studio and Excel 2017. Continuous variables were expressed as mean ± standard deviation. P value less than 0.05 was considered significant.

Results: Amongst 104 children, were 67 (64%) girls and 37 (36%) boys. The age structure is presented in the table 1. The CHD with left-to-right shunt was established in all children with echocardiography, the full structure is presented in Table 2. All patients demonstrated APAH-CHD symptoms as dyspnoea, low weight, cyanosis, often respiratory infections. Oxygen saturation (sO_2) was <90% in 17 children, 90-94% in 54 patients and normal ranges in 33.

Table 1. The gender-age structure of the group.

	girls	boys	%
6 - 12 m.o.	19	9	27%
1-3 yrs.o.	15	10	24%
3-7 yrs.o.	16	9	24%
7-11 yrs.o.	12	5	16%
11-16 yrs.o.	5	4	9%

Table 2. The structure of congenital heart disease in group.

CHD	**girls**	**boys**	**%**
ASD	8	4	12%
CS	16	9	24%
AVSD	7	0	7%
other	4	0	4%
PDA	16	2	17%
VSD	16	22	37%

Abbreviations: ASD – atrial septal defect, CHD – congenital heart disease, CS – combined shunt, AVSD – atrioventricular septal defect, PDA – patent ductus arteriosus, VSD – ventricular septal defect.

Echocardiographically for all group mean right ventricular systolic pressure (RVSP) was 56.77 ± 15.51. Right to left ventricle ratio (RV/LV) was 0.54±0.51. Depending to the level of sO_2, RVSP level and RV/LV ratio with shunt direction (mPAP/mSAP ratio), we divided all children in 4 categories (Table 3).

Table 3. The 4 categories of patients depending on oxygen saturation, right ventricle systolic pressure level and right to left ventricle, mean pulmonary arterial pressure to mean systemic arterial pressure ratios.

	Category 1 (n=4)	Category 2 (n=53)	Category 3 (n=44)	Category 4 (n=3)
sO_2 (%)	97-100	91-97	<95	<91
RVSP (mmHg)	36-50	36-70	42-90	>50
RV/LV	0,4 – 0,5	0,5 – 0,7	0,7-1,5	0,5 – 2,0
Shunt direction	LRS	LRS	LRS / BDS / RLS	RLS

Abbreviations: RVSP – right ventricle systolic pressure, RV – right ventricle, LV – left ventricle, LRS – left-to-right shunt, BDS – bidirectional shunt, RLS – right-to-left shunt.

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Left-to-right shunt (LRS) was registered in 92 kids, right-to-left (RLS) in 4, and bidirectional (BDS) in 8 children. Left ventricle (LV) end diastolic index (EDI) showed LV dilation in 52 cases.

On RHC reports mean pulmonary arterial pressure (mPAP) was 49.19±22.87mmHg. The AVRT was performed in 29 patients with positive response in 9 children.

Cardiac surgery correction was performed in 53 children, 3 patients were not operated due to Eisenmenger syndrome. For other 48 patients transcatheter device closure was considered as a best option. After operation 11 patients had complications with APAH-CHD progression and 5 patients had had a pulmonary hypertension crisis in early postoperative period. While 19 children did not present any signs of APAH-CHD after shunt correction.

Based on our analysis and the outcome of the option we suggest the following criteria that may help in the clinical management:

1. Pseudo APAH-CHD: Patients have congenital left-to-right shunt with the clinical presentation on sO_2 97-100%, echocardiography measurements of RVSP are >36mmHg., RV/LV ratio is usually normal (0,4 – 0,5), shunt direction is only left-to-right. For this category no RHC needed, full operability, no specific drug treatment (SDT) is needed;

2. Reversal APAH-CHD: Patients have congenital left-to-right shunt with the clinical presentation on sO_2 91-97%, echocardiography measurements of RVSP are between 36 and 50 mm.Hg., RV/LV ratio shows RV dilatation (0,5 – 0,7), shunt is predominantly left-to-right. For this category RHC is mandatory with AVRT what has positive response. Patients would have full operability, no SMT needed as preoperative preparation or monotherapy for 3-6 months after operation;

3. Persistent APAH-CHD: Patients have congenital left-to-right shunt with the clinical presentation on sO_2<95%, echocardiography measurements of RVSP are between 36 and 70mm.Hg., RV/LV ratio is >0,7, what is RV dilatation. Shunt's direction might reverse in diastolic phase and be as left-to-right, as bidirectional. RHS is required and AVRT could be as negative as positive (what is rare). For this category of patients, no radical repair options available for the moment of diagnosis, possible palliation as pulmonary artery banding or patch fenestration. Specific drug therapy must be prescribed as life-long.

4. Irreversible APAH-CHD: This is category of patients with Eisenmenger syndrome presentation. For them, no radical operability options available. However, the Rashkind procedure could be considered at some point of the management. Mandatory life-long SDT is required. SDT could be as monotherapy as combination of different pharmacological groups.

Conclusion: On the basis of our data, the difference between the categories of the same group of patients with congenital left-to-right shunt could clearly be seen. We believe, that simplified clinical criteria described in results can help in guiding the clinical management of the APAH-CHD.

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ТҮЙІНДІ

Қанның туа біткен сол-оң шунттауымен қауымдастырылған өкпелік артериялық гипертензияның (АЛАГ-ДПО) көптеген клиникалық көріністері бар. АЛАГ-ДПО бар ересектер мен балалар үшін бірнеше жіктеулері бар.

Мақсаты: қанның туа біткен сол-оң шунттауы бар балаларды қарау үшін клиникалық тәжірибе негізінде АЛАГ-ДПО клиникалық сатыларын жіктеуді әзірлеу.

Материалдар және әдістер: Қазақстан Республикасы Денсаулық сақтау министрлігінің Педиатрия және балалар хирургиясы ғылыми орталығында 2012-2016 жж. кезеңде АЛАГ-ДПО бар балалардың 104 ауру тарихына ретроспективті талдау. Ауруханаға түскен кездегі клиникалық мәртебесі, эхокардиография деректері, жүректің оң жақ бөлімдерін катетерлеу деректері (КПОС), жіті вазореактивті тест нәтижесі, пациенттердің ерте операциядан кейінгі мәртебесімен операциялық хаттама талданды.

Нәтиже: АЛАГ-ДПО осындай клиникалық көріністері ретінде ентігу, төмен салмақ, цианоз, жиі респираторлық аурулар, оттегінің 90% кем сатурациясы 17 балада тіркелді, 54 пациентте және 33 балада норма шегінде 90-94%.

«Эхокардиографияда, орташа деңгейі-систолиялық қысым құқығымен қарыншада (СДПЖ) 56,77±15,51 мм. сын.бағ.ст. Оң жақ қарыншаның сол жақ қарынша диаметріне қатынасы (ПЖ/ЛЖ) 0,54±0,51. Сол-оң шунттау 90 балада тіркелді, оң-сол - 8 және айқас түрі бойынша 11 бала.

Жүректің оң жақ бөлімдерін катетерлеу хаттамасына сәйкес орта өкпенің қан қысымы 49,19±22,87 мм. сын.бағ.ст. болды. 29 балаға жіті вазореактивті тест өткізілді.

Операциядан кейін 11 пациентте АЛАГ-ДПО біртіндеп күшей түсті. Ал 19 пациентте операциядан кейін АЛАГ-ДПО белгілерінің толық жоқтығын көрсетті. Алынған деректер және жедел емдеу нәтижелері негізінде науқастарға клиникалық көмек көрсету үшін мынадай өлшемдер ұсынылады:

1. Жалған АЛАГ-ДПО: sO2 97-100%, СДПЖ> 36 мм. сын.бағ.ст., ПЖ/ЛЖ 0,4 – 0,5, сол-оң шунттау. КПОС талап етілмейді, толық операция жасауға болады, арнайы дәрі-дәрмек терапиясы (СМТ) талап етілмейді;

2. Қайтымды АЛАГ-ДПО: sO2 91-97%, СДПЖ 36-мм. сын.бағ.ст., ПЖ/ЛЖ 0,5 – 0,7, көбінесе сол-оң шунттау. ОВРТ оң, толық операция жасауға болады. Операциядан кейін СМТ тағайындаудың қажеттілігі жоқ, операциядан кейінгі кезеңде 3-6 айға монотерапия тағайындалуы мүмкін;

3. Ұзақ сақталатын АЛАГ-ДПО: sO20,7, сол-оң жақ немесе екі бағытты шунттау. Теріс ОВРТ, радикалды түзету мүмкін емес, паллиативтік хирургия мүмкін. Ғұмырлық СМТ көрсетілген.

4. Жазылмайтын АЛАГ-ДПО: Эйзенменгер синдром, операция жасау сатысы. Ғұмырлық СМТ міндетті түрде тағайындау.

Қорытынды: нәтижелерінде сипатталған жеңілдетілген клиникалық критерийлер АЛАГ-ДПО бар пациенттерді клиникалық жүргізуді айтарлықтай оңтайландыруы мүмкін.

Кілт сөзер: өкпе гипертензиясы, жіктелуі, пациенттерді қарау, стратегия, балалар.

АННОТАЦИЯ

Легочная артериальная гипертензия, ассоциированная с врожденным лево-правым шунтированием крови, имеет множество клинических проявлений, существует несколько классификаций для взрослых и детей.

Цель: разработать классификацию клинических стадий легочной артериальной гипертензией, для ведения детей с врожденным лево-правым шунтированием крови, на основе клинического опыта.

Материалы и методы: ретроспективный анализ 104 историй болезни детей с легочной артериальной гипертензией, ассоциированной с врожденным лево-правым шунтированием крови в Научном центре педиатрии и детской хирургии Министерства здравоохранения Республики Казахстан за период 2012-2016 гг. Проанализирован клинический статус при поступлении, данные эхокардиографии, данные катетеризации правых отделов сердца, результат острого вазореактивного теста, операционные протокола с ранним послеоперационным статусом пациентов.

Результаты: такие клинические проявления легочной артериальной гипертензии, ассоциированной с врожденным лево-правым шунтированием крови, как одышка, низкий вес, цианоз, частые респираторные заболевания, сатурация кислорода менее 90% была зарегистрирована у 17 детей, 90-94% у 54 пациентов и в пределах нормы у 33 детей.

На эхокардиографии, средний уровень систолического давления в правом желудочке 56,77±15,51 мм.рт.ст. Соотношение диаметра правого желудочка к левому желудочку 0,54±0,51. Лево-правый шунт был зарегистрирован у 90 детей, право-левый у 8 и перекрестный у 11 детей.

Согласно протоколам катетеризации правых отделов сердца, среднее легочное артериальное давление было 49,19±22,87 мм.рт.ст. Острый вазореактивный тест был проведен 29 детям.

После операции у 11 пациентов легочная артериальная гипертензия, ассоциированная с врожденным лево-правым шунтированием крови, прогрессировала. В то время, как 19 пациентов после операции демонстрировали полное отсутствие симптомов легочной артериальной гипертензии. На основе полученных данных и исходов оперативного лечения, предлагаются следующие критерии, для помощи в клиническом ведении пациентов:

1. Псевдо АЛАГ-ВПС: sO2 97-100%, СДПЖ> 36 мм.рт.ст., ПЖ/ЛЖ 0,4 – 0,5, лево-правое шунтирование. КПОС не требуется, операбельность полная, специфическая медикаментозная терапия не требуется;

2. Обратимая АЛАГ-ВПС: sO2 91-97%, СДПЖ 36-мм.рт.ст., ПЖ/ЛЖ 0,5 – 0,7, преимущественно лево-правый шунт. ОВРТ положительный, полная операбельность. Отсутствует необходимость в предоперационном назначении специфической медикаментозной терапии, в послеоперационном периоде возможно назначение монотерапии на 3-6 месяцев;

3. Персистирующая АЛАГ-ВПС: sO2<95%, СДПЖ 36-70 мм.рт.ст., RV/LV>0,7, шунт лево-правый или двунаправленный. Отрицательный ОВРТ, радикальная коррекция невозможна, возможна паллиативная хирургия. Показана пожизненная специфическая медикаментозная терапия.

4. Необратимая АЛАГ-ВПС: синдром Эйзенменгера, неоперабельная стадия. Обязательно назначение пожизненной специфической медикаментозной терапии.

Заключение: описанные в результатах упрощенные клинические критерии могут значительно оптимизировать клиническое ведение пациентов с легочной гипертензией.

Ключевые слова: легочная гипертензия, классификация, ведение пациентов, стратегия, дети.

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