Maria Roszkowska-Blaim, Piotr Skrzypczyk

PROCEEDING IN ACUTE KIDNEY INJURY IN ASPHYXIATED NEONATES – DIFFICULTIES AND SUCCESS

POSTĘPOWANIE W OSTRYM USZKODZENIEU NEREK U NIEDOTLENIONYCH NOWORODKÓW – TRUDNOŚCI I SUKCESY

Department of Pediatrics and Nephrology
Medical University of Warsaw, Warsaw, Poland

Abstract

Acute kidney injury (AKI) is a common consequence of perinatal asphyxia reported in 30 to 70% cases.
We present 4 full-term neonates with oliguric/anuric AKI caused by perinatal asphyxia requiring renal replacement therapy (RRT) and their long-term outcomes. Patient No. 1 was dialyzed for 12 days (continuous ambulatory peritoneal dialysis (CAPD)/continuous venovenous hemodiafiltration (CVVHDF)), then was treated conservatively, and received pre-emptive kidney transplantation (KTx) at the age of 3 3/12 years. Patient No. 2 was treated with CAPD/automated peritoneal dialysis (APD) for 15 months, due to recovery of renal function, dialysis was withdrawn. He is now 8 5/12 years old and has chronic kidney disease (CKD) stage III. Patient No. 3 after 5 days of continuous arteriovenous hemofiltration (CAVH) required CAPD for 17 days. The child is now 8 4/12 years old and has CKD stage III. Patient No. 4, dialyzed from 3rd day of life for 51 months (CAVH followed by CAPD/APD), was given cadaver KTx at the age of 4 3/12 years. Psychomotor development is good in 2 patients, whereas patients No. 3 and 4 have tetraplegic spastic infantile cerebral palsy, severe mental retardation, and epilepsy.
Conclusions: *Severe perinatal asphyxia with oliguric/anuric AKI is a risk factor for chronic kidney disease sometimes end-stage renal disease.*

Key words: acute kidney injury, neonates, perinatal asphyxia, peritoneal dialysis

Streszczenie

Ostre uszkodzenie nerek to częste powikłanie niedotlenienia okołoporodowego stwierdzane w 30 do 70% przypadków.
Przedstawiamy 4 donoszone noworodki z oligoanurycznym ostrym uszkodzeniem nerek spowodowanym niedotlenieniem okołoporodowym, wymagających leczenia nerkozastępczego oraz ich odległe losy. Pacjent nr 1 był dializowany przez 12 dni (ciągła ambulatoryjna dializa otrzewnowa – CADO/ciągła żylno-żylna hemodiafiltracja (continuous venovenous hemodiafiltration (CVVHDF)), następnie był leczony zachowawczo i otrzymał wyprzedzający przeszczep nerki w wieku 3 lat 3 miesięcy. Pacjent nr 2 był leczony CADO/ADO (automatyczną dializą otrzewnową) przez 15 miesięcy, leczenie nerkozastępcze zakończono z powodu poprawy funkcji nerek. Obecnie jest w wieku 8 lat 5 miesięcy i ma przewlekłą chorobę nerek (PChN) w stadium III. Pacjent nr 3 po 5 dniach ciągłej tętniczo-żylnej hemofiltracji (continuous arteriovenous hemofiltration – CAVH) wymagał leczenia CADO przez 17 dni. Dziecko jest obecnie w wieku 8 lat 4 miesięcy i ma PChN w stadium III. Pacjent nr 4, dializowany od trzeciej doby życia przez 51 miesięcy (CAVH, następnie CADO/ADO), otrzymał przeszczep nerki ze zwłok w wieku 4 lat 3 miesięcy. Rozwój psychomotoryczny jest dobry u 2 pacjentów, podczas gdy pacjenci nr 3 i 4 mają mózgowe porażenie dziecięce (tetraplegia spastyczna), ciężkie upośledzenie umysłowe i padaczkę
Wnioski: *Ciężkie niedotlenienie okołoporodowe z oligoanurycznym ostrym uszkodzeniem nerek stanowi czynnik ryzyka przewlekłej choroby nerek, a nawet schyłkowej niewydolności nerek.*

Słowa kluczowe: ostre uszkodzenie nerek, noworodki, niedotlenienie okołoporodowe, dializa otrzewnowa

INTRODUCTION

Perinatal asphyxia is a common neonatal problem and contributes significantly to neonatal morbidity and mortality. It ranks as the second most important cause of neonatal death after infections, accounting for around 30% mortality worldwide. The incidence rate of perinatal asphyxia is between 1-10 per 1000 live births [1]. Newborns with asphyxia often develop multiorgan dysfunction affecting every organ system [2]. Acute kidney injury (AKI) is a common consequence of perinatal ischemia, and has been reported in 30 to 70% of asphyxiated neonates [3-8, 9]. This data may be lowered as renal failure in asphyxiated neonates is often nonoliguric [3, 10] and these patients are commonly overlooked in statistics. Despite progress in treatment, AKI in asphyxiated neonates increases mortality rate to 61% [2], particularly in those with low 5-minute Apgar score, oliguria, and fluid overload >20% [1]. In world literature, there is no reliable data on long-term renal outcome in children with perinatal asphyxia and AKI.

We present 4 cases of neonates (3 boys and 1 girl) with severe asphyxia resulting in AKI, who required renal replacement therapy (RRT), and their long-term outcomes.

CASE REPORTS

Clinical data on perinatal period in 4 studied children were shown in table I. No complications were present in the pregnancies except for 2 episodes of urinary tract infection in mother of child No. 4. All neonates were full-term, born in severe asphyxia (Apgar score ≤5 in 5th minute), with birth weight above 3500 g. Patient No. 2 required 20-minute-resuscitation to restore life signs. All children needed further treatment in intensive care unit (ICU).

Clinical and biochemical parameters in ICU were presented in table II. Patients No. 1 and 2 became anuric in 2nd and 3rd day of life, respectively, whereas patients No. 3 and 4 were anuric from birth. Apart from anuria, indications to RRT were: high serum level of urea and creatinine, metabolic acidosis and hyperkalemia in two children, reaching almost 10 mmol/L in patient No. 2. In abdominal US all of them had hyperechoic kidneys with blurred corticomedullary differentiation. In initial transfontanelle US brain structures were normal, except for most deeply asphyxiated patient No. 2, in whom brain edema was found.

Modes and course of RRT used in the studied children were presented in table III. Renal replacement therapy was initiated between second and fifth day of life. Continuous ambulatory peritoneal dialysis (CAPD), using single cuff Tenckhoff catheter, was initial method in two children (patients No. 1 and No. 2). Patient No. 1, due to catheter migration below the liver and ultrafiltration failure, had to be transferred to continuous venovenous hemodiafiltration (CVVHDF), using 6.5 Fr. double-lumen catheter placed in internal jugular vein. This RRT modality was continued till 20th day of life. The patient No. 2 was on CAPD for

Table I. Perinatal period.

Tabela I. Okres okołoporodowy.

Pregnancy ***Ciąża* (No./*nr*)**	**Patient's number/*Numer pacjenta***			
	1	**2**	**3**	**4**
	I	II	I	I
Course of pregnancy ***Przebieg ciąży***	Normal *Prawidłowa*	Normal *Prawidłowa*	Normal *Prawidłowa*	UTI/ZUM 2x (31, 36 Hbd)
Delivery ***Poród***				
Gestational age ***Wiek ciążowy***	39 week/Hbd	39 week/Hbd	40 week/Hbd	40 week/Hbd
Delivery/*Poród*	Cesarean section Placental abruption *Cięcie cesarskie Odklejenie łożyska*	Spontaneous Neck wrapped by umbilical cord *Siłami natury Szyja owinięta pępowiną*	Cesarean section Fetal asphyxia/ *Cięcie cesarskie Niedotlenienie wewnątrzmaciczne*	Cesarean section Fetal asphyxia *Cięcie cesarskie Niedotlenienie wewnątrzmaciczne*
Gender ***Płeć***	Boy *Chłopiec*	Boy *Chłopiec*	Girl *Dziewczynka*	Boy *Chłopiec*
Apgar score ***Punktacja Apgar 1' – 5'***	1 – **4**	1 – **5**	0 – **0** 20-min-resuscitation *resuscytacja przez 20 min.*	2 – **5**
Birth weight ***Masa urodzeniowa***	3680 g	4850 g	3540 g	4660 g
Birth length ***Długość urodzeniowa***	52 cm	61 cm	51 cm	54 cm

No./*Nr* – number/*numer*, UTI/*ZUM* – urinary tract infection/*zakażenie układu moczowego*

Table II. Clinical data in 4 neonates with acute kidney injury in Intensive Care Unit.

Tabela II. Dane kliniczne 4 noworodków z ostrym uszkodzeniem nerek w oddziale intensywnej terapii.

		Patient's number/*Numer pacjenta*			
		1	**2**	**3**	**4**
Admission *Przyjęcie*	**[day of life]** **[*doba życia*]**	2	3	1	1
Discharge *Wypis*		10	26	37	11
DIAGNOSIS – AKI ***DIAGNOZA – OSTRE USZKODZENIE NEREK*** **(2-3 day/*doba*)**					
Kidney function ***Funkcja nerek:*** **Diuresis/*Diureza* [mL/kg/h]/[ml/kg/godz.]**		0.22	0.25	0	0.25
Creatinine ***Kreatynina* [mg/dL]**		3.45	3.84	2.36	2.42
Urea ***Mocznik* [mg/dL]**		145	69.4	123	59
Na+ [mmol/L]		134	129	130	132
K+ [mmol/L]		5.4	9.7	4.8	6.0
HCO_3^- [mmol/L]		18.5	14.2	12.6	16.8
US/*USG*	**Kidney right/left** ***Nerka prawa/lewa*** **[mm]**	**Hyperechoic kidneys without corticomedullary differentiation** ***Nerki hiperechogenne z zatartym zróżnicowaniem korowo-rdzeniowym***			
		45/45	54/55	48/50	35/54
	Brain ***Mózg***	Normal *Prawidłowy*	Normal *Prawidłowy*	Brain edema *Obrzęk mózgu*	Normal *Prawidłowy*

AKI – acute kidney injury, US/USG – ultrasonography/*badanie ultrasonograficzne*

two months. After a month single cuff Tenckhoff catheter was exchanged for 2-cuff Spi-Argent catheter. Dialysis was complicated with bilateral inguinal hernia. As renal function did not improve, the child was transferred to automated peritoneal dialysis (APD) and remained with end-stage renal disease (ESRD) after 3 months. Continuous arteriovenous hemofiltration (CAVH), using two 5 Fr. catheters, was initial method of RRT in two children (patients No. 3 and No. 4). In patient No. 4 the procedure was complicated by intracranial hemorrhage. Because of ongoing uremia, both patients were transferred to CAPD in 6th and 9th day of life, respectively. In patient No. 3 dialysis was withdrawn in 23rd day of life. Patient No. 4, who was anuric from first day of life, underwent in 3rd month surgical removal of Tenckhoff catheter and implantation of swan-neck presternal catheter (SNPC) with concomitant bilateral inguinal hernia repair. This child remained with ESRD after 3 months.

In abdominal US performed in 3rd month of life all patients still had hyperechoic kidneys with blurred corticomedullary differentiation; in transfontanelle US periventricular leukomalacia was found in 2 children (patients No. 2 and No. 4). Echocardiography revealed patent foramen ovale (PFO) in patients No. 1 and 4, persistent ductus arteriosus (PDA) in patient No. 2, and atrial septal defect t. II (ASD II) in patient No 3.

Long-term outcome was shown in table IV. Patient No. 1, who experienced partial improvement of renal function in neonatal period, became end-stage in the age of 3 3/12 years and was given a pre-emptive kidney transplant from his father. Patient No. 2 was on peritoneal dialysis for 15 months; afterwards dialysis was withdrawn due to improvement of renal function. This child is now 8 5/12 year old and is on conservative treatment with GFR slightly above 30 mL/min/1.73 m^2. Patient No. 3 is at present in CKD stage III treated conservatively. In patient No. 4 no improvement in renal function was found, he was on a long-term PD (CAPD – 3.5 years, APD – 10 months), and finally received cadaver kidney transplantation. In 2 children requiring chronic peritoneal dialysis (patients No. 2 and 4) no complications, except for bilateral inguinal hernias were observed. In child No. 2 hernias were repaired in the age of 15 months during removal of Tenckhoff catheter.

All children required in first year erythropoiesis-stimulating agents (ESA). Additionally, patient No. 1 was treated with ESA from birth for 51 months to kidney transplantation. Among 4 patients with AKI in neonatal period only 1 child is normotensive (patient No. 2). Two children (patients No. 1 and 3) developed arterial hypertension in neonatal period, patient No. 4 in second year of life. All 3 patients require one antihypertensive

Table III. Renal replacement therapy in neonates with acute kidney injury.

Tabela III. Leczenie nerkozastępcze u noworodków z ostrym uszkodzeniem nerek.

	Patient's number/*Numer pacjenta*			
	1.	2.	3.	4.
First method of RRT/*Pierwsza metoda leczenia nerkozastępczego*				
Modality/*Metoda*	**CAPD/*CADO***	**CAPD/*CADO***	**CAVH/*CAVH***	**CAVH/*CAVH***
Dialysis access Catheter *Dostęp dializacyjny cewnik*	1-cuff Tenckhoff *1-mufkowy cewnik Tenckhoffa*		5 Fr femoral art. axillary vein tętnica *udowa żyła udowa*	5 Fr femoral art. femoral vein tętnica *udowa żyła udowa*
Dialysis treatment *Leczenie dializami* [days of life] [*doba życia*]	5-12	4-65	2-6	3-8
Dialysis protocol *Schemat dializy*	Dianeal, Baxter, 5-10 → 20 mL/kg exchange *5-10 → 20 ml/kg wymianę*		Ultrafiltration *Ultrafiltracja* [mL/24h]	
			670-1380	540-850
Complications *Powikłania*	Ineffective dialysis (catheter transposition under the liver, ultrafiltration failure) *Nieskuteczna dializa (przemieszczenie cewnika pod wątrobę, niewydolność ultrafiltracyjna)*	Catheter exchange - Spi Argent (1mth), bilateral inguinal hernia *Wymiana cewnika - Spi Argent (1 miesiąc), obustronne przepukliny pachwinowe*	None *Brak*	Intracranial hemorrhage *Krwawienie śródczaszkowe*
Second method of RRT/*Druga metoda leczenia nerkozastępczego*				
Modality/*Metoda*	**CVVHDF/*CVVHDF***	**APD/*ADO***	**CAPD/*CADO***	**CAPD/*CADO***
Dialysis treatment *Leczenie dializami* [days of life] [*doba życia*]	12-20	65-3 months *miesiące*	6-23	9-3 months *miesiące*
Dialysis access Catheter *Dostęp dializacyjny cewnik*	6.5 Fr double-lumen *Cewnik dwuświatłowy*	2-cuff Spi Argent *2-mufkowy cewnik Spi Argent*	1-cuff Tenckhoff/ *1-mufkowy cewnik Tenckhoffa*	1-cuff Tenckhoff → swan-neck presternal (3 mths) *1-mufkowy cewnik Tenckhoffa → cewnik przedmostkowy (3 miesiące)*
Complications *Powikłania*	None/*Brak*	None/*Brak*	None/*Brak*	Bilateral inguinal hernia *Obustronne przepukliny pachwinowe*
Anuria *Bezmocz* [days of life] [*doby życia*]	2-13	3-10	1-11	1-8
Arterial hypertension *Nadciśnienie tętnicze*	13th day of life *doba życia*	No/*Nie*	17th day of life *doba życia*	No/*Nie*

Table III. cd.

Tabela III. cont.

AKI – OUTCOME AFTER 3 months/*OSTRE USZKODZENIE NEREK – ZEJŚCIE PO 3 miesiącach*					
Diuresis/*Diureza* [mL/kg/24 h]		**CKD/PChN**	**ESRD/SNN**	**CKD/PChN**	**ESRD/SNN**
Creatinine/*Kreatynina* [mg/dL]		61.8 2.9	58.7 2.5	75.3 2.46	76.5 2.76
Urea/*Mocznik* [mg/dL]		80.6	31.3	81.2	79.4
GFR[mL/min 1.73m^2]		8.83	7.83	10.07	1.72
US *USG*	**Kidney right/left *Nerka prawa/lewa* [mm]**	**Hyperechoic kidneys without corticomedullary differentiation /*Nerki hiperechogenne z zatartym zróżnicowaniem korowo-rdzeniowym***			
		45/50	50/50	42/40	35/53
	Brain *Mózg*	Normal *Prawidłowy*		Periventricular leukomalacia *Leukomalacja okołokomorow*a	
	Heart *Serce*	PFO	PDA	ASD II	PFO

RRT – renal replacement therapy, CAPD/*CADO* – continuous ambulatory peritoneal dialysis/*ciągła ambulatoryjna dializa otrzewnowa*, CAVH – continuous arteriovenous hemofiltration/*ciągła tętniczo-żylna hemofiltracja*, CVVHDF – continuous venovenous hemodiafiltration/*ciągła żylno-żylna hemodiafiltracja*, APD/ADO – automated peritoneal dialysis/*automatyczna dializa otrzewnowa*, AKI – acute kidney injury, CKD/PChN – chronic kidney disease/*przewlekła choroba nerek*, ESRD/SNN – end-stage renal disease/*schyłkowa niewydolność nere*k, GFR – glomerular filtration rate/*stopień przesączania kłębuszkowego*, US/USG – ultrasonography/*badanie ultrasonograficzne*, PFO – patent foramen ovale/*drożny otwór owaln*y, PDA – persistent ductus arteriosus/*drożny przewód tętniczy*, ASD II – atrial septal defect type II/*otwór w przegrodzie międzyprzedsionkowej t. II.*

medication: amlodipine (2 children) and enalapril (1 child). Regardless from renal function, at the end of observation in US all patients had hyperechoic kidneys without corticomedullary differentiation. Two patients had vesicoureteral refluxes: unilateral (patient No. 2) and bilateral (patient No. 3). All children, except for patient No. 2, are growth-retarded.

Patent foramen ovale closed spontaneously in patients No. 1 and 4 in infancy; patient No. 2 underwent successful transcatheter coil occlusion of PDA at the age of 4 years; patient No. 3 has hemodinamically insignificant ASD II. Psychomotor development is good in two patients, whereas 2 children (patients No. 3 and 4), with a history of fetal asphyxia and periventricular leukomalacia, have tetraplegic spastic infantile cerebral palsy with severe mental retardation and epilepsy.

DISCUSSION

The pathogenesis of acute kidney injury in perinatal asphyxia is complex and only partially understood. In case of hypoxemia blood flow is redistributed into brain, heart and adrenal glands, facilitating perfusion of other organs like gastrointestinal tract, skin, and kidneys [11]. Apart from this central hemodynamic mechanism, adenosine, which is generated in hypoxemic tissue, causes afferent arteriolar vasoconstriction and efferent arteriolar dilatation, leading to further decrease in glomerular filtration [12-14]. In case of prolonged ischemia, initially prerenal AKI progresses into structural and functional tubular damage (acute tubular necrosis – ATN), and finally cortical necrosis.

In this study we have presented 4 newborns, in whom perinatal asphyxia led to oliguric acute kidney injury. All the children required renal replacement therapy, and two of them were dialyzed over perinatal period. Chronic kidney disease in different stages was an outcome for all of them.

There are only few studies documenting dialysis therapy in AKI in asphyxiated neonates. Yu et al. reported their experience with acute peritoneal dialysis in 16 very low birth weight neonates using a 14-gauge Arrow vascular catheter for PD access. In this group there was one premature (30 Hbd, birth weight 1200 g) neonate dialyzed for 6 days with recovery of renal function [15].

Severity of asphyxia correlates with both neurologic and renal outcomes [4, 10]. Results of studies by Perlman and Nouri suggest that renal failure is associated with significant long-term neurologic defects in asphyxiated neonates [16, 17]. Two of 4 our patients have spastic tetraplegic infantile cerebral palsy, severe mental retardation, and epilepsy. They both had fetal asphyxia;

Table IV. Long-term outcome and kidney function.
Tabela IV. Odległe losy i funkcja nerek.

	Patient's number/*Numer pacjenta*			
	1	2.	3.	4.
OUTCOME/*WYNIK*				
Age/*Wiek* [years/*lata*]	3 3/12	8 5/12	8 4/12	4 3/12
Height *Wysokość ciała* [cm][percentile/ *centyl*]	82 (<3 c.)	130 (25-50 c.)	102 (<3c.)	90 (<3c.)
Weight *Masa ciała* [kg] [percentile/*centyl*]	9.2 (<3 c.)	27 (25-50 c.)	13 (<3c.)	10.3 (<3c.)
CKD stage *PChN stadium* **Creatinine *Kreatynina* [mg/dL]** **Urea *Mocznik*[mg/dL]** **GFR [mL/min/1.73m²]**	Preemptive KTx *Przeszczep wyprzedzający* 2.90 176 15.94	CKD stage III *PChN stadium III* 1.6 74 30.97	CKD stage III *PChN stadium III* 1.23 58 34.2	Cadaver KTx *Przeszczep nerki ze zwłok* 3.0 104.6 4.76
Psychomotor development *Rozwój psychomotoryczny*	Normal/*Prawidłowy*		Severe mental retardation, spastic tetraplegic infantile cerebral palsy *Głębokie upośledzenie umysłowe, mózgowe porażenie dziecięce (tetraplegia spastyczna)*	
Concomitant diseases *Choroby współistniejące*		Hypothyroidism *Niedoczynność tarczycy* VUR I° left kidney *OPM I° do lewej nerki*	gastro-esophageal reflux *refluks żołądkowo-przełykowy* epilepsy/*padaczka* ASD II	VUR III° right kidney II° left kidney/*OPM III° do prawej nerki II° do lewej nerki* epilepsy/*padaczka*
Arterial hypertension *Nadciśnienie tętnicze*	Yes *Tak* Amlodipine *Amlodypina*	No/*Nie*	Yes/*Tak* Enalapril	Yes/*Tak* (21st month/*od 21 miesiąca*) Amlodipine *Amlodypina*
US/*USG*	Hyperechoic kidneys without corticomedullary differentiation *Nerki hiperechogenne z zatartym zróżnicowaniem korowo-rdzenio*wym			
	45/45	62/53	65/65	40/50

KTx – kidney transplantation, CKD/*PChN – przewlekła choroba nerek*/chronic kidney disease, GFR – glomerular filtration rate/*stopień przesączania kłębuszkowego*, VUR/*OPM* – vesicoureteral reflux/*odpływ pęcherzowo-moczowodowy*, ASD II – atrial septal defect type II/*otwór w przegrodzie międzyprzedsionkowej t. II*, US/USG – ultrasonography/*badanie ultrasonograficzne*

one of them was born with 0 pts in Apgar score and was resuscitated for 20 minutes. Both these children had on US periventricular leucomalacia in first 3 months of life. Noteworthy, mental development was very good in remaining two children.

In world literature, there is also little information on renal outcome after AKI in neonates. Limited evidence suggests permanent renal disfunction in at least 40% of patients with acute renal failure in this period of life [6, 8, 18]. A persistent tubular dysfunction at 1 year, measured by urinary excretion of beta-2-microglobulin, has been described in infants with a history of AKI associated with perinatal asphyxia, despite normalization in GFR [19]. All our patients had oliguric form of AKI with at least 7-day anuria and all required RRT in neonatal period. Moreover, two out of 4 our patients required long-term dialysis. Interestingly, they were not more asphyxiated and did not have longer anuria period than two patients who experienced rapid partial recovery of renal function. We can hypothetize that asphyxiated newborns who experience prolonged anuria are at risk of chronic kidney disease and end-stage renal failure,

despite initial partial recovery of renal function. Further long-term observational studies are needed to assess renal function in this group of patients.

In our group both CAVH and CAPD were used as initial RRT modality. It would be beneficial to establish which method is best suited and favors best renal outcome in asphyxiated neonates.

Diagnosing AKI in neonates may be quite a challenge not only due to high percentage of non-oliguric forms but also due to difficulties and limitations in using blood serum creatinine level as marker of renal function in this group of patients. Akcan-Arikan et al. proposed in 2007 a pediatric version of RIFLE criteria, based on estimated clearance of creatinine and urine output, but this classification can be used in children older than 2 years [20]. Koralkar et al. proposed neonatal RIFLE criteria using only serum creatinine level [21]. Owing to limitations in measuring serum creatinine level in neonates, there is an obvious need for usage of sensible, early biomarkers of AKI in first days of life. Several molecules have been found to rise in early phases of AKI in adults and in older children, and were suggested to be useful in neonatal period, too. The most intensively investigated biomarkers are: neutrophil gelatinize-associated lipocalcin (NGAL), cystatin C (CysC), kidney injury molecule-1 (KIM-1), and interleukin 18 (IL-18) [22]. Sarafidis et al. found that serum NGAL, urinary CysC and urinary NGAL were elevated in a small group of 13 asphyxiated neonates compared to healthy peers, and measurement of these markers on the 1st day of life could be predictive of post-asphyxia-AKI [23]. Further studies on larger groups of patients are necessary to assess biomarkers' usefulness in AKI in these children.

Further efforts should be focused on investigating early markers of AKI in asphyxiated neonates, establishing indications to dialysis treatment in this group of children, with the aim being decrease in risk for late cerebral and renal consequences.

CONCLUSIONS

Severe perinatal asphyxia with oliguric/anuric AKI is a risk factor for chronic kidney disease sometimes end-stage renal disease.

REFERENCES

1. Durkan AM, Alexander RT. Acute kidney injury post neonatal asphyxia. Journal of Pediatrics. 2011;158:(suppl. 2);29-33.
2. Jayashree G, Dutta AK, Sarna MS, Saili A. Acute renal failure in asphyxiated newborns. Indian Pediatrics. 1991;28:19-23.
3. Agras PI, Tarcan A, Baskin E, Cengiz N, Gürakan B, Saatci U. Acute renal failure in the neonatal period. Renal Failure. 2004;26;305-309.
4. Aggarwal A, Kumar P, Chowdhary G, Majumdar S, Narang A. Evaluation of renal functions in asphyxiated newborns. Journal of Tropical Pediatrics. 2005;51:295-299.
5. Gupta BD, Sharma P, Bagla J, Parakh M, Soni JP. Renal failure in asphyxiated neonates. Indian Pediatrics. 2005;42:928-934.
6. Chevalier RL, Campbell F, Brenbridge AN. Prognostic factors in neonatal acute renal failure. Pediatrics. 1984;74:265-272.
7. Norman ME, Asadi FK. A prospective study of acute renal failure in the newborn infant. Pediatrics. 1979;63;475-479.
8. Askenazi DJ, Ambalavanan N, Goldstein SL. Acute kidney injury in critically ill newborns: what do we know? What do we need to learn? Pediatric Nephrology. 2009;24:265-274.
9. Shah P, Riphagen S, Beyene J, Perlman M. Multiorgan dysfunction in infants with post-asphyxial hypoxic-ischaemic encephalopathy. Archives of Diseases in Childhood. Fetal and Neonatal Edition. 2004;89:152-155.
10. Karlowicz MG, Adelman RD. Nonoliguric and oliguric acute renal failure in asphyxiated term neonates. Pediatric Nephrology. 1995;9:718-722.
11. M. Roszkowska-Blaim M. Ostra niewydolnosc nerek u noworodkow w: M. Borszewska-Kornacka, M. Roszkowska-Blaim (red.) Nefrologia noworodka, Medpress, Warsaw, 2012;12-138.
12. Gouyon B, Guignard JP. Theophylline prevents hypoxemia-induced renal hemodynamic changes in rabbits. Kidney International. 1988;33:1078-1083.
13. Osswald H, Schmitz HJ, Kemper R. Tissue content of adenosine, inosine and hypoxanthine in the rat kidney after ischemia and postischemic recirculation. Pflügers Archiv: European Journal of Physiology. 1977;371:45-49.
14. Churchill PC, Bidani AK. Hypothesis: adenosine mediates hemodynamic changes in renal failure. Medical Hypotheses. 1982;8:275-285.
15. Yu JE, Park MS, Pai KS. Acute peritoneal dialysis in very low birth weight neonates using a vascular catheter. Pediatric Nephrology. 2010;25:367-371.
16. Perlman JM, Tack ED. Renal injury in the asphyxiated newborn infant: relationship to neurologic outcome. The Journal of Pediatrics. 1988;113:875-879.
17. Nouri S, Mahddaoui N, Beizig S, Zakhama R, Salem N, Ben Dhafer S, Methlouthi J, Seboui H. Acute renal failure in full term neonates with perinatal asphyxia. Prospective study of 87 cases. Archives de Pediatrie. 2008;15:229-235.
18. Mammen C, Al Abbas A, Skippen P, Nadel H, Levine D, Collet JP, Matsell DG. Long-term risk of CKD in children surviving episodes of acute kidney injury in the intensive care unit: a prospective cohort study. American Journal of Kidney Diseases. 2012;59:523-530.
19. Di Pietro A, Proverbio MR, Pescatore L, Chianese F, Coletta S, Race G, Ponticelli R, Atronne L, and Coletta A. Evaluation of kidney damage in neonatal anoxia syndrome: a 1-year follow-up. La Pediatr medica et chirurgica. 1989;11:637-638.
20. Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein LS. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney International. 2010;71;1028-1035.
21. Koralkar R, Ambalavanan N, Levitan EB, McGwin G, Goldstein SL, Askenazi D. Acute kidney injury reduces survival in very low birth weight infants. Pediatric Research. 2011;69:354-358.

22. Argyri I, Xanthos T, Varsami M, Aroni F, Papalois A, Dontas I, Fanos V, Iacovidou N. The role of novel biomarkers in early diagnosis and prognosis of acute kidney injury in newborns. American Journal of Perinatology. 2013;30:347-352.
23. Sarafidis K, Tsepkentzi E, Agakidou E, Diamanti E, Taparkou A, Soubasi V, Papachristou F, Drossou V. Serum and urine acute kidney injury biomarkers in asphyxiated neonates. Pediatric Nephrology. 2012;27:1575-1582.

Author's contributions/Wkład Autorów
According to the order of the Authorship/Według kolejności

Conflicts of interest/Konflikt interesu
The Authors declare no conflict of interest.
Autorzy pracy nie zgłaszają konfliktu interesów.

Received/Nadesłano: 04.08.2015 r.
Accepted/Zaakceptowano: 25.08.2015 r.

Published online/Dostępne online

Address for correspondence:
Piotr Skrzypczyk
Department of Pediatrics and Nephrology
Medical University of Warsaw, Warsaw
24 Marszałkowska Street, 00-576 Warsaw
tel. 502-507-822
fax (22) 621-98-63
e-mail: pskrzyp@gmail.com