Paediatrica Indonesiana
Paediatr Indones 2001; 41:175-179

Original article

The effect of neonatal asphyxia on renal function

Ellya Nova Lubis, Srie Yanda, Khainir Akbar, Guslihan Dasa Tjipta, Dachrul Aldy

Department of Child Health, Medical School University of North Sumatera / H. Adam Malik Hospital, Medan

ABSTRACT Neonatal asphyxia can cause renal perfusion and dilution disorders and also glomerular filtration abnormality. The purpose of this study was to find renal dysfunction, which caused by neonatal asphyxia. The study was performed by cross sectional for newborn babies with asphyxia based on Apgar score in the first minute. Newborn babies without asphyxia were as control. In both group, the first micturition times were recorded, total urine output in 24 hours were counted, the mean of blood urea and creatinine serum level value examined and also glomerular filtration rate. Statistical analysis has been performed by using Fisher Exact test, Student t test and Wilcoxon Rank Sum test. All of babies in the asphyxiated and non asphyxiated group had the first micturition in 24 hours after delivery. Significant difference of oliguria incidence was found in the asphyxiated group compared to the control group ($p<0,05$). The mean of blood urea and creatinine serum level was significantly higher in asphyxiated ($p<0,05$). The mean of glomerular filtration rate in the asphyxiated group was not significantly different to the control group ($p>0,05$). According to the degree of asphyxia we found significantly different of renal dysfunction ($p<0,05$). It was concluded that the asphyxia could cause the occurrence of renal dysfunction. **[Paediatr Indones 2001; 41:175-179]**

Keywords*: neonatal asphyxia, renal function, Apgar scores.*

IN NEONATES, HYPOXIA AND ISCHEMIA MAY OCCUR AS result of various abnormalities or perinatal diseases. The most common abnormality which result in hypoxia and ischemia is neonatal asphyxia.[1] Neonatal asphyxia will occur if a baby has gas exchange and oxygen transportation disorders at birth then result lack of oxygen supply and difficulties in carbondioxide expiration. In this condition, the baby usually can not respire spontaneously and regularly soon after birth.[2,3,4] In the initial stage, hypoxia and ischemia process rise reaction of systemic circulatory adaptation.

Correespondence: Ellya Nova Lubis, M.D., Department of Child Health, Medical School University of North Sumatera / H. Adam Malik Hospital, Medan Jalan Bunga Lau No. 17 Medan, Indonesia. Phone: (061) 8361721

Cardiac output attempt to maintain blood flow to vital organ as heart, central nervous system, and also reduce blood flow to another organ like kidney, gastrointestinal and the other peripheral organ.[1] When the asphyxia occur in along period, reduce oxygen saturation will emerge and decrease blood perfusion in tissue which cause ischemia of the sensitive organ. The condition will effect cell body function particularly in the vital organs such as brain, kidney, heart and lung.[4] Brain and kidney are the most common involved.[6,7] The various studies demonstrated hypoxia and ischemia process that caused by neonatal asphyxia has not only resulted poor to one certain organ but also might caused functional disorder in some organs simultaneously.[7,8,9] The organ function disorder might be transient, but not uncommon to rise permanent abnormality and interfered further the growth and development of the infant.[1]

In the urogenital system, neonatal asphyxia may result renal function disorder as renal perfusion and dilution abnormality or glomerulus filtration disorder.[10] Acute renal failure can occur and give a poor prognosis and may result in permanent renal damage.[11,12] The purpose of this study is to find the effect of neonatal asphyxia in renal function by assessing first urination time after birth, daily urine output, blood creatinine and urea level, and glomerulus filtration rate.

Methods

This cross sectional study was performed in Perinatology Sub Division Department of Child Health, Medical School, University of North Sumatera, H. Adam Malik Hospital in Medan from October 1998 to January 1999.

In this study period, there were 249 deliveries which 72 newborn babies had asphyxia. Fifty-nine of 72 asphyxiated newborn babies were eligible for the criteria of the study and considered as asphyxiated group. Out of 177 babies without asphyxia, there were 60 newborn babies eligible for the criteria of the study and formed the non-asphyxiated group. The criteria for inclusion was newborn babies with appropriate for gestational age. The exclusion criteria consisted of: (1) newborn babies with congenital heart disease which determined by virtue of clinical features, (2) newborn babies who had not micturition within 48 hours, proved by USG examination to find urogenital abnormalities, (3) uncompleted examination.

The evaluated Apgar score in first minute to determine degree of asphyxia was done by the author or residents in Pediatrics, Department of Child Health, Medical School, University of North Sumatera. The degrees of asphyxia might be divided on: (1) Normal (without asphyxia), Apgar score of 7 to 10; (2) Mild-moderate asphyxia, Apgar score of 4 to 6; (3) severe asphyxia, Apgar score of 0 to 3.

In asphyxiated and non asphyxiated group we did measurement of: (1) body weight and body length, (2) physical examination, (3) recording of first urination time after birth, (4) urine output was collected during 24 hours after birth. For male babies, the collecting urine used plastic bag, whereas for female babies, it used pediatric urine specimen collector (Urograd) made in Terumo Corporation Tokyo. The urine output was measured by measuring glass. (5) Examinations of creatinine serum and blood urea level were done on the second day of life. The creatinine serum level assay used Jaffe reaction by Vitalab Selecta two devices, and blood urea level assay used Barthelot reaction by Vitalab Selecta two devices. Normal creatinine serum level is 0,2 to 1 mg/dl[13], and normal blood urea level is 10 to 30 mg/dl.[13] (6) Assessment of renal function used formula :[14,15] $GFR = \frac{0,45 \times BL}{S_{Cr}}$

GFR: glomerular filtration rate (ml/minute/1,73m^2), Normal GFR in newborn : 20 to 25 ml/minute/1,73m^2 (20% of GFR in adults)[14], B L : body length (cm), S_{Cr} : level of creatinine serum (mg/dl), 0,45 : empiric constanta for appropriate for gestational age babies.

The operational definition were: (1) Oliguria was defined as urinary excretion less than 1 ml/kg body weight/hours.[2] (2) There was renal dysfunction if GFR less than 20 ml/minute/1,73 m^2. (3) Gestational age was determined first day in the last menstrual sickle.

Data were tabulated and analyzed by using computer. Correlation between two qualitative data was tested by Chi-Square test, if found expected value less than 5 used Fisher Exact test. To evaluate the correlation between two quantitative data was tested by t-test, if found extreme value and abnormal distribution, used Wilcoxon Rank Sum test. The level of significance was $p<0,05$.

Results

The study was conducted from October 1998 to January 1999, there were 119 newborn babies included, which 59 babies had asphyxia (6 among them were severe asphyxia), while 60 other babies were not asphyxia.

All of babies in asphyxiated and non-asphyxiated group had micturition in 24 hours of life. Thirty-eight babies (64%) of the asphyxiated group and 44 babies (73%) of non-asphyxiated group had micturition 8 hours after birth (Table 1).

In the asphyxiated group, there were six babies (10%) had oliguria whereas in the non-asphyxiated group was none. We found statistically significant difference with $p<0,05$ (Table 2). The mean creatinine serum level in asphyxiated group was 0,8300 $\pm$0,2922 mg/dl, significantly different with non

TABLE 1. THE TIME OF FIRST MICTURITION IN BOTH ASPHYXIATED AND NON-ASPHYXIATED GROUP

Group	0 - 8 hrs	>8-24 hrs	Total
Asphyxiated	38	21	59
Non-asphyxiated	44	16	60
Total	82	37	119

TABLE 2. RELATIONSHIP BETWEEN ASPHYXIA WITH OLIGURIA

Group	Oliguria	Non oliguria	Total
Asphyxiated	6	53	59
Non-asphyxiated	0	60	60
Total	6	113	119

Prob. Fisher Exact test : 0,027

TABLE 3. COMPARISON OF MEAN CREATININE SERUM LEVEL BETWEEN ASPHYXIATED AND NON-ASPHYXIATED GROUP

Group	N	Creatinine Serum Level x ± SD(mg/dl)
Asphyxiated	59	0,8300 ± 0,2922
Non-asphyxiated	60	0,6278 ± 0,1619

df : 90 t : 4,657 $p < 0,05$

TABLE 4. COMPARISON OF MEAN BLOOD UREA LEVEL ASPHYXIATED AND NON-ASPHYXIATED GROUP

Group	N	Blood Urea Level Mean Ranking(mg/dl)
Asphyxiated	59	77,6
Non-asphyxiated	60	42,62

W test : 2558,00 $p < 0,05$

TABEL 5. COMPARISON OF MEAN GFR VALUE BETWEEN ASPHYXIATED AND NON-ASPHYXIATED GROUP

Group	N	GFR Value x ± SD(ml/minute/1,73 m^2)
Asphyxiated	59	29,7686 ± 10,8190
Non-asphyxiated	60	32,3202 ± 6,5803

df : 95 t : 1,551 $p > 0,05$

TABEL 6. RELATION BETWEEN ASPHYXIA DEGREE WITH RENAL DYSFUNCTION

Group Asphyxia	Renal Function Abnormal	Normal	Total
Mild-moderate	0	53	53
Severe	5	1	6
Total	5	54	59

Prob. Fisher Exact test < 0,0001

asphyxiated 0,6278 ± 0,1619 mg/dl with $p<0,05$ (Table 3). There were significant difference in blood ureum level between asphyxiated group with non asphyxiated group $p<0,05$ (Table 4). The mean glomerular filtration rate value were not significantly different between asphyxiated group and non asphyxiated group $p>0,05$ (Table 5).

In the mild-moderate asphyxiated group there were no renal dysfunction, while in severe asphyxiated group there were five babies with renal dysfunction. There was significant difference between both groups with $p>0,05$ (Table 6).

Discussion

In this study, all of babies in non-asphyxiated had micturition in first 24 hours of life (Table 1). This study is similar with Clark[16] and Mawardi[17] study which newborn babies with appropriate for gestational age, 100% had micturition during 24 hours after birth. While Sherry and Kramer reported that among 500 newborn babies, appropriate for gestational age, 92,4% had micturition during 24 hours after birth and the remains in the second day.[18]

In the asphyxiated newborn babies, a transient paralysis of the blast may occur. This condition resulted in urine excretion which usually emerge in the first 24 hours after birth, will be delayed.[1] In this study, asphyxiated group did not delay in micturition which 59 babies (100%) had micturition in 24 hours after birth (Table 1). Mawardi reported that among 44 babies who had asphyxia, only one babies (2,8%) had micturition in the second day of life and 43 babies (97,2%) had micturition in the first day after birth.[17]

The major feature of renal failure is oliguria.[11] If we found oliguria we should have suspicion for renal

dysfunction.[19,20] For further clarification, it is necessary to perform blood urea and creatinine serum level to determine the occurance of renal failure.[14,15] In this study, oliguria was found in 6 babies (10%) from asphyxiated group (Table 2), which five babies with severe asphyxia and one babies was moderate asphyxia.

The main renal function is to clean the plasma from unnecessary agents for human body, particularly protein metabolic output. Creatinine serum and blood urea are two blood chemical agents which in normal condition is excreted through kidney. If the disorders occur in nephron due to hypoperfusion or hypoxia, therefore, clearance of those two agents will decrease and their levels will increase in the blood. Creatinine serum is still a reliable indicator to evaluate newborn renal function.[17] In this study we found significantly different in mean creatinine serum and blood urea level, which asphyxiated group was higher compare with non asphyxiated group (Table 3,4). Although mean creatinine serum and blood urea level in asphyxiated group were higher compare to non asphyxiated group, but the value in both group was in normal limit. If we excluded severe asphyxia in asphyxiated group, mean creatinine serum and blood urea level in mild-moderate asphyxia were 0,7610 ± 0,2922 mg/dl and this value is in normal limit, while mean creatinine serum and blood urea level in severe asphyxia were 1,4351 ± 0,3225 mg/dl. Mean creatinine serum level in severe asphyxia was higher compared to normal value. In Mawardi's study, they found mean creatinine serum and blood urea level in study group (asphyxia baby and respiratory syndrome), not significantly different compare with control group.[17]

In the asphyxiated newborn babies GFR were commonly lower than newborn glomerular filtration rate of the non-asphyxiated group but with the same gestational age. In that condition, decreased GFR was strongly related to the severity of asphyxia.[14] In this study we did not find differences of mean GFR in asphyxiated and non asphyxiated group (Table 5). In mild and moderate group, all babies have normal GFR value, similar with non-asphyxiated group, while in severe asphyxia group, we found low GFR value in 83% (5 from 6 babies). We found significantly different according to incidence. Low GFR of severe asphyxia was compared to mild-moderate in this study (Table 6).

The major characteristic of acute renal failure was azotemia with or without oliguria.[20,21] Chronic renal failure was established base on urine output less than 1 ml/kg BW/hour with creatinine serum level more than 1,5 mg/dl in 2 until 5 days of life. In acute renal failure non oliguric we found normal urine or more and creatinine serum level was high.[14] Karlowicz and Adelman reported that acute renal failure was found in 61% of severe asphyxia baby, which acute renal failure was established as creatinine serum level more than 1,5 mg/dl.[22] Dauber reported that in seven asphyxia babies, three of them have renal failure (± 40%).[11] In this study, creatinine serum level was assessed in two days of life. In mild and moderate asphyxiated babies, we did not find renal dysfunction, while in severe asphyxiated babies associated with acute renal failure, we found oliguria and two from six babies who had oliguria got renal failure and they both died.

In summary, all of babies in both groups had micturition during the first 24 hours after birth. There was significant difference between babies who had oliguria in the asphyxiated group and non-asphyxiated group. The mean creatinine serum and blood urea level was significantly different between asphyxiated and non-asphyxiated group. The mean GFR value did not significantly different among asphyxiated group and non asphyxiated group. While based on asphyxiated degree, there was correlation between the severity of asphyxia with renal dysfunction. According to diagnoses of oliguric renal failure we found renal failure in 33% (two of six babies with severe asphyxiated).

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