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The variation of serum Cystatin C and urinary microalbumin in Neonatal asphyxia

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Abstract: Objectives: To explore the detection of Serum cystatin C (Cys C) and urinary microalbumin (UMA) in diagnosing renal impairment of early neonatal asphyxia. Methods: We had 120 cases of full-term neonates who experience asphyxia from our hospital between June 2009 and December 2012, then they were divided into two arms, mild asphyxia and severe asphyxia group, by the admission sequence. 60 cases of health full-term neonates during the same period were as the control group. After 24h birth, we got an approximate blood sample varies from around 2 to 3ml in each neonate among three arms. Automatic biochemistry analyzer made in Hitachi was used to test for renal function, Latex enhance nephelometry immune assay was for serum Cys C, within two days old neonate, we collected 2ml urine and UMA were measured by immunoturbidimetric method. Results: The serum Cys C and UMA of asphyxia groups, Cys C (mg/L)：(1.74±0.21)、(1.510±0.21) UMA (rag/L)：(22.1±5.3)、(14.1 ±3.2), were higher than the control group, Cys C (mg/L)：(1.201±0.23) UMA (rag/L)：(10.1±3.2), the P value was under 0.05. Between asphyxia groups, severe asphyxia group was higher, and the difference was statistically significant. The abnormal rates of serum Cys C single test, UMA single test and combination of both were 60%、62.5%、90% respectively. Conclusion: Serum cystatin C (Cys C) and urinary microalbumin (UMA) can be used to diagnose renal impairment of early neonatal asphyxia. The combination of two technics is better than single one.
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Keyword: Serum cystatin C; urinary microalbumin; asphyxia; renal impairment

1. Introduction

The most important cause of neonatal death and disability of children is neonatal asphyxia, asphyxia is an eventuality having far reaching consequences in the neonatal period. Overall incidence of asphyxia is reported to vary from 1 to 1.5% at various centers [1] and is related to birth weight and gestational age of the baby. Hypoxia and ischaemia can cause damage to almost every tissue and organ of the body and various target organs involved have been reported to be kidneys in 50% followed by CNS in 28%, CVS in 25% and lungs in 23% cases [2]. Kidney is the first organ that will be impaired in the multiple organ injury, a direct complication of asphyxia, so diagnosing renal impairment in an early stage and then planning interventions means a lot [3]. Most studies reveal that serum cystatin C (Cys C) and urinary microalbumin (UMA) are sensitive indicators in reflecting renal impairment, this study will use the combination of two sensitive indicators to explore the diagnostic significance in neonatal renal impairment, specially for neonatal asphyxia.

2. Material and Methods

We had 120 cases of full-term neonates who experience asphyxia from our hospital between June 2009 and December 2012, then they were divided into two arms, mild asphyxia and severe asphyxia group, by the admission sequence. Inclusion criteria: The admission to Hospital must be within 24h after birth, the gestational age must be 37~42weeks, the weight must be 2500~4000g, and who has 4~7 scores to be included in severe asphyxia group while who has 0~3 scors in mild asphyxia group, the score is judged in 1 minute Apgar score grading standard. Exclude the disease which can cause renal dysfunction, such as severe infections、cardiopulmonary disease induced by non-asphyxia、urinary tract malformation and so on, also the disease may have an effect on serum Cys C, for example, sever jaundice、hematolysis and so on. On the other hand we have 60 cases of health full-term neonates during the same period as the control group. (The healthy neonates had been made an agreement by their parents before they accept the tests, and this was already been approved by the Ethics Committee).

Sample collection: We got an approximate blood sample varies from around 2 to 3 ml After 24h birth in each arm, renal function and serum Cys C were tested. We collected 2 ml urine with neonatal urine collection bags in neonate within two days old, and UMA were measured. Test method: Automatic biochemistry analyzer ROCHE. MODULARP800 made in Hitachi Japan was used to test for renal function, Latex enhance nephelometry immune assay was for serum Cys C and immunoturbidimetry was for UMA. Test results Criteria: The reference ranges of these indicators are listed separately, Cys C: 0.92~1.45 mg/L, the UMA: 0.62~11.7 mg/L, BUN: 1.0~3.6 mmol/L, Scr: 26.5~88.0 umol/L. Every data that over the upper limit is abnormal.

3. Results

General information: there are 30 cases male, 30 cases female in mild asphyxia group, gestational age (39.6±1.4) weeks, weight (3301±420) g, days of age for blood sample (11.4±1.7) h, days of age for urine sample (15.50±3.7) h. There are 10 cases male, 10 cases female in sever asphyxia group, gestational age (39.6±1.5) weeks, weight (3213±511) g, days of age for blood sample (5.5±1.6) h, days of age for urine sample (17.4±2.7) h. There are 9 cases male, 11 cases female in control group, gestational age (39.5±1.5) weeks, weight (3220±520) g, days of age for blood sample (13.0±1.7) h, days of age for urine sample (16.4±3.5) h. Comparisons of gestational age、days of age and weight among three groups have no significant statistical differences (P> 0.05).

The blood and urine indicators compare: Serum Cys C and UMA tested in the mild asphyxia and severe asphyxia group were higher than the control group, and severe asphyxia group was higher to mild asphyxia group, they had a significant statistical difference (P<0.01), there are no differences in BUN and Scr among the groups (P> 0.05). Table 1.

Table 1. The blood and urine indicators compare

	N	UMA (mg/L)	Cys C (mg/L)	BUN (mmol/L)	Scr (umol/L)
The control	60	8.13±2.4	1.07±0.54	5.01±1.52	39.10±5.20
Mild asphyxia	60	14.21±4.27*	1.25±0.42*	4.89±1.13	40.15±3.30
Severe asphyxia	60	20.17±6.11#	1.81±0.71#	5.91±1.45	46.17±6.21
F		29.41	11.34	1.02	1.46
P		<0.05	<0.05	>0.05	>0.05

Note： * compared with the control，P <0.05； # compared with the mild asphyxia，P <0.05;

The abnormal rate of each indicators: In 120 cases of asphyxial neonate, 72 cases were abnormal in serum Cys C, make a percentage of 60%, 75 cases were abnormal in UMA, make a percentage of 62.5%, 108 cases who had at least one test abnormal, make a percentage of 90%. The combination of two technics has a higher abnormal rate than the single one, and has a significant statistical difference (P<0.05).

4. Discussions

Neonatal asphyxia can cause multiple organ injury, and it may lead to death in sever cases. The rate of multiple organ or single organ impairment that cased by asphyxia is 70%, and the renal impairment constitutes 57% of these [4]. According to report, there are more than 40% asphyxial neonates will develop into acute renal failure, 61%~70% to the severe asphyxial neonates [5]. Urinary output was slightly less in neonates with severe birth asphyxia but it was statistically insignificant when compared with cases of mild and oderate asphyxia. But oliguria has been reported in higher number of neonates by other authors with figures ranging from 25% to 69.2% babies [6-7]. After 1 day birth of asphyxial neonate, the renal artery flow velocity and volume decrease, while resistance increase, the severer the asphyxia, the worser the condition, we can find oliguria、anuria、proteinuria and acute tubular necrosis. The renal impairment will improve following the improvement of hypoxia. If there are sever intrauterine fetal distress or persistent hypoxia condition after birth, both can develop into acute renal failure, and finally threat to life. BUN and Scr are widely used clinically as indicators to evaluate renal function, but it has some interference factors which result in a poor sensitiveness, especially in the early stage of acute renal dysfunction.

we will probably find out that BUN and Scr are in the reference ranges, and there are no significant symptoms and signs, but if we ignore these, then the disease may have a progression. Therefore, to diagnose neonatal acute renal dysfunction in early stage requires indicators that have more sensitivity and specificity, such as serum Cys C、UMA and so on. Cys C is a kind of low molecular weight protein [8-11], secreted by karyocyte, released into the blood at a constant rate, it can be filtered freely by kidney tubules, reabsorbed and degraded in the proximal convoluted tubule, and gender、diet、inflammation、muscle mass have little effect on it, the Cys C is an ideal endogenous indicator to reveal glomerular

filtration which is discovered in recent years, in our study, Neonates that after 1 day birth in the control group have a mean serum Cys C at (1.19±0.27) mg/L. UMA has a molecular weight of 60 kD, synthesized by the liver, belonged to glomerular urine protein, it can't pass through the glomerular filtration membrane normally, only a trace in the urine; when glomerulus impair, filtration barrier that works as the molecular sieve to prevent protein infiltration is damaged, and increased permeability, as a result, increased UMA excretion, so UMA is an sensitive indicator for diagnosing glomerular impairment in early stage. This study shows that both serum Cys C and UMA have a significant rise in mild asphyxia and severe asphyxia group, and the severer the asphyxia, the higher the serum Cys C、UMA. Hence, serum cys C and UMA can be used as the sensitive indicators, reveal GFR, for renal impairment of asphyxial neonate, its sensitivity is better than BUN and Scr. The study also shows that the abnormal rates of serum Cys C single test, UMA single test were 60%、62.5% respectively, but when we combined both, the rate rose up to 90%.

The result reveals that the combination of two technics is better than single one. So we make a conclusion that serum cys C and UMA can be a diagnostic guide in early renal impairment of neonatal asphyxia, the combination of two technics will decrease the false negative rate of early renal impairment, and the detection method is simple, fast, worthy to be popularized.

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