Research Article

Lamellar Body Count has Higher Sensitivity and Specificity in the Prediction of Neonatal Respiratory Distress Syndrome

Hitung Badan Lamella Memberikan Sensitivitas dan Spesifisitas yang Tinggi dalam Memprediksi Respiratory Distress Syndrome pada Neonatus

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Abstract

Objective: The study was designed to acquire the cut-off value for lamellar body count and its role in predicting the presence of Respiratory Distress Syndrome (RDS) in pregnancy with gestational age above 28 weeks.

Method: Amniotic fluid specimens were collected by amniotomy during cesarean section from women with gestational age above 28 weeks. A haematology analyzer (Advia 120) was used to determine the lamellar body counts. We also performed foam stability test and observed the development of respiratory distress syndrome. Receiver operating characteristics curve was estimated to assess the threshold of lamellar bodies count that may predict the presence of Respiratory Distress Syndrome.

Result: Fifty nine specimens were collected from woman with 29 - 42 weeks gestational age. The incidence of Respiratory Distress Syndrome was 15.3%. Area under the curve for lamellar body count was 0.94. Lamellar body count, with the best cut-off point of 50,000 cell/µl had sensitivity 89% and specifity 92% for predicting the presence of RDS, while the sensitivity of foam stability test was 67% and specificity was 90%. The negative predictive value of the lamellar body count was 98% slightly better than the negative predictive value of the foam stability test 94 %.

Conclusion: Although both test are good predictor of RDS, lamellar body count has higher sensitivity and specificity. It also has more advantages as it only requires small amount of sample, fast, easy and more objective.

[Indones J Obstet Gynecol 2012; 36-4: 176-80]

Keywords: foam stability test, lamellar body, respiratory distress syndrome

Abstrak

***Tujuan**: Mengetahui nilai ambang hitung badan lamelar pada usia kehamilan di atas 28 minggu dan perannya dalam memprediksi terjadinya RDS apabila dibandingkan dengan tes busa.*

***Metode**: Sampel cairan ketuban diperoleh melalui amniotomi saat melakukan seksio sesarea pada perempuan hamil dengan usia kehamilan di atas 28 minggu. Nilai hitung badan lamelar dihitung menggunakan mesin hematologi Advia 120. Tes busa juga dilakukan terhadap sampel cairan ketuban, sementara bayi diobservasi dan dinilai apakah mengalami RDS. Titik potong nilai hitung badan lamelar dalam memprediksi RDS dihitung menggunakan grafik Receiver Operating Characteristic.*

***Hasil**: Lima puluh sembilan sampel cairan ketuban diperoleh dari perempuan dengan usia kehamilan 29-42 minggu. Angka kejadian RDS pada penelitian ini adalah 15,3%. Didapatkan nilai Area Under the Curve 0,94 untuk pemeriksaan hitung badan lamelar. Pada titik potong 50.000 sel/µl, hitung badan lamelar memiliki nilai sensitivitas 89 % dan spesifisitas 92%, sementara tes busa memiliki nilai sensitivitas 67% dan spesifisitas 90%. Nilai negative predictive value untuk hitung badan lamelar pada titik potong 50.000 sel/µl adalah 98%, sedikit lebih tinggi dari tes busa yaitu 94%.*

***Kesimpulan**: Pemeriksaan tes busa dan nilai hitung badan lamelar merupakan alat yang dapat dipakai dalam memprediksi terjadinya RDS, namun nilai hitung badan lamelar memiliki nilai sensitivitas dan spesifisitas yang lebih tinggi dan memiliki beberapa kelebihan, yaitu lebih objektif, mudah dan cepat dikerjakan, serta hanya memerlukan sedikit sampel cairan ketuban.*

[Maj Obstet Ginekol Indones 2012; 36-4: 176-80]

***Kata kunci**: badan lamelar, respiratory distress syndrome, tes busa*

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INTRODUCTION

Respiratory Distress Syndrome (RDS) is the most common complication experienced by preterm infants at birth. An epidemiological study in the United States estimates that there are approximately 80,000 cases of neonatal RDS each year and resulting in approximately 8,500 infant deaths per year. The incidence of RDS is almost 1% of all live birth but occurs in 10-15% of all infants with a birth weight less than 2,500 grams. The risk of RDS significantly increased in babies born by planned caesarean section between 37 weeks and 38 weeks 6 days, compared with the planned operation at 39 weeks gestation and above. In a retrospective study of 1,284 planned caesarean section, it was found that the incidence of RDS is 25 per 100 live births at 37-38 weeks 6 days of gestation, while at over 39 weeks gestation the incidence of RDS is 7 out of 100 births.[1-4]

To avoid the occurrence of RDS, the American College of Obstetricians and Gynecologists (ACOG) recommends to terminate the pregnancy at 39 weeks gestation and to confirm fetal lung maturity at elective birth that will be performed under 39 weeks' gestation. To assess fetal lung maturity, there are two types of tests that test indirectly or directly. Indirect tests did not evaluate pulmonary function directly, but evaluate the age, size of the fetus or a physical profile that can be used as parameters in predicting fetal lung maturity. While direct tests consist of tests of biochemistry and biophysics. Biochemical test is the most widely used test to evaluate lung maturity. One example is lecithin-sphingomyelin test. But there are some drawbacks of this test, namely the high cost, time consuming, specialized equipment with a fairly complex procedure, and until has not been done routinely in Indonesia. Lamellar body count test with amniocentesis procedure is one test that can be used as an alternative biophysical examination of lung maturity. Lamellar body count is relatively easier, less expensive, faster, and can be done with the equipment available in most hospitals. In a meta-analysis of six studies comparing the two tests, it is said that the lamellar body count tests have an accuracy similar to the L/S ratio test. A protocol has been published to promote the same standard to test lamellar body count. The threshold value of 50,000 cells/µl is proposed as a determinant for fetal lung maturation.[5-13]

Surfactant is stored in pneumocyte type II in the form of lamellar bodies. Lamellar bodies are actively secreted into the alveoli, and then out into the amniotic fluid. Lamellar body size is similar to platelet cells (1-5 µm), so the standard hematology calculators can be used to determine the concentration of lamellar bodies. This technique is simple, fast, inexpensive, and reliable enough to predict lung maturity. The possibility of RDS is reduced if the lamellar body count result is high. In a cohort of 527 neonates, 2 cut-off value were used, 30,000 cells/µl and 50,000 cells/µl. The need of neonatal respiratory support, care in the NICU and complications were generally rare in cut-off numbers above 50,000 cells/µl. Another study performed on 80 subjects also stated that the prediction rate of RDS was 93% when the cut-off point was 50,000 cells/µl.[4,6,14,15]

In Indonesia, there is no research data comparing lamellar body count with foam testexamination, which has been used as the standard tests to determine fetal lung maturity. In the current study, we expected to obtain data on the cut-off values for lamellar body count obtained using a brand Advia 120 hematology analyzer, as well as comparing of the diagnostic value of lamellar body count with foam test. Data generated from this study is expected to establish lamellar body count as one of the procedures used in assessing intrauterine fetal lung maturity.

METHODS

The design of this study was cross-sectional. We aimed to find a cut-off value for lamellar body count and its role as a diagnostic test to assess the occurrence of RDS. Samples of amniotic fluid obtained by amniotomy during c-section operation on pregnant women with gestational age above 28 weeks. The study was conducted at Dr. Cipto Mangunkusumo Hospital (RSCM), Fatmawati Hospital (RSF), and the Maternal and Child Hospital Mother Aliyah (RSIA-BA) from April 2012 to September 2012.

Lamellar body count value is calculated using the Advia 120 hematology machine. Foam test was also conducted on samples of amniotic fluid. The infant was observed and assessed to determine whether they had RDS based on Downes score. Cut-off value of lamellar body count in predicting RDS was calculated using Receiver Operating Characteristic chart.

RESULT

Fifty nine samples of amniotic fluid were obtained from women with gestational age of 29-42 weeks. The incidence of RDS in this study was 15.3%. Obtained value of Area Under the Curve for lamellar body count examination was 0.94 (Figure 1). At the cut-off value of 50,000 cells/µl, lamellar body count has a sensitivity value of 89% and specificity of 92%, while the foam test has a value of 67% sensitivity and 90% specificity. Rated negative predictive value for the lamellar body count at cut-off value of 50,000 cells/µl was 98%, slightly higher than the 94% foam tests. From the agreement test of both clinical examination with the Kappa approach, we obtained that the best agreement was the lamellar body count with cut-off value of 50,000 cells/µl (Kappa 0.713), followed by the foam test (Kappa 0.521), then the lamellar body count with the cut-off value of 45,000 cells/µl

Table 1. Lamellar body Count Cut-off point with the best sensitivity and specificity in predicting the occurrence of RDS

		RDS						
		Present	**No**	**Sn**	**Sp**	**PPV**	**NPV**	**LR+**
LBC 45,000 cells/µl	Under CU	6	4	0.67	0.92	0.60	0.94	8.33
	Over CU	3	46					
LBC 50,000 cells/µl	Under CU	8	4	0.89	0.92	0.67	0.98	11.11
	Over CU	1	46					
LBC 75,000 cells/µl	Under CU	9	20	1.00	0.60	0.31	1.00	2.50
	Over CU	0	30					

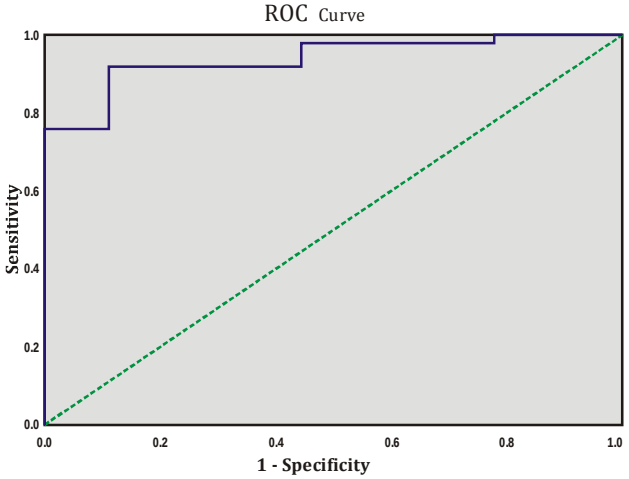

Figure 1. ROC for Lamellar body count

(Kappa 0.477), while the weakest agreement was the lamellar body count with cut-off value of 75,000 cells/µl.

DISCUSSION

The study was conducted on 59 samples obtained from subjects who met the inclusion criteria, with each sample obtained equal treatment. RDS incidence in this study were 15.3% (9 of 59 subjects). In the few studies that have been done before, the incident of RDS was 17% in the study by Salim et al, 19% in research conducted by Wijnberger et al, and 18.6% in the study by Ramadauskaite et al.5,8,9 This difference could be due to several factors, namely the difference in gestational age, inclusion criteria, sample size, and corticosteroid regime. In this study, the inclusion criteria were gestational age of 28 weeks and above, while the number of samples with gestational age below 36 weeks was only 5 samples. this is in contrast to some other studies where the limit is 32 weeks. But the number of cases of RDS in this study can be considered eligible for this study, because the incidence of RDS in this case as much as 15.3% was in line with the incidence of RDS in these studies were used as a reference in calculating the number of samples for this study ie 10.5% on research by Djanas et al, and 14.6% in the study Visnjevac et al.[16]

In this study, the results of foam test has sensitivity rate of 67% and specificity of 90%, slightly better when compared with the results of the study Visnjevac et al. that resulted in a sensitivity rate 67.6% and specificity of 72.2% for the foam test.[16] In predicting the occurrence of RDS, the test foam is superior to ensure no RDS. It is shown from the value of negative predictive value that is much higher when compared to the value of the positive predictive value (94% to 55%). Of the 11 subjects who tested negative for foam test, 6 subjects experienced events RDS. in this study, the Likelihood Ratio of this foam test was 6.8, suggesting that as a tool that has been used, the foam test has a pretty good ability in predicting RDS.

Meanwhile, in this study, the lamellar body count examination resulted in an excellent sensitivity and specificity with cut-off value <50,000 cells/µl it gave sensitivity of 89% and specificity of 92% with a negative predictive value of 98%. When compared with results from Khazardoost et al are using 80 samples with the same subject gestational age is 28-40 weeks, lamellar bodies cut point value <50,000 cells/µl had similar results, obtained a sensitivity of 85% and a specificity of 70% with a negative predictive value 93%. In the handling of the sample, the study Khazardoost et al also have the same method, ie by centrifugation before calculation using the machine, even though the machines used different STKR Coulter. It is also in accordance with the recommendations of ACOG 2008 which concluded that the incidence of neonatal complications with lamellar bodies cut-off values >50,000 cells/µl less occur.[4]

Of the 59 subjects, there were 9 subjects with preeclampsia as complicating factors, and from 9 infants with RDS, there were 3 subjects whose mothers had preeclampsia with gestational age below 36 weeks. Of the 3 subjects, there was 1 subject who was not managed to be diagnosed by lamellar bodies (false negative). The subject had a gestational age of 30 weeks, severe preeclampsia complications factors and the infant weight was 1,500 grams with lamellar body count value of 66,000 cells/µl. There were several possible causes for this, one of which was that the baby was already in a state of chronic hypoxia caused by preeclampsia, which then causes the lamellar bodies to be formed from the start, which then stimulates cells produce surfactant pneumosit type 2, so then lamellar body count value produced false negative. Another possibility of false negative that could not be ruled out was the contamination of the sample in the sample handling or lab error.

In conducting this study, the diagnosis of RDS was made by using Downes scoring system, but then we grouped the subjects into two categories: with RDS and no RDS, so the data analysis was not conducted to analyze the relationship between the score and the value of lamellar body count. Each education and health care centers have a different way of assessment in diagnosing RDS, thus scoring points in this study have no clinical significance. And the assessment of the scoring in this study was carried out by several assessor different examiner, so the bias will be high.

In this study, we did not conduct follow-up observations of the infants who had RDS. Further data using a larger sample were required to oserve the outcome of the baby, especially infants who have RDS. Thus, the cut-off value of lamellar bodies that can predict the severity of RDS and the infant's outcomes later in life could be found.

Based on the results of a diagnostic tool that tests both foam and lamellar body count of this study, the lamellar body count obtained good results in predicting RDS. Cut-off value of lamellar body count of 50,000 cells/µl had Kappa values which categorized as goo (Kappa 0.60-0.80), while the foam test had a Kappa value that categorized as adequate (Kappa 0.4 to 0.6). Thus the cut point values of 50,000 cells/µl for lamellar body count was better than the foam test in diagnosing RDS.

Lamellar bodies also had a higher number for negative predictive value, where the ability to predict the absence of RDS is the most important characteristic in analyzing fetal lung maturity. Lamellar bodies also had a higher sensitivity and specificity values than the foam test. Meanwhile the lamellar body count also had many advantages, such that it is easier to perform, requires a smaller sample size, cheaper in terms of cost and more objective and can be checked in any laboratory that has a regular hematology machine.

CONCLUSION

Examination of the foam test and the value of lamellar body count is a tool that can be used in predicting the occurrence of RDS, but the value of lamellar body count has a higher sensitivity and specificity values several advantages, namely more objective, easily and quickly done, and requires only a small sample amniotic fluid.

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