

## Efficacy of dexamethasone for lung maturity in preterm delivery in association with lamellar bodies count

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### Abstract

**Background** Organ immaturities in preterm infants may result in perinatal death. One of the diseases is respiratory distress syndrome (RDS) which is caused by lung immaturity. Dexamethasone is often used to accelerate maturity of infant lungs.

**Objective** To determine the efficacy of dexamethasone on lung maturity measured by lamellar bodies count.

**Methods** A quasi experimental study was done at Perinatology Division, Department of Child Health, Medical School, Udayana University, Sanglah Hospital, Denpasar. We recruited 72 subjects; 36 subjects were given four times intramuscular dexamethasone 5 mg every twelve hours before delivery. Thirty six subjects who did not receive dexamethasone belonged to control group. Infants' lungs maturity assessment was performed using lamellar bodies count taken from amniotic fluid.

**Results** The gestational age ranged between 28 to 36 weeks, with the mean gestational age in dexamethasone group was 32.2 (SD 1.76) weeks and that in control group was 31.7 (SD 2.65) weeks. The efficacy of dexamethasone therapy on lung maturity was significant with Fisher's exact test  $P < 0.0001$ , 95%CI 2.546; 11.173. Using multivariate logistic regression analysis, there was significant correlation between dexamethasone and lung maturity measured by lamellar bodies count [OR=239.39;  $P < 0.0001$ , 95%CI 22.12;526.53].

**Conclusion** Administration of dexamethasone in pregnant women during preterm delivery significantly improves lung maturity measured by lamellar bodies count. [Paediatr Indones 2007;47:115-119].

**Keywords:** Preterm delivery, dexamethasone, lamellar bodies, lung maturity

Immaturity of the organs is the most important problem in prematurity.<sup>1</sup> A preterm delivery is defined as the delivery that occurred at the gestational age between 28-37 weeks;<sup>2</sup> the prevalence of preterm delivery is 4-12.9% of all deliveries.<sup>3</sup> Respiratory distress syndrome (RDS) and its complications are the key factor affecting mortality and morbidity in preterm infants. RDS in premature infants is caused by hyaline membrane disease (HMD), which is related with surfactant deficiency due to lung immaturity.<sup>4,6</sup> In Sanglah Hospital, HMD accounts for 21.1% neonatal death, after asphyxia and congenital abnormalities.<sup>7</sup>

The efficacy of intramuscular glucocorticoid as the basic therapy for preterm delivery has been well documented.<sup>8-10</sup> Understanding lung maturity is important to predict the development of RDS caused by HMD. Thus, its assessment is very important in preterm infant management.<sup>11-14</sup> A study on the association of lamellar bodies with lung maturity by Atlanta Maternal Fetal medical suggests cut off point of lung maturity is 16,000/mL.<sup>15</sup> This study aimed to determine the efficacy of dexamethasone for lung maturity in preterm delivery measured by lamellar bodies count.

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## Methods

This was a single blind quasi experimental clinical study conducted at Perinatology Division, Department of Child Health, Medical School, Udayana University, Sanglah Hospital, Bali, from January to November 2004. The inclusion criteria were (1) pregnancy with gestational age between 28-37 weeks; (2) single birth; (3) premature rupture of the membrane <6 hours, and (4) a signed informed consent. The exclusion criteria were (1) medical diseases such as asthma, congenital heart disease, diabetes mellitus, fever, preeclampsia, eclampsia; (2) the infant had congenital abnormality; (3) mother suffered from chorioamnionitis; (4) amniotic fluid contaminated by maternal blood or meconium and (5) fetal distress. Amniotic fluid sampling was performed in the delivery room in Sanglah Hospital and lamellar bodies test was carried out in the laboratory of Obstetric and Gynecology Department, Dr. Sutomo Hospital, Surabaya. This study was approved by Research Committee of Sanglah Hospital.

The number of subjects needed for each group was 36. Subjects were allocated in consecutive order and divided into two groups. The study subjects were not *in partu* and received 5 mg intramuscular dexamethasone every 12 hours for four times, with the total dose of 20 mg. The control group received no treatment.

Amniotic fluid specimen was collected in the delivery room at Sanglah Hospital. This was done by transvaginal puncture with insertion of nasal canule no. 22 through the cervical canal. Lamellar bodies test was done in Obstetric and Gynecology laboratory, Dr Sutomo Hospital Surabaya.

Statistical analysis was performed using SPSS for Windows v. 13.00. Relative risk and X<sup>2</sup> test were used to compare proportion of lung maturity between dexamethasone and control group. Independent *t*-test was used to compare lamellar bodies count between dexamethasone and control groups. Multivariate logistic regression analysis was used to find any association of dexamethasone therapy, lamellar bodies and confounding variables. A P value of less than 0.05 was considered statistically significant.

### Interpretation of lamellar bodies count

Maturity of lungs	Lamellar bodies count
Mature Lung	≥16 K/μL
Immature Lung	<16 K/μL

## Results

During the study period, there were 3,470 infants born at Sanglah Hospital Denpasar and 402 (12%) of them were preterm. Seventy two (17%) of those preterm infants were enrolled in this study. The baseline characteristics of the subjects are shown in **Table 1**. Mothers' age, gestational age, birth weight, gender, mode of delivery and parity were similar both in dexamethasone and control group. Distribution of gestational age was in the range of 28-36 weeks, with mean age of that in dexamethasone and control group was 32.2 (SD 1.76) weeks and 31.7 (SD 2.65) weeks, respectively.

The lamellar bodies count (**Table 2**) showed statistically significant difference between dexamethasone and control group [OR=4.25; 95%CI 2.55;11.17; P<0.0001]. The mean difference of lamellar bodies in both group were statistically significant [mean difference 8.69; 95%CI 6.69;10.69; P<0.0001].

Using multivariate logistic regression analysis, there was a strong association between dexamethasone and lung maturity based on lamellar bodies count [OR=263.39; 95%CI 22.12;526.53; P<0.0001] whereas gestational age, mode of delivery and birth weight had a weak association with lung maturity (**Table 3**).

**Table 1.** Baseline characteristics of the study subjects

Variables	Group	
	Dexamethasone n=36	Control n=36
Mothers' age y, mean (SD)	29.7 (2.65)	29.0 (2.90)
Gestational age wk,mean (SD)	32.2 (1.76)	31.7 (2.65)
Birthweight g, mean (SD)	1845.8 (436.6)	1979.0 (396.7)
Mode of delivery		
Spontaneous, n (%)	25 (69)	25 (69)
Cesarean section, n (%)	11(31)	11(31)
Parity		
Primipara, n (%)	11 (31)	10 (28)

**Table 2.** Efficacy of dexamethasone in maturity of lungs

Group	Maturity of lungs		Total
	Mature	Immature	
Dexamethasone	34 (94%)	2 (6%)	36(100%)
Control	8(22%)	28(78%)	36(100%)
Total	42	30	72

## Discussion

Preterm birth is the main cause of morbidity and mortality in neonatal period. Immaturity of the lungs commonly occurs in preterm infants and may lead to RDS caused by the deficiency of surfactant called as HMD.<sup>3,8,11,15-19</sup>

Because of its efficacy, our hospital policy recommends the use of prenatal dexamethasone for women at risk of preterm delivery.<sup>20</sup> Antenatal dexamethasone therapy may decrease the incidence of RDS caused by HMD in preterm infants.

In preterm pregnancy, intramuscular dexamethasone will reach fetal blood circulation through the placenta. In lungs, dexamethasone binds to receptor III in pneumocyte cell type II and then after passing through the cytoplasm, it will bind to receptor III in nuclear cell. Dexamethasone stimulates the production of several enzymes such as cholinephosphotransferase enzyme, phosphatidate phosphatase enzyme and phosphatidate cytidyltransferase.<sup>9-11</sup>

The ideal method for assessing lung maturity is lung profile. This is a modified method that combines lecithine/sphingomyeline (L/S) ratio and chromatography method. Basically, it divides phospholipids into small components and then each component is counted. This method is a gold standard for lung maturity but this method is very invasive.<sup>4,13</sup>

In this study, we used lamellar bodies count to assess the lung maturity. The basic principle of this test is to detect surfactant secreted by pneumocyte II by assessing lamellar bodies. The lamellar bodies count is associated with gestational age and lung maturity.

We found strong association between dexamethasone and lung maturity ( $P < 0.0001$ ). In nuclear cell, dexamethasone stimulates the production of some enzyme such as cholinphosphotransferase enzyme, phosphatidate phosphatase enzyme and phosphatidate cytidyltransferase that increase production of surfactant which is important

for lung maturity.<sup>21-24</sup> This result was in accordance with previous study done by Scottish Neonatal Consultants Collaboration<sup>25</sup> in their meta analysis of 11 randomized trials using the same method as our study. They reported a decrease mortality rate of 70% of HMD after given antenatal dexamethasone for 24h or more in infants born before 37 weeks of gestational age ( $X^2 = 12.0$ ;  $P < 0.001$ ). Junara<sup>23</sup> with shake test had suggested the benefit of antenatal dexamethasone for lung maturity. We also found significant effect of dexamethasone for lung maturity associated with lamellar bodies count using independent *t*-test with mean different of 8.68. With the same method Henderson<sup>24</sup> found an increase of lamellar bodies count in parallel with lung maturity.

Tarnow and Mordi<sup>26</sup> compared the efficacy of antenatal dexamethasone, betamethasone and hydrocortisone for lung maturity in preterm delivery measured by shake test. They found dexamethasone had greater beneficial effect on lung maturity [OR = 32.02; 95% CI 15.38; 190.57;  $P < 0.001$ ]. Sinclair<sup>27</sup> found from metaanalysis of randomized trial a decreased mortality of 65% of HMD after given antenatal dexamethasone therapy for 24h.

The effect of confounding factors like birth weight, gestational age and mode of delivery can be reduced by comparable distribution of both groups. Logistic regression analysis showed no significant association between confounding factors and lung maturity. Henderson<sup>24</sup> reported similar results in his study of 132 premature infants.

In conclusion, dexamethasone administered in pregnant women during preterm delivery significantly improves lung maturity as measured by lamellar bodies count.

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**Table 3.** Multivariate logistic regression analysis

Variable	Beta	SE	Wald	df	P	Odds ratio	95%CI
Dexamethasone	5.465	1.21	20.444	1	0.000	236.39	22.12;526.53
Mode of delivery	1.333	1.28	1.083	1	0.298	0.26	0.02;3.25
Gestational age	0.429	0.31	1.890	1	0.169	0.65	0.35;1.20
Birth weight	0.00	0.01	0.43	1	0.835	1.00	1.00;1.00

$\beta$  logistic regression coefficient; SE: Standard Error; df: degree of freedom; P:Probability; CI: Confidence Interval

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