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Pregnancy outcome after oral salbutamol tocolysis in preterm labor at King Chulalongkorn Memorial Hospital

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Objective : *To evaluate pregnancy outcomes in patients receiving oral salbutamol as a tocolytic agent for the inhibition of labor at King Chulalongkorn Memorial Hospital.*

Method : *All singleton patients with preterm labor who received oral salbutamol for tocolysis and delivered at King Chulalongkorn Memorial Hospital between 1996-1998 were retrospectively evaluated. The main outcome measures were its efficacy in prolongation of pregnancy, perinatal and neonatal mortality rates, the rates of respiratory distress syndrome, other neonatal complications and the need for intensive care unit admission.*

Result : *Only four women were able to continue pregnancy until term, the remainder delivered prematurely. A delay of delivery for more than 48 hours occurred in 75.0 % and for more than one week in 31.3 %. No perinatal and neonatal death found in our study. Respiratory distress syndrome occurred in 18.8 % neonates. Sixty three percent of preterm infants needed intensive care unit admission.*

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Conclusion : *Salbutamol is an effective tocolytic agent in delaying delivery during corticosteroid administration, with the advantages of simplicity and good compliance. As there are several confounding factors, its effect on the prolongation of pregnancy and neonatal outcome in this study is inconclusive.*

Key words : *Preterm labor, Tocolysis.*

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วันทนา ธารามาศ, บุญชัย เอื้อไพโรจน์กิจ, ธีระพงศ์ เจริญวิทย์. ผลการยับยั้งการคลอดก่อนกำหนดด้วยยาซัลบูทามอลชนิดรับประทานในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2544 พ.ค; 45(5): 393 - 401

วัตถุประสงค์ : *เพื่อศึกษาผลของการยับยั้งการคลอดก่อนกำหนดด้วยยาซัลบูทามอลชนิดรับประทานในโรงพยาบาลจุฬาลงกรณ์*

วิธีการ : *ทบทวนแฟ้มข้อมูลของหญิงตั้งครรภ์เดี่ยวผู้เจ็บครรภ์คลอดก่อนกำหนดที่มาคลอดที่โรงพยาบาลจุฬาลงกรณ์ ระหว่าง พ.ศ. 2538 – 2541 โดยศึกษาประสิทธิภาพในการยืดอายุการตั้งครรภ์ อัตราการตายของทารกแรกเกิดอัตราการเกิดภาวะ respiratory distress syndrome และภาวะแทรกซ้อนอื่น และการรับไว้ใน neonatal intensive care unit*

ผลการศึกษา : *สามารถยับยั้งการคลอดไปจนครบกำหนดได้เพียง 4 รายจาก 48 ราย แต่สามารถยืดระยะเวลาการคลอดไปได้ 48 ชั่วโมงได้ถึง 75 % ทั้งนี้ 32.3 % ยืดระยะการคลอดได้นานมากกว่าหนึ่งสัปดาห์ พบภาวะ respiratory distress syndrome 18.96 % ต้องรับไว้ดูแลใน neonatal intensive care unit 62.5 % และไม่พบทารกแรกเกิดเสียชีวิตเลย*

สรุป : *ซัลบูทามอลเป็นยาที่มีวิธีการใช้ง่ายและสะดวก สามารถยับยั้งการคลอดก่อนกำหนดได้ดี โดยเฉพาะในระหว่างที่รอผลการเร่งการพัฒนาปอดของทารกใน 48 ชั่วโมง แต่เนื่องจากเป็นการศึกษาย้อนหลังจึงยังไม่สามารถสรุปประสิทธิภาพในการยืดอายุการตั้งครรภ์ได้*

Salbutamol has been used as a tocolytic agent in preterm labor for many years. Being used as oral administration is its advantage. Its low cost makes its attractive especially during our economic turmoil. Surprisingly, there are few studies reporting its efficacy in delaying delivery, prolonging pregnancy and improving neonatal outcome. In Chulalongkorn Memorial Hospital, it is the most popular tocolytic agent for decades. Unfortunately, there has been no previous available report in our population. Its efficacy should be proved before being replaced by such a new agent with very high expense.

This study was designed to investigate the pregnancy outcome of patients with preterm labor after oral salbutamol treatment at King Chulalongkorn Memorial Hospital. This study is proposed to be useful as a primary database for further study to improve the outcome of these patients in the future.

Method

Data were collected retrospectively from all singleton diagnosed preterm who received oral salbutamol for tocolysis and delivered at King Chulalongkorn Memorial Hospital between 1996-1998. Preterm labor was defined as a labor pain starting before 37 weeks' gestation. Cervical progression or 2 centimeters dilatation and 80 percents effacement coexisting with regular uterine contraction were required for diagnosis. Digital examination was abandoned in any cases complicated with placenta previa and premature rupture of membranes. Maternal and neonatal records were reviewed for specific information regarding the pregnancy, labor, delivery and neonatal course. The data were entered into a computerized database. The information recorded included demographic characteristics, underlying maternal disease, gestational age at diagnosis and delivery, precipitating causes, use of tocolytic drugs and glucocorticoids, latency period, route of delivery and the specific reason for the preterm birth. The neonatal charts were reviewed for the presence of specific complications contained in the final discharge diagnosis approved by the responsible neonatologist. The outcome measures were duration of delaying delivery, prolongation of pregnancy, perinatal and neonatal mortality rates, the rates of respiratory distress syndrome and other neonatal complications. Newborn intensive care unit admission time was coded in whole number of days.

Descriptive statistics determined the incidence and frequency of the major and minor morbidities.

Result

From 471 women with confirmed preterm labor, there were 64 patients who received tocolytic agents. These consist of 60 singleton, three twins and one quadrupet. For singleton the tocolytic agent most frequently used was salbutamol (N = 48). Only one patient in this group started treatment via the intravenous route, while 52 patients received an oral form of salbutamol. The oral regimen for acute tocolysis started with 32 milligram daily. Salbutamol dosage was then decreased to the lowest effective dose for maintenance. Terbutaline, indomethacin and magnesium sulfate were used in 8, 2 and 1 cases respectively.

Population characteristics of the study group are shown in table 1. The study group age ranged from 14 to 38 years. There were 30 primipara,12 patients with one child, six patients with two children

and one patient with three children. The fetal presentation was cephalic in 41 patients, breech in 4 patients and scapula in 4 patients.

As shown in table 2, the most common associated obstetric complication was placenta previa followed in order by PROM, anemia and preechampsia. Nineteen patients had no associated complication.

The cervical dilatation of all 25 cases that underwent pelvic examination was less than 4 centimeters. There were 23 cases in whom pelvic examination was not performed due to the presence of an obstetric contraindication such as placenta previa or PROM.

Thirty eight patients received dexamethasone to enhance fetal lung maturity. The most frequently - used regimen was dexamethasone 12 milligrams intramuscularly every 12 hours for two doses. This regimen was used in 36 patients, however, nine of these patients received only one dose before delivery from failure inhibition. One patient received dexamethasone 6 milligram every 6 hours for four doses and the other one received dexamethasone 6 milligram every 12 hours for four doses.

Table 1. Population characteristic.

	Oral salbutamol receivers N = 48
Average age	25.9 ± 5.8
Primipara	30 (62.5 %)
ANC ≥ 4	30 (62.5 %)
No ANC	1 (2.1 %)
Chula ANC	32 (66.7 %)
Cephalic presentation	41 (85.4 %)

Table 2.Common associated obstetric complications.

	Oral salbutamol receivers N = 52
Placenta previa	17 (37.4 %)
PROM	8 (16.7 %)
PIH	2 (4.2 %)
Anemia	2 (4.2 %)
Gestational diabetes	1 (2.1 %)
HIV infection	1 (2.1 %)

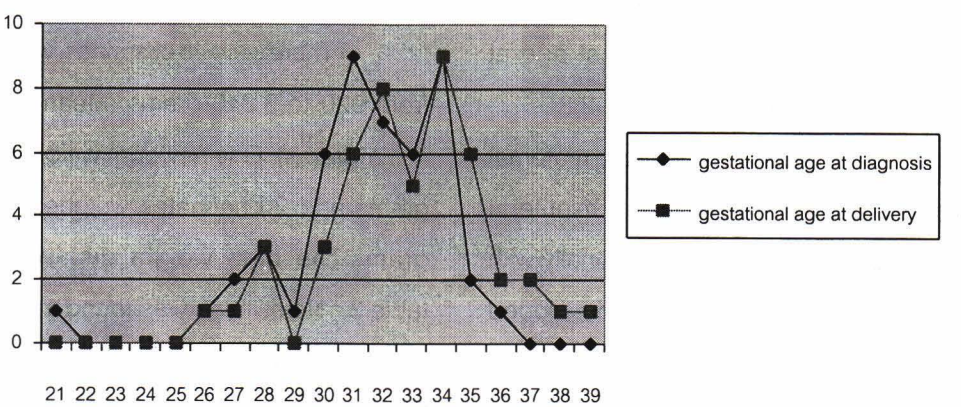

Figure 1. Distributions of age at diagnosis and delivery.

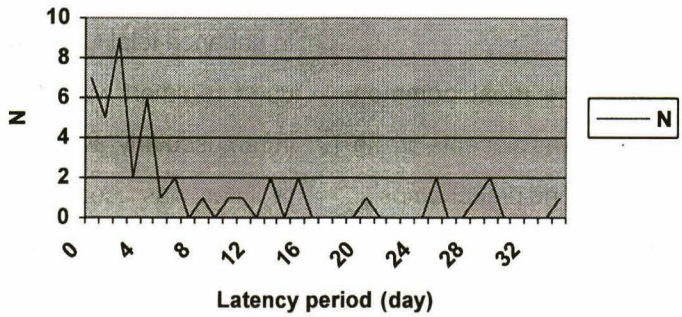

Figure 2. Latency period

The gestational age distributions are shown in figure 1. The gestational age at diagnosis ranged from 21-36 weeks (mean ± SD = 31.4 ± 2.7 weeks). After tocolysis treatment, the pregnancy was prolonged for 8 days 22 hours ± 11 days 2 hours on average. The longest latency period was 40 days (Figure 2). Only four patients were able to continue their pregnancy until 37 weeks. These consisted of one case of 32 weeks' gestation, two cases of 33 weeks' gestation and one case of 34 weeks' gestation. Uterine contraction was not able to be diminished in five patients resulting in progression of labor and delivery. A delay of delivery for more than 48 hours was found in 36 patients (75.0 %). and for more than 1 week in fifteen patients (31.3 %). The gestational age at delivery ranged from 26 -39 weeks (32.8 ± 2.8).

Although tachycardia is common, maternal heart rate was less than 120 beats per minute in most cases. Palpitations occurred occasionally with spontaneous resolution. Only one patient developed tachycardia up to 148 beats per minute, which was reversible after discontinuation of salbutamol. One case of gestational diabetes developed fetal distress with birth asphyxia. We found three cases of puerperal fever without definite cause and one case of post-partum hemorrhage with underlying placenta previa.

The specific reasons for discontinuing salbutamol were advanced labor in 15 patients, massive bleeding in 10 patients, term pregnancy in 7 patients, rupture of membranes in 8 patients, and failure of inhibition in 6 patients. Tocolytic agents were found to be withdrawn without any reason noted in one patients.

The cesarean section rate was 36.5%. The indications were composed of 11 cases (22.9 %) of placenta previa, 2 cases of fetal distress, 2 cases of previous cesarean section and one case of breech presentation.

There were 48 offsprings, which weight ranged from 920 to 3,040 grams (Mean ± SD = 1,943.9 ± 481.1 grams). One newborn weighed less than 1,000 grams and 20 neonates weighed more than 2,000 grams.The birth weight distribution is shown in table 3. No stillbirth was found in the study. Most of the neonates had five – minute. Apgar score more than seven (N = 47) except one with birth asphyxia that no Apgar score presented. No perinatal and neonatal death found in our study.

Table 3. Neonatal birth weight.

Birth weight	Inhibited offsprings	Steroid receivers
≤ 1,000	1	0
1,001-1,500	10	4
1,501-2,000	17	10
2,001-2,500	17	10
> 2,501	3	3
Total	48	27

The most common neonatal complication was hyperbilirubinemia (58.3 %), followed by hypoglycemia (27.1 %) and hypothermia (22.9 %). RDS was found in 18.8 %. Other lung complications found were pneumonia and bronchopulmonary dysplasia. There were two neonates with apnea of prematurity and seven cases of respiratory distress of unknown cause. Moreover, severe complications related to prematurity such as intraventricular hemorrhage and necrotizing enterocolitis, were found in two and one cases respectively.

Thirty neonates (62.5 %) needed intensive care unit admission (Mean ± SD = 5.3 ± 9.4 days). Mean hospital stay was 21.2 ± 21.0 days (range from 2 days to 79 days).

The most common congenital anomaly was patent ductus arteriosus, which was found in 7 neonates. Also, we found one case of Downs' syndrome and one neonate with absent septum pellucidum. Undescended testis was another finding in 3 premature neonates.

Table 4. Neonatal complications.

Neonatal complications	Inhibited offspring N = 58	Steroid receivers N = 27
Hyperbilirubinemia	28 (58.5 %)	13 (48.1 %)
Hypoglycemia	13 (27.1 %)	8 (29.6 %)
Hypothermia	11 (22.9 %)	5 (18.5 %)
RDS	9 (18.8 %)	1 (3.7 %)
Birth asphyxia	4 (8.3 %)	2 (7.4 %)
Pneumonia	7 (14.6 %)	2 (7.4 %)
Cold stress	7 (14.6 %)	2 (7.4 %)
Sepsis	2 (4.2 %)	1 (2.1 %)
G6PD	2 (4.2 %)	1 (2.1 %)
IVH	2 (4. 2 %)	0 (0.0 %)
NEC	1 (2.1 %)	1 (2.1 %)
BPD	1 (2.1 %)	1 (2.1 %)

Discussion

Prematurity of neonates is an extensive responsibility for medical workers in our hospital. We found that some preterm labor patients treated with tocolytic agents were able to reach as near term as 36 weeks and to avoid any effects of prematurity.

As a simple administrative tocolytic agent, oral salbutamol is an effective method to delay delivery. Our study showed 75.0 % effectiveness in delaying delivery for more than 48 hours. The result is comparable to Haswell's report of 208 preterm labor patients that received 32 milligram daily salbutamol.[1] His study presented 89.4 % effectiveness. While Hastwell et al.[1] reported high efficacy of salbutamol in prolongation of pregnancy (77.5 % for one week and 66.8 % for two weeks), in our study we found only 28.85 % of cases could be prolonged for more than one week. Furthermore, Ashworth et al.[2] did not found a benefit on prolonging the length of gestation in 74 twin pregnancy received oral salbutamol For the pregnancy that could be prolonged until 37 weeks, Gummerus[3] reported as high as 61% of 54 intact membranes preterm labor patients treated with intravenous salbutamol follow by 24 miligram daily oral salbutamol. In contrast, this incidence was very low in our study as the result of the following factors. First, the high incidence of associated obstetric complications such as placenta previa, PROM, multiple pregnancy. Second, the difference of salbutamol dosage. Since the study is retrospective and some data are not available (especially concerning the reason to discontinue salbutamol), its effect on prolongation of pregnancy needs further investigation.

Magowan et al.[4] reported perinatal mortality rate as 41/1000 livebirth of Scottish preterm births. In our experience we found no perinatal and neonatal death in three years. However three neonates of one quadruplet woman dead from remote from term during the same period.

The incidence of respiratory distress syndrome in these preterm neonate was as high as in the previous reports of Owen et al.[5] (17.4 %) and Wigton et al.[6] (19.5 %). In contrast Hastwell et al.[1,7] reported only 4.1% RDS in premature labor treated with salbutamol as a result of effectively prolonged pregnancy.

As in previous studies the most frequent neonatal complications did not differ from general premature neonates. Hyperbilirubinemia was found in more than half of the cases. Hypoglycemia and hypothermia[1] often occured also. We found a very high incidence of NICU admission in our study due to the complications of prematurity especially RDS, IVH and NEC.

Salbutamol is an effective tocolytic agent for delaying delivery during corticosteroid administration. Its advantages are simplicity and good compliance. As there are several confounding factors in this study, its effect on prolongation of pregnancy and neonatal outcome were inconclusive. Although the data concerning delaying delivery for more than 48 hours is encouraging, a prospective study is warranted.

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