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A study of efficacy of Turbutaline in inhibition of labour and Glucocorticoid therapy for the improvement of the lungs of the new born in preterm premature rupture of the membranes at Sawanpracharak Hospital

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- Objective** : *To study the results of treatments in premature rupture of the membranes in preterm labour.*
- Setting** : *The labour room, Department of Obstetrics and Gynecology, Sawanpracharak Hospital.*
- Design** : *Descriptive study.*
- Subject** : *Preterm pregnant woman with premature rupture of the membranes (PROM) in the labour room of the Department of Obstetrics. Sawanpracharak Hospital from January 2004 to April 2008.*
- Method** : *A retrospective study of preterm pregnant women with premature rupture of the membranes with gestational age of 20 - 36 weeks, primigravida and multigravida in 15 - 44 years old who had no medical and obstetrics underlying. no contraindication for inhibition of the labour, and no history of trauma. After confirmation of the premature rupture of the membranes and confirmation of the gestational age by ultrasound. The patient would be admitted into the labour room. After the patient is put on bed rest and a sedative drug would be injected intramuscularly. Turbutaline (bricanyl) was then given intravenous as well as intramuscular steroid therapy.*

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Results : *The patients went on labour within 48 hours with 82.90 percent rate. Average time for inhibit of labour was approximately 1.14 ± 1.7 days. According to the procedure of treatment in cases of premature rupture of the membranes in preterm labour. We found that the effectiveness of the treatment depended on gestational age. Moreover, neither maternal age nor parity had any statistic significance in relationship to the incidence.*

Conclusion : *Most cases of PROM went into labour within 24 hours. Delay or inhibition of the labour at least 48 hours or more, it had benefit in the decrease of respiratory distress syndrome (RDS) in newborns.*

Keywords : *Preterm labour, Premature rupture of the membranes, Respiratory distress syndrome.*

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อรรถกฤต นิตินาวรัตน์. ประสิทธิภาพของ Turbutaline ในการยับยั้งการคลอตร่วมกับ Glucocorticoid therapy เพื่อกระตุ้นการทำงานของปอดของทารกที่มีภาวะถุงน้ำคร่ำแตกในอายุครรภ์ไม่ครบกำหนดในโรงพยาบาลสวรรค์ประชารักษ์. จุฬาลงกรณ์เวชสาร 2551 พ.ย. - ธ.ค.; 52(6): 447 - 56

- วัตถุประสงค์** : ศึกษาผลการรักษาหญิงมีครรภ์ที่มีภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอด ในอายุครรภ์ที่ไม่ครบกำหนด
- สถานที่ศึกษา** : ห้องคลอดกลุ่มงานสูติ-นรีเวชกรรม โรงพยาบาลสวรรค์ประชารักษ์
- รูปแบบการวิจัย** : การวิจัยเชิงพรรณนา
- กลุ่มตัวอย่าง** : ผู้ป่วยที่มาคลอดที่โรงพยาบาลสวรรค์ประชารักษ์ ตั้งแต่ มกราคม 2547 - เมษายน 2551 ที่มีอายุครรภ์ ไม่ครบกำหนดร่วมกับมีภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอด จำนวน 158 คน
- วิธีการศึกษา** : เป็นการศึกษาย้อนหลัง จากแบบบันทึกข้อมูลผู้ป่วยที่มาคลอดที่ห้องคลอดกลุ่มงานสูติ-นรีเวชกรรม โรงพยาบาลสวรรค์ประชารักษ์ ตั้งแต่ มกราคม 2547 - เมษายน 2551 ที่มีอายุครรภ์ตั้งแต่ 20 - 36 สัปดาห์ มีภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอด ไม่มีภาวะแทรกซ้อนทั้งทางอายุรศาสตร์และสูติศาสตร์ ไม่มีประวัติได้รับการบาดเจ็บหรือภัยอันตรายใด ๆ มีอายุตั้งแต่ 15 - 44 ปี ทั้งครรภ์แรกและครรภ์หลัง หลังจากการตรวจพิสูจน์ทราบว่ามีถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอดและยืนยันอายุครรภ์ โดยการตรวจ Ultrasound แล้วผู้ป่วยทุกราย จะได้รับการนอนพักรักษาในห้องคลอดร่วมกับการให้ยา sedative รวมทั้งจะได้รับยา Turbutaline (bricanyl) เพื่อยับยั้งการคลอต ในขณะเดียวกันก็จะได้รับยา glucocorticoid เพื่อเป็นการกระตุ้นการทำงานของปอดของทารก
- ผลการศึกษา** : ผู้ป่วยมีการคลอตภายใน 48 ชั่วโมง ร้อยละ 82.90 ระยะเวลายับยั้งหรือชะลอการคลอต เฉลี่ย 1.14 ± 1.7 วัน โดยผลของการยับยั้งหรือชะลอการคลอต ในผู้ป่วยที่มีอายุครรภ์ ไม่ครบกำหนด และมีภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์ขึ้นกับอายุครรภ์ในขณะนั้น อายุมารดาหรือจำนวนการตั้งครรภ์ไม่มีความแตกต่างกันทางสถิติ จากการศึกษาในครั้งนี้

วิจารณ์และสรุป : ผู้ป่วยที่มีภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอด ส่วนใหญ่จะคลอดภายใน 24 ชั่วโมง ทั้งในอายุครรภ์ที่ครบและไม่ครบกำหนด การยับยั้งหรือชะลอการคลอดให้ได้อย่างน้อย 48 ชั่วโมงหรือมากกว่าในผู้ป่วยที่อายุครรภ์ยังไม่ครบกำหนด จะช่วยลดภาวะการหายใจลำบากในทารกแรกเกิดได้ (RDS)

คำสำคัญ : การคลอดก่อนกำหนดที่มีอายุครรภ์ ไม่ครบ 37 สัปดาห์, ภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอด, การหายใจลำบากของทารกแรกเกิด

The incidence of premature rupture of the membranes is about 10 percent in overall normal labours. Nevertheless, there is about 0.7–2.0 percent that can occur in the preterm period. The situation is hazardous to both the mother and the fetus. Preterm labour imposes a significant morbidity and mortality on newborns ^(1,2) Most obstetricians have tried conservative treatments to delay or inhibit the labour. because the longer the gestational age is prolonged the less morbidity and mortality of the fetus has. There are strong evidences that a premature newborn has a greater chance to develop a number of complications such as respiratory distress syndrome (RDS), necrotizing enterocolitis and intraventricular hemorrhage. ^(3,4) The aim of conservative treatment is to delay or inhibit the labour for at least 48 hours or longer. This should result in higher benefit to both the mother and her fetus. Because steroid treatment in the mother will improve the overall organ functions of the fetus especially the lung function, this will also normally decrease the rate of RDS. ^(1, 3, 5)

The Department of Obstetrics and Gynecology of Sawanpracharak Hospital had the protocol of treatment : absolute bedrest and sedation by Meperidine (pethidine) 50 mg. plus Diazepam (valium) 10 mg. was injected intramuscularly. Turbutaline was given intravenous 10 microgram/min the dose of Turbutaline can be adjusted according to the uterine contraction but not more than 40 microgram/min as long as the side effect did not occur. Glucocorticoid was administered intramuscularly, dexamethasone 6 mg every 12 hours, 4 time. Avoiding unnecessary digital cervical examination. If the patient developed strong uterine contraction or cervical dilatation more than 4 cm, effacement more than

80% Turbutaline would be completely taken off. After confirmation of the premature rupture of the membranes and confirmation of the gestational age by ultrasound, the patient would be admitted into the labour room and then routine laboratory testings would be performed. After the patient is put on bed rest and a sedative drug would be injected intramuscularly, Turbutaline was then given intravenous as well as intramuscular steroid (dexamethasone) therapy. However, there has been no study on the result of this protocol. Therefore the author would like to find the connection between the treatment and morbidity and mortality rate in both the mother and the newborn.

At present, obstetricians and pediatricians believe that the delay or inhibition of labour in the preterm period is the goal to pursue, given that there is no further complication. It has obviously decreased the incidence of RDS. ^(3,6) According to most experts administration of antenatal corticosteroids are responsible for much of this decrease. ⁽³⁾

Material and Method

The author used retrospective descriptive study from the data collected at the Department of Obstetrics and Gynecology of Sawanpracharak Hospital. One hundred and fifty-eight preterm patients with premature rupture of the membranes came to the labour room from January 2004 to April 2008. Our records showed that their age were from 15 - 44 years old, the gestational age, 20 - 36 weeks which included primigravida and multigravida. The mean of maternal age was 24.5 ± 7.6 years old, 33.2 ± 2.6 weeks of gestational age, 96 (60.76 %) of primigravida and 62 (39.24 %) of multigravida (Table 1). The inclusion criteria of the subject in this

study are gestational age less than 37 weeks, with premature rupture of the membranes. Primigravida and multigravida, vertex presentation. No evident of infection at the time of premature rupture of the membranes. No medical or Obstetric underlying, no genetic underlying, no history of trauma. No contraindication for inhibit of labour and not in active phase of labour, The condition of the cervical dilatation of less than 3 cm with effacement less than 80%.

Every patient under these criteria who were proved to have premature rupture of the membranes by the doctor in charge was recruited. Sterile speculum exam was then performed to access the condition of the cervix. In the case of suspected PROM an examination of discharge from vagina by nitrazine paper would be conducted.^(3,4) Among the subject under these criteria, also the result of laboratory investigations indicated the normal limit and anti HIV negative. The condition of the cervical dilatation of less than 3 cm with effacement less than 80%. Additional every patient had no contraindication for inhibit of labour and not in active phase of labour.^(3,4)

When PROM was confirmed and the gestational age by ultrasound showed no obvious cause of PROM. The patient would be admitted into the labour room and the routine laboratory investigation was then administrated as well as the vital signs were checked. The same procedure was conducted for every patient as follow : Bed rest and sedation by Meperidine 50 mg plus Diazepam 10 mg was injected intramuscularly. Turbutaline was given intravenous 10 microgram/min for not more than 40 microgram/min. The dose of Turbutaline can be adjusted according to the uterine contraction. It was believed that Turbutaline affects uterine contraction but with out any teratogenic effect to the fetus. Turbutaline could be given as long as the side effect did

not occur.⁽⁷⁻¹²⁾

Every patient was closely observed : their vital signs and fetal heart sound were monitored every 30 min and uterine contraction every 60 min. If there was any sign of side effect of Turbutaline such as maternal heart rate more than 140/min or tremor, the dose of Turbutaline would be decrease. If the patient developed strong uterine contraction or cervical dilatation more than 4 cm, effacement more than 80 % Turbutaline would be completely taken off. Also during the procedure, steroid was administered to the patient, dexamethasone 6 mg every 12 hours, 4 time, for the improvement of the lungs of the newborn⁽⁶⁾

Result

There were 158 patients who fulfilled the criteria for this treatment procedure. The mean maternal age was 24.5 ± 7.6 years old, with 33.2 ± 2.6 weeks mean of gestational age: 96 (60.76 %) were primigravida multigravida and 62 (39.24 %) multigravida (Table 1) This treatment procedure could delay or inhibit labour for 17.1 % for more than 48 hours .The rest delivered with in 48 hours. The study found that the mean time to delay or inhibit labour was 1.14 ± 1.7 days. (Table 2) Also the records showed that the time to delay or inhibit labour depended on gestational age. There was statistical significance (p-value = 0.026). The study showed no statistical significance in maternal age and parity i.e. p-value = 0.495 and 0.861 respectively. There were 4 fetal deaths in 158 deliveries. Nine newborns had Apgar score 4 - 7 at 1 minute, 141 newborn, 8 - 10 at 1 minute 150 newborn 8 - 10 at 5 minutes. The 4 fetal death were due to low gestational age 20 - 24 weeks (2 newborn) and the other two were less than 28 weeks .

Table 1. Detail of the subject.

Maternal age	Frequency	Percentage
15 - 19	50	31.6
20 - 24	40	25.3
25 - 29	33	20.9
30 - 34	15	9.5
35 - 39	15	9.5
40 - 44	5	3.2

Age distribution ($\bar{X} \pm SD$) 24.5 \pm 7.6 yrs. N = 158

Gestational age	Frequency	Percentage
20 - 24	2	1.3
25 - 28	7	4.4
29 - 32	38	24.0
33 - 36	111	70.3

Gestational age distribution 33.2 \pm 2.6 weeks. N = 158

Parity	Frequency	Percentage
Primigravida	96	60.76
Multigravida	62	39.24

Table 2. Time (day) around to delay or inhibit labour.

Day (s)	Frequency	Percentage
0 - 2 days (48 hrs)	131	82.9
3 days	10	6.3
4 days	9	5.8
5 days	4	2.6
6 days	1	0.6
7 days	1	0.6
8 days	1	0.6
9 days	1	0.6

Distribution of time to delay or inhibit labour ($\bar{X} \pm SD$) 1.14 \pm 1.7 days. N = 158

Table 3. Comparison between patient delivery within 48 hours with delivery more than 48 hours.

Detail of patient	Delivery \leq 48 hrs N = 131	Delivery \geq 48 hrs N = 27	P-value
Maternal mean age	24.3 \pm 7.7	25.4 \pm 7.1	0.495
Gestational mean age	33.4 \pm 2.6	32.2 \pm 2.1	0.026
Parity			
Primigravida	80 (83.3 %)	16 (16.7 %)	0.861
Multigravida	51 (82.3 %)	11(17.7 %)	

Discussion

Premature labour means the delivery of gestational age less than complete 37 weeks. It was accounted for 60 % of the fatality rate of the newborns. Furthermore, in the case of the newborns who survived the premature labour, they still had a risk of poor development for the brain and functions of other organs,^(3,4) especially the lungs. Respiratory distress syndrome (RDS) was often diagnosed in prematurely delivered infants which is one of the major problems in public health. Preterm neonates are more prone to infection morbidity respiratory and gastrointestinal compromise, and neurological deficits than their term counter parts⁽¹⁾ The causes of premature labour were partly from the mother herself such as poverty, and malnutrition. Smoking, drug abuse and alcohol consumption of the mother were also probable factors. Additionally, mother with medical underlying such as heart, kidney, thyroid disease^(1,3) or pregnancy complications such as pregnancy-induced hypertension, twin abruptio placenta or premature rupture of the membranes; all these conditions cause tendency to develop premature labour. However the exact cause was still unknown.⁽³⁾

Therefore, PROM in preterm patients posed a great risk to both the mother and her child because

the development of fatal chorioamnionitis. Infants who survived the premature labour had a high tendency to develop RDS (Respiratory distress syndrome) which is also fatal. Therefore the prevention of premature labour would greatly reduce the fatality rate for both the mother and the infant.⁽²⁾ At admission, 75 percent of the women were already in labour, 5 percent were delivered for other complications and another 10 percent were delivered following spontaneous labour within 48 hours. In only 7 percent were delivered delayed 48 hours or more after membranes rupture^(3,4) The study by this protocols showed that delay delivery more than 48 hours was about 17 percent

The exact cause of premature rupture of the membranes is still unknown. However patients with vagina and cervical infection, or obstetrics complication such as twins, abruption, placenta previa, had a high risk of premature rupture of the membranes. From the study, the author still could not pinpoint the exact cause of the phenomenon. However, strong evidence indicated that the delay or inhibit of young gestational age was more effective than the mature gestational age with exactly the same procedure. The study showed no significant difference between mother age and parity (Table 3). There were various

procedures to inhibit or prolong the labour such as bed rest together with sedative to lessen the patient anxiety, followed by administration of Turbutaline and steroid therapy. The study showed a decrease in fatality rate and RDS in newborns. There were 4 fetal deaths in this study due to young gestational age. The drug also has minimal side effect on the fetus (e.g., teratogenic effect). To reduce the risk of RDS, the author found that steroid therapy was effective.⁽⁷⁻¹²⁾ According to most experts administration of antenatal corticosteroids are responsible for much of this decrease.⁽³⁾ But it could also increase the infection rate in the mother and the child. The study showed 8 mother developed metritis (5 percent) and 13 newborns were infected (8.2%). Because of there is no antimicrobial therapy in this protocol. Once the infection was found, the pregnancy should be terminated as soon as possible.^(2,6) For prevention of group B streptococcal infection in the newborn, ampicillin 2 gm. is given intravenously every 6 hours when labour is subsequently diagnosed.⁽³⁾

Between the two groups of patients, one with the delay and complete administration of 48 hours steroid and the other with less delay with incomplete 48 hours steroid. The records showed that the latter had significant higher tendency to develop RDS. By the study of the author, he concluded that even the procedure was sometimes effective, it was not highly successful.

Conclusion

Labour could be inhibited through conservative treatments such as bed rest and sedation, as well as intravenous Turbutaline and

steroid therapy. The study found that the time to delay or inhibit labour depends only on gestational age, whereas maternal factors and parity have no statistical significance in relationship to PROM because most cases of PROM developed labour within 24 hours before labour.

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