The influence of preterm premature rupture of membranes on maternal and neonatal outcome

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Abstract

Introduction: The aim of the study was to evaluate the influence of the interval between preterm premature rupture of membranes (PPROM) and delivery on maternal and neonatal complications in cases of PPROM occurring at different gestational ages.

Material and methods: The study was conducted among 80 pregnant women with PPROM and their 85 newborns. Pregnant women were divided into two groups: 1) 46 patients with PPROM before 31 weeks gestation and 2) 34 women with PPROM at or after 31 weeks gestation. In each group, two subgroups of patients were formed: 1) patients with an interval between PPROM and delivery < 48 h and 2) patients with an interval between PPROM and delivery ≥ 48 h. Analysis of newborns concerned the frequency of various complications, including infections and complications of prematurity.

Results: The frequency of almost all neonatal complications, including infections, was significantly higher in children delivered by mothers with PPROM before 31 weeks gestation than in babies of patients with PPROM at or after 31 weeks gestation. After taking the time between PPROM and delivery into account, there was a significant increase of neonatal sepsis and pneumonia only in newborns born ≥ 48 h after PPROM which occurred before 31 weeks gestation.

Conclusions: The length of the interval between PPROM and delivery does not have a significant influence on the frequency of neonatal complications associated with prematurity but may slightly increase the risk of infection in newborns delivered after PPROM before 31 weeks gestation.

Key words: preterm premature rupture of membranes, complications, prematurity, infections, gestational age.

Introduction

Preterm premature rupture of membranes (PPROM) affects 5 to 10% of pregnant women and is responsible for around 30% of preterm deliveries. The diagnosis of PPROM is made by obtaining a history of leaking amniotic fluid, clinical assessment, including speculum examination, and laboratory tests such as nitrazine and fern tests [1]. Additionally, both ultrasound evaluation of amniotic fluid volume and assessment of vaginal pH may be helpful in diagnosis of PPROM [2].

In spite of the fact that the pathogenesis of PPROM has not been completely explored, there are some possible causes of this pathology of pregnancy, including infections of the lower genital tract, polyhydramnios, multiple pregnancies and iatrogenic factors. Neonatal outcome after PPROM mostly depends on gestational age at the time of delivery which, in turn, determines the likelihood of possible complications associated with prematurity. In the case of rupture of membranes before fetal viability, a very important prognostic factor is the interval between PPROM and delivery [3]. The most common complication of prematurity in newborns is respiratory distress syndrome (RDS). Other frequent diseases of premature neonates are: 1) infections, 2) necrotizing enterocolitis (NEC), 3) intraventricular haemorrhages (IVH), 4) retinopathy and 5) bronchopulmonary dysplasia (BPD).

The most common maternal complication of PPROM is intrauterine infection [2]. A less frequently observed complication of PPROM in mothers is placental abruption. A diagnosis of intrauterine infection requires presence of maternal fever (> 37.8°C) and two of the following pathological findings: 1) maternal tachycardia, 2) fetal tachycardia, 3) leucocytosis in the mother, 4) uterine tenderness or 5) foul-smelling amniotic fluid [4].

Management in cases of PPROM mainly depends on gestational age and maternal and fetal condition. The presence of an intrauterine infection is an indication for delivery. Induction of labour should be considered after 34 weeks gestation. Expectant management is popular before 34 weeks gestation. Tocolytics, steroids and antibiotics are recommended drugs in such cases [4, 5].

Expectant management in cases of PPROM allows the fetus to gain maturity but, at the same time, increases the risk of intrauterine infection, with all the consequences, for both the mother and the newborn.

The aim of the study was to evaluate the influence of the interval between PPROM and delivery on maternal and neonatal complications in cases of PPROM occurring at different gestational ages.

Material and methods

The study was conducted among 80 patients with PPROM and their 85 newborns. All pregnant women were hospitalized in the Division of Reproduction of the University of Medical Sciences in Poznan between 1999 and 2005. All neonates were patients of the Department of Neonatal Infectious Disease.

Patients with PPROM were divided into two groups according to the gestational age at the time of PPROM. The first group consisted of 46 patients with PPROM before 31 weeks gestation. Thirty-four pregnant women with PPROM, at or after 31 weeks gestation, formed the second studied group. In each group two subgroups of patients were formed: 1) patients with an interval between PPROM and delivery < 48 h, 2) patients with an interval between PPROM and delivery ≥ 48 h.

Only patients with PPROM diagnosed by visualization of amniotic fluid leakage during speculum examination were recruited. In all these patients the amount of amniotic fluid found in ultrasound examination was significantly reduced – amniotic fluid index (AFI) below 5 cm.

A single course of betamethasone (2 doses of 12 mg 24 h apart) was administered to most patients with an interval between PPROM and delivery ≥ 48 h and to less than half of the women who delivered less than 48 h after PPROM.

All patients received antibiotics (ampicillin and erythromycin) until the results of bacteriological examinations of vaginal secretions were obtained. If the results of bacteriological cultures were negative, antibiotics were not administered further. Positive results of culture indicated the need to continue treatment for at least 7 days. This regimen of antibiotic administration is in line with the recommendations of the Polish Society for Perinatal Medicine [5].

Tocolytics (β-sympathomimetics) were administered to all patients with PPROM, except in cases showing symptoms of intrauterine infection [4]. Firstly tocolytics were given intravenously for 48 h, then, if the patient remained undelivered, orally until 34 weeks gestation [5].

All pregnant women with PPROM were monitored for the presence of symptoms of intrauterine infection. Intrauterine infection was diagnosed in cases of fever (> 37.8°C) and in the presence of at least two of the following additional findings 1) maternal tachycardia (> 100 beats/min), 2) fetal tachycardia (> 160 beats/min), 3) leucocytosis in the mother (> 15,000/mm^3), 4) uterine tenderness, and 5) foul-smelling amniotic fluid [3].

Clinical analysis of all newborns from the studied groups concerned the frequency of the following complications: 1) infections, including sepsis, pneumonia, urinary tract infections and meningitis, 2) respiratory distress syndrome (RDS), 3) intraventricular haemorrhages (IVH), 4) necrotizing enterocolitis (NEC), 5) retinopathy of prematurity (ROP), or 6) bronchopulmonary dysplasia (BPD).

The Shapiro-Wilk test was used to analyze the character of distribution. For further evaluation of the variables between groups, the following tests were used: Mann-Whitney, Fisher, and Student's *t*-test. Statistical significance was accepted as being $p < 0.05$.

Results

The mean gestational ages at PPROM among women with PPROM before 31 weeks gestation and in patients with PPROM at or after 31 weeks were 27.1 (22-30) and 33.0 weeks (31-36), respectively.

The mean gestational age at delivery was 28.7 ±2.8 in the first group and 34.3 ±1.8 in the second. No significant difference was observed between these groups, in terms of the length of the interval between PPROM and delivery. The clinical characteristics of patients from both studied groups are presented in Table I.

The mean weight, at birth, of neonates delivered by mothers from the first group was 1287.0 ±532.1 g and from the second group 2221.1 ±496 g. The frequency of almost all neonatal complications, including sepsis, pneumonia, urinary tract infections and meningitis, was significantly higher among children from the first group than in neonates from the second group.

The incidence of neonatal death in the first group was 16%. Two babies died after delivery at 22 gestational week. These were spontaneous labours, which both occurred within 24 h after PPROM at 22 weeks. The cause of death in both cases was extreme immaturity. Another six neonatal deaths concerned newborns delivered at 27 weeks (n = 2), at 26 (n = 1), at 28 (n = 1), at 29 (n = 1) and at 32 weeks (n = 1). In all these cases except one, the cause of neonatal death was respiratory failure. The newborn delivered at 32 weeks gestation died because of sepsis. None of the newborns from the second studied group died. The clinical characteristics of newborns from both studied groups are presented in Table II.

Table I. Clinical characteristics of patients from two studied groups

Data	Group 1 (n = 46)	Group 2 (n = 34)	p
Age [years]	31.7 ±6.6	29.1 ±5.2	NS
Gestational age at PPROM [weeks]	27.1 ±2.2 (min 22, max 30)	33.0 ±1.6 (min 31, max 36)	< 0.00001
Interval from PPROM to delivery [days]	10.9 ±10.2 (min 1, max 56)	10.6 ±9.4 (min 1, max 35)	NS
Gestational age at delivery [weeks]	28.7 ±2.8 (min 22, max 37)	34.3 ±1.8 (min 31, max 38)	< 0.00001
WBC [g/l]	18.8 ±6.3	16.5 ±6.5	NS
CRP [mg/l]	29.0 ±22.2	18.1 ±15.9	NS
Intrauterine infection [%]	40	26	NS

Group 1 – PPROM before 31 weeks gestation, group 2 – PPROM at or after 31 weeks gestation
WBC – white blood cell count, CRP – C-reactive protein

Table II. Clinical characteristics of newborns from two studied groups

Data	Group 1 (n = 50)	Group 2 (n = 35)	p
Apgar score at 1' (median)	5	8	0.0002
Apgar score at 5' (median)	7	9	0.002
Birth weight [g]	1287 ±532.1	2221.14 ±496.0	< 0.0001
Percentage of newborns' death [%]	16	0	0.02
Pneumonia [%]	59	31	0.02
Sepsis [%]	12	0	0.038
Urinary tract infection [%]	14	6	NS
Meningitis [%]	2	0	NS
RDS (1st and 2nd degree) [%]	30	3	0.002
RDS (3rd and 4th degree) [%]	18	3	0.04
IVH (1st and 2nd degree) [%]	28	9	0.03
IVH (3rd and 4th degree) [%]	16	0	0.02
NEC [%]	4	3	NS
ROP [%]	32	3	0.004
BPD [%]	24	0	0.003
Intrauterine hypoxia [%]	15	0	0.03
Percentage of newborns needing ventilation [%]	76	29	< 0.0001
Percentage of newborns needing mechanical ventilation (% of ventilated newborns) [%]	62	20	0.03
Percentage of infants on nCPAP (% of ventilated newborns) [%]	38	80	0.03
Duration of ventilatory support [days]	13.13 ±17.74	1.27 ±1.48	< 0.0001
Administration of surfactant [%]	32	6	0.003
Leucocytosis [%]	55	37	NS
Leucopenia [%]	2	0	NS
Increase of CRP [%]	22	6	NS
Increase of I/T ratio [%]	12	9	NS
Hypoglycaemia [%]	6	17	NS
Hyperbilirubinaemia [%]	69	83	NS

Group 1 – PPROM before 31 weeks gestation, group 2 – PPROM at or after 31 weeks gestation
nCPAP – nasal continuous positive air pressure, CRP – C-reactive protein, I/T ratio – immature/total neutrophil ratio

After taking the time between PPROM and delivery into account (more or less than 48 h), no significant differences in the frequency of intrauterine infections between the two subgroups of mothers could be observed, either when analyzed in the group of women with PPROM before (Table III) or at and after 31 weeks gestation (Table IV).

With regards to the interval (more or less than 48 h) between PPROM and delivery in the group of newborns delivered after PPROM occurring before 31 weeks gestation, a significant difference was found in the frequency of neonatal sepsis, pneumonia, leucocytosis, the need for mechanical ventilation and the proportion of neonatal deaths (Table V). In this subgroup of neonates, pneumonia and sepsis were both found to occur more frequently in newborns delivered 48 h or more after PPROM than in neonates delivered before 48 h after PPROM. Both leucocytosis and the need for mechanical ventilation were also more frequently observed in this subgroup of newborns. The percentage of neonatal deaths was, however, significantly higher in neonates delivered before 48 h after PPROM than in children born 48 h or more after PPROM.

In the second group of children, born by mothers whose pregnancy was complicated by PPROM occurring at or after 31 weeks, no significant differences were found in the frequency of clinical complications (Table VI).

Discussion

Despite significant improvements in perinatal care, premature rupture of membranes remains a problem for obstetricians and, subsequently, for neonatologists. Management in cases of PPROM is

Table III. Clinical characteristics of mothers with PPROM before 31 weeks gestation considering interval between PPROM and delivery

Data	Delivery < 48 h after PPROM (n = 8)	Delivery ≥ 48 h after PPROM (n = 38)	p
Age [years]	36.7 ±7.3	31.2 ±6.5	NS
Gestational age at PPROM [weeks]	26.5 ±2.8 (min 22, max 30)	27.2 ±2.1 (min 23, max 30)	NS
Length of interval between PPROM and delivery [days]	1.7 ±0.5 (min 1, max 2)	12.9 ±10.2 (min 4, max 56)	< 0.001
Gestational age at delivery	26.7 ±2.9 (min 22, max 30)	29.2 ±2.6 (min 25, max 37)	0.014
Percentage of caesarean section [%]	56	54	NS
Administration of steroids [%]	44	80	0.04
WBC [g/l]	15.7 ±9.3	19.1 ±6.1	NS
CRP [mg/l]	32.2 ±15.7	28.2 ±23.8	NS
Intrauterine infection [%]	44	39	NS

WBC – white blood cell count, CRP – C-reactive protein

Table IV. Clinical characteristics of mothers with PPROM at or after 31 weeks gestation considering interval between PPROM and delivery

Data	Delivery < 48 h after PPROM (n = 8)	Delivery ≥ 48 h after PPROM (n = 26)	p
Age [years]	27.6 ±6.1	29.58 ±4.9	NS
Gestational age at PPROM [weeks]	32.5 ±1.2 (min 31, max 34)	33.8 ±1.7 (min 31, max 36)	NS
Length of interval between PPROM and delivery [days]	1.9 ±0.3 (min 1, max 2)	13.3 ±9.2 (min 4, max 35)	< 0.001
Gestational age at delivery	32.6 ±1.30 (min 31, max 34)	34.8 ±1.6 (min 32, max 38)	0.002
Percentage of caesarean section [%]	38	41	NS
Administration of steroids [%]	63	59	NS
WBC [g/l]	17.6 ±3.1	16.1 ±7.3	NS
Intrauterine infection [%]	38	41	NS

WBC – white blood cell count

Table V. Clinical characteristics of newborns born by mothers with PPROM before 31 weeks gestation considering interval between PPROM and delivery

Data	Delivery < 48 h after PPROM (n = 9)	Delivery ≥ 48 after PPROM (n = 41)	p
Apgar score at 1' (median)	4	5	0.0002
Apgar score at 5' (median)	6	7	0.002
Birth weight [g]	1051 ±404	1339 ±546	< 0.0001
Percentage of newborns' death [%]	22	15	0.02
Pneumonia [%]	56	60	0.02
Sepsis [%]	0	15	0.038
Urinary tract infection [%]	11	15	NS
Meningitis [%]	0	3	NS
RDS (1st and 2nd degree) [%]	11	34.15	NS
RDS (3rd and 4th degree) [%]	11	20	NS
IVH (1st and 2nd degree) [%]	22	30	NS
IVH (3rd and 4th degree) [%]	0	20	NS
NEC [%]	0	5	NS
ROP [%]	30	32	NS
BPD [%]	0	29	NS
Intrauterine hypoxia [%]	17	14	NS
Percentage of newborns needing ventilation [%]	44	83	0.026
Percentage of newborns needing mechanical ventilation (% of ventilated newborns) [%]	60	62	NS
Percentage of infants on nCPAP (% of ventilated newborns) [%]	40	38	NS
Duration of ventilatory support [days]	9.20 ±11.18	13.7 ±18.56	NS
Administration of surfactant [%]	22	34	NS
Leucocytosis [%]	22	63	0.059
Leucopenia [%]	0	3	NS
Increase of CRP [%]	11	25	NS
Increase of I/T ratio [%]	0	15	NS
Hypoglycaemia [%]	0	7	NS
Hyperbilirubinaemia [%]	56	73	NS

nCPAP – nasal continuous positive air pressure, CRP – C-reactive protein, I/T ratio – immature/total neutrophil ratio

Table VI. Clinical characteristics of newborns born by mothers with PPROM at or after 31 weeks gestation considering interval between PPROM and delivery

Data	Delivery < 48 h after PPROM (n = 8)	Delivery ≥ 48 after PPROM (n = 27)	p
Apgar score at 1' (median)	8	8	NS
Apgar score at 5' (median)	10	9	NS
Birth weight [g]	2098 ±469	2257 ±506	NS
Pneumonia [%]	25	33	NS
Sepsis [%]	0	0	NS
Urinary tract infection [%]	13	4	NS
Meningitis [%]	0	0	NS
RDS (1st and 2nd degree) [%]	0	4	NS
RDS (3rd and 4th degree) [%]	13	0	NS
IVH (1st and 2nd degree) [%]	0	4	NS
IVH (3rd and 4th degree) [%]	0	0	NS
NEC [%]	0	0	NS
ROP [%]	0	4	NS
BPD [%]	0	0	NS
Intrauterine hypoxia [%]	0	0	NS
Percentage of newborns needing ventilation [%]	13	33	NS
Percentage of newborns needing mechanical ventilation (% of ventilated newborns) [%]	0	22	NS
Percentage of infants on nCPAP (% of ventilated newborns) [%]	100	88	NS
Administration of surfactant [%]	25	0	0.047
Leucocytosis [%]	25	41	NS
Leucopenia [%]	0	0	NS
Increase of CRP [%]	0	7	NS
Increase of I/T ratio [%]	0	11	NS
Hypoglycaemia [%]	0	22	NS
Hyperbilirubinaemia [%]	75	85	NS

nCPAP – nasal continuous positive air pressure, CRP – C-reactive protein, I/T ratio – immature/total neutrophil ratio

focused both on the prolongation of pregnancy and on the avoidance of intrauterine infection [6].

Tanir *et al*. [7] compared the frequencies of complications (maternal, fetal or neonatal) in cases of preterm delivery associated with PPROM to spontaneous preterm delivery. The incidence of intrauterine infection found in that study was 25% in patients with PPROM and 2% in mothers with spontaneous preterm labour. In our study, the frequency of intrauterine infection was 40% in patients with PPROM before 31 weeks gestation and 25% in patients with PPROM at or after 31 gestational weeks. A much smaller proportion of intrauterine infections (13%) was noted by Spinillo *et al*. [8] among patients with PPROM, occurring between 24 and 31 weeks gestation.

A correlation between the interval from PPROM to delivery, and the incidence of intrauterine infections among pregnant women, was found by Cox *et al*. [9]. The authors showed an almost 10-fold increase in the frequency of intrauterine infection in mothers who delivered after a mean time of 72 h from PPROM in comparison to patients in whom the mean interval from PPROM to delivery was 16 h. Surprisingly, we did not find such correlations in our study. This lack of correlation between the incidence of intrauterine infections in mothers, and the interval between PPROM and delivery, concerned both studied groups of patients, those before 31 weeks gestation and those at or after 31 gestational weeks. Our finding may indicate the need for proper monitoring of the signs of intrauterine infection in patients with PPROM, as well as the need for immediate delivery in cases concerning the occurrence of early clinical symptoms of infection, or pathological laboratory findings.

Considering the influence of PPROM on neonatal mortality and morbidity, we found a significant relationship between the length of the interval between the rupture of membranes and delivery on the incidence of neonatal infection, though only in newborns born after PPROM occurring before 31 weeks of gestation. No such correlation was seen among neonates delivered by mothers in whom PPROM had occurred at or after 31 weeks.

Similar results concerning the frequency of neonatal infections, in newborns born to mothers who were managed conservatively after PPROM at 30-34 weeks gestation, were found by Cox *et al*. [9]. The authors of the study found no difference in the incidence of infections amongst neonates born up to 48 h after PPROM in comparison to newborns delivered more than 48 h after PPROM. However, the authors did not evaluate the influence of the length of the interval between PPROM and delivery on the incidence of neonatal infections when PPROM occurred earlier than 30 weeks gestational age.

Analyzing the eventual benefits of delaying the onset of labour by expectant management in cases of PPROM, we observed no significant decrease in the incidence of RDS, IVH or NEC in neonates born at or more than 48 h after PPROM in comparison to newborns delivered before 48 h after PPROM. This tendency concerned both analyzed groups. The only positive influence of the length of the interval between PPROM and delivery concerned the incidence of perinatal death, which was reduced in newborns delivered at or more than 48 h after PPROM, occurring before 31 weeks gestation. The results of our study are consistent with the data published by Cox *et al*. [9], who also showed no advantages from expectant management of PPROM at 30-34 weeks' gestation, on neonatal outcome, including the incidence of IVH, NEC, RDS and perinatal death.

Considering the incidence of different neonatal complications, except infections, we found that the gestational age at delivery, though not rupture of the membranes alone or the interval between the PPROM and delivery, was the most important factor influencing neonatal outcome. This is consistent with the results of a study by Tanir *et al*. [7], which found neither significantly higher numbers of RDS, perinatal asphyxia or neonatal death, or a higher incidence of sepsis in babies delivered before 34 weeks gestation after PPROM in comparison to neonates delivered preterm but not as a consequence of PPROM.

An analysis of maternal and neonatal morbidity in pregnancies complicated by PPROM allows us to reflect on the optimal timing of delivery in such cases. According to Matteson [10] the optimal gestational age at the time of delivery in cases of PPROM should be at least 33 weeks. However, Mercer [6] regards 32 weeks gestation as the age at which both decreases in complications associated with prematurity and increases in intrauterine infection after PPROM may be observed. In our material, and contrary to the study of Mercer [6], we found a higher frequency of intrauterine infections in patients with conservative management of PPROM at or after 31 weeks in comparison to women with PPROM which occurred earlier in pregnancy.

The results of our study lead us to doubt the sense of accepted, but still controversial, conservative management in cases of PPROM occurring before 34 weeks gestation. Controversies especially concern cases of PPROM at or after 31 (32) weeks gestation in which a delay of labour is often not associated with a decrease in neonatal complications of prematurity. Expectant management is potentially more beneficial for newborns in cases of PPROM which occur before 31 (30) weeks gestation, though the reduction in the incidence of some complications, including

perinatal death, may also be associated with an increase in the frequency of severe neonatal infections.

The results of this study underline the significance of precise monitoring of both the mother and the fetus with regards to possible signs of infection, as well as reasonable antibiotic therapy and proper timing of delivery as being the most important elements of expectant management in patients with PPROM.

In conclusion, because of the fact that delivery occurs within 7 days of PPROM in over 80% of cases, the most important factor which influences the frequency of all neonatal complications is gestational age at the time of PPROM. This concerns not only neonatal complications associated with prematurity, but also infections including sepsis and pneumonia, which occur more frequently in babies delivered after PPROM occurring before 31 weeks gestation.

The length of the interval between PPROM and delivery does not have a significant influence on reduction of neonatal complications associated with prematurity but may slightly increase the risk of neonatal infections in babies delivered after PPROM occurring before 31 weeks gestation.

Reasonable antibiotic treatment, precise monitoring of early signs of intrauterine infection and proper timing of delivery seem to be crucial in the effective limitation of increased risks of infection associated with the delay of labour in cases of PPROM.

References

1. Canavan TP, Simhan HN, Caritis S. An evidence – based approach to the evaluation and treatment of premature rupture of membranes, part I. Obstet Gynecol Surv 2004; 59: 669-77.
2. Oszukowski P, Pięta-Dolińska A. Premature rupture of membranes [Polish]. In: Bręborowicz GH (ed.) Obstetrics and Gynecology. PZWL, Warszawa 2005; 2: 178-82.
3. Scott JR, Di Saia PJ, Hammond SB, Spellacy WN. Danforth, Danforth's Obstetrics and Gynecology, 9th ed. Lippincott Williams & Wilkins Publishers. Philadelphia 2003.
4. Drews K, Pieńkowski W. Correlation between ascending vertical infection and premature labor [Polish]. In: Bręborowicz GH, Paszkowski T (eds). Premature labor. Ośrodek Wydawnictw Naukowych, Poznań 2006; 79-94.
5. Skrzypczak J, Bręborowicz GH. Premature rupture of membranes – recommendations [Polish]. Klin Perinat Ginek 2003; 39: 76-8.
6. Mercer BM. Preterm premature ruptrure of the membranes. Obstet Gynecol 2003; 101: 178-93.
7. Tanir HM, Sener T, Tekin N, Aksit A, Ardic N. Preterm premature rupture of membranes and neonatal outcome prior to 34 weeks of gestation. Int J Gynaecol Obstet 2003; 82: 167-72.
8. Spinillo A, Montanari L, Sanpaolo P, Bergante C, Chiara A, Fazzi E. Fetal growth and infant neurodevelopmental outcome after preterm premature rupture of membranes. Obstet Gynecol 2004; 103: 1286-93.
9. Cox SM, Leveno KJ. Intentional delivery versus expectant management with preterm ruptured membranes at 30-34 weeks' gestation. Obstet Gynecol 1995; 86: 875-9.
10. Matteson JJ, Ramsey PS, Brumfield CG, Carlo W. Preterm premature rupture of membranes: is there an optimal delivery gestational age? Obstet Gynecol 2002; 4 (Suppl): 74-5.