AICOG 2025
Mumbai
67th All India Congress of Obstetrics & Gynaecology
FOGSI celebrates 75 years - Diamond Jubliee
8-12 January, 2025 | JIO World Convention Centre

Poster Number: EP 081 Name: **Dr. POOJA GUPTA**, Professor, Dept Of Obstetrics & Gynecology, Dr. Ram Manohar Lohia Institute Of Medical Sciences, Lucknow

Title: A COMPARISON OF ANTIBIOTIC REGIMENS IN THE TREATMENT OF PRETERM PREMATURE RUPTURE OF MEMBRANES

Introduction: Rupture of amniotic membranes before labor that occurs before 37 weeks of gestation is referred to as "Preterm Prelabor Rupture Of Membranes" (PPROM). Preterm PROM complicates 3 percent of pregnancies whereas, at term, PROM complicates approximately 8% of pregnancies which is usually followed by spontaneous labor and delivery (1). To reduce maternal and neonatal infections during expectant management of women with PPROM, the substitution of azithromycin for erythromycin is a suitable alternative antibiotic regimen secondary to its ease of administration, better side effect profile, and decreased cost.

Materials and Methods: The study was carried out in the Department of Obstetrics and Gynecology, Dr. RMLIMS, Lucknow after getting ethical clearance from the Institute's Ethical Committee. It will be a single-center, prospective observational cohort study. Pregnant women with singleton, between 24 0/7 to 36 0/7 weeks of gestation presenting with PPROM were included in the study. The Erythromycin group consisted of erythromycin 250 mg and ampicillin 2 g every 6 hours IV for 48 hours followed by amoxicillin 250 mg and erythromycin 333 mg every 8 hours PO for 5 days (7 Days total). The azithromycin group consisted of azithromycin 1 g PO once. Patients were followed till delivery. The specific antibiotic regimen, including which macrolide was used and the duration, timing, and route of administration, was recorded. The primary outcome was to evaluate the latency from diagnosis of rupture of membranes to delivery and development of chorioamnionitis assessed clinically or biochemically using TLC, CRP, urine and high vaginal swab cultures and the secondary outcome was to evaluate the fetomaternal outcomes in terms of the need for cesarean delivery, postpartum sepsis, and neonatal morbidity in terms of low APGAR score, need of resuscitation at the time of delivery, NICU admissions and need of intravenous antibiotics for neonatal sepsis in case of positive blood culture. Statistical methods The SPSS (Version 26.0) program was used for statistical analysis.

Result: 394 patients who met inclusion criteria were identified. 197 study participants received an erythromycin-based antibiotic regimen in the first half of the study and the remaining 197 received an Azithromycin-based regimen in the second half of the study. There was no statistical difference in the primary outcome of latency to delivery. Unadjusted median time from PPROM to delivery was 9 days for the azithromycin group and 7 days for erythromycin (P = .98). The clinical rates of chorioamnionitis was seen in 50 pregnant women of Group 1 and 33 pregnant women of Group2 and this difference was statistically significant (p value=0.04).

Our study shows no difference in the primary outcome of latency until delivery when comparing single-dose azithromycin with standard erythromycin however clinical rates of chorioamnionitis were significantly lower in the Azithromycin Group.

Table 1 - Maternal demographics

	GROUP 1 (ERYTHROMYCIN)	GROUP 2 (AZITHROMYCIN)	P-value
NO OF PATIENTS ENROLLED	197 (N1=197)	7 (N2=197)	
MATERNAL AGE (YEARS)	31± 0.5(20-39)	29.8 ± 5.8	.40
NULLIPAROUS	71(36.4)	79(40.3)	.85
GESTATIONAL AGE AT DIAGNOSIS/ RUPTURE (WEEKS) ±2SD	32.9±1.76 -34.7± 1.08	31.6 ± 3.2-34.1-2.17	.38
RANGE OF GESTATIONAL AGE AT DIAGNOSIS OF RUPTURE (WEEKS)	(24-36/7)	(24-36/7)	
BMI (Kg/m2)	27.8±5.1(21-35.9)	25.4±4.1(21-35.9)	0.30
GDM	35(17.77)	37(18.78)	0.15
HYPERTENSION	29(14.72)	25(12.6)	0.40
IHCP	19(9.64)	18(9.13)	0.16
HYPOTHYROIDISM	17(8.63)	19(9.6)	0.55
DEXAMETHASONE	171(86.80)	165(84)	0.46
NEUROPROTECTION MGSO4	55(27.92)	50(25.38)	0.17

Table 2 - Prolongation of pregnancy latency period and prevalence rates of chorioamnionitis

NO OF PATIENT ENROLLED	197 (N1=197)	7 (N2=197)	
CLINICAL CHORIOAMNIONITIS	50(25.8)	33(16.7)	0.04
TLC (c/mm)	25,000 (18,000-35,000)	16,000 (9,000-20,000)	0.03
hsCRP (mg/dl)	19 (15-45)	15(5-35)	0.04
LATENCY INTERVAL(days) RANGE	7 (5-45)	9 (6-20)	0.98

Table 3- Delivery data

GA AT DELIVERY (weeks)	35.2± 3.3	35.6± 3.1	0.87
CESAREAN DELIVERY	76 (38.57)	79 (40.3)	0.45
BIRTH WEIGHT	1800±250	2100±179	0.55
5 MIN APGAR<7	40(20.30)	21(10.6)	0.002
NEONATAL SEPSIS	38(19.2)	28(14.2)	<0.001
POSTPARTUM ENDOMETRITIS	21(10.65)	18(9.13)	0.07

Discussion: Daniel Martingano et al 2020 study suggests that latency antibiotic regimens substituting azithromycin for erythromycin have lower rates and decreased risk of clinical chorioamnionitis, neonatal sepsis, and postpartum endometritis with no difference in pregnancy latency in PPROM(2). Finneran et al 2020 study concluded that there is no difference in latency to delivery when a single oral dose of azithromycin 1g is substituted for erythromycin used in PPROM as evidenced by our study as well (3).

The spectrum of microbial coverage of azithromycin is similar to erythromycin, but the pharmacokinetic properties are different. Azithromycin has a significantly longer half-life of approximately 3 days compared with 1.6 for erythromycin. Additionally, because of nationwide shortages of IV erythromycin, many institutions have advocated for the use of azithromycin instead of erythromycin. This may represent an opportunity for health system cost savings because of lower cost of azithromycin compared with erythromycin. The ORACLE trial showed that the macrolide component of treatment improved neonatal outcomes not just by increasing latency but also by specifically reducing fetal exposure to intrauterine infection and inflammation (4).

Conclusion: Patients with PPROM who are treated with azithromycin have similar latency periods but lower rates of clinical chorioamnionitis when compared to those treated with erythromycin. We speculate this may be due to azithromycin's longer half-life, higher tissue concentration, and increased activity against enteric pathogens such as E. coli. Secondary to national shortages of erythromycin, ease of administration, better side effect profile, and decreased cost of azithromycin compared with erythromycin, Azithromycin could be considered as an alternative to erythromycin (as also stated on ACOG 2020 update) in the expectant management of Preterm Premature Rupture Of Membranes if erythromycin is unavailable or contraindicated.

References:

1-Middleton P, Shepherd E, Flenady V, McBain RD, Crowther CA. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more). Cochrane Database of Systematic Review 2017, Issue 1. Art. No.: CD005302. (Systematic Review and Meta-Analysis)

2- Martingano D, Singh S, Mitrofanova A. Azithromycin in the Treatment of Preterm Prelabor Rupture of Membranes Demonstrates a Lower Risk of Chorioamnionitis and Postpartum Endometritis with an Equivalent Latency Period Compared with Erythromycin Antibiotic Regimens. Infect Dis Obstet Gynecol. 2020 Jul 9;2020:2093530. doi: 10.1155/2020/2093530. PMID: 32694907; PMCID: PMC7368187.

3 - Matthew M. Finneran, Ashley Appiagyei, Megan Templin, Heather Mertz. Comparison of Azithromycin versus Erythromycin for Prolongation of Latency in Pregnancies Complicated by Preterm Premature Rupture of MembranesAm J Perinatol 2017; 34(11): 1102-1107, DOI: 10.1055/s-0037-1603915

4 -Kenyon S.L.,Taylor D.J.,Tarnow-Mordi W,ORACLE Collaborative Group Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. ORACLE Collaborative Group.*Lancet*. 2001; 357: 979-988