**Abstract**

Although the use of broad-spectrum antibiotics in women with preterm premature rupture of membranes (PPROM) is recommended to prolong pregnancy and decrease short-term neonatal complications, the optimal regimen remains undetermined. The objective of this study was to compare the efficacy of cefazolin plus macrolide (erythromycin or clarithromycin) versus cefazolin alone in reducing neonatal morbidity and placental inflammation for women with PPROM. This prospective study included singleton pregnancies with PPROM (23-33 weeks gestation). The primary outcome was neonatal composite morbidity and the secondary outcomes were the incidence of abnormal brain sonography and infant neurological outcome at one year of age. The presence and the stage of acute histological chorioamnionitis and funisitis were also reviewed blinded to all clinical information. 120 women were randomly assigned to cefazolin (n = 40), cefazolin plus erythromycin (n = 40), or cefazolin plus clarithromycin (n = 40). The neonatal composite morbidity, the incidence of abnormal brain sonography, and infant neurological outcome at one year of age were similar between the comparison treatments (combination of cefazolin plus erythromycin or clarithromycin) and cefazolin. However, the presence and stage of histological funisitis showed significant difference between cefazolin plus clarithromycin versus cefazolin alone (p = 0.314). This study is the first clinical trial of the use of cefazolin with either clarithromycin or erythromycin compared to cefazolin alone in the management of PPROM in which the primary and secondary analyses showed no difference among the three antibiotic regimens. The only noted difference was from a lesser degree of histological funisitis associated with clarithromycin exposure. Our data suggests that clarithromycin may be an alternative worth considering with potentially beneficial effects compared to erythromycin in PPROM.

**Keywords:** Cefazolin, Clarithromycin, Placental Inflammation, Preterm Premature

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