CHAPTER 4
RESULTS OF THE STUDY

4.1 Characteristics of the study population

There were 46 preterm infants enrolled into the study; 23 infants in each group. Almost all infants were less than 32 weeks of gestation, except 4 infants (2 in each group). Baseline characteristics were similar between the two groups as shown in table 3. Respiratory status as indicated by fractional inspiratory oxygen concentration (FiO_2) was similar, most of the infants were in room air or low oxygen supplement at time of enrollment. Age at enrollment was approximately one week of age after stable clinical condition. Factors effecting feeding tolerability; e.g. perinatal asphyxia (low Apgar score), prenatal steroid, PDA, umbilical artery catheterization, and breast milk were not statistically different between the two groups.

Table 3. Baseline characteristics of the study infants

Characteristics	Erythromycin n = 23 median (IQR)	Placebo n = 23 median (IQR)
Birth weight (g)	1100 (870, 1500)	1065 (940, 1270)
Gestational age (wk)	30 (29, 32)	29 (28, 31)
Small for gestational age [n,(%)]	7 (30)	3 (13)
Male gender [n,(%)]	9 (39)	13 (56)
Apgar score at 1 min.	6 (3, 8)	7 (4, 9)
Apgar score at 5 min.	8 (6, 9)	9 (8, 10)
FiO_2 at enrollment	0.21 (0.21, 0.30)	0.21 (0.21, 0.30)
Age at enrollment (day)	7 (6, 8)	6 (6, 8)
Prenatal steroid [n,(%)]	15 (65)	17 (74)
Presence of PDA [n,(%)]	12 (52)	17 (73)
Indomethacin use [n,(%)]	11 (48)	14 (61)
Presence of umbilical catheter [n,(%)]	15 (65)	19 (82)
Duration of umbilical catheter (day)	7 (6, 8)	8 (6, 10)
Breast milk [n,(%)]	9 (39)	4 (17)
Volume of feeding at enrollment (ml/kg/day)	25 (9, 40)	15 (7, 31)

4.2 Time to full feeding after enrollment

Time to full feeding after enrollment was significantly shorter in erythromycin group with a median of 7 days compared to a median of 13 days in placebo group with p value < 0.001(table 4). Fifty percent of infants in erythromycin group reached full feeding in one week after treatment and all of them achieved within two weeks, whereas only half of infants in placebo were able to achieve during the same period (figure 3). The effect of erythromycin demonstrated even analyzed separately according to age strata (<32 weeks, and ≥ 32 weeks) as shown in figure 4.

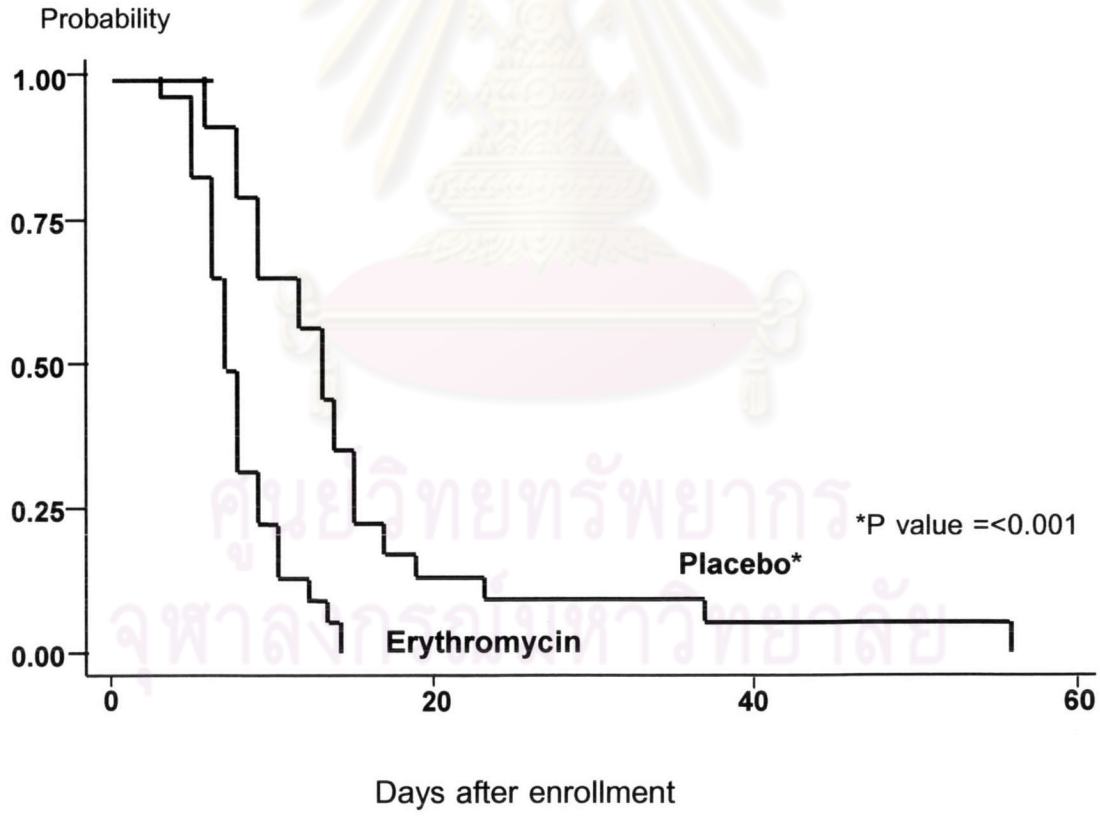

Figure 3. Kaplan-Meier Survival Curve by group of treatment

* Log-rank test significant p value < 0.05

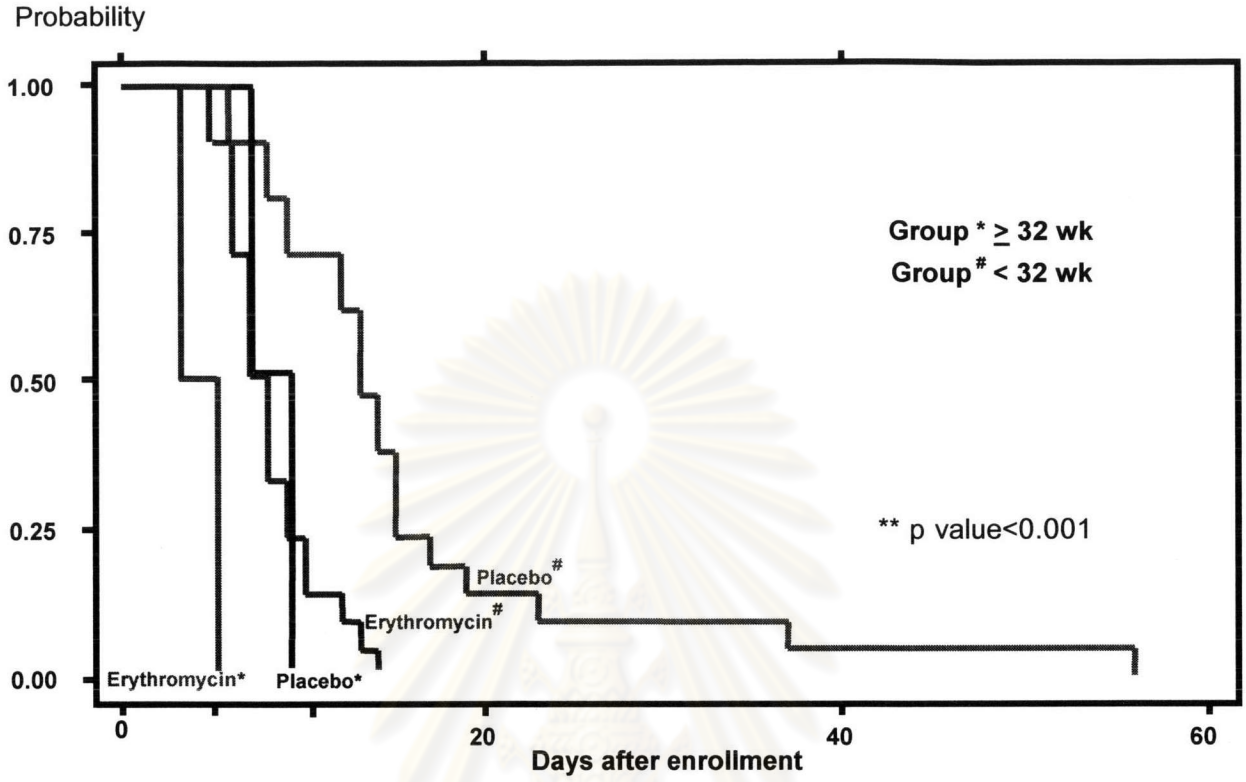

Figure 4. Kaplan-Meier Survival Curve by age strata and treatment group

** Log-rank test significant p value < 0.05 in infants less than 32 weeks

4.3 Secondary outcomes

Duration of parenteral nutrition, and numbers of holding feeds or significant gastric residuals (> 50% of feeding volume) were significantly less in erythromycin group than that of placebo group (table 4). There was a trend of shorter length of hospital stay in erythromycin group, thus discharge weight was less than that of placebo.

Table 4. Clinical outcomes between the two groups

Characteristics	Erythromycin n = 23 median (IQR)	Placebo n = 23 median (IQR)	P value
Time to full feeding (day)	7 (6, 9)	13 (9, 15)	<0.001*
Duration of parenteral nutrition (day)	13 (11, 15)	17 (13, 25)	0.03*
Numbers of holding feeds or gastric residuals > 50%	1(0, 2)	9 (2, 13)	<0.001*
Day to regain birth weight (day)	11 (10, 14)	12 (11, 15)	0.49
Length of stay (day)	46 (24, 74)	60 (43, 89)	0.07
Discharge weight (g)	2170 (1987, 2587)	2560 (2130, 3600)	0.06

* Mann-Whitney test significant p value < 0.05

IQR = Interquartile ranges

4.4 Complications of parenteral nutrition and side-effects related to medication

There were no significant differences in episode of sepsis, necrotizing enterocolitis (NEC), cholestatic jaundice and mortality rate (table 5). Two infants died in erythromycin group; one from severe bronchopulmonary dysplasia and died on the 92 days of life, the other from NEC stage III that occurred after 4 days of full feeding and 11 days after discontinue erythromycin. There were 3 infants (13%) in placebo group also developed definite NEC stage II. No significant side-effect related to erythromycin, e.g. elevated liver enzyme, abnormal electrocardiogram, or pyloric stenosis, was observed.

Table 5. Possible complications related to parenteral nutrition or erythromycin between the two groups

Characteristics	Erythromycin n (%)	Placebo n (%)	P value
Sepsis	3 (13)	4(17)	1.0
Necrotizing enterocolitis	1 (4)	3 (13)	0.61
Cholestatic jaundice	3 (13)	2 (9)	1.0
Prolonged QTc interval	0	0	-
Hypertrophic pyloric stenosis	0	0	-
Dead	2(9)	0	0.49