Effect of Erythromycin on Gastric Emptying Time of Low Birth Weight Babies

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Abstract

Background: To study the promotility effects of low dose erythromycin on gastric emptying time in a population of normal low birth weight (LBW) neonates on breast feeds with or without nutritional supplements and human milk fortifier (HMF).

Method: A randomised control trial involving 50 neonates was undertaken and they were given 6mg/kg/day of oral erythromycin or placebo in three divided doses for four consecutive days in the first two weeks of life. The gastric emptying time (GET) was assessed ultrasonographically by measuring the decrease in the antral cross sectional area (ACSA). The time taken for the ACSA to become half the prefeed value, was taken as t/2 or half GET. The babies were also assessed for pre and post intervention side effects of the drug. The results were analysed using SPSS ver 11.5.

Results: The test group showed a significant decrease in GET after the intervention. This effect was mainly seen in the preterm babies as compared to term Small for Gestational Age (SGA) babies. The decrease in GET was more in babies born after 34 weeks of gestation as compared to smaller babies. The reduction in GET was seen in babies on breast milk alone and nutritional supplements with breast milk but not when HMF was added. No side effects of the drug were noted.

Conclusion: Low dose erythromycin is a safe way of decreasing gastric emptying in preterm babies born after 34 weeks of gestation in the first two weeks of life.

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Key Words : Low dose erythromycin; Gastric emptying time; Low birth weight

Introduction

Despite advances in the care of low birth weight (LBW) babies, feed intolerance, increased gastric residues and delayed time to full feeds remains a problem in these neonates. This is common in preterm babies. A gastrointestinal polypeptide hormone, motilin, synthesized and released from endocrine cells of intestinal mucosa, mediates gastrointestinal motility. It stimulates propagatory contractile activity during phase III of the migratory motor complex in the interdigestive state [1]. Circulating motilin concentration and motilin receptors increase with increasing gestational age. Erythromycin also induces gastrointestinal contractility by the release of motilin as well as by direct binding with motilin receptors [2]. However, studies using erythromycin in antimicrobial dose of 30-45mg/kg/day, have found it ineffective in improving feed tolerance in babies < 36 weeks of gestation [3]. The same drug in the dose of <12 mg/kg/day q 6-8 hours, shortens the gastric emptying time and whole gut transit time in infants [4,5]. Erythromycin appears to be equally effective when given orally (ethyl succinate, stearate or estolate) or intravenously (lactobionate) [6].

Real time ultrasonography is a safe and noninvasive method for measuring gastric emptying time (GET). This is done by evaluating the antral cross sectional area (ACSA) before and after a feed [7]. This study was undertaken to determine the effect of low dose erythromycin on gastric emptying time in LBW babies.

Material and Methods

A randomised controlled trial was done on a study population consisting of 50 LBW neonates. The sample size was calculated assuming a 20% decrease in GET to be significant. The average GET was taken from previous studies on normal preterm neonates [8]. The study included LBW neonates weighing less than 2.2 kg at birth, babies on breast-milk feeds of at least 100 ml/kg/day with or without supplements or human milk fortifier (HMF). The exclusion criterion were babies requiring resuscitation at birth, neonates with evidence of sepsis, abdominal distension/vomiting, those with congenital or electrocardiographic abnormality, jaundice below chest level or icterus suggestive of pathological jaundice, abnormal liver enzymes and neonates on any drug therapy except maintenance intravenous (IV) fluids.

GET was measured using Ultrasonic Imaging System Model Logi Q 100 MP with 5 MHz probe (Wipro GE). Natcal

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syrup (calcium 60 mg, phosphorous 30mg in 5 ml manufactured by American Remedies), vitamin drops with zinc (Zincovit by Apex Labs) and human milk fortifier (Lactodex HMF by Raptakos Brett) were the nutritional supplements used. Syrup erythromycin stearate (Alembic Pharma, 125mg/5ml) and a placebo was used for the study. Informed consent was taken from parents and neonates classified into groups according to feed type:

1. Exclusive breast milk (BM) feeds in term small for gestational age (SGA) babies weighing >1800 gms
2. BM with HMF (all babies weighing < 1800 gms)
3. BM with supplements of calcium, phosphorus, iron and multivitamins (preterm babies weighing > 1800 gms)

Babies were randomised in each group to receive oral erythromycin or placebo in the dose of 6 mg/kg/day in three divided doses for four consecutive days any time in the first two weeks of life. The researcher doing the GET estimation was blinded to the drug being administered. ACSA was measured before a feed while the measurements after the feed were done at five minute intervals till ACSA decreased to half the prefeed value ($t/2$). GET is double this time. The average of three GET readings was taken after three feeds over one day. The babies were then administered erythromycin @ 2mg/kg/dose q 8 hourly or placebo along with feeds. The ultrasonographic measurement for GET was repeated after four days of drug therapy. The babies were monitored for clinical features of sepsis or jaundice during the course of drug therapy and laboratory screening was repeated again on completion of drug therapy.

Analysis of statistical data was done using SPSS version 11.5. Chi square test was used for categorical variables. Fischer's paired t test was used for continuous variables. ANOVA was used for inter variable comparison in data with more than two variables.

Results

Term SGA babies constituted a third of the study group. There were larger number of term SGA babies in the control group, since randomisation was done on birth weight and not on gestational age. More babies were on breast feeds with supplements or HMF in the test group while there were more on exclusive breast feeds in the control group (Table 1),

Table 1
Demographic characteristics of study population

Characteristic	Test	Control	p value
Number	27	23	NS
Term SGA	5	13	<.05
Preterm	22	10	NS
Mean birth weight (gms)	1952	2165	NS
Mean gestational age (weeks)	35.5	37.2	<.05
Only on BM	9	19	<.05
BM+S	13	3	<.05
BM+HMF	5	1	<.05

BM=Breast Milk; S=Supplements; HMF=Human Milk Fortifier;
SGA=Small for Gestational Age

since term SGA babies weighing > 1800 grams were not supplemented.

There was a significant reduction in the GET in the test group after intervention as compared to controls (Table 2). This was seen in babies on exclusive breast milk and those on breast milk with supplements but not in babies on breast milk and HMF. On analysis of factors affecting the GET (Table 3), preterm babies showed a better response with erythromycin as compared to term SGA babies. Babies born after 34 weeks of gestation showed a better response with the intervention. When birth weight was compared, babies weighing > 2 kgs showed a statistically significant decrease in GET with the intervention as compared to smaller babies. When the postnatal age was analysed, there was no difference in the response to the intervention before or after one week of life.

Discussion

Our study showed that there was a significant decrease in GET in the test group after erythromycin. Weight for gestational age analysis showed that there were more preterm babies in the test group and it was these babies who showed a better response to the promotility effect of erythromycin as compared to term SGA babies (Table 3). This is the only study which suggests that growth retarded babies may have a poorer response to motilin. When changes in GET were analysed in relation to the type of feed, we found that the group on BM+HMF group did not show a change in GET with intervention (Table 2). Mclure et al [8], studied the effect of fortifying breast milk on gastric emptying and showed no significant difference in GET in the group receiving breast milk with HMF as compared to those receiving breast milk alone. This is contrary to observations by Ewer et al [9], who concluded that fortification of BM significantly delayed gastric emptying. Our observations are comparable to this study and the prokinetic effect of erythromycin appeared to be negated in presence of HMF.

In our study, babies > 34 weeks of gestation showed better response to erythromycin as compared to less

Table 2
Mean gastric emptying time (in minutes) and type of feed

	Pre intervention GET	Post intervention GET	p value
Test BM (n=9)	76.44	71.33	0.016
BM+S (n=13)	86.31	78.92	0.022
BM+ HMF (n=5)	76	74.48	0.773
Control BM (n=19)	72.63	71.79	0.563
BM+S (n=3)	76	76.67	0.918
BM+HMF(n=1)	112	104	*

BM=Breast Milk; S=Supplements; HMF=Human milk fortifier

*There was only one baby in this group, hence statistics could not be computed

Table 3**Factors affecting mean gastric emptying time (in minutes)**

Factor		Pre intervention	Post intervention	p value
Gestational age	Test			
	? 34 weeks (n=9)	85.33	79.78	0.118
	> 34 weeks(n=18)	79.0	73.44	0.017
	Control			
	? 34 weeks (n=2)	96	98	0.874
	>34 weeks(n=21)	72.7	71.5	0.359
Weight for gestational age	Test			
	Preterm (n=19)	79.68	72.95	0.006
	Term SGA (n=8)	84.5	81.75	0.346
	Control			
	Preterm (n=10)	73.67	72	0.300
	Term SGA (n=13)	76	75.82	0.934
Birth weight	Test			
	? 2kg (n=18)	84.67	79.67	0.053
	>2kg (n=9)	74	67.33	0.011
	Control			
	? 2kg (n=6)	79.33	81	0.700
	> 2kg (n=17)	73.18	71.29	0.138
Age at intervention	Test			
	? 7 days (n=22)	79	71.5	0.001
	> 7 days (n=5)	87.14	81.14	0.05
	Control			
	? 7 days (n= 10)	87.0	83.2	0.145
	> 7 days (n=13)	79.2	72.3	0.542

mature babies (Table 3). Oei et al [10], showed significant effect of low dose erythromycin on gastric aspirates and time to full feeds in babies with birth weight ranging between 1216 ± 380 gms. In our study there was a decrease in GET in babies of all weights in the test group, but it was more in babies weighing > 2 kgs (Table 3). In a recent study by Ng et al [11], erythromycin in doses of 15mg/kg/day, did not improve feed tolerance in smaller and more preterm babies which has been collaborated by other studies [12]. Babies in our study were larger and more mature which explains the better results. No side effects of the drug were seen. Low dose oral erythromycin shortens GET in bigger and more mature preterm babies.

Conflicts of Interest

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