CHAPTER I

BACKGROUND AND RATIONALE

Provision of adequate nutrition is a critical factor to an increased survival of preterm infants especially for very low birth weight infants. Aims of nutritional support are to provide nutrients and energy for their metabolism and growth. However, preterm infants of very low birth weight usually have some limitations both in digestion and in absorption due to immaturity of digestive enzymes and gastrointestinal function, making the parenteral nutrition invariably employed during the first few weeks of life. Nevertheless, prolonged parenteral nutrition carries some potential risks such as catheter-related sepsis, metabolic disturbances and cholestatic jaundice. Therefore, initiating enteral feeding in preterm infants as soon as possible is a common practice as a trophic feeding or gut priming(1, 2).

Several studies have shown the benefits of early enteral feeding including faster weight gain, shortening hospital stay, decreasing feeding intolerance and shortening the duration of parenteral nutrition, and avoiding the chance of parenteral nutrition related complications. However, feeding intolerance is a common problem and frequently complicates the clinical course of preterm infants. Previous studies using prokinetic drug such as cisapride reported contradictory results(3-5). In addition, current studies reported fatal adverse effect such as long QT syndrome, causing sudden death and it was not approved by FDA to use in preterm infant any more(6-8).

Erythromycin, a macrolide antibiotic, has been found to have potent prokinetic properties by action on a motilin receptor(9, 10). The potent prokinetic action of erythromycin has been shown to act principally at the level of the stomach and the proximal small intestine in both human and animal studies(11, 12). Stimulation of the motilin pathways results in greater amplitude and more frequent antral contractions, an increased in proximal gastric tone, suppression of pyloric pressure waves, which is associated with reduced pyloric outlet resistance, and an increase in duodenal contraction frequency(12-14). Combination of these mechanisms is thus likely to produce powerful

propulsive forces, which effectively propel the gastric luminal contents distally towards the small and large intestines.

Theoretically, the pattern of distribution of motilin in gastrointestinal tract at 20 weeks gestation closely resembles adult patterns, and the development of the gastrointestinal neuroendocrine network is almost complete by 25 weeks gestation(15, 16). It has also been shown that infusion of exogenous motilin may promote an earlier appearance of the migrating motor complex(17) and the introduction of enteral feeding to the neonatal gut has resulted in premature detection of phase III motor activity than would normally be expected for the gestational age(18). Thus it seems that preterm infants are already equipped with necessary anatomical and physiological apparatus at a very early gestation, and it is possible that erythromycin, a competitive analogue of motilin, can act on such motilin receptors and enhance upper gastrointestinal motility.

Since there is no standard treatment available for this condition at this moment due to non-effective and potential serious side effect, erythromycin as a pro-kinetic agent may offer an alternative option to treat feeding intolerance in preterm infants. A randomized controlled trial is needed to confirm its effectiveness in clinical practice.