

# **Erythromycin in Feeding Intolerance in Preterm Infants**

“systematic Review”

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## **Abstract**

Premature infants frequently suffer from feeding intolerance and are exposed to nasoduodenal feeding and parenteral nutrition with their complications for prolonged times. Establishing enteral feeding is therefore a critical milestone during management of premature infants. Erythromycin, is a motilin agonist with prokinetic effect which improve feeding tolerance however its use should be reserved for only high risk preterm neonates with persistent and severe feeding intolerance while limiting the duration of exposure and ensuring long term follow up.

### **Key words:**

Erythromycin – Enteral feeding – Preterm infants.

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### **List of Abbreviations**

CI	:	Confidence Interval
EES	:	Erythromycin – Ethyl – Succinate
ELBW:		Extremely Low Birth Weight
EM	:	Erythromycin
GRV's:		Gastric Residual Volumes
MMC's:		Migratory Motor Complexes
NEC	:	Necrotizing Enterocolitis
OR	:	Odds Ratio
RR	:	Relative Risk
TPN	:	Total Parenteral Nutrition
VLBW:		Very Low Birth Weight
WMD:		Weighted Mean Difference

Important Definitions  
in  
This Review

### **Confidence interval (CI)**

The range of numerical values in which we can be confident (to a computed probability, usually 95%) that the population value being estimated will be found. Confidence intervals indicate the strength of evidence. Where confidence intervals are wide they indicate less precise estimates of effect. It also means that if the same clinical trial was repeated 100 times we can be 95% sure that the data would fall within the calculated range (or in 95 times the data would fall in the range).

### **P Value:**

Refers to the probability that any particular outcome would have arisen by chance. The smaller the P value the less likely the data was by chance. Standard scientific practice usually deems a P value of less than 1 in 20 (expressed as  $P < 0.05$ ) as “statistically significant”. The smaller the P value the higher the significance. A P value of  $P < 0.01$  (less than 1 in 100) is considered statistically “highly significant”.

### **Randomized controlled trial:**

Study design where treatments, interventions or enrollment into different study groups are assigned by random



allocation rather than by conscious decisions of clinicians or patients. If the sample size is large enough, this study design avoids problems of bias and confounding variables by assuring that both known and unknown determinants of outcome are evenly distributed between treatment and control groups.

### **Allocation concealment**

It is concealing (hiding) the allocation sequence from those assigning the groups.

It prevents researchers from directing certain participants to a given group (selection bias)

Inadequate concealment exaggerates the treatment effect by 30-40%.

### **Blindness**

Means ensuring that a person remains unaware of which arm a subject has allocated to.

Trials are often describes as:

- Single-blind: The subject participating in the trial.
- Double-blind: The subject and investigators (interviewers, clinicians, laboratory personnel).

- Triple-blind: The subjects, investigators and committee responsible for monitoring outcome as well as persons who perform data entry, analysis and statistics.

**Relative risk or risk ratio (RR):**

The ratio of the probability of developing, in a specified period of time, an outcome among those receiving the treatment of interest or exposed to a risk factor, compared with the probability of developing the outcome if the risk factor or intervention is not present = the ratio of risk in the experimental group to the risk in the control group .

# Introduction to Systematic Review

## **Evidence – Based Medicine (EBM)**

The conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.

The science of integrating the best available evidence from clinical research with physicians' experience and patient's unique values and preferences.

## **Systematic Review**

A review addressing a specific research question (on treatment, diagnosis, prognosis or etiology using explicit methodology of collecting, selecting and appraising studies (qualitative assessment) and, whenever appropriate, synthesizing their results quantitatively (Meta-analysis).

Structured process involving several steps:

- Well formulated question.
- Comprehensive data search
- Thorough assessment of quality
- Unbiased extraction of data
- Critical appraisal of data
- Synthesis of data

## **Meta-analysis**

A statistical technique for combining the results of several studies, addressing the same research question, into a single numerical estimate.

## **The Cochrane Collaboration**

The Cochrane collaboration is an international non-profit and independent organization that aims to help people make well-informed decisions about healthcare by preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions.

The Cochrane Collaboration was founded in 1993 and named for the British epidemiologist Archie Cochrane. He wrote in 1972, “It is surely a great criticism of our profession that we have not organized a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomized controlled trials.” (Cochrane, 1972).

The Cochrane Collaboration has grown rapidly since its launch in 1993. There are now more than 15 Cochrane Centers around the world. There are 48 review groups which cover most of health care. Currently, new reviews are being published on The Cochrane Database of Systematic reviews at the rate of about 300 each year.

## **What is a Systematic Review?**

Systematic review or overview comprehensively locates, evaluates, and synthesizes all the available literature on a given topic, using a strict scientific design, which must itself be reported in the review. A systematic review, therefore, aims to be:

Systematic (e.g. in its identification of literature)

Explicit (e.g. in its statement of objectives, materials and methods)

Reproducible (e.g. in its methodology and conclusions).

## **Advantages**

Explicit methods limit bias in identifying and rejecting studies.

Conclusions are more reliable and accurate.

Large amounts of information can be assimilated quickly and efficiently by health care providers, researchers, and policymakers to plan research, purchasing and guidelines.

Delay between research discoveries and implementation of effective diagnostic and therapeutic strategies is potentially reduced.

Results of different studies can be formally compared to establish generalisability of findings and consistency of results.

Reasons for heterogeneity (inconsistency in results across studies) can be identified and new hypotheses generated about particular subgroups.

Quantitative systematic reviews (meta-analyses) increase the precision of the overall result.

### **Stages of a systematic review**

Planning the review – i.e. identifying the need for a review, and documenting the methodology.

Conducting the review – i.e. finding, selecting, appraising, extracting and synthesizing primary research studies.

Reporting and dissemination – i.e. writing up and disseminating the result of the review.

### **How to conduct a systematic review?**

#### **1- A well formulated PICO question:**

Defining an appropriate therapeutic question with four components PICO: patient or population, intervention,