

Design of a prospective multicenter randomized controlled trial evaluating the effects of gastric lavage on coffee-ground emesis in neonates: study protocol

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ABSTRACT

Neonates who swallow a considerable amount of maternal blood may exhibit vomiting and suckling disorder during the first few days of the postnatal period. Some clinicians treat these neonates with gastric lavage (GL) to prevent vomiting and the establishment of enteral feeding empirically, but there was no study assessing the effect of GL for neonates with coffee-ground emesis. We designed a multicenter randomized controlled trial to evaluate the efficacy and safety of GL in neonates with coffee-ground emesis. Vigorous neonates with birth weight ranging from 2500 g to 3999 g and gestational age between 37w0d and 41w6d who presented with coffee-ground emesis on more than twice and diagnosed as false melena, were divided into two groups using computerized randomization. We defined feeding intolerance (FI) as (1) ≥ 2 vomiting episodes in 4h or ≥ 3 episodes in 24h and/or (2) feeding failure on at least two occasions because of retching or poor sucking. Primary outcome is percentage of infants who present FI within 24 hours from admission. We also assessed the residual volumes, number of vomiting episodes, percentage of weight reduction at postnatal day 4, rates of body weight gain at 1 month of age, and peak serum total bilirubin value before discharge. To our knowledge, this is the first study to evaluate the safety and efficacy of GL for neonates with coffee-ground emesis. This trial is registered at UMIN Clinical Trials Registry as UMIN000026483.

Keywords: gastric lavage, feeding intolerance, coffee-ground emesis, false melena

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BACKGROUND

Almost all infants swallow some amount of maternal blood during birth. However, neonates who swallow a large amount of maternal blood are considered more likely to experience feeding problems than those who swallow less maternal blood. The presence of maternal blood in the stomach is believed to act as a chemical irritant, causing vomiting, retching, and feeding intolerance (FI). FI can result in hypoglycemia, delayed establishment of breast feeds, need for parenteral fluids, and an increased risk of infections. It is believed that gastric lavage (GL) may benefit these infants by removal of the irritant maternal blood.

Conventionally, GL has been performed in several institutions for preventing feeding problems, preventing admission to the neonatal intensive care unit. Previously, several reports have shown that in neonates born with meconium-stained amniotic fluid, GL did not have a significant impact in terms of reduction in feeding problems.¹⁻⁵ A recent systematic review has also shown that although there were some possible benefits of GL in infants born through meconium-stained liquor, the evidence was limited.⁶ To our knowledge, thus far, there have been no reports regarding the treatment effect of GL on coffee-ground emesis.

Nevertheless, nasogastric tube insertion and subsequent GL is not always without complications, including bradycardia, apnea, vomiting, trauma, aspiration, and/or esophageal/gastric perforation.⁷ A previous report has revealed that gastric suction undertaken at birth is associated with a long-term risk of functional intestinal disorder.⁸ Routine gastric suction may overestimate FI and delay the initiation of breast-feeding; furthermore, a slight elevation of the mean arterial blood pressure and increased retching have also been reported.⁹

This study was designed to evaluate the safety and efficacy of GL on the neonates who have swallowed a large amount of maternal blood and present with coffee-ground emesis and diagnosed false melena.

METHODS

Design and setting

This nonblinded, multicenter, randomized controlled trial is coordinated at the Nagoya University Hospital and conducted at eight institutions (Anjo Kosei Hospital, Japan Red Cross Nagoya Daiichi Hospital, Konan Kosei Hospital, Nagoya University Hospital, Okazaki City Hospital, Ogaki municipal Hospital, Tosei General Hospital, and Toyota Memorial Hospital). Figure shows a flow diagram of the study protocol.

Ethical consideration and registration

The study protocol is in accordance with the Helsinki declaration. We obtained approval from the ethical committee at the Nagoya University on August 17, 2017 (IRB number 2017-0405). This trial was registered at the UMIN Clinical Trials Registry as UMIN000026483 (<http://www.umin.ac.jp/ctr/index.htm>).

Eligibility criteria

The inclusion criteria are as follows:

- Vigorous neonate status, defined as that with strong respiratory effort and good muscle tone
- Gestational age between 37w0d and 41w6d
- Birth weight: from 2500 to 3999g

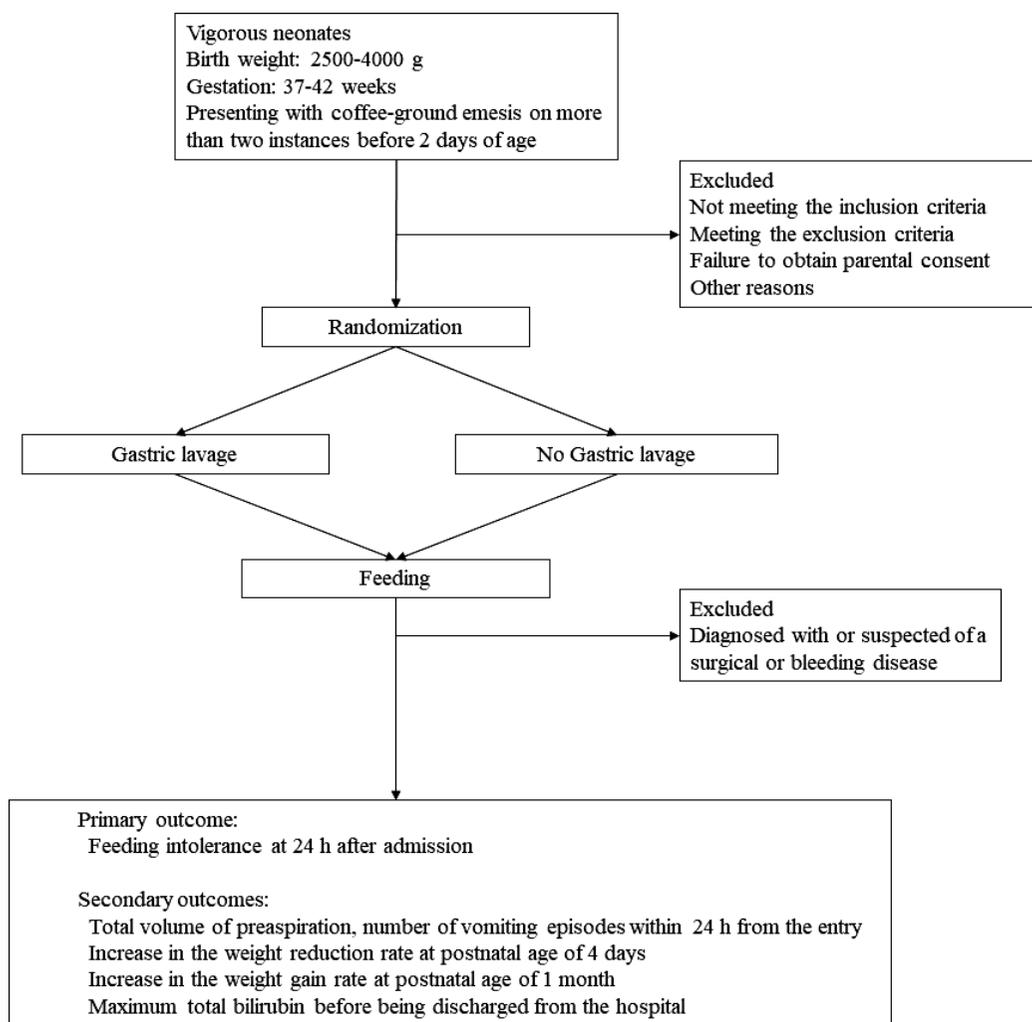


Fig. 1 A flow diagram of a prospective multicenter randomized controlled trial evaluating the effects of gastric lavage on coffee-ground emesis in neonates.

- Presenting with coffee-ground emesis on more than two instances before 2 days of age
- Normal and stable vital signs, such as heart rate, blood pressure, and oxygen saturation
- Provision of written informed consent for study participation from the parents

The exclusion criteria are as follows:

- Diagnosed or suspected with a surgical disease on radiological or clinical examination
- Diagnosed or suspected with gastrointestinal bleeding, requiring treatment
- Abnormal platelet count ($\leq 100,000/\text{mm}^3$) or coagulation test (PT ≥ 22 s, APTT ≥ 85 s) and suspected hemorrhagic disease
- Presence of other problems, such as infection or respiratory distress, requiring any other treatments
- Presence of major congenital malformation

- Failure to obtain informed consent of substitute

Patient registration

After confirming the eligibility criteria and obtaining informed consent, eligible patients will be registered and allocated to the GL group that will receive GL or the non-GL group that will not receive GL. The enrolment will start in April 2018, and the randomization will be performed by the independent data center of Nagoya University Hospital using web-based software that generates a random number and includes a minimization procedure by prognostic factors (gestational age: ≤ 38 weeks or > 38 ; birth body weight: ≤ 3000 g or > 3000 g; 5-minute Apgar score: ≤ 7 or ≥ 8).

Intervention

After being enrolled in the trial and being allocated to a group, each patient will receive continuous intravenous infusion, and an 8-Fr nasogastric tube will be inserted. The nasogastric tube will be correctly placed under the guidance of abdominal X-ray examination. In neonates belonging to the GL group, GL will be performed using a 20 mL/kg dose of normal saline that will be repeated until the suction fluids become clean. Neonates in the non-GL group will not receive GL.

Enteral nutrition

Enteral nutrition will be started within 5 h. Until 24 h after the start of nutrition, neonates will be fed 10 mL every 3 hours. The medical staff will check the nature and quantity of the gastric content before feeding every time using the nasogastric tube, and if the gastric content shows biliary or fresh bleeding, the patient will be excluded from this study because a surgical disease or gastrointestinal bleeding cannot be ruled out. When the gastric content is coffee-ground emesis, undigested milk, or gastric juice, the medical staff will return it to the stomach using a nasogastric tube and subsequently continue feeding. Irrespective of the amount of residual volume, feeding will be performed in patients without presenting FI. At the point of presenting FI, whether continuing feeding or not, whether returning gastric content or not, will be decided at the discretion of the chief physician. .

Protocol suspension

The protocol treatment will be terminated if a surgical or hemorrhagic disease is diagnosed or suspected; if there were any symptoms of respiratory, circulatory, or neurological disorders after the first feeding; or if serious adverse events occur.

Definition of vomiting, regurgitation, retching, and feeding intolerance

Vomiting is defined as an episode of expulsion of gastric contents with effort; regurgitation is defined as effortless milk expulsion during or immediately after the feeding. Regurgitation can be distinguished from vomiting by examining the contents; regurgitation contains only milk, whereas vomit may contain other food material as well. Retching or nausea is defined as attempted vomiting without the expulsion of gastric contents.

FI is defined as follows: (1) ≥ 2 vomiting episodes in 4 h or ≥ 3 episodes in 24 h, and/or (2) feeding failure on at least two occasions because of retching or poor sucking.

OUTCOME

The primary outcome will be FI within 24 h from the point of study enrolment. The secondary outcomes will include the total residual volume of preaspiration, number of vomiting episodes within 24 h from study enrolment, decrease in the weight reduction rate at postnatal age of 4 days, increase in the weight gain rate at postnatal age of 1month, and maximum total bilirubin before being discharged from the hospital.

Sample size determination and statistical consideration

The sample size of this study is calculated to achieve 80% power of testing with α error rate of 5.0% under the assumption that the proportions of patients with FI for GL and non-GL groups are 80% and 50%, respectively. Thus, we will enroll forty patients for each group. The primary analysis for primary endpoint is Pearson's chi-square test. Differences between the continuous variables of the GL and non-GL groups will be analyzed using two-sample t-tests or Mann–Whitney U tests for non-normally distributed data. Categorical variables will be analyzed using Pearson chi-square test or Fisher's exact test. $P < 0.05$ will be considered statistically significant.

DISCUSSION AND CONCLUSION

This study was designed to determine whether GL can prevent (or reduce) retching, vomiting, and FI in neonates who have swallowed a large amount of maternal blood. If this procedure proves to be beneficial, both the incidence of adverse events associated with FI and the risk of separation between mothers and neonates during the postnatal period may reduce. In case this method is not proven beneficial, potential procedure-related complications, including bradycardia, apnea, vomiting, trauma, aspiration, esophageal/gastric perforation,⁷ functional intestinal disorder,⁸ and/or delayed initiation of breast-feeding can be prevented.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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