Original Article

Phentolamine and B vitamins for feeding intolerance in late preterm infants: a randomised trial

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Background and Objectives: Feeding intolerance (FI) is a common problem in late preterm infants (34 weeks $\leq$ gestational age < 37 weeks). This study aimed to evaluate the efficacy and safety of phentolamine combined with B vitamins in treating FI in late preterm infants and to explore its effects on gastrointestinal symptoms, inflammation and complications. **Methods and Study Design:** We randomly assigned 118 late preterm infants with FI to a treatment group (n = 56) or a control group (n = 62). The treatment group received intravenous phentolamine and intramuscular B vitamins, whereas the control group received basic treatment only. We measured the time of disappearance of gastrointestinal symptoms, the time of basal attainment, the time of hospitalisation, the incidence of complications, the concentrations of inflammatory markers and the overall effective rate of treatment. **Results:** The treatment group had a shorter duration of gastrointestinal symptoms than did the control group ($p < 0.01$). The treatment group also had lower concentrations of inflammatory markers and a higher overall effective rate than did the control group ($p < 0.05$). There was no difference between the two groups in the time of hospitalisation, basal attainment, weight recovery and the incidence of complications ($p > 0.05$). **Conclusions:** Phentolamine and B vitamins can reduce gastrointestinal symptoms and inflammation in late preterm infants with FI but do not affect the occurrence of complications.

Key Words: phentolamine, B vitamins, feeding intolerance, late preterm infants, prematurity

INTRODUCTION

Feeding intolerance (FI) is a group of clinical syndromes characterised by intolerance to enteral nutrition caused by gastrointestinal dysfunction in neonates. The incidence of FI is as high as 7.9% in full-term infants, 25% in premature infants with a body weight >2,500 g, 50% in premature infants with a body weight of 2,001–2,500 g and over 70% in very low birth-weight infants.[1,2] Feeding intolerance can prevent infants from meeting the optimal nutritional criteria and increase the length of hospitalisation. Meanwhile, studies show that FI is closely associated with other neonatal diseases and may continue to develop into life-threatening necrotising enterocolitis (NEC) and late-onset sepsis (LOS) that reduce the survival rate of infants.[3-5] Some studies also report that FI can cause delayed psychological development in infants.[6] Therefore, exploring the treatment strategy of FI in premature infants is of great significance. Clinical observations indicate that late premature infants with gestational ages >34 weeks suffering from FI are not rare. Given a larger gestational age or weight, FI in this group of infants can easily be ignored. However, FI in late preterm infants can also have adverse effects on their growth and development, such as increased risk of infection, hyperbilirubinaemia and neurodevelopmental impairment.[2] For the above reasons, it is necessary to further summarise the treatment plan for FI in late preterm infants. The treatment of FI is mainly sup-

portive, such as gastric lavage, temporary fasting, nutritional support and abdominal massage.[7,8] However, these measures may not be sufficient to relieve the symptoms and improve the outcomes of FI. Therefore, there is a need for more effective and safe interventions for FI in late preterm infants. Some traditional treatment drugs for FI include prokinetic agents, such as metoclopramide and erythromycin, antacids, such as ranitidine and omeprazole and probiotics, such as *Lactobacillus* and *Bifidobacterium*. However, these drugs have some disadvantages or drawbacks, such as adverse effects, limited efficacy and lack of evidence.[9,10] For example, metoclopramide can cause extrapyramidal symptoms, erythromycin can induce bacterial resistance, ranitidine and omeprazole can increase the risk of infections and probiotics can have variable quality and safety.[9,10] Therefore, there is a need for alternative treatment options for FI in late preterm infants. In this study, we adopted a combination therapy

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with phentolamine and B vitamins to treat FI in late preterm infants, resulting in good clinical outcomes. Phentolamine is an alpha-adrenergic blocker that can improve intestinal blood flow and motility by reducing the vasoconstrictive effect of norepinephrine. B vitamins are essential for maintaining normal nervous system function and can enhance vagus nerve activity, which regulates gastric emptying and intestinal peristalsis. We hypothesised that phentolamine and B vitamins could have synergistic effects on improving the gastrointestinal function and reducing the inflammation in FI and thus enhance the efficacy and safety of the treatment. In this study, we aimed to assess the efficacy and safety of phentolamine and B vitamins for treating FI in late preterm infants.

METHODS
General data
A total of 118 cases of late premature infants aged <1.0 day and diagnosed with FI that were admitted to the neonatology department between January 2018 and July 2022 were selected. The infants were divided into the treatment group and control group using a random number table. The two groups, containing 56 and 62 cases, respectively, had no statistically significant differences ($p > 0.05$) in sex, gestational age, weight and method of delivery before treatment, as shown in Table 1. This study was approved by the Ethics Committee of Baoding First Central Hospital (Approval No.: K[2018] 070). We used a web-based randomization system to generate and conceal the allocation sequence, which was only accessible to an independent statistician. The treatment and control groups received identical-looking injections of phentolamine and B vitamins or placebo, respectively. The investigators, study staff, and participants were blinded to the group assignments throughout the study. The blinding was maintained until the data analysis was completed.

Inclusion and exclusion criteria
The inclusion criteria were as follows: (1) The infants met at least one of the criteria specified by the Clinical Guidelines for the Diagnosis and Treatment of Feeding Intolerance in Preterm Infants (2020),[11] namely (i) the gastric residual volume exceeded 50% of the previous feeding amount, with vomiting and/or bloating or (ii) there was a failure of the feeding plan, including reduced, delayed or disrupted enteral feeding, (2) the infants were appropriate

for gestational age (weight between 10th and 90th percentile) with gestational age <37 weeks (250 d) and ≥34 weeks (238 d) and (3) the infants were admitted to hospital within 24 h after birth.

The exclusion criteria were as follows: (1) the infants could not be fed normally due to surgical conditions, such as congenital digestive tract malformation or NEC, genetic metabolic disease or chromosomal abnormalities and (2) the data were incomplete.

Treatment method
After admission, infants diagnosed with FI were divided into treatment and control groups using a random number table. Both groups of infants were kept warm and given supportive care, such as total parenteral nutrition and anti-infection, to ensure a water, electrolytes and acid–base balance. When necessary, enhanced immunotherapy, such as infusion of plasma and intravenous immunoglobulin, was administered. The control group received treatments such as gastric lavage, abdominal massage and supplement of intestinal probiotics. In addition to the treatments given to the control group, the treatment group also received phentolamine (Shanghai Fudan Fuhua Pharmaceutical Co., GYZZ No. H10890046) administered by intravenous pump combined with intramuscular injections of B vitamins (Vitamin B1: Tianjin Pharmaceutical Group Xinzheng Holdings Co., Ltd., GYZZ No. H41021262; Vitamin B12: Suicheng Pharmaceutical Co., Ltd., GYZZ No. H41021261). The liquid was configured as follows: A solution of 1.8 mg/kg of phentolamine with 10 mL 5% glucose injection was continuously pumped for 10 h at a rate of 1 mL/h, with the phentolamine pumping rate being 0.3 μg/(kg·min). The pumping was administered once per day and one session lasted 5–7 days. The configuration of B vitamins was as follows: Vitamin B1 and vitamin B12, 25 mg and 125 μg, respectively, were intramuscularly administered once per day and a session lasted 3 days. Parenteral nutrition support for both groups stopped after total enteral nutrition was fulfilled. The enteral nutrition was given by nasogastric tube or oral feeding, depending on the infant's condition and tolerance. The enteral nutrition consisted of breast milk or formula milk, with the volume and frequency adjusted according to the infant's weight and growth. The enteral nutrition was gradually increased until the infant reached the basal standard of 100 mL/(kg·d) milk via oral feeding. Daily changes in the

Table 1. General data of comparisons of two groups of infants prior to treatment

	Treatment group (n=56)	Control group (n=62)	t/X²	p
Gestational age (d)	247 ± 6.38	245 ± 5.02	1.895[†]	0.061
Sex				
Male (%)	54 (30/56)	44 (27/62)	2.001[‡]	0.157
Female (%)	46 (26/56)	56 (35/62)		
Weight (g)	2432 ± 298	2403 ± 333	0.487[†]	0.627
Method of delivery				
Natural birth (%)	59 (33/56)	47 (29/62)	2.890[‡]	0.089
C-section (%)	41 (23/56)	53 (33/62)		
Prenatal hormones (%)	45 (25/56)	37 (23/62)	0.081[‡]	0.776
Maternal history of hypertension (%)	36 (20/56)	48 (30/62)	2.956[‡]	0.086
Maternal history of diabetes (%)	55 (31/56)	60 (37/62)	0.512[‡]	0.474

[†]unpaired Student's t test
[‡]X² test

infants' conditions, such as basic vital signs, daily milk volume, residual milk volume, daily weight change and presence of symptoms such as vomiting or abdominal distension, were recorded during the study.

Observation indicators

The observation indicators were as follows: (1) time of digestive tract symptoms (vomiting, abdominal distension and clearance of meconium), (2) time for meeting basic standards (time needed to reach 100 mL/(kg·d) milk via oral feeding after birth), (3) time of weight recovery, (4) length of hospitalisation, (5) incidence of complications of NEC, LOS or hyperbilirubinaemia during hospitalisation and (6) C-reactive protein (CRP) and interleukin-6 (IL-6) concentrations before and after treatment.

Efficacy evaluation

The efficacy evaluation was based on the following criteria: significant efficacy – infants exhibited good sucking, absence of vomiting or abdominal distension, significantly relieved gastric retention and increased milk intake, with stomach rumble returning to normal; efficacy– infants demonstrated good sucking, relieved symptoms such as vomiting, abdominal distension or gastric retention, increased milk intake and enhanced stomach rumble; non-efficacy–no improvement in times of vomiting or abdominal distension, presence of significant gastric retention and non-progress in milk intake. Total treatment efficacy = significant efficacy + efficacy.

Statistical processing

Analysis was carried out using the SPSS 25.0 statistical software suite. All measurement data were presented as mean value ± standard deviation (±SD). Two groups of data satisfying normal distribution and homogeneity of variances underwent independent sample t-test. Two independent sample ordinal data underwent the Mann–Whitney U test. Count data were presented as percentages, and the total sample size N ≥ 40. When all theoreti-

cal values T ≥ 5, the Pearson chi-squared test was adopted. If T < 5, then Fisher's exact probability method was used. A value of $p < 0.05$ indicates a statistically significant difference.

RESULTS

Comparison of gastrointestinal symptom indicators of the two groups after treatment

The times needed for the disappearance of vomiting, abdominal distension and meconium in the treatment group were invariably shorter than those of the control group, with a statistically significant difference ($p < 0.01$). However, no significant difference was found in time for meeting basic standards, weight recovery and hospitalisation, which was statistically insignificant ($p > 0.05$), as shown in Table 2.

Comparison of incidence of complications between the two groups

After treatment, the treatment group had 1 case of NEC (2%), 1 case of LOS (2%) and 22 cases of hyperbilirubinaemia (39%). Comparatively, the control group had 2 cases of NEC (3%), 30 cases of hyperbilirubinaemia (48%) and 0 cases of LOS. The two groups showed no statistical differences ($p > 0.05$), as shown in Table 3.

Comparison of efficacy results

After 5 days of treatment, the total efficacy of the treatment group was 77%, significantly higher than the 56% efficacy in the control group, pointing to a significant statistical difference ($p < 0.05$), as shown in Table 4.

Comparison of C-reactive protein and interleukin-6 levels between the two groups

Before treatment, infants in the two groups showed no statistically significant difference in CRP concentrations ($p > 0.05$). After the treatment, the CRP concentrations dropped in both groups and showed a statistically significant difference ($p < 0.01$). After the treatment, the CRP concentration of the treatment group was lower than the

Table 2. Comparison of treatment outcomes of two groups of infants with FI (±SD, d)

Group	Vomiting time	Time of abdominal distension	Time of clearance of meconium	Time for weight recovery	Time for meeting basic standards	Time of hospitalization
Treatment group	2.3±0.6*	3.1±0.6*	4.5±1.0*	8.3±1.2	8.4±1.6	8.0±1.5
Control group	3.7±0.7	4.3±0.9	5.8±1.1	8.2±1.3	8.6±1.7	8.5±1.6
t value	-11.284	-8.114	-6.329	0.034	-0.558	-1.770
p	< 0.001	< 0.001	< 0.001	0.973	0.578	0.079

FI: Feeding intolerance
Comparison with the control group *p<0.01

Table 3. Comparison of incidence of complications in FI infants between the two groups n (%)

Group	Case	Number of NEC (%)	Number of LOS (%)	Number of hyperbilirubinemia (%)
Treatment group	56	1 (2)	1 (2)	22 (39)
Control group	62	2 (3)	0 (0)	30 (48)
X^2				0.989
p		1.000	0.475	0.320

NEC: Necrotizing enterocolitis; LOS: Late-onset sepsis. FI: Feeding intolerance
X^2 test was used to compare the incidence of complications between the two groups.

Table 4. Comparison of efficacy in FI infants between the two groups n (%)

Group	Case	Significant efficacy (%)	Efficacy (%)	Non-efficacy (%)	Z[†]	p
Treatment group	56	18 (32)	25 (45)	13 (23)	-2.010	0.044
Control group	62	10 (16)	25 (40)	27 (44)		

FI :Feeding intolerance
[†]Mann-Whitney U test

Table 5. Comparative analysis of CRP and IL-6 concentrations in FI infants between treatment and control groups before and after treatment

	Before Treatment (Mean ± SD)	After Treatment (Mean ± SD)	t	p
CRP (mg/L)				
Treatment Group	1.99 ± 0.35	0.980 ± 0.18	19.242	< 0.001
Control Group	2.08 ± 0.31	1.31 ± 0.24	15.399	< 0.001
t	-1.817	-2.952		
p	0.072	0.004		
IL-6 (pg/mL)				
Treatment Group	23.7 ± 5.75	9.33 ± 2.23	17.467	< 0.001
Control Group	25.8 ± 6.45	10.6 ± 2.36	17.429	< 0.001
t	-1.972	-3.087		
p	0.054	0.003		

CRP: C-reactive protein; IL-6: Interleukin-6; FI: Feeding intolerance

control group, showing a statistically significant difference ($p < 0.01$), as shown in Table 5.

Before treatment, infants in the two groups showed no statistically significant difference in IL-6 concentrations ($p > 0.05$). After the treatment, the IL-6 concentrations dropped in both groups and showed a statistically significant difference ($p < 0.01$). After the treatment, the CRP concentrations in the treatment group were lower than those in the control group, showing a statistically significant difference ($p < 0.01$), as shown in Table 5.

Comparison of Total Parenteral Nutrition (TPN) parameters between the two groups

We used TPN as a supplementary nutritional support for our study population, which were late preterm infants with immature gastrointestinal function and unable to meet their nutritional needs. Moreover, due to the presence of FI, their intestinal absorption capacity was also impaired, increasing the risk of malnutrition. Therefore, we used TPN to ensure their growth and development. We have provided related clinical data, including the amount of energy and protein supplied by TPN, and the comparison between the two groups. We have also added a table to show the TPN parameters and their differences (Table 6).

Safety evaluation

(1) Vital signs monitoring

After receiving phentolamine and B vitamins, no significant abnormality was monitored in respiration, heart rate or blood pressure in the treatment group.

(2) Incidence of adverse drug reactions in the treatment group

In this study, no adverse reactions, such as nasal congestion, rash, flushed complexion, arrhythmia or redness, swelling or erosion at the site of injection, were found in the treatment group.

DISCUSSION

During the neonatal period, a variety of factors can cause reduced gastrointestinal blood flow, abnormal secretion of gastrointestinal hormones and changes in gastrointestinal motility; these can lead to FI, which further results in long-term nutrition therapy and complications, such as cholestasis, bleeding and infection.[12,13] Premature infants with a gestational age <33 weeks have an insufficiently developed central nervous system and can barely be fed orally,[14] leading to a relatively high incidence of FI. Hence, there has been a larger body of literature focusing on FI premature infants with a gestational age <34 weeks.[15] However, few studies address late premature infants with a gestational age >34 weeks. Clinical observations show that, subject to the effects of maternal and delivery factors, infants of this gestational age still have a high incidence of FI.1 Thus, this study is meaningful in summarising the clinical experience in FI of late premature infants to provide new methods for treating FI in extremely and ultra-early premature infants by expanding the treatment scope.
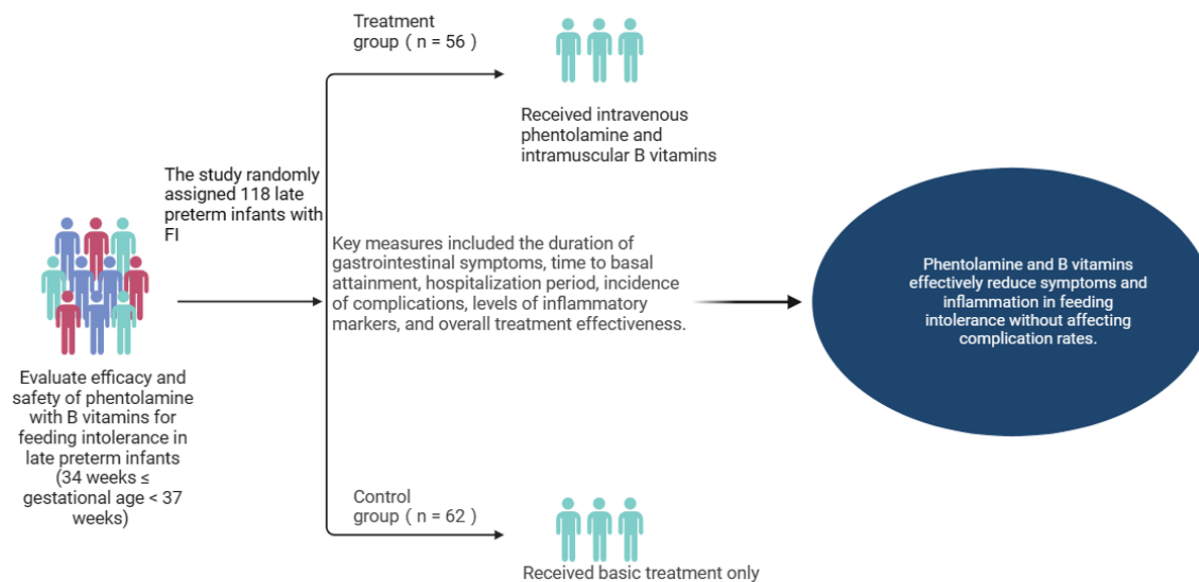
As an alpha receptor blocker, phentolamine competitively blocks the binding of norepinephrine with the alpha receptor, reducing its vasoconstriction effect and improving systemic microcirculation. When intestinal microcirculation improves, the congestion and oedema of the intestinal wall are alleviated and the gastrointestinal smooth muscles are excited to enhance intestinal motility, thereby helping the dispersion of accumulated intestinal gas and recovery of intestinal mobility and absorption. Given its improvement in microcirculation, it is mainly used as a topical medicine for neonates, and few studies have reported treatment of FI with phentolamine.[16]

Both vitamin B1 and vitamin B12 are water-soluble vitamins and nourish nerves when used in combination. For adults, they can treat neuritis, neuralgia caused by herpes zoster, sequelae of cerebrovascular disease and neuropathies caused by diabetes. Near-term and prema-

Table 6. TPN parameters and comparison between the two groups

Parameter	Treatment group (n=56)	Control group (n=62)	t	p
TPN energy (kcal/kg/d)	80.3 ± 12.4	79.8 ± 11.7	0.213	0.832
TPN protein (g/kg/d)	2.50 ± 0.4	2.40 ± 0.3	1.234	0.220
TPN duration (d)	5.20 ± 1.6	5.40 ± 1.8	-0.542	0.589

Phentolamine and B vitamins for feeding intolerance in late preterm infants: a randomised trial

Graphical abstract. Phentolamine and B vitamins effectively reduce gastrointestinal symptoms and inflammation in late preterm infants with feeding intolerance, demonstrating improved treatment efficacy without affecting the incidence of complications.

ture infants have relatively sophisticated intestinal development, and their FI is largely associated with intrauterine distress and infection. Affected infants largely show a vagus nerve disorder. B vitamins help maintain normal functions of the nervous system, as they cause a gradual expansion in stomach receptivity and improvement in contractility that help accelerate the emptying of stomach contents.

The current clinical experiment shows that phentolamine combined with B vitamins can shorten the duration of vomiting and abdominal distension when treating FI in premature infants. Compared with the treatment group, the treatment plan advances clearance of meconium (p < 0.01), significantly alleviating the clinical symptoms of affected infants. The total efficacy of the treatment group was significantly higher than that of the control group (p < 0.01). However, compared with the control group, the treatment group showed no reduction in the incidence of NEC, LOS or hyperbilirubinaemia. The literature shows that the risk factors of FI in late premature infants are mainly premature rupture of membranes, perinatal infection and apnoea.[17,18] As an acute-phase response protein, CRP can increase in the case of tissue damage and inflammation. However, non-Chinese literature reports that premature infants with FI may show abnormal concentrations of the inflammatory factor IL-6 and a low neurodevelopmental score.[19] Chinese literature demonstrates that phentolamine can alleviate the inflammatory factor concentrations of NEC, severe pneumonia combined with respiratory failure.[20,21] Our study shows that the CRP and IL-6 concentrations both dropped after treatment in the

two groups (p < 0.01). After the treatment, the CRP and IL-6 concentrations in the treatment group were lower than those in the control group (p < 0.01). This suggests that phentolamine combined with B vitamins may alleviate inflammatory reactions, but the specific mechanism requires further exploration.

To summarise, phentolamine and B vitamins can significantly alleviate the clinical symptoms of FI in late premature infants, reduce inflammation, improve total efficacy, promote early initiation of breastfeeding and thus help infants recover early. The study also provides reference medication for treating FI in extremely and ultra-early premature infants.

REFERENCES

1. Hu X, Chang Y, Wang Z, Bao W, Li Z. Altered gut microbiota is associated with feeding intolerance in preterm infants. Turk J Pediatr. 2021;63:206-17. doi: 10.24953/turkjped.2021.02.004.
2. Stellon M, Joshi D, Lee-Miller C, Brinkman A. Neonatal rhabdoid tumor presenting as feeding intolerance and vomiting: A case report. Pediatr Blood Cancer. 2024;11:e31013. doi: 10.1002/pbc.31013.
3. Neu J, Walker WA. Necrotizing enterocolitis. N Engl J Med. 2011;364:255-64. doi: 10.1056/NEJMra1005408.

4. Patel RM, Kandefer S, Walsh MC, Bell EF, Carlo WA, Laptook AR et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Causes and timing of death in extremely premature infants from 2000 through 2011. N Engl J Med. 2015;372:331-40. doi: 10.1056/NEJMoa1403489.

5. Deshpande G, Jape G, Rao S, Patole S. Benefits of probiotics in preterm neonates in low-income and medium-income countries: a systematic review of randomised controlled trials. BMJ Open. 2017;7:e017638. doi: 10.1136/bmjopen-2017-017638.

6. Maller VV, Cohen HL. Neurosonography: Assessing the Premature Infant. Pediatr Radiol. 2017;47:1031-45. doi: 10.1007/s00247-017-3884-z.

7. Singh P, Kumar M, Basu S. Gastric lavage for prevention of feeding intolerance in neonates delivered through meconium-stained amniotic fluid: a systematic review and meta-analysis. Indian Pediatr. 2021;58:973-7.

8. Chaudhary RK, Chaurasia S, Singh P, Priyadarshi M, Bhat NK, Chaturvedi J, Basu S. Impact of Delivery Room Gastric Lavage on Exclusive Breastfeeding Rates Among Neonates Born Through Meconium-Stained Amniotic Fluid: A Randomized Controlled Trial. Indian Pediatr. 2023;60:719-25. doi: 10.1007/s13312-023-2984-8

9. Thomas JP, Raine T, Reddy S, Belteki G. Probiotics for the prevention of necrotising enterocolitis in very low-birth-weight infants: a meta-analysis and systematic review. Acta Paediatr. 2017;106:1729-41. doi:10.1111/apa.13902

10. Calhoun LK. Pharmacologic management of apnea of prematurity. J Perinat Neonatal Nurs. 1996;9:56-62. doi:10.1097/00005237-199603000-00007

11. Evidence-Based Medicine Group, Neonatologist Society, Chinese Medical Doctor Association. Clinical guidelines for the diagnosis and treatment of feeding intolerance in preterm infants (2020). Chin J Contemp Pediatr. 2020;22:1047-55. doi: 10.7499/j.issn.1008-8830.2008132

12. Hunter CJ, Upperman JS, Ford HR, Camerini V. Understanding the susceptibility of the premature infant to necrotizing enterocolitis (NEC). Pediatr Res. 2008;63:117-23. doi: 10.1203/PDR.0b013e31815ed64c.

13. Maeda T, Sato Y, Hirakawa A, Nakatochi M, Kinoshita F, Suzuki T, et al. Nagoya Collaborative Clinical Research Team. Design of a prospective multicenter randomized controlled trial evaluating the effects of gastric lavage on coffee-ground emesis in neonates: study protocol. Nagoya J Med Sci. 2019;81:227-32. doi: 10.18999/nagjms.81.2.227.

14. Morgan J, Young L, McGuire W. Slow advancement of enteral feed volumes to prevent necrotising enterocolitis in very low birth weight infants. Cochrane Database Syst Rev. 2015;D001241..doi: 10.1002/14651858.CD001241.pub6.

15. Schanler RJ, Shulman RJ, Lau C, Smith EO, Heitkemper MM. Feeding strategies for premature infants: randomized trial of gastrointestinal priming and tube-feeding method. Pediatrics. 1999;103:434-39. doi: 10.1542/peds.103.2.434.

16. Liu Y, Ran S. Phentolamine combined with Xiliaotol external application for the treatment of neonatal fluid extravasation. J Jilin Med. 2020;41:2182-3. doi: 10.3969/j.issn.1004-0412.2020.09.057.

17. Wu MH, Zhao YN, Zheng Z. Factors affecting feeding intolerance in preterm infants of different gestational ages. Medical Science Journal Central South China. 2017;45:160-4. doi: 10.15972/j.cnki.43-1509/r.2017.02.013.

18. Abiramalatha T, Ramaswamy VV, Bandyopadhyay T, Somanath SH, Shaik NB, Pullattayil AK, Weiner GM. Interventions to Prevent Bronchopulmonary Dysplasia in Preterm Neonates: An Umbrella Review of Systematic Reviews and Meta-analyses. JAMA Pediatr. 2022;176:502-16. doi: 10.1001/jamapediatrics.2021.6619.

19. Moore TA, Pickler RH. Feeding intolerance, inflammation, and neurobehaviors in preterm infants. J Neonatal Nurs. 2017;23:134-41. doi: 10.1016/j.jnn.2016.09.009.

20. Zhu XQ. The efficacy of phentolamine, dopamine, and dobutamine combined with nasal continuous positive airway pressure ventilation in the treatment of severe pneumonia combined with respiratory failure in children and their impact on inflammatory cytokine concentrations. Matern Child Health Care China. 2021;36:2773-6. doi: 10.19829/j.zgfybj.issn.1001-4411.2021.12.029

21. Zhang RJ. The efficacy of phentolamine pump maintenance to neonatal necrotizing enterocolitis. J Jining Med Univ. 2016;39:258-60. doi: 10.3969/j.issn.1000-9760.2016.04.009.