Section: Paediatrics

Systematic Review

TWO-HOURLY VERSUS THREE-HOURLY FEEDING IN LOW-BIRTH-WEIGHT PRETERM INFANTS: A SYSTEMATIC REVIEW

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Received : 10/12/2025
Received in revised form : 20/01/2026
Accepted : 07/02/2026

Keywords:
Enteral Nutrition, Feeding Interval, Low Birth Weight Infant, Necrotising Enterocolitis, Preterm Neonates.

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DOI: 10.47009/jamp.2026.8.1.126

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (1); 662-668

ABSTRACT

Background: Optimising enteral feeding strategies is a critical component of care for preterm low-birth-weight (LBW) infants, as early nutritional adequacy supports gastrointestinal maturation, growth, and reduces dependence on parenteral nutrition. Intermittent bolus feeding at two-hourly or three-hourly intervals is commonly practised in neonatal intensive care units (NICUs), yet the optimal feeding frequency remains uncertain, with inconsistent evidence regarding feeding tolerance, safety, and clinical outcomes. **Objective:** This systematic review aimed to compare the effectiveness and safety of two-hourly versus three-hourly enteral feeding schedules in preterm LBW infants, focusing on time to achieve full enteral feeds, feeding intolerance, necrotising enterocolitis (NEC), hypoglycaemia, growth outcomes, and hospital-related measures. **Materials and Methods:** A comprehensive literature search of PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library was conducted for studies published up to December 2025, in accordance with PRISMA guidelines. Randomised controlled trials and observational cohort studies involving preterm LBW, very low birth weight (VLBW), or extremely low birth weight (ELBW) infants comparing two-hourly and three-hourly bolus feeding schedules were included. Data extraction focused on feeding outcomes, neonatal morbidities, growth parameters, duration of hospital stay, and parenteral nutrition exposure. **Results:** Twelve studies encompassing 1,673 preterm infants were included. Overall, no consistent difference was observed between two-hourly and three-hourly feeding schedules in time to achieve full enteral feeds, with results varying by gestational age and birth weight. Rates of feeding intolerance, NEC (2–13%), hypoglycaemia, mortality, and short-term growth outcomes were comparable across feeding intervals. Two-hourly feeding demonstrated potential benefit in selected ELBW subgroups for earlier feed attainment, whereas three-hourly feeding consistently reduced nursing workload without compromising safety or efficacy. **Conclusion:** Two-hourly and three-hourly enteral feeding schedules are equally safe and effective for most preterm LBW infants. Feeding frequency does not uniformly influence major clinical outcomes, and the choice of schedule should be individualised based on infant maturity, clinical stability, and unit resources. Further large-scale, multicentre trials are required to clarify subgroup-specific benefits and optimise evidence-based feeding protocols.

INTRODUCTION

Preterm birth and low birth weight (LBW) are the main contributors to neonatal illness and death worldwide. The World Health Organisation (WHO) estimates 13.4 million babies were born preterm in 2020, and preterm birth complications are a leading cause of mortality for children under 5 years. About 6500 newborns die every day, but most of these deaths are preventable using feasible interventions.[1,2] Preterm infants commonly require prolonged inpatient care and intensive monitoring during the early neonatal period.[1] As nutrition is a key modifiable factor in this population, optimising feeding practices is important for improving short-

term stabilisation and longer-term growth and neurodevelopment.[3]

Early start of enteral nutrition in preterm infants supports gastrointestinal maturation and helps reduce reliance on parenteral nutrition, which is associated with infection risk and other complications.[4] However, achieving enteral nutrition is difficult in LBW preterm babies because of the physiological immaturity of the gut, including limitations in motility and functional adaptation.[5] Therefore, it's important to achieve full enteral feeds with the avoidance of feeding-related morbidity. In many neonatal intensive care units (NICUs), intermittent bolus feeding via tube is commonly delivered at 2–3-hourly intervals, but this practice varies with institute, and there is no standard on the optimal interval.6 On a theoretical basis, two-hourly schedules provide smaller volumes per feed, which are often proposed to reduce gastric distension and reflux-related issues, improving tolerance.[7] In contrast, three-hourly schedules may reduce handling and nursing workload and have been suggested as a better alternative without worsening of outcomes.[8]

Feeding interval may also affect adverse outcomes in LBW preterm infants. Feeding intolerance, characterised by vomiting, abdominal distension, or increased gastric residuals, can delay advancement to full enteral nutrition and prolong hospitalisation.[9] Serious complications, like the necrotising enterocolitis (NEC) and hypoglycaemia, are some important issues that are to be considered while determining the feeding strategies.[9,10] Given ongoing discrepancy in NICU practice and mixed findings across studies and reviews, a focused review is needed to clarify all benefits or harms in LBW preterm babies provided by the two-hourly and three-hourly feeding method. Therefore, this systematic review aims to compare: time to achieve full enteral feeding, incidence of feeding intolerance, NEC, hypoglycaemia, weight gain, and time to regain birth weight. To evaluate the effects on hospital stay and other clinical outcomes in preterm infants following either a two-hourly or three-hourly feeding method.

Objectives

Primary objective

To compare the effectiveness and safety of two-hourly versus three-hourly intermittent bolus enteral feeding schedules in preterm low-birth-weight infants.

Secondary objectives

To evaluate differences in (i) time to achieve full enteral feeding, (ii) feeding intolerance, (iii) necrotising enterocolitis, (iv) hypoglycaemia, (v) growth outcomes including weight gain and time to regain birth weight, and (vi) duration of hospital stay and feeding-related care burden.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The review protocol was not registered in PROSPERO, as the review was undertaken as an academic synthesis with predefined objectives, eligibility criteria, and outcomes established prior to study selection.

Search strategy

A comprehensive electronic search was conducted in PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library for studies published up to December 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms, including “preterm infant,” “low birth weight,” “enteral feeding,” “two-hourly feeding,” and “three-hourly feeding,” using appropriate Boolean operators. Reference lists of included studies were manually screened to identify additional relevant articles.

Study selection

Studies were considered eligible for inclusion if they met the following criteria: preterm infants, including LBW, very low-birth-weight (VLBW), or extremely low-birth-weight (ELBW) neonates admitted to NICU, were included in the study. The intervention involved a two-hourly enteral feeding schedule, and the comparator was a three-hourly enteral feeding schedule. Eligible studies were required to report at least one relevant outcome, including time to achieve full enteral feeding, feeding intolerance, NEC, hypoglycaemia, weight gain, time to regain birth weight, duration of hospital stay, or other relevant neonatal outcomes.

Only randomised controlled trials (RCTs), quasi-randomised trials, and prospective or retrospective observational cohort studies published in the English language were included. The exclusion criteria include case reports, case series without a comparator, editorials, letters to the editor, conference abstracts, and unpublished studies. Studies involving term infants, infants with major congenital anomalies or chromosomal abnormalities, or studies evaluating feeding modalities other than intermittent bolus feeding, such as continuous enteral feeding, were also excluded.

Data extraction

All retrieved records were imported into EndNote X9 for deduplication. Two independent reviewers screened the titles and abstracts for relevance, followed by a full-text evaluation of the potentially eligible studies. Any disagreements during the selection process were resolved through discussion or by consulting a third reviewer. The final selection of studies is summarised using a PRISMA flow diagram. [Figure 1]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

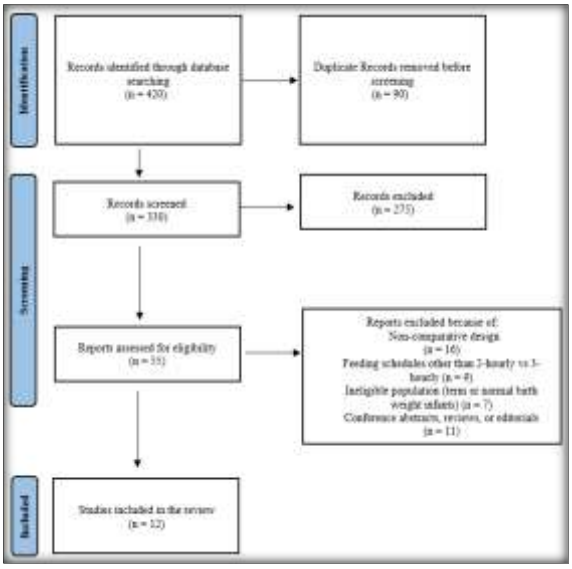

Figure 1: PRISMA 2020 flow diagram showing study selection process

Data extraction was performed independently by two reviewers using a standardised data extraction template. The following information was collected from each eligible study: first author and year of publication, study design, study setting, sample size, and baseline neonatal characteristics, including gestational age, birth weight, and sex distribution. Details of the feeding protocol were extracted, including feeding interval (two-hourly or three-hourly), type of enteral feed (breast milk, formula, or mixed feeding), initial feed volume, and feed advancement strategy, where reported.

Outcome data extracted included time to achieve full enteral feeding, incidence of feeding intolerance, NEC, hypoglycaemia, weight gain, time to regain birth weight, duration of hospital stay, and other reported outcomes, such as need for parenteral nutrition, sepsis, or mortality. Information on outcome definitions, follow-up duration, and subgroup analyses by birth weight or gestational age was recorded when reported. Discrepancies during data extraction were addressed through discussion between the two reviewers. A third reviewer was consulted when consensus could not be reached. When outcome data were missing or unclear, analyses were restricted to the information available in the published reports, and no data imputation was performed.

Risk of bias, data synthesis, and certainty of evidence

Risk of bias was assessed independently by two reviewers. Randomised controlled trials were evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool, while observational studies were assessed using the Newcastle–Ottawa Scale. Disagreements were resolved through discussion. Effect measures, including risk ratios, odds ratios, and mean differences, were extracted as reported in the original studies. Due to clinical and methodological heterogeneity across studies, such as differences in gestational age, birth weight categories, feeding schedules, and outcome definitions, a quantitative meta-analysis was not undertaken. Findings were analysed narratively and summarised in tables. Publication bias was not assessed, as meta-analysis was not performed, and the number of studies per outcome was limited. Certainty of evidence was evaluated qualitatively, considering study design, risk of bias, consistency of results, and precision of reported outcomes.

RESULTS AND DISCUSSION

A total of 420 records were identified through database searching. After removal of 90 duplicate records, 330 records were screened based on titles and abstracts, of which 275 were excluded. Fifty-five full-text articles were assessed for eligibility, and 43 were excluded due to non-comparative study design, inappropriate feeding schedules, ineligible populations, or publication type. Finally, 12 studies met the inclusion criteria and were included in the systematic review. [Figure 1]

1. Study selection and characteristics

The present systematic review included 12 studies, comprising seven randomised controlled trials and five observational cohort studies, evaluating two-hourly versus three-hourly enteral feeding schedules in preterm neonates. Overall, 1,673 preterm infants were analysed across studies, with sample sizes ranging from 60 to 362 neonates. Gestational age ranged from <28 weeks in ELBW cohorts to 36 weeks in late preterm infants, while birth weights spanned <1000 g (ELBW), 1000–1500 g (VLBW), and up to 2000 g (LBW). The studies were conducted in tertiary NICUs across India, Europe, the United States, Malaysia, and Turkey, with enteral feeding delivered mostly via intermittent bolus gavage using expressed breast milk, donor human milk, or preterm formula.

2. Time to achieve full enteral feeding

Definitions of full enteral feeding (FEF) varied across studies, ranging from 100 to 150 mL/kg/day maintained for 24–48 hours without parenteral nutrition (PN). In ELBW <1000 g infants, Rüdiger et al. reported no significant difference in time to FEF, with median times of 26 days in the two-hourly feeding group vs 20 days in the three-hourly feeding group ($p = 0.15$).[11] Similarly, Dhingra et al., Yadav et al., Parashar et al., Tali et al., Ibrahim et al., and Anushree et al. found comparable time to FEF between feeding schedules, with mean or median times ranging from 5 to 10 days in very low birth weight (VLBW; 1000–1500 g) and more mature preterm infants.[6-8,12-14] In contrast, DeMauro et al. demonstrated significantly faster attainment of FEF with two-hourly feeding, with adjusted analyses showing a 3.7-day decrease overall, which was most noticeable in infants born at <28 weeks' gestation, where time to FEF was reduced by 7.2 days.[15] But, Sunil et al., Chalasani and Prasad, and Chu et al. reported earlier achievement of FEF with three-

ISSN (O): 2687-5365; ISSN (P): 2753-6556

hourly feeding, with mean differences of approximately 2–3 days, particularly among infants weighing >1000 g.[5,16,17] Therefore, the effect of feeding interval on time to FEF was heterogeneous and appeared to vary by gestational age and birth weight, with no consistent advantage of either schedule across all preterm populations.

3. Feeding intolerance

Feeding intolerance definitions varied and included vomiting, abdominal distension, increased gastric residuals, or the need for feed interruption. Dhingra et al. reported feeding intolerance in 13% of infants fed three times a day vs 19% of infants fed twice a day, with no significant difference.[12] Anushree et al. observed comparable rates (30% vs. 23.3%, p = 0.56).[6] Yadav et al. and Tali et al. also reported no significant difference in feeding intolerance between schedules.[7,14]

High rates of feed interruption were noted by Rüdiger et al., particularly in ELBW infants, but these were not differentially associated with feeding interval.[11] Across studies, feeding intolerance was numerically but not statistically higher in the two-hourly groups. Thus, the available data suggest that feeding intolerance is affected more by infant maturity and condition than by the choice of two-hourly or three-hourly feeding intervals.

4. Necrotising enterocolitis (NEC)

The incidence of NEC across studies ranged from 2% to 13% in most cohorts. Rüdiger et al. reported comparable NEC rates between two-hourly and three-hourly feeding schedules (7.1% vs. 6.3%).[11] Dhingra et al., Anushree et al., Yadav et al., Parashar et al., Tali et al., and Unal et al. found no statistically significant difference in NEC incidence or severity, including Bell stage ≥ II NEC.[6,7,12-14,18] Particularly, Parashar et al. reported an unusually high incidence of stage II NEC (35.5%) in both feeding groups, without a significant intergroup difference.[13] Ibrahim et al. observed NEC in 6.7% of infants receiving three-hourly feeds compared with 12.0% of those receiving two-hourly feeds; however, this difference did not reach statistical significance.8 These available evidence indicates that altering feeding frequency alone does not appear to modify the risk or severity of NEC in preterm infants.

5. Hypoglycemia

The incidence of hypoglycemia varied across studies, ranging from 1.7% to approximately 26%, with most trials reporting rates below 10%. Dhingra et al., Anushree et al., Yadav et al., Parashar et al., Ibrahim et al., and Tali et al. reported no statistically significant difference in hypoglycemia between two-hourly and three-hourly feeding schedules.[6-8,12-14]

Yadav et al. demonstrated that hypoglycemic episodes in both groups occurred predominantly within the first 48 hours of life, with no difference in timing or recurrence between feeding intervals. No study reported an increased risk of severe or recurrent hypoglycemia attributable to feeding frequency, indicating that glucose homeostasis is maintained with either schedule when standard neonatal monitoring and care practices are followed.

6. Weight gain and growth outcomes

Rüdiger et al. reported identical postnatal growth trajectories, with a mean daily weight gain of 14 ± 4 g/kg/day in both groups.[11] Unal et al. similarly observed comparable early weight gain (15.7 vs. 14.1 g/kg/day) and no difference in weight at discharge.18 Dhingra et al., Chu et al., Tali et al., and Ibrahim et al. found no differences with significance in discharge weight, length, or head circumference between feeding schedules.[12,14,17,8] Growth outcomes were constant across feeding intervals. Thus, changing the feeding frequency does not affect the short-term somatic growth in preterm infants once adequate caloric intake is achieved.

7. Time to regain birth weight

The time to regain birth weight ranges from 10 to 15 days across studies. Dhingra et al., Chu et al., and Tali et al. reported no significant difference between two-hourly and three-hourly feeding schedules.[12,14,17] In contrast, Ibrahim et al. demonstrated a significantly shorter time to regain birth weight with three-hourly feeding (12.9 vs. 14.8 days; p = 0.04), particularly among infants born at >32 weeks' gestation and those who were small for gestational age (SGA).[8]

Subgroup analysis by Tali et al. suggested that infants weighing ≤1000 g achieved full enteral feeds earlier with two-hourly feeding; however, this advantage was observed for time to FEF rather than reliably for time to regain BW.[14] Overall, these findings indicate that birth-weight recovery may be affect primarily by gestational maturity and factors, with feeding interval exerting variable effects in selected subgroups rather than a uniform impact across all preterm infants.

8. Duration of hospital stay

Length of NICU stay varied, from 26 to 86 days. Rüdiger et al., Dhingra et al., Chu et al., Yadav et al., Ibrahim et al., and Unal et al. reported no significant difference in hospital stay between feeding schedules.[7,8,11,12.17,18] Parashar et al. observed a longer NICU stay in the three-hourly group; however, this finding was not consistent across other trials.[13] Therefore, hospital length of stay appears to be affected mainly by baseline neonatal risk and comorbidities rather than the interval of enteral feeding alone.

9. Parenteral nutrition and central line exposure

DeMauro et al. reported that infants fed three-hourly were 4.7 times more likely to require prolonged parenteral nutrition (>28 days).15 In contrast, Chu et al. found longer central catheter and parenteral nutrition exposure in two-hourly-fed infants.[17] Rüdiger et al. observed minimal differences in central venous access duration.[11] This difference suggests that the duration of parenteral support is affect by multiple clinical and institutional factors beyond feeding interval alone.

10. Other neonatal morbidities

Several studies reported additional neonatal morbidities, including apnoea, sepsis, respiratory morbidity, and mortality. Dhingra et al. and Anushree

ISSN (O): 2687-5365; ISSN (P): 2753-6556

et al. found no significant difference in the incidence of apnoea or sepsis between feeding schedules.[6,12] In contrast, Sunil et al. reported a significantly higher incidence of apnoea in the two-hourly feeding group compared with the three-hourly feeding group (28% vs. 4%; p = 0.001),[16] a finding that was not replicated in other trials. Mortality rates were low and comparable across feeding schedules in all studies reporting this outcome. These findings suggest that most neonatal morbidities are not changed by feeding interval, while more frequent feeding may be associated with increased apnoea in selected low-birth-weight cohorts.

11. Nursing workload and feeding-related care burden

Dhingra et al. demonstrated significantly higher nursing time with two-hourly feeding (82 vs. 60 minutes/day, p = 0.03).[12] Tali et al. similarly reported reduced nursing workload with three-hourly feeding (50 vs. 74 minutes/day, p = 0.04).[14] Unal et al. noted reduced handling frequency with longer feeding intervals.[18] These findings supported three-hourly feeding in terms of care burden.

12. Subgroup analyses based on birth weight and gestational age

DeMauro et al. and Tali et al. reported that ELBW infants (<1000 g) may achieve full feeds earlier with two-hourly feeding.[15,14] In contrast, Sunil et al., Chalasani & Prasad, and Ibrahim et al. found that VLBW and more mature preterm infants achieved full feeds earlier or regained birth weight sooner with three-hourly feeding.[5,8,16] Therefore, no uniform subgroup effect was observed across all studies.

13. Summary of key findings

Across 12 studies, two-hourly and three-hourly feeding schedules showed comparable safety profiles, with no consistent differences in the incidence of necrotising enterocolitis, hypoglycaemia, growth outcomes, or mortality. The time required to achieve full enteral feeding varied according to gestational age and birth weight, and no single feeding interval showed clear superiority across all populations. Three-hourly feeding was associated with reduced nursing workload, whereas two-hourly feeding had benefits in extremely low birth weight subgroups.

Table 1: Characteristics of studies included in the systematic review

Studies (Year)	Study design / Population	Feeding schedules compared	Time to full enteral feeds	Key safety outcomes (Feeding intolerance / NEC / Hypoglycaemia)	Growth & hospital stay	Key findings/remarks
Rüdiger et al.[11]	Retrospective cohort; ELBW (<1000 g), n = 74	2-hourly vs 3-hourly	Median 26 vs 20 days (p = 0.15)	NEC 7.1% vs 6.3%; frequent feed interruptions in both groups	Weight gain identical (14 ± 4 g/kg/day); LOS 84 vs 86 days	Feeding interval did not influence feeding advancement, growth, NEC, or LOS; two-hourly feeding associated with shorter CPAP duration and reduced phototherapy exposure
De Mauro et al.[15]	Retrospective cohort; VLBW (500–1500 g), n = 362	2-hourly vs 3-hourly	6.7 ± 3.2 vs 9.4 ± 8.6 days; adjusted −3.7 days (p = 0.001)	NEC 13% vs 12%; mortality similar	No significant difference reported; prolonged PN (>28 days) more common with 3-hourly feeding	Two-hourly feeding independently associated with faster attainment of full feeds, particularly in infants <28 weeks' gestation
Dhingra et al.[12]	Randomised controlled trial; ≤1750 g, n = 87	2-hourly vs 3-hourly	8.1 ± 5.9 vs 8.1 ± 3.9 days	Feeding intolerance 19% vs 13%; NEC 7% in both groups; hypoglycaemia 26% vs 21%	Birth-weight regain 12.8 vs 12.0 days; LOS 26 vs 31 days	Comparable clinical outcomes; three-hourly feeding significantly reduced nursing workload
Chu et al.[17]	Retrospective cohort; ≤1250 g, n = 113	2-hourly vs 3-hourly	Median 15 vs 14 days (adjusted p = 0.054)	NEC 5.6% vs 3.4%; mortality similar	Birth weight regained at 12 days in both groups; LOS similar	Two-hourly feeding associated with longer parenteral nutrition and central line exposure without feeding advantage
Chalasani & Prasad[5]	Open-label comparative study; <2 kg, n = 90	2-hourly vs 3-hourly	13.5 ± 1.4 vs 11.0 ± 2.1 days (p < 0.001)	Feeding intolerance 8.9% vs 4.4%; NEC 4.4% vs 0%	Not reported	Three-hourly feeding achieved full feeds earlier; interpretation may be influenced by greater baseline maturity in the three-hourly group
Anushree et al.[6]	Observational study; VLBW (<1500 g), n = 60	2-hourly vs 3-hourly	Median 10 vs 10 days (p = 0.99)	Feeding intolerance 30% vs 23.3%; NEC 6.7% in both groups; hypoglycaemia similar	Not reported	Both feeding schedules were equally safe and effective in VLBW neonates

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Yadav et al.[7]	Randomised controlled trial; VLBW (1000–1500 g), n = 350	2-hourly vs 3-hourly	Median 5 vs 5 days (p = 0.665)	Feeding intolerance 7.4% vs 6.9%; NEC 2.3% vs 2.9%; hypoglycaemia similar	Not reported	Three-hourly feeding non-inferior to two-hourly feeding with comparable safety outcomes
Sunil et al.[16]	Randomised controlled trial; LBW (1.0–1.8 kg), n = 100	2-hourly vs 3-hourly	13.7 ± 3.5 vs 11.9 ± 3.0 days (p = 0.008)	Apnoea significantly higher with two-hourly feeding; NEC numerically higher with two-hourly feeding (not statistically significant)	Not reported	Three-hourly feeding independently predicted earlier attainment of full enteral feeds
Parashar et al.[13]	Randomised controlled trial; VLBW (1000–1500 g), n = 62	2-hourly vs 3-hourly	9.29 ± 3.02 vs 9.60 ± 3.53 days	Feeding intolerance 74.2% vs 64.5%; NEC 35.5% in both groups	LOS longer with three-hourly feeding	No clear advantage of either feeding schedule for feeding progression or safety outcomes
Ibrahim et al.[8]	Multicentre randomised controlled trial; VLBW (1.0–1.5 kg), n = 150 (144 analysed)	2-hourly vs 3-hourly	10.2 ± 3.7 vs 11.3 ± 4.9 days (p = 0.14)	NEC 12.0% vs 6.7%; hypoglycaemia similar	Birth-weight regain faster with three-hourly feeding (12.9 vs 14.8 days; p = 0.04)	Three-hourly feeding improved birth-weight regain without increasing morbidity
Tali et al.[14]	Randomised controlled trial; ≤1500 g, n = 120	2-hourly vs 3-hourly	9.53 ± 4.26 vs 9.85 ± 5.48 days	Feeding intolerance 40.0% vs 46.7%; NEC 3.3% vs 8.3%	LOS 43.7 vs 46.0 days	Overall equivalence; two-hourly feeding beneficial only in ≤1000 g subgroup; nursing workload lower with three-hourly feeding
Unal et al.[18]	Randomised controlled trial; VLBW (<32 weeks), n = 100	2-hourly vs 3-hourly	Postmenstrual age at full oral feeds: 35 vs 35 weeks	Low and comparable adverse events	LOS 51 vs 49 days; growth outcomes similar	Longer feeding interval did not delay oral feeding or growth and reduced handling burden

Footnotes: ELBW – Extremely Low Birth Weight; VLBW – Very Low Birth Weight; LBW – Low Birth Weight; NEC – Necrotising Enterocolitis; PN – Parenteral Nutrition; LOS – Length of Stay; CPAP – Continuous Positive Airway Pressure. Data are presented as mean ± standard deviation, median, frequencies and percentages. Chi-square test was used for comparison, and a statistical significance was set at $p < 0.05$.

CONCLUSION

In preterm low-birth-weight infants, two-hourly and three-hourly feeding schedules in preterm low-birth-weight infants are equally safe and effective, with no reliable differences in NEC, hypoglycaemia, growth, mortality, or length of hospital stay. Neither feeding schedule showed an advantage in achieving full enteral feeds. Two-hourly feeding may offer benefit in selected extremely low-birth-weight infants, whereas three-hourly feeding reduces nursing workload without adversely affecting clinical outcomes. Feeding intervals should therefore be individualised according to gestational age, clinical stability, and available unit resources. Larger multicentre studies are required to clarify subgroup-specific benefits and to improve enteral feeding protocols.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556