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Systematic Review

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Evaluating Preventive Strategies for Bronchopulmonary Dysplasia in Preterm Neonates: A Systematic Review

Madiha Gul[1], Sadaf Alam[2*], Aisha Durani[3], Mahnoor Raziq[2], Hafiz Muhammad Nouman Javed[2] and Hameed Ullah[3]

[1]Department of Paediatrics, Khyber Teaching Hospital, Peshawar, Pakistan
[2]Department of Paediatrics, Pak International Medical College, Peshawar, Pakistan
[3]Department of Paediatrics, Frontier Crops Teaching Hospital, Peshawar, Pakistan

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Corresponding Author:
Sadaf Alam
Department of Paediatrics, Pak International Medical College, Peshawar, Pakistan
peshawarmc01@gmail.com

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ABSTRACT

Bronchopulmonary dysplasia (BPD) remains a major complication in preterm neonates, affecting long-term respiratory health and quality of life. Despite advances in neonatal care, identifying consistently effective preventive strategies remains a clinical challenge. **Objectives:** To evaluate recent evidence on interventions used to prevent BPD in preterm neonates, focusing on identifying effective strategies and addressing current research gaps. **Methods:** A structured literature search was conducted using PubMed, Embase, Cochrane Library, and Web of Science for studies published between January 2016 and March 2025. Eligible studies included randomized controlled trials, prospective cohorts, and observational studies evaluating interventions in neonates born before 32 weeks of gestation or weighing under 1500 grams. Screening and data extraction were performed independently. Methodological quality was assessed using standard tools. **Results:** Eighteen studies met the inclusion criteria. Interventions evaluated included non-invasive ventilation, minimally invasive surfactant therapy (MIST), pharmacologic agents (melatonin, corticosteroids, intra-tracheal budesonide), and nutritional supplementation (vitamins A and D, fatty acids). MIST, melatonin, budesonide with surfactant, and early vitamin D supplementation consistently reduced BPD incidence. In contrast, vitamin A, maternal DHA supplementation, and systemic hydrocortisone showed limited or inconsistent benefit. **Conclusions:** Several interventions, particularly MIST, budesonide with surfactant, melatonin, and vitamin D, appear effective in preventing BPD in preterm infants. However, inconsistencies in outcomes from other therapies underscore the need for further high-quality trials to guide clinical practice.

INTRODUCTION

Bronchopulmonary dysplasia (BPD) remains a serious and common complication among preterm neonates, especially those born at ≤32 weeks of gestation or with birth weights less than 1500 grams [1]. Despite advances in neonatal care, BPD continues to impact neonatal survival and long-term respiratory and neurodevelopmental outcomes significantly [2]. Preterm infants with BPD often experience extended hospital stays, increased healthcare costs, and higher risks of chronic lung disease, making its prevention a priority in neonatal intensive care settings [3, 4]. Over recent years, various strategies have been investigated to prevent or reduce the severity of BPD. These include non-invasive respiratory support modalities, pharmacological agents, nutritional supplementation, and early developmental interventions [5]. While multiple individual studies and previous systematic reviews have explored these options, most have focused on isolated interventions or a narrow subset of strategies [6]. Furthermore, many existing reviews are outdated and do not incorporate findings from the most recent randomized controlled trials or observational studies. Importantly, the available evidence often lacks consistency in recommendations, partly due to heterogeneity in study design, outcomes assessed, and

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population characteristics. For example, while some reviews report the benefits of non-invasive ventilation, others fail to demonstrate a clear advantage over conventional methods. Similarly, studies investigating pharmacological therapies like corticosteroids or antioxidants like melatonin vary widely in methodology and outcomes. Thus, there remains a lack of consolidated and up-to-date evidence to guide clinicians in selecting the most effective preventive measures. By analysing recent evidence from randomized controlled trials, cohort studies, and prospective observational studies, this review seeks to identify evidence-based interventions that show promise in reducing the incidence and severity of BPD. Interventions covered include non-invasive ventilation, minimally invasive surfactant therapy (MIST), pharmacologic therapies (such as corticosteroids and melatonin), nutritional approaches (including vitamin and fatty acid supplementation), and early developmental care strategies. This review synthesizes current evidence and highlights knowledge gaps and areas for future investigation, supporting evidence-based clinical decision-making in neonatal care.

This study aims to evaluate original research studies published between 2016 and 2025 that assess various preventive strategies for BPD in preterm neonates.

METHODS

A comprehensive search was performed in four major databases: PubMed, Embase, Web of Science, and Cochrane CENTRAL, covering studies published between January 2016 and March 2025. This systematic review evaluated recent evidence on interventions to prevent bronchopulmonary dysplasia (BPD) in preterm neonates. Keywords and MeSH terms included: bronchopulmonary dysplasia, BPD, preterm neonates, prevention, non-invasive ventilation, surfactant therapy, vitamin supplementation, corticosteroids, and melatonin. Boolean operators such as "AND" were used to improve search specificity. Reference lists of selected studies were also checked to identify additional eligible articles. Studies were included if they involved preterm infants (≤32 weeks' gestation or ≤1500g birth weight) and evaluated interventions aimed at preventing BPD. These included non-invasive ventilation strategies (NIPPV, NCPAP, NHFOV, MIST), pharmacological agents (e.g., budesonide, melatonin, corticosteroids), nutritional supplements (e.g., vitamin A, vitamin D, DHA), and early developmental care. Only randomised controlled trials, prospective /retrospective cohort studies, and observational studies reporting BPD-related outcomes were included. Exclusion criteria included studies on term infants, animal models, reviews or editorials, and non-English publications. Two independent reviewers screened the identified studies' titles, abstracts, and full texts. A third reviewer resolved disagreements. Data were extracted using a standardised form, including the author's name, year, study design, sample size, intervention type, outcomes, and key findings. Eighteen studies met the inclusion criteria. Risk of bias was assessed using the Cochrane Risk of Bias Tool for RCTs and the Newcastle-Ottawa Scale for cohort and observational studies. Due to heterogeneity in interventions and outcome measures, data were synthesized narratively rather than through meta-analysis. The PRISMA 2020 flow diagram summarises the selection process (Figure 1).

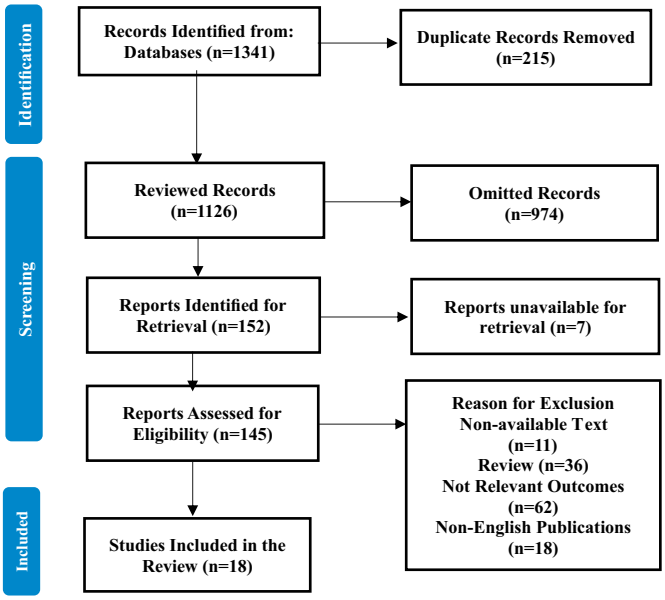

Figure 1: Process of Study Selection for This Systematic Review, Including Identification, Screening, Eligibility Assessment, and Final Inclusion of Studies

RESULTS

This systematic review included 18 studies assessing interventions to prevent bronchopulmonary dysplasia (BPD) in preterm neonates. The interventions comprised non-invasive ventilation, nutritional and pharmacological therapies, and early developmental support. Non-invasive ventilation strategies showed varied effectiveness. Foglia *et al.*, compared nasal intermittent positive-pressure ventilation (NIPPV) to nasal continuous positive airway pressure (NCPAP) in infants ≤28 weeks of gestation and found no significant reduction in BPD or mortality [7]. In contrast, Rachana *et al.*, demonstrated that non-invasive high-frequency oscillatory ventilation (NHFOV) significantly reduced BPD incidence and need for mechanical ventilation compared to non-invasive intermittent mandatory ventilation (NIMV). Nutritional interventions had mixed results [8]. Wendel *et al.*, and Abiramalatha *et al.*, investigated arachidonic acid (ARA) and docosahexaenoic acid (DHA) supplementation, but neither study showed significant benefits [9, 10]. Similarly, Ndiaye *et al.*, found that SMOF lipid emulsion failed to improve BPD-free survival [11]. Marc *et al.*, also reported no benefit from maternal DHA supplementation. Vitamin

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supplementation yielded inconsistent outcomes [12]. Ge *et al.*, found that early vitamin D supplementation (800 IU/day) significantly reduced BPD and inflammatory markers [13]. However, Rakshasbhuvankar *et al.*, reported no benefit of enteral vitamin A on BPD incidence or inflammation. Pharmacological therapies produced variable effects [14]. Manley *et al.*, and Liu *et al.*, noted that intra-tracheal budesonide combined with surfactant significantly reduced BPD and mortality [15, 16]. Conversely, systemic hydrocortisone administered after the first week of life showed no effect on BPD or death in a trial by Onland *et al* [17]. As reported by Remy *et al.*, oral betamethasone was beneficial for patent ductus arteriosus (PDA) closure and ventilator weaning [18]. Melatonin demonstrated significant reduction in BPD, mortality, and hospital stay when used with surfactant [19]. Surfactant delivery techniques were also explored. Dai *et al.*, suggested that optimising surfactant administration angle may reduce BPD and intracranial haemorrhage [20]. Dargaville *et al.*, showed that minimally invasive surfactant therapy (MIST) significantly decreased BPD and mortality compared to CPAP alone [21]. Developmental interventions also proved valuable. Van *et al.*, found that early behavioural programs enhanced long-term motor and cognitive outcomes in preterm infants with BPD [22]. In summary, the most promising interventions were MIST, intra-tracheal budesonide with surfactant, melatonin, and early vitamin D supplementation. Other therapies, particularly nutritional supplements and systemic steroids, showed limited or inconsistent benefits (Table 1).

Table 1: Study Involved for This Research

Sr. No.	References	Study Design	Sample Size	Intervention	Primary Outcome (s)	Key Findings
1	[7]	RCT	1009	NIPPV vs. NCPAP (non -invasive ventilation)	(BPD incidence, mortality	NIPPV was not superior to NCPAP in reducing BPD or mortality.
2	[8]	RCT	140	NHFOV vs. NIMV (non-invasive modes)	BPD incidence, need for ventilation	NHFOV is more effective in reducing BPD and ventilation need.
3	[9]	RCT	200	ARA + DHA supplementation	BPD incidence, respiratory morbidities	No significant impact on BPD or other neonatal morbidities.
4	[10]	RCT	251	Enteral ARA + DHA	Severe ROP, BPD	Reduced ROP risk, but no effect on BPD, sepsis, or IVH.
5	[11]	Cohort	222	SMOF lipid emulsion vs. standard	BPD-free survival	No improvement in BPD-free survival among very preterm infants.
6	[12]	RCT	528	Maternal DHA supplementation	BPD-free survival	No significant improvement in BPD-free survival.
7	[13]	RCT	112	Vitamin D (800 IU/day)	BPD incidence, inflammation	Early vitamin D reduced BPD and inflammatory markers.
8	[14]	Nested Observational	66	Enteral Vitamin A	BPD incidence, faecal calprotectin	No significant change in BPD or inflammation biomarkers.
9	[15]	RCT	1160	Budesonide + surfactant (intra-tracheal)	BPD incidence, mortality	Significantly reduced BPD and mortality in preterm neonates.
10	[16]	RCT	122	Budesonide + surfactant	BPD severity, Oxygen therapy duration	Improved ventilation outcomes without steroid -related complications.
11	[17]	RCT	372	Postnatal hydrocortisone	Death or BPD at 36 weeks PMA	No significant reduction in BPD or mortality.
12	[18]	Retrospective Cohort	101	Oral betamethasone	BPD incidence, PDA closure	Improved PDA closure and ventilator weaning; aided BPD recovery.
13	[19]	RCT	80	Melatonin + surfactant vs. surfactant alone	BPD incidence, mortality	Melatonin reduced BPD, mortality, and length of hospital stay.
14	[20]	RCT	96	Surfactant administration angles	BPD, intracranial haemorrhage	Certain angles reduced BPD and intracranial haemorrhage rates.
15	[21]	RCT	485	MIST vs. CPAP	Death or BPD at 36 weeks PMA	MIST significantly lowered rates of death or BPD.

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16	[22]	RCT	176	Early behavioural program	Motor and cognitive outcomes	Improved long-term development in infants with BPD.
17	[23]	Prospective Cohort	2693	Combined perinatal interventions	Severe BPD or death	Synergistic interventions reduced the risk of severe BPD or death.
18	[24]	RCT	800	Inhaled nitric oxide (iNO)	Neurodevelopmental outcomes	No significant benefit on long-term outcomes at 7 years.

DISCUSSION

A systematic review highlights multiple strategies for preventing bronchopulmonary dysplasia (BPD) in preterm neonates. Several interventions demonstrated promising clinical benefits, while others showed inconsistent or limited effects. Existing literature largely supports these findings, though some discrepancies persist [25, 26]. Non-invasive ventilation techniques effectively reduced BPD incidence, particularly non-invasive high-frequency oscillatory ventilation (NHFOV). Rachana *et al.*, reported significantly lower rates of BPD and reduced mechanical ventilation needs with NHFOV [8]. This aligns with a meta-analysis by Minamitani *et al.*, which confirmed superior outcomes for high-frequency non-invasive ventilation over conventional methods such as NCPAP and NIPPV [27]. However, Jensen *et al.*, observed no significant advantage of nasal intermittent positive-pressure ventilation (NIPPV) over nasal continuous positive airway pressure (NCPAP) [25]. This finding is also supported by earlier systematic reviews conducted by Mitra *et al.*, [28]. These mixed outcomes suggest that timing, technique, and patient characteristics may influence the effectiveness of non-invasive respiratory strategies. Pharmacological agents showed variable effectiveness. Melatonin, for example, demonstrated consistent benefit in reducing BPD, mortality, and hospital stay duration^10. This is supported by Häusler *et al.*, who emphasised melatonin's antioxidant and anti-inflammatory properties as protective against neonatal lung injury [29]. Similarly, intra-tracheal administration of budesonide mixed with surfactant significantly reduced the incidence and severity of BPD [14]. These findings are consistent with prior meta-analyses such as Venkataraman *et al.*, which endorsed the safety and efficacy of this combined therapy [30]. Vitamin-based interventions yielded mixed results. Ge *et al.*, found that early vitamin D supplementation reduced BPD incidence and inflammatory markers [13]. This aligns with other systematic reviews that support vitamin D's anti-inflammatory role in improving respiratory outcomes [31]. On the other hand, vitamin A supplementation showed no clear benefit. Rakshasbhuvankar *et al.*, observed no improvement in BPD outcomes or faecal inflammation [14]. This mirrors the findings by Ding *et al.*, who questioned the practical value of routine vitamin A use in this population [32]. Maternal supplementation with docosahexaenoic acid (DHA) also produced a limited benefit. Marc *et al.*, reported no significant improvement in BPD-free survival [33]. This result corresponds with findings from Tanaka *et al.*, who also noted negligible respiratory advantages in preterm infants whose mothers received DHA [34]. These outcomes highlight the need for more targeted nutritional interventions and larger studies to confirm clinical efficacy. Minimally invasive surfactant therapy (MIST) consistently showed positive results. Dargaville *et al.*, reported a significant reduction in BPD [21] and mortality when MIST was used compared to standard CPAP [23]. These outcomes align with earlier systematic reviews, such as Rigo *et al.*, which emphasised the effectiveness of MIST in spontaneously breathing preterm infants [35]. Postnatal corticosteroid therapy produced contrasting outcomes. Oral betamethasone aided ductus arteriosus closure and supported ventilator weaning [13]. Systemic hydrocortisone therapy did not significantly affect BPD or survival outcomes^23. This is consistent with a meta-analysis by De *et al.*, who advised caution in using systemic corticosteroids due to their limited benefits and potential risks [36]. Lastly, developmental care strategies also warrant consideration. Van *et al.*, demonstrated that early behavioural intervention programs significantly improved motor and cognitive outcomes in infants with BPD^24. These findings support previous systematic reviews that promote early neurodevelopmental support for high-risk preterm infants [22].

CONCLUSIONS

This systematic review identifies several preventive strategies that show meaningful potential in reducing the incidence and severity of bronchopulmonary dysplasia (BPD) in preterm neonates. Among the most consistently effective interventions were minimally invasive surfactant therapy (MIST), intra-tracheal budesonide with surfactant, melatonin, and early vitamin D supplementation. These strategies demonstrated favourable outcomes across multiple high-quality studies and may serve as reliable options in neonatal clinical practice. On the other hand, interventions such as systemic hydrocortisone, vitamin A, and maternal DHA supplementation showed limited or inconsistent benefits. While they hold theoretical and biological plausibility, current evidence does not support their routine use without further validation through large-

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scale, well-designed trials. In conclusion, a combination of non-invasive respiratory techniques, targeted pharmacological therapies, and early nutritional support appears to be the most effective approach for BPD prevention. Continued research is needed to standardize treatment protocols, evaluate long-term safety, and identify patient-specific factors influencing intervention effectiveness.

Authors Contribution

Conceptualization: MG
Methodology: MG, SA, AD, MR, HMNJ
Formal analysis: MG, HU
Writing review and editing: SA, AD, MR, HMNJ, HU

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Li Ching Ng ML. The Association Between BMI Trajectories and the Development of Bronchopulmonary Dysplasia among Preterm Infants Born at Less Than 30 Weeks of Gestational Age. 2022.doi:10.1038/s41390-022-02358-4.

[2] Principi N, Di Pietro GM, Esposito S. Bronchopulmonary Dysplasia: Clinical Aspects and Preventive and Therapeutic Strategies. Journal of Translational Medicine.2018Dec;16:1-3.doi:10.1186/s12967-018-1417-7.

[3] Kugelman A and Durand M. A Comprehensive Approach to the Prevention of Bronchopulmonary Dysplasia.Pediatric Pulmonology.2011Dec;46(12):1153-65. doi: 10.1002/ppul.21508.

[4] Zimmermann LJ, Kostenzer J, Mader S. Tackling Bronchopulmonary Dysplasia to Improve Preterm Health: A Call for Family-Centred Care at World Prematurity Day 2020. American Journal of Physiology-Lung Cellular and Molecular Physiology. 2020Nov;319(5):L867-70.doi:10.1152/ajplung.00415.2020.

[5] Beam KS, Aliaga S, Ahlfeld SK, Cohen-Wolkowiez M, Smith PB, Laughon MM. A Systematic Review of Randomized Controlled Trials for the Prevention of Bronchopulmonary Dysplasia in Infants. Journal of Perinatology.2014 Sep;34(9):705-10.doi:10.1038/jp.2014.126.

[6] Muehlbacher T, Bassler D, Bryant MB. Evidence for the Management of Bronchopulmonary Dysplasia in Very Preterm Infants. Children.2021Apr;8(4):298.doi:10.3390/children8040298.

[7] Foglia EE, Jensen EA, Kirpalani H. Delivery Room Interventions to Prevent Bronchopulmonary Dysplasia in Extremely Preterm Infants. Journal of Perinatology. 2017 Nov; 37(11): 1171-9. doi: 10.1038/jp.2017.74.

[8] Rachana RD, Oleti T, Saikiran D, Vardhelli V, Thiruveedi S, Hussain A *et al.* Non-Invasive High-Frequency Oscillatory Ventilation Versus Non-Invasive Intermittent Mandatory Ventilation as A Rescue Mode In Preterm Infants with Respiratory Distress on Nasal CPAP—A Randomized Control Trial. European Journal of Paediatrics.2025 Mar; 184(3): 1-8. doi: 10.1007/s00431-025-06041-8.

[9] Wendel K, Aas MF, Gunnarsdottir G, Rossholt ME, Bratlie M, Nordvik T *et al.* Effect of Arachidonic and Docosahexaenoic Acid Supplementation on Respiratory Outcomes and Neonatal Morbidities in Preterm Infants. Clinical Nutrition.2023 Jan; 42(1): 22-8. doi: 10.1016/j.clnu.2022.11.012.

[10] Abiramalatha T, Ramaswamy VV, Bandyopadhyay T, Somanath SH, Shaik NB, Pullattayil AK *et al.* Interventions to Prevent Bronchopulmonary Dysplasia in Preterm Neonates: An Umbrella Review of Systematic Reviews and Meta-Analyses.JAMA Paediatrics.2022May;176(5):502-16.doi:10.1001/jamapediatrics.2021.6619.

[11] Ndiaye AB, Mohamed I, Pronovost E, Angoa G, Piedboeuf B, Lemyre B *et al.* Use of SMOF Lipid Emulsion in Very Preterm Infants Does Not Affect the Incidence of Bronchopulmonary Dysplasia–Free Survival. Journal of Parenteral and Enteral Nutrition. 2022 Nov; 46(8): 1892-902. doi: 10.1002/jpen.2380.

[12] Marc I, Piedboeuf B, Lacaze-Masmonteil T, Fraser W, Mâsse B, Mohamed I *et al.* Effect of Maternal Docosahexaenoic Acid Supplementation On Bronchopulmonary Dysplasia–Free Survival in Breastfed Preterm Infants: A Randomized Clinical Trial. Journal of the American Medical Association. 2020 Jul; 324(2): 157-67. doi: 10.1001/jama.2020.8896.

[13] Ge H, Qiao Y, Ge J, Li J, Hu K, Chen X *et al.* Effects of Early Vitamin D Supplementation on the Prevention of Bronchopulmonary Dysplasia in Preterm Infants. Pediatric Pulmonology.2022Apr;57(4):1015-21.doi:10.1002/ppul.25813.

[14] Rakshasbhuvankar AA, Pillow JJ, Patole SK, Nathan EA, Simmer K. Effect of Enteral Vitamin A on Faecal Calprotectin in Extremely Preterm Infants: A Nested Prospective Observational Study. Neonatology.2021 Sep; 118(6): 720-6. doi: 10.1159/000518680.

[15] Manley BJ, Kamlin CO, Donath SM, Francis KL, Cheong JL, Dargaville PA, Dawson JA, Jacobs SE, Birch P, Resnick SM, Schmölzer GM. Intra-tracheal Budesonide Mixed with Surfactant for Extremely Preterm Infants: The PLUSS Randomized Clinical Trial. Journal of the American Medical Association. 2024 Dec; 332(22): 1889-99.

DOI: https://doi.org/10.54393/pjhs.v6i5.3015

[16] Liu MM, Ji L, Dong MY, Zhu XF, Wang HJ. Efficacy and Safety of Intra-Tracheal Administration of Budesonide Combined with Pulmonary Surfactant in Preventing Bronchopulmonary Dysplasia: A Prospective Randomized Controlled Trial. Chinese Journal of Contemporary Paediatrics. 2022 Jan; 24(1): 78-84.

[17] Onland W, Cools F, Kroon A, Rademaker K, Merkus MP, Dijk PH *et al.* Effect of Hydrocortisone Therapy Initiated 7 to 14 Days After Birth on Mortality or Bronchopulmonary Dysplasia among Very Preterm Infants Receiving Mechanical Ventilation: A Randomized Clinical Trial. Journal of the American Medical Association.2019Jan;321(4):354-63.doi: 10.1001/jama.2018.21443.

[18] Remy A, Vincent M, Pastor-Diez B, Picaud JC. Late Postnatal Steroid Treatment Using Oral Beta-methasone Can Help to Close Ductus Arteriosus in Extremely Preterm Infants Who Cannot Be Weaned from Ventilation. European Journal of Paediatrics. 2024 Nov; 184(1):50.doi:10.1007/s00431-024-05840-9.

[19] Gharehbaghi MM, Yeganedoust S, Shaseb E, Fekri M. Evaluation of Melatonin Efficacy in Prevention of Bronchopulmonary Dysplasia in Preterm New-born Infants. The Turkish Journal of Paediatrics.2022 Feb; 64(1): 79-84. doi: 10.24953/turkjped.2021.1334.

[20] Dai XF, Zhu AA, Xie TT, Xiong YH, Meng L, Chen MW. Impact of Different Angles of Pulmonary Surfactant Administration on Bronchopulmonaryplasia and Intracranial Haemorrhage in Preterm Infants: A Prospective Randomized Controlled Study. Chinese Journal of Contemporary Paediatrics.2024 Apr;26(4): 337-42.

[21] Dargaville PA, Kamlin CO, Orsini F, Wang X, De Paoli AG, Kutman HG *et al.* Effect of Minimally Invasive Surfactant Therapy Vs Sham Treatment on Death or Bronchopulmonary Dysplasia in Preterm Infants with Respiratory Distress Syndrome: The OPTIMIST-A Randomized Clinical Trial. Journal of the American Medical Association. 2021 Dec; 326(24): 2478-87.

[22] Van Hus JW, Jeukens-Visser M, Koldewijn K, Holman R, Kok JH, Nollet F *et al.* Early Intervention Leads to Long-Term Developmental Improvements in Very Preterm Infants, Especially Infants with Bronch-opulmonary Dysplasia.Acta Paediatric.2016Jul; 105(7): 773-81. doi: 10.1111/apa.13387.

[23] Chen X, Yuan L, Jiang S, Gu X, Lei X, Hu L *et al.* Synergistic Effects of Achieving Perinatal Interventions on Bronchopulmonary Dysplasia in Preterm Infants. European Journal of Paediatrics. 2024 Apr; 183(4): 1711-21.

[24] Greenough A, Decobert F, Field D, Hallman M, Hummler HD, Jonsson B *et al.* Inhaled Nitric Oxide (INO) or Preventing Prematurity-Related Bronchopulmonary Dysplasia (BPD): 7-Year Follow-Up of the European Union Nitric Oxide (EUNO) Trial. Journal of Perinatal Medicine.2021 Jan; 49(1): 104-10. doi: 10.1515/jpm-2020-0164.

[25] Jensen EA. Prevention of Bronchopulmonary Dysplasia: A Summary of Evidence-Based Strategies. Neo-reviews.2019Apr;20(4):e189-201.doi:10.1542/neo.20-4-e189.

[26] Durlak W and Thébaud B. BPD: latest Strategies of Prevention and Treatment. Neonatology.2024Sep; 121(5): 596-607. doi: 10.1159/000540002.

[27] Minamitani Y, Miyahara N, Saito K, Kanai M, Namba F, Ota E. Non-Invasive Neutrally-Adjusted Ventilatory Assist in Preterm Infants with Respiratory Distress: A Systematic Review and Meta-Analysis.2023.doi: 10.21203/rs.3.rs-2900977/v1.

[28] Mitra S, Disher T, Pichler G, D'Souza B, McCord H, Chayapathi V *et al.* Delivery Room Interventions to Prevent Bronchopulmonary Dysplasia in Preterm Infants: A Protocol For A Systematic Review and Network Meta-Analysis. British Medical Journal Open. 2019Aug;9(8):e028066.doi:10.1136/bmjopen-2018-028066.

[29] Häusler S, Robertson NJ, Golhen K, van den Anker J, Tucker K, Felder TK. Melatonin as a Therapy for Preterm Brain Injury: What Is the Evidence? Antioxidants.2023Aug;12(8):1630.doi:10.3390/antiox12081630.

[30] Venkataraman R, Kamaluddeen M, Hasan SU, Robertson HL, Lodha A. Intra-tracheal Administration of Budesonide-Surfactant in Prevention of Bronchopulmonary Dysplasia in Very Low Birth Weight Infants: A Systematic Review and Meta-Analysis. Pediatric Pulmonology.2017Jul;52(7):968-75.doi:10.1002/ppul.23680.

[31] Álvarez-Fuente M, Moreno L, Mitchell JA, Reiss IK, Lopez P, Elorza D et al. Preventing Bronchopulmonary Dysplasia: New Tools for an Old Challenge. Pediatric Research.2019Mar;85(4):432-41.doi:10.1038/s41390-018-0228-0.

[32] Ding Y, Chen Z, Lu Y. Vitamin A Supplementation Prevents the Bronchopulmonary Dysplasia in Premature Infants: A Systematic Review and Meta-Analysis.Medicine.2021Jan;100(3):e23101.doi:10.1097/MD.0000000000023101.

[33] Marc I, Boutin A, Pronovost E, Herrera NM, Guillot M, Bergeron F *et al.* Association Between Enteral Supplementation with High-Dose Docosahexaenoic Acid and Risk of Bronchopulmonary Dysplasia in Preterm Infants: A Systematic Review and Meta-Analysis. Journal of the American Medical Association Network Open.2023Mar;6(3):e233934-.doi:10.1001/jamanetworkopen.2023.3934.

[34] Tanaka K, Tanaka S, Shah N, Ota E, Namba F. Docosahexaenoic Acid and Bronchopulmonary

DOI: https://doi.org/10.54393/pjhs.v6i5.3015

Dysplasia in Preterm Infants: A Systematic Review and Meta-Analysis. The Journal of Maternal-Fetal and Neonatal Medicine.2022May;35(9):1730-8.doi:10.1080/14767058.2020.1769590.

[35] Rigo V, Lefebvre C, Broux I. Surfactant Instillation in Spontaneously Breathing Preterm Infants: A Systematic Review and Meta-Analysis.European Journal of Paediatrics.2016 Dec; 175: 1933-42. doi:10.1007/s00431-016-2789-4.

[36] De Luca D, Ferraioli S, Watterberg KL, Baud O, Gualano MR. Hydrocortisone in Very Preterm Neonates for BPD Prevention: Meta-Analysis and Effect Size Modifiers. Archives of Disease in Childhood-Fetal and Neonatal Edition.2024Sep;109(5):481-7.doi:10.1136/archdischild-2023-326254.