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Non-Invasive Respiratory Support for 22–23-week Gestational age infants

ADVANCING PREMATURE LUNG PROTECTION AT UT SOUTHWESTERN (APLUS) 2024

Angela Kribs

Children's Hospital University of Cologne, Neonatology and Pediatric Intensive Care

Medical Faculty University of Cologne

Conflict of interest

During the last three years, I received fees as a member of advisory boards from Chiesi and for lectures from Chiesi and Vygon.

Agenda

Background behind our concept of non invasive respiratory support

Description of the concept

Results

Clinical observations and resulting questions

Most preterm infants – also those with a gestational age of 22-23 weeks- show respiratory efforts after birth and are not dead.

So they need no resuscitation and not obligatory positive pressure ventilation but they certainly need respiratory support!

But:

The rhythm of breathing can easily be disturbed and they show mostly signs of dyspnea and respiratory distress

So the questions are:

What can we do to help the infants to start sponaneous breathing and to preserve respiratory function?

What are the causes of dyspnea?

What is the best way to support breathing and what can we do to avoid and to treat dyspnea?

Measures to help the baby to start breathing

Cooperation with obstreticans, anesthesiologists and midwives

- Antenatal steroids
- Avoidance of asphyxia and inflammation
- Avoidance of general anesthesia
- Optimization of birth mode
- Optimization of umbilical cord management

Standardization of delivery room management

- Optimization of temperature (heated, humidified gas)
- Minimizing of any kind of stress
- Lung recruitment
- Surfactant
- Caffeine

Establishing stable respiration, creating a balance of oxygen consumption and oxygen intake

Oxygen consumption

Any stress

Low temperature

Light

Noise

Pain

Loss of postural control

Separation from the mother

Oxygen intake

Oxygen

CPAP

Mechanical ventilation

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What are infants‘ needs during neonatal transition?

Replacement of pulmonary fluid by air

(influenced by gestational age, mode of delivery, application of antenatal steroids)

Opening of the pulmonary circulation

(aeration preceeds perfusion, need for blood to fill pumonary vessels, influence of umbilical cord management)

Carakteristics of the immature respiratory system

Unstable upper airways

Stiff alveoli

- reduced surface area, less capacity for gas exchange
- thick interstitial tissue, high vulnerability
- less elastic recoil, high susceptility to overinflation

Unstable thoracic wall

Weak muscles

Immature regulation of breathing

Closed glottis during apnea

Most important problem:

Creating a balance between atelectasis and overinflation

Effects of CPAP (CDP)

Stabilization of airways

Stabilization of the thoracic wall >> reduction of work of breathing

Increase of the intraalveolar pressure

- reduction of the intraalveolar fluid
- avoidance of the end-expiratory alveolar collapse
- preservation of surfactant

Stimulation of breathing

But: How to find the right CDP - level?

Phases of respiratory transition

Stuart B Hooper et al. Respiratory transition in the newborn: a three-phase process
Arch Dis Child Fetal Neonatal Ed 2016;101:F266-F271

1. Phase of fluid clearance
2. Phase of accumulation of fluid in the interstitial tissue
3. Phase of resorption of fluid in the interstitial tissue and of gas exchange

It is very unlikely that one fixed level of distending pressure fits the needs of the different phases of transition!

Therapy during phase 1 –
Characteristics and theoretical considerations

Phase 1:

Gas exchange not yet possible, replacement of fluid in the airways and the alveoli by air, movement of the fluid/air interface until transfer into the interstitial tissue.

Aim: uniform aeration of the lung by opening of the glottis and allowing deep inspirations

Duration in healthy term infants: seconds to minutes, perhaps longer in preterm infants, after CS and if no antenatal steroids were applied.

Therapeutic options:

Sustained inflation: long inspiration with defined pressure until the whole lung is aerated

or:

Increasing distending pressure, allowing spontanuous breathing, if necessary applying positive pressure ventilation with defined tidal volumes until the whole lung is aerated

Most important therapeutic element: Continuous distending pressure, perhaps need of high pressure levels

Therapy during phase 2 – Characteristics and theoretical considerations

Phase 2:

Fluid accumulation in interstitial tissue, increasing pressure in interstitial tissue, possibility of reentry of fluid into the alveoli and the airways, impaired gas exchange, decrease of tidal volume

Aim: Avoidance of reentry of fluid into the airways, preservation of aeration

Duration in healthy term newborns 4-6 hrs, longer in preterm infants

Problems: thickened alveolar wall and diffusion line, low oxygen uptake, impaired CO_2 elimination, low compliance

Therapeutic options:

Adaquate CDP, oxygen, surfactant

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Therapy during phase 3 – Characteristics and theoretical considerations

Phase 3:

Phase of resorption and after complete resorption of pulmonary fluid phase of stable gas exchange

Aim: maintenance of FRC and blood gas homeostasis

Problems: Overlapping with phase 2, still thickened alveolar wall and lower compliance, adaptation of all parameters continuously necessary

Therapeutic options:

adaquate and titrated CDP, adapted and titrated FiO_2

During respiratory transition CDP has continuously to be re-evaluated and adopted!

How to find the optimal distending pressure?

By stepwise increasing and, after that, decreasing of positive end-expiratory pressure (PEEP) during conventional positive pressure ventilation or the distending pressure during HFOV or CPAP the upper and lower deflection point of the pressure volume curve can be identified.

(Dargaville PA, Tingay DG *J Paediatrics and Child Health 48 (2012) 740–746)*.

The optimal CDP is clinically characterized by the fact that with a constant Delta P the highest Delta V is reached and that the FiO_2 for an adaquate saturation is minimal. Furthermore infants show the lowest signs of dyspnoea.

The value of optimal CDP together with the FiO2 describe the actual state of the lung!

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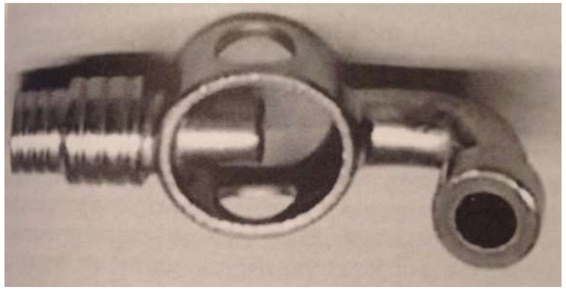
Brit. J. Anaesth. (1968), 40, 464

A VALVE SUBSTITUTE WITH NO MOVING PARTS, FOR ARTIFICIAL VENTILATION IN NEWBORN AND SMALL INFANTS

BY

D. BENVENISTE AND J.-E. POUL PEDERSEN

Flow



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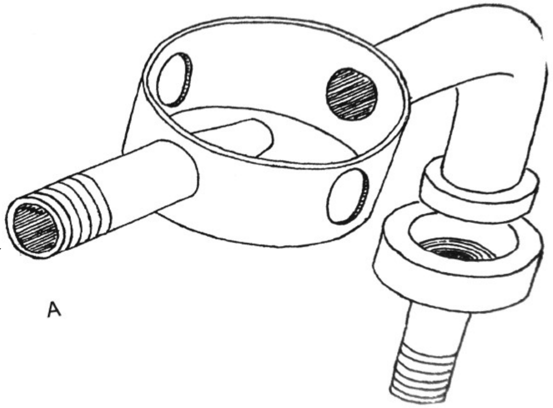

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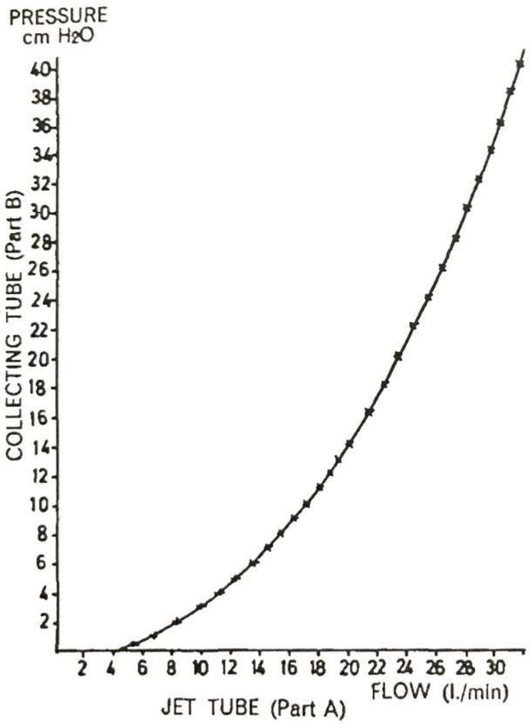
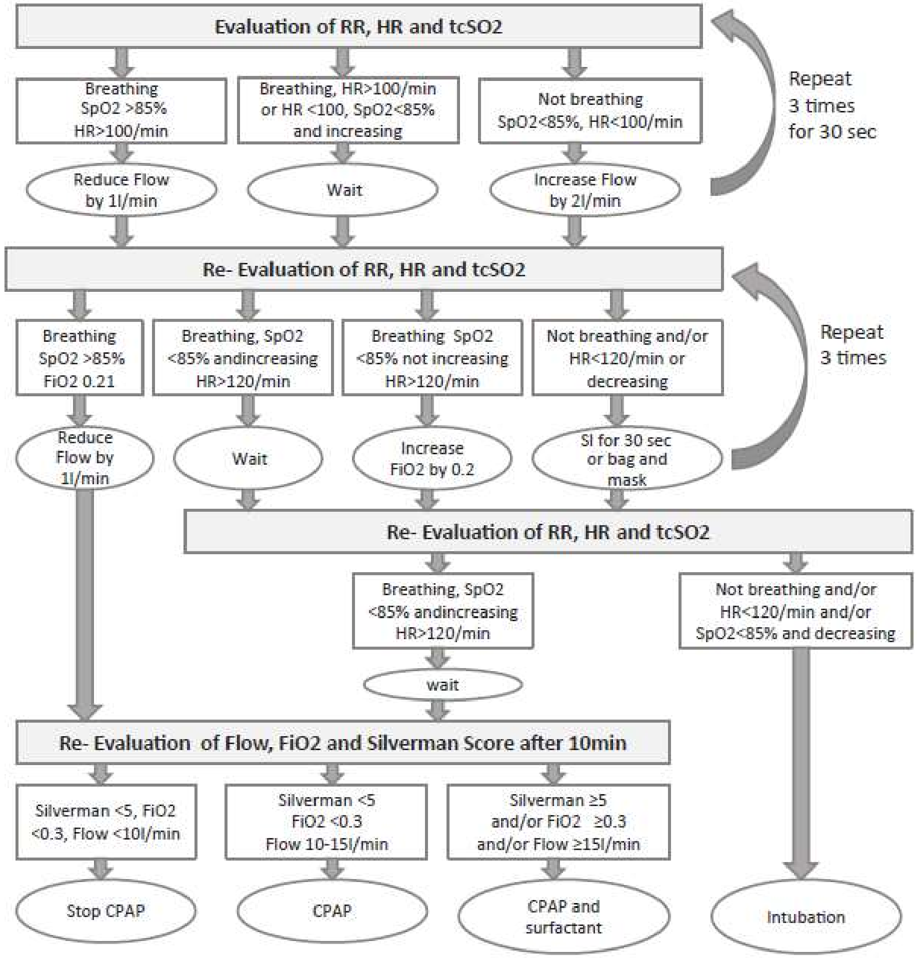




Mehler K et al *2012 Acta paediatrica*

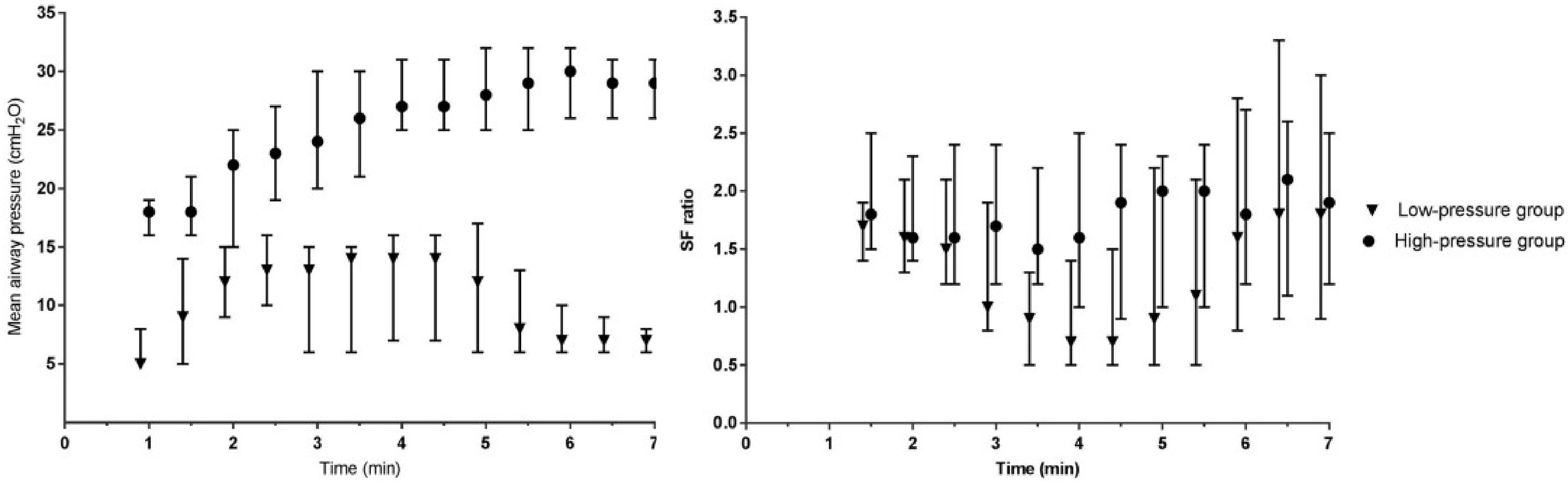
Aim:

Reduction of CDP below 15 cm H2O at end of stabilization

Further reduction during the next 8 hrs below 10 cm H2O

Comparison of Two Respiratory Support Strategies for Stabilization of Very Preterm Infants at Birth: A Matched-Pairs Analysis

Martherus T et al *Front Pediatr. 2019 Jan 29;7:3*



SF ratio. The SF ratio (SpO2/FiO2) represents gas exchange over the lungs and corrects the SpO2 for the given FiO2. Data is presented as median (IQR). At 1.5 and 2 min, the mean of the high-pressure group is calculated based on n = 9 and n = 16, respectively. All other presented data is based on n ≥ 20.

The high pressure strategy went along with a lower intubation rate during the course of RDS and during the whole hospital stay

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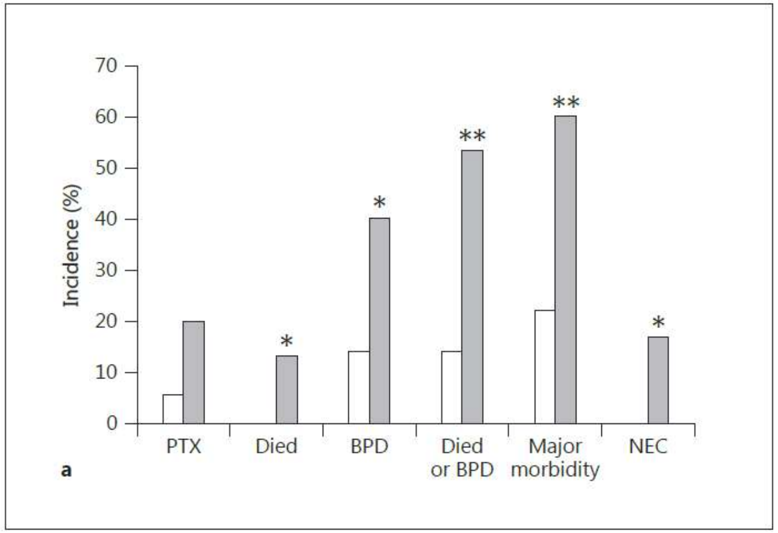
Continuous Positive Airway Pressure Failure in Preterm Infants: Incidence, Predictors and Consequences

Dargaville PA et al. *Neonatology 2013;104:8–14*



Neonatal outcomes in the CPAP groups. 25–28 weeks' gestation. White bars = Initial CPAP, successful; grey bars = initial CPAP, failed; PTX = pneumothorax. Higher incidence in infants failing CPAP, * p < 0.05. * * p < 0.01

Predictor	Univariate logistic regression			Multivariate logistic regression model 1			Multivariate logistic regression model 2		
	OR	p value	95% CI	OR	p value	95% CI	OR	p value	95% CI
Gestational age	0.61	0.044	0.38, 0.99	0.41	0.087	0.15, 1.14	0.48	0.193	0.16, 1.45
Birth weight	0.99	0.018	0.99, 0.99	0.99	0.265	0.99, 1.00	0.99	0.387	0.99, 1.00
Multiple birth	2.63	0.069	0.93, 7.43	1.62	0.555	0.32, 8.12	2.59	0.305	0.42, 16.03
Caesarean delivery	5	0.004	1.65, 15.17	11.12	0.024	1.37, 90.10	14.77	0.022	1.47, 148.55
FiO_2 by 2 h	1.21	<0.001	1.10, 1.33	1.20	0.001	1.08, 1.33	1.19	0.002	1.06, 1.33
CPAP level	3.21	0.001	1.57, 6.56	–	–	–	3.04	0.054	0.98, 9.40

Logistic regression analysis examining prediction of CPAP failure at 25–28 weeks' gestation (n = 66). OR, p values and 95% CI for univariate analysis, and multivariate logistic regression using model 1 (excluding CPAP level) and model 2 (with CPAP level included).

CPAP- failure is related to a high risk of mortality and morbidity

Surfactant therapy via thin catheter in preterm infants with or at risk of respiratory distress syndrome

Abdel-Latif ME, Davis PG, Wheeler KI, De Paoli AG, Dargaville PA. Cochrane Database Syst Rev. 2021 May 10;5(5):CD011672

	RR	95% CI	RD	95% CI	NNTB	95% CI
Death or BPD	0,59	0,48-0,73	-0,1	-0,15 - -0,07	9	7-16
Intubation during the first 72 hrs	0,63	0,54-0,74	-0,14	-0,18 - -0,09	8	6-12
Severe IVH	0,63	0,42-0,96	-0,04	-0,08 - -0,00	22	12-193
Death	0,63	0,47-0,84	-0,02	-0,10 - -0,06	20	12-58
BPD in survivers	0,57	0,45-0,74	-0,09	-0,11 - -0,04	13	9-24

Surfactant should be applied early in the course of RDS by LISA!

Caffeine

	Caffeine DR group (13 patients) $N = 1{,}091$ breaths	Caffeine NICU group (10 patients) $N = 779$ breaths	*P* value	OR (95% confidence interval)
Minute volume (ml/kg)[a]	189 ± 74	162 ± 70	< 0.05	53.1 (18.0 to 88.3)
Average rate of rise to maximum tidal volumes (ml/kg/s)[b]	14.3 (11.2 to 19.8)	11.2 (7.9 to 15.2)	< 0.001	5.5 (4.8 to 6.3)
Average inspired tidal volume (ml/kg)[b]	5.2 (3.9 to 6.4)	4.4 (3.0 to 5.6)	< 0.001	0.8 (0.5 to 1.0)
Recruitment (number of breaths with inspired tidal volume/kg > 8 ml)[c]	142/1,061 (13%)	67/779 (9%)	0.001	1.6 (1.2 to 2.2)
Respiratory rate/min at 7–9 min after birth[a]	35 ± 10	33 ± 10	NS	4.7 (−0.5 to 9.9)
Heart rate (b.p.m.)[b]	157 (141 to 170)	146 (135–160)	< 0.001	9.7 (8.2 to 11.2)
Maximum fraction of inspired oxygen at 7–9 min after birth[a]	0.55 ± 0.21	0.63 ± 0.27	NS	10.0 (−15.7 to 35.7)
Fraction of inspired oxygen when leaving the delivery room[b]	0.35 (0.31 to 0.40)	0.39 (0.32 to 0.63)	NS	7.8 (−12.2 to 27.7)
Oxygen saturation (%) at 7–9 min after birth[b]	91 (87 to 94)	91 (88 to 94)	NS	−0.2 (−0.7 to 0.4)

DR, delivery room; IQR, interquartile range; NICU, neonatal intensive care unit; OR, odds ratio; NS, not significant.
[a]Data are presented as mean ± SD for parametric data.
[b]Median (IQR) for nonparametric data.
[c]*n* (%) for categorical data.

Dekker J et al. *Pediatr Res. 2017 Aug;82(2):290-296*

Caffeine, if applied in the delivery room, increases minute volume, tidal volume and recruitment breaths and can thereby facilate transition!

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What is NHFOV and how does it work?

Pharyngeal oscillations produced by bubble CPAP are assumed to improve CO2- elimination.

Pulmonary oscillations during invasive HFOV are known to improve CO2 –elimination.

Non invasive HFOV may be an increased bubble-CPAP with the effects observed in invasive HFOV

NHFOV may be a usefull tool to escalate non invasive respiratory support!

Biology of the Neonate

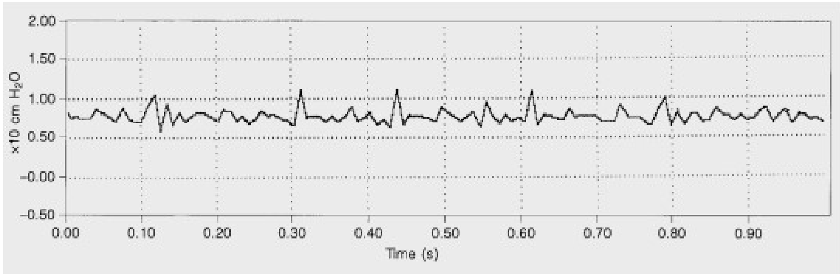
Original Paper

Biol Neonate 1998;73:69–75

A Comparison of Underwater Bubble Continuous Positive Airway Pressure with Ventilator-Derived Continuous Positive Airway Pressure in Premature Neonates Ready for Extubation

Kyong-Soon Lee
Michael S. Dunn
Marsha Fenwick
Andrew T. Shennan

Department of Newborn and Developmental Paediatrics, Regional Perinatal Unit, Women's College Hospital and Department of Paediatrics, University of Toronto, Toronto, Ont., Canada



Waveform produced at airway with bubble CPAP. Flow set at 8 liters/min; amplitude of waveform 2–4 cm H2O; waveform frequency approximately 15–30 Hz

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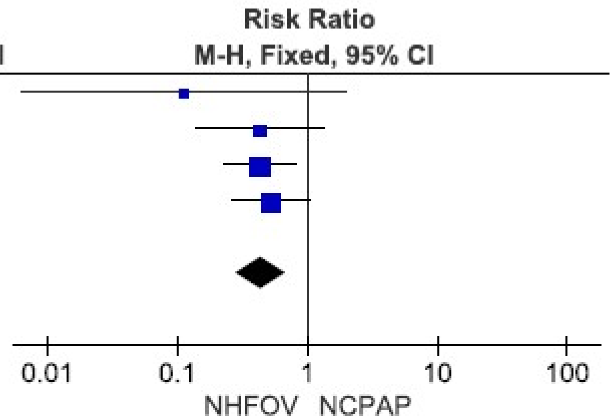
Nasal high-frequency oscillatory ventilation versus nasal continuous positive airway pressure as primary respiratory support strategies for respiratory distress syndrome in preterm infants: a systematic review and meta-analysis

Li J et al *Eur J Ped (2022) 181:215–223*

Outcome: Intubation

	NHFOV		NCPAP			Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Fixed, 95% CI**
Iranpour et al. 2019	0	34	4	34	8.0%	0.11 [0.01, 1.99]
Malakian et al. 2019	4	63	9	61	16.3%	0.43 [0.14, 1.32]
Zhu et al 2017	9	37	22	39	38.1%	0.43 [0.23, 0.81]
Zhu et al. 2021	11	152	21	150	37.6%	0.52 [0.26, 1.03]
Total (95% CI)		**286**		**284**	**100.0%**	**0.44 [0.29, 0.67]**
Total events	24		56			

Heterogeneity: Chi² = 1.09, df = 3 (P = 0.78); I² = 0%
Test for overall effect: Z = 3.78 (P = 0.0002)



nHFOV: Practical aspects

Settings at start of nHFOV

MAP: CPAP- Level + 2 cm H_2O

Freq: (6)-8-(10) Hz

Ampl.: visible vibrations of the chest

Interfaces:

- Nasopharyngeal tube
- Nasal prongs
- Nasal mask

Effects of the respiratory management on pulmonary perfusion

Rapid and homogenous aeration

>> decrease of pulmonary vascular resistance

>> risk of left to right shunting via the duct

At the same time:

Lower endothoracic pressure than in infants on invasive mechanical ventilation

>> increased risk of early left to right shunting via the duct

>>>>

Systematic echocardiographic screening starting at 12 hrs after birth!

Medical closing of the duct as early as a continuous left to right shunting is observed!

Indications for intubation and invasive ventilation

Persistent or recurrent apnea

Respiratory acidosis pH < 7,20 despite optimized non invasive respiratory support

FiO2 > 0,6 despite optimized non invasive respiratory support and after surfactant

Severe abdominal distension

Pneumoperitoneum

Preferred mode of invasive mechanical ventilation

HFOV

Parameter- Settings

MAP: CPAP- Level + 2 cm H2O

Freq: (6)-8-(10) Hz

Ampl.: visible vibrations of the chest

Key elements of the Cologne approach of early respiratory management

Use of prenatal steroids after parental counseling from 22 weeks of gestation

Cesarean delivery with local anesthesia as prefered mode of delivery

Delayed cord clamping or physiology-based cord clamping by extra-uterine placental perfusion

Soft landing with comfort (mostly) lateral positioning of the infant

Establishment of spontaneous breathing via a stepwise increasing continuous distending pressure by use of a variable flow device (Benveniste valve)

Less invasive surfactant application early in the course of RDS (usually about 30 min after birth)

Early use of Caffeine already during stabilization in the delivery room

Escalation to nHFOV in cases of respiratory insufficiency or apnea

Early screening for PDA

Early targeted medical closure of duct

Results

82 ELGANs (n=35 with a GA of 22 weeks, n=47 with a GA of 23 weeks) born 2019-2022

Survival	77 %
Intubated within first hour	8 %
Intubated ever in NICU	79 %
Mean age at first intubation in survivors	110 hrs
Mean duration of invasive ventilation in survivors	21 days
Pneumothorax	11 %
Mechanical ventilation at 36 weeks	3 %
Nasal canula at discharge	14 %
Grade 3-4 IVH	19 %
Treated ROP	5 %
Focal intestinal perforation	19 %
PDA management	
Echo within 24 hrs	100 %
Medical treatment	90 %
Surgical / Cath closure	3 %

Summary

The focus of our approach is establishing and preservation of spontaneous breathing by minimizing stress and individualizing respiratory support.

The primary respiratory support is use of a continuous distending pressure adopted to the three phase process of pulmonary transition by individualized titration.

Infant comfort is a priority during the whole process as it minimizes oxygen consumption.

Caffeine is given soon after birth to stimulate spontaneous breathing.

Early less invasive surfactant therapy is routinely performed as it is a cornerstone to minimize need of respiratory support.

nHFOV is the preferred mode to escalate respiratory support in cases of respiratory insufficiency.

Early targeted medical closure of PDA is performed based on early echocardiographic screening starting at 12 hrs after birth

More than 75 % of infants ≤23 weeks can successfully be managed with this protocol!

Thank you for your attention!