COVER PAGE

Official Title: NON-INVASIVE NEURALLY ADJUSTED VENTILATORY ASSIST VERSUS NASAL INTERMITTENT POSITIVE PRESSURE VENTILATION FOR PRETERM INFANTS AFTER EXTUBATION: A RANDOMIZED CONTROLLED TRIAL

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Study Results

Study Type	**Interventional**
Study Design	Allocation: Randomized; Intervention Model: Parallel Assignment; Masking: None (Open Label); Primary Purpose: Treatment
Condition	Non-invasive neurally adjusted ventilatory assist versus nasal intermittent positive pressure ventilation for preterm infants after extubation
Intervention	Device: noninvasive respiratory support with **NAVA** mode and **NIPPV**
Enrollment	36

Participant Flow

Recruitment Details	Patients recruited from single tertiary center neonatal intensive care unit (NICU) level 3 at the King Fahad Armed Forces Hospital in Saudi Arabia between May 2017 and April 2019
Pre-assignment Details	41 assessed for eligibility, 5 excluded, 36 randomized subsequently equally

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description	NI-NAVA after extubation Initial ventilatory settings were NAVA level of 2; Positive End Expiratory Pressure (PEEP) of 5-6 cm H2O; apnea time 5-10 seconds; and target electrical activity of the diaphragm (Edi) maximum between 10-15 and minimum <5 for 72 hours post extubation.	NIPPV after extubation Positive Inspiratory Pressure (PIP) incremented at 2 cm H2O from the pre-extubation PEEP of 5-6 cm H20 for 72 hours post extubation. The set respiratory rate was same as prior to extubation.
Period Title: **Overall Study**		
Started	18	18
Completed	18	18
Not Completed	0	0
Reason Not Completed		
Adverse Event (Death)	2	1

Baseline Characteristics

Arm/Group Title		NI-NAVA Group	NIPPV Group	Total
▼ Arm/Group Description		Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants	Total of all reporting groups
Overall Number of Baseline Participants		18	18	36
▼ Baseline Analysis Population Description		[Not Specified]		
Age at extubation, Continuous Mean (Standard deviation) Unit of measure: Days				
	Number Analyzed	18 participants	18 participants	36 participants
		1.67 (1.49)	1.17 (0.38)	1.41(1.11)
Sex: Female, Male				

Measure Type: Count of Participants **Unit of measure: Participants**				
	Number Analyzed	18 participants	18 participants	36 participants
	Female	8 44.4%	8 44.4%	16 44.4%
	Male	10 55.6%	10 55.6%	20 55.6%%
Gestational Age, continuous **Mean (Standard Deviation)** **Unit of measure: Weeks**				
	Number Analyzed	18 participants	18 participants	36 participants
		28.94 (1.83)	28.55 (1.18)	28.74 (1.53)
Birth Weight, continuous **Mean (Standard deviation)**				

Unit of measure: g				
	Number Analyzed	18 participants	18 participants	36 participants
		1251.94 (329.13)	1051.0 (376.99)	1151.47 (363.36)
Antenatal Steroid usage Measure Type: Count of Participants Unit of measure: Frequency				
	Number Analyzed	18 participants	18 participants	36 participants
	YES	14 (77.8%)	11 (61.1%)	25 (69.4%)
Presence of IUGR Measure Type: Count of Participants Unit of measure: Frequency				
	Number Analyzed	18 participants	18 participants	36 participants
		0 (0%)	1 (5.6%)	1 (2.8%)
CRIB Score				

Mean (Standard Deviation) **Unit of measure: number**				
	Number Analyzed	18 participants	18 participants	36 participants
		1.72 (2.02)	1.88 (1.40)	1.80 (1.72)
Duration of invasive ventilation **Mean (Standard Deviation)** **Unit of measure: hours**				
	Number Analyzed	18 participants	18 participants	36 participants
		22.77 (35.05)	10.22 (11.55)	16.50 (26.49)
Caffeine usage **Measure Type: Count of Participants** **Unit of measure: Participants**				
	Number Analyzed	18 participants	18 participants	36 participants

	YES	18 (100%)	18 (100%)	36 (100%)
Patent Ductus Arteriosus (PDA) at birth **Measure Type: Count of Participants** **Unit of measure: Participants**				
	Number Analyzed	18 participants	18 participants	36 participants
	Present	7 (38.9%)	4 (22.2%)	11 (30.6%)

Outcome Measures

1. **Primary Outcome**

Title	**Treatment failure**
Description	hypoxia (FiO2 requirement >0.35), respiratory acidosis (pH < 7.2 & PCO 2 > 60 mm Hg) or major apnea requiring mask ventilation or >4 episodes/hour. Rescue treatment with NIPPV was also considered as treatment failure.
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
Overall Number of Participants Analyzed	18	18
Measure Type: Count of Participants **Unit of measure: Participants**		
	1 (5.5%)	0 (0%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	0.310
	Comments	[Not Specified]
	Method	Pearson's chi-square
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	
	Estimated Value	
	Confidence Interval	
	Parameter Dispersion	
	Estimation Comments	

2. **Primary Outcome**

Title	**Reintubation**
Description	Treatment failure leading to reintubation of infant within 72 hours
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
Overall Number of Participants Analyzed	18	18
Measure Type: Count of Participants **Unit of measure: Participants**		
	4 (22.2%)	2 (11.1%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	0.371
	Comments	[Not Specified]
	Method	Pearson’s chi-square
	Comments	[Not Specified]

Method of Estimation	Estimation Parameter	
	Estimated Value	
	Confidence Interval	
	Parameter Dispersion	
	Estimation Comments	

3. **Secondary Outcome**

Title	**Intraventricular Hemorrhage**
Description	IVH (grades III & IV) classified according to Papile et al after evaluation of head ultrasound by a pediatric radiologist
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
Overall Number of Participants Analyzed	18	18

Measure Type: Count of Participants **Unit of measure: Participants**		
	2 (11.1%)	0 (0%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	0.486
	Comments	[Not Specified]
	Method	Fisher's exact
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	
	Estimated Value	
	Confidence Interval	
	Parameter Dispersion	
	Estimation Comments	

4. **Secondary Outcome**

Title	**Necrotizing Enterocolitis**
Description	Necrotizing enterocolitis defined according to modified Bell's criteria (stage 2 to 3)
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
Overall Number of Participants Analyzed	18	18
Measure Type: Count of Participants **Unit of measure: Participants**		
	4 (22.2%)	0 (0%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV

	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	0.034
	Comments	[Not Specified]
	Method	Pearson's chi-square
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	
	Estimated Value	
	Confidence Interval	
	Parameter Dispersion	
	Estimation Comments	

5. **Secondary Outcome**

Title	**Pneumothorax**
Description	Air leak within pleural cavity diagnosed radiologically
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	NI-NAVA	NIPPV
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
Overall Number of Participants Analyzed	18	18
Measure Type: Count of Participants **Unit of measure: Participants**		
	0 (0%)	0 (0%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	-
	Comments	[Not Specified]
	Method	-
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	
	Estimated Value	

	Confidence Interval	
	Parameter Dispersion	
	Estimation Comments	

6. **Secondary Outcome**

Title	**GI Perforation**
Description	Gastrointestinal perforation diagnosed radiologically or at operation
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
Overall Number of Participants Analyzed	18	18
Measure Type: Count of Participants **Unit of measure: Participants**		

	1 (5.6%)	0 (0%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	0.310
	Comments	[Not Specified]
	Method	Pearson's chi-square
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	
	Estimated Value	
	Confidence Interval	
	Parameter Dispersion	
	Estimation Comments	

7. Secondary Outcome

Title	**Sepsis**
Description	Nosocomial sepsis defined as presence of clinical signs of sepsis or positive blood or cerebrospinal fluid (CSF) cultures taken after five days of age
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
Overall Number of Participants Analyzed	18	18
Measure Type: Count of Participants **Unit of measure: Participants**		
	2 (11.1%)	2 (11.1%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	1.000

	Comments	[Not Specified]
	Method	Pearson's chi-square
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	
	Estimated Value	
	Confidence Interval	
	Parameter Dispersion	
	Estimation Comments	

8. **Secondary Outcome**

Title	**Retinopathy of prematurity**
Description	Retinopathy of prematurity (ROP) stage 3 or greater according to International classification
Time Frame	72 hours

Outcome Measure Data

- **Analysis Population Description**

The analysis was "per protocol". 36 patients who had completed the study was used for the analysis.

Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description:	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV)

		after extubation in preterm infants
Overall Number of Participants Analyzed	18	18
Measure Type: Count of Participants **Unit of measure: Participants**		
	2 (11.1%)	1 (5.6%)

Statistical Analysis 1

Statistical Analysis Overview	**Comparison Group Selection**	NI-NAVA, NIPPV
	Comments	[Not Specified]
	Type of Statistical Test	Superiority or Other
	Comments	[Not Specified]
Statistical Test of Hypothesis	**P-Value**	0.546
	Comments	[Not Specified]
	Method	Pearson's chi-square
	Comments	[Not Specified]
Method of Estimation	Estimation Parameter	
	Estimated Value	
	Confidence Interval	
	Parameter Dispersion	

	Estimation Comments	

Adverse Events

Time Frame	72 hours	
Adverse Event Reporting Description	[Not Specified]	
Arm/Group Title	**NI-NAVA**	**NIPPV**
Arm/Group Description	Non-invasive Neurally adjusted ventilatory assist (NAVA) after extubation in preterm infants	Non-invasive positive pressure ventilation (NIPPV) after extubation in preterm infants
All-Cause Mortality		
	NI-NAVA	**NIPPV**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	2/18 (11.1%)	1/18 (5.6%)
Serious Adverse Events		
	NI-NAVA	**NIPPV**
	Affected / at Risk (%)	Affected / at Risk (%)
Total	0/18 (0.00%)	0/18 (0.00%)
▼ **Other (Not Including Serious) Adverse Events**		
Frequency Threshold for Reporting Other Adverse Events	5%	
	NI-NAVA	**NIPPV**
	Affected / at Risk (%)	Affected / at Risk (%)

Total	0/18 (0.00%)	0/18 (0.00%)	