High Flow Nasal Cannula (HFNC)

Prof Sunil Sinha University of Durham & James Cook University Hospital, UK

High-flow nasal cannula

- Humidified gas and can blend oxygen with air
- Perception that it is easy to use and comfortable
- Greater access to face and improved bonding & feeding
- Experience in children with Respiratory Tract Infection

Indications for use of HFNC

- Signs of Respiratory Distress
- Slow to wean off CPAP
- Chronic Lung Disease with long term dependency on CPAP
- Alternative to CPAP with nasal trauma
- Alternative to CPAP following extubation
- ?? Early treatment of RDS

Contraindications of HFNC

- The need for intubation and/or Mechanical Ventilation
- Unstable Respiratory Drive with recurrent
 apnoea
- Inability to maintain acceptable blood gases
- Upper airway abnormality e.g. Cleft, TOF, Choanal atresia

Settings for HFNC

- Start at 4-6L/min
- Aim for oxygen saturations between 91-94%
- Maximum Flow 6L/min in infants <1 kg, can go higher in bigger babies
- Generation of higher distending pressure with decreasing weight and higher flow !
- Depends on leak around the nasal prongs

Weaning

• <u>If Fio2</u> ,0.25

Reduce flow rate by 0.5L/min 12 hrly

• <u>If Fio2 0.25 to 0.3</u>

Reduce flow rate by 0.5L/min 24 hrly

• <u>If FiO2 >0.3</u>

Do not wean flow rate

<u>When flow rate <2L/min</u>, change to Low Flow oxygen therapy

HFNC- Mode of action

- Reduction in respiratory dead space leading to Improved Tidal volume delivery
- Improved thoracic-abdominal synchrony
- Stabilisation of respiratory rate
- Prolonged inspiratory time

EVIDENCE FOR HF USE FROM CLINICAL TRIALS

- 1. Post-extubation
- 2. 'Weaning' from CPAP
- 3. Primary support

HF vs. CPAP POST-EXTUBATION IN PRETERM INFANTS



Cochrane Database of Systematic Reviews

High flow nasal cannula for respiratory support in preterm infants (Review)

Wilkinson D, Andersen C, O'Donnell CPF, De Paoli AG, Manley BJ



Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD006405. DOI: 10.1002/14651858.CD006405.pub3.

Treatment Failure <7 Days



	HEN	С	CPA	2		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
3.4.1 <28 weeks							
Collins 2013a	11	30	15	29	19.1%	0.71 [0.39, 1.28]	
Manley 2013	43	83	32	91	38.2%	1.47 [1.04, 2.09]	
Subtotal (95% Cl)		113		120	57.4%	1.22 [0.91, 1.64]	•
Total events	54		47				
Heterogeneity: Chi ² = 4.41, df:	= 1 (P = 0	.04); I²	= 77%				
Test for overall effect: Z = 1.31	(P = 0.19)					
2 4 2 20 22 weeks							
3.4.2 28-32 weeks			-		0.000	0.00 10 40 4 7 4	
Collins 2013a	4	37	(36	8.9%	0.56 [0.18, 1.74]	
Maniey 2013 Maatafa Okanakka nii 2014	9	69		60	9.4%	1.12 [0.44, 2.82]	
Mostata-Gharenbaghi 2014	2	14	4	13	5.2%	0.46 [0.10, 2.12]	
Yoder 2013 Subtotal (05% CI)	3	175	3	58 167	3./%	1.05 [0.22, 5.00]	
Subtotal (95% CI)	4.0	175	24	107	27.170	0.60 [0.44, 1.44]	
Liotorogonoity: Chiž - 1 51 df.	18 - 270 - 0	COV-12	_ 00 ⁷				
Toot for everall effect: 7 = 0.74	= 3 (P = 0 70 = 0.40	.08), F N	= 0%				
Test for overall effect. $\Sigma = 0.74$	(F = 0.40	9					
3.4.3 ≥32 weeks							
Mostafa-Gharehbaghi 2014	3	28	4	30	4.8%	0.80 [0.20, 3.28]	
Yoder 2013	8	52	6	61	6.9%	1.56 [0.58, 4.22]	
Subtotal (95% CI)		80		91	11.8 %	1.25 [0.56, 2.79]	~
Total events	11		10				
Heterogeneity: Chi ² = 0.58, df	= 1 (P = 0	.45); I²	= 0%				
Test for overall effect: Z = 0.55	(P = 0.58)					
3.4.4 <37 weeks' (subaroup a	data not a	vailab	le)				
Campbell 2006	12	20	-, 2	20	3.8%	4 00 [1 33 12 05]	
Subtotal (95% CI)	12	20		20	3.8%	4.00 [1.33, 12.05]	
Total events	12		3			. / .	
Heterogeneity: Not applicable			-				
Test for overall effect: Z = 2.46	(P = 0.01)				╺┫┠╸ ◢	
Total (95% CI)		388		398	100.0%	1.21 [0.95, 1.55]	•
Total events	95		81				
Heterogeneity: Chi² = 12.89, d	f= 8 (P =	0.12);1	≈ = 38%				
Test for overall effect: Z = 1.54	(P = 0.12)					Eavours HENC Eavours CPAP
Test for subaroup differences	: Chi ² = 6.	42. df=	= 3 (P = 0	09), I ^z	= 53.2%		Tavouis FIFING Favouis OFAF

Treatment Failure <7 Days



	HEN	С	CPA	Р		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
3.4.1 <28 weeks							
Collins 2013a	11	30	15	29	19.1%	0.71 [0.39, 1.28]	
Manley 2013	43	83	32	91	38.2%	1.47 [1.04, 2.09]	
Subtotal (95% CI)		113		120	57.4%	1.22 [0.91, 1.64]	•
Total events	54		47				
Heterogeneity: Chi ² = 4.41, df:	= 1 (P = 0	.04); I ^z	= 77%				
Test for overall effect: Z = 1.31	(P = 0.19)					
3.4.2 28-32 weeks							
Collins 2013a	4	37	7	36	8.9%	0.56 [0.18, 1.74]	_
Manley 2013	9	69	7	60	9.4%	1.12 [0.44, 2.82]	_
Mostafa-Gharehbaghi 2014	2	14	4	13	5.2%	0.46 [0.10, 2.12]	
Yoder 2013	3	55	3	58	3.7%	1.05 [0.22, 5.00]	
Subtotal (95% Cl)		175		167	27.1%	0.80 [0.44, 1.44]	
Total events	18		21				
Heterogeneity: Chi ² = 1.51, df:	= 3 (P = 0	.68); I ^z	= 0%				
Test for overall effect: Z = 0.74	(P = 0.48	i)					
3.4.3 ≥32 weeks							
Mostafa-Gharehbaghi 2014	3	28	4	30	4.8%	0.80 [0.20, 3.28]	
Yoder 2013	8	52	6	61	6.9%	1.56 [0.58, 4.22]	
Subtotal (95% CI)		80		91	11.8%	1.25 [0.56, 2.79]	•
Total events	11		10				
Heterogeneity: Chi ² = 0.58, df:	= 1 (P = 0	.45); I²	= 0%				
Test for overall effect: Z = 0.55	(P = 0.58)					
3.4.4 <37 weeks' (subgroup o	lata not a	wailabl	le)				
Campbell 2006	12	20	3	20	3.8%	4.00 [1.33, 12.05]	
Subtotal (95% Cl)		20		20	3.8%	4.00 [1.33, 12.05]	
Total events	12		3				
Heterogeneity: Not applicable							
Test for overall effect: Z = 2.46	(P = 0.01)					
Total (05% CI)		200		200	100.0%	4 24 [0.05 4 55]	
Total (95% CI)	0.5	388	0.1	298	100.0%	1.21 [0.95, 1.55]	
i otal events	95	0.4.00	81 7 0001				
Teet fax everyall effects 7 4 5	1 = 8 (P =	0.1Z);1 N	-=38%				0.05 0.2 1 5 20
Test for overall effect: Z = 1.54	(P = 0.12)	() 10.46	2 (D - 2	000.12	60.00V		Favours HFNC Favours CPAP
iest for subgroup differences	: Chi r = 6.	42, at =	= 3 (P = U	.09), (*:	= 53.2%		

Treatment Failure <7 Days



Study or Subgroup	HEN	C	CPA	D Total	Woight	Risk Ratio	Risk Ratio
3.4.1 <28 weeks	Events	TULA	Events	TULAI	weight	M-n, Fixed, 95% Ci	м-п, гіхец, 95% сі
Collins 2013a	11	30	15	29	191%	0 71 (0 39 1 28)	_ _
Manley 2013	43	83	32	91	38.2%	1.47 [1.04, 2.09]	- - -
Subtotal (95% CI)		113		120	57.4%	1.22 [0.91, 1.64]	◆
Total events	54		47				
Heterogeneity: Chi ² = 4.41, df	'= 1 (P = 0	.04); I ^z	= 77%				
Test for overall effect: Z = 1.31	1 (P = 0.19))					
3 / 2 29 32 wooke							
Collins 2013a	A	27	7	26	8 0%	0.56 (0.19.1.74)	
Manley 2013a	a a	69	7	60	9.4%	1 1 2 [0 44 2 82]	
Mostafa-Gharehbaghi 2014	2	14	. 4	13	5.2%	0.46 [0.10, 2.12]	_
Yoder 2013	3	55	3	58	3.7%	1.05 [0.22, 5.00]	
Subtotal (95% CI)		175		167	27.1%	0.80 [0.44, 1.44]	
Total events	18		21				
Heterogeneity: Chi ² = 1.51, df	'= 3 (P = 0	l.68); I ²	= 0%				
Test for overall effect: Z = 0.74	4 (P = 0.46	i)					
3.4.3 > 32 weeks							
Mostafa-Gharebhanbi 2014	3	28	4	30	4 8%	0.80 (0.20, 3.28)	
Yoder 2013	8	52	- 6	61	6.9%	1 56 [0.58 4 22]	
Subtotal (95% CI)	Ŭ	80	Ŭ	91	11.8%	1.25 [0.56, 2.79]	
Total events	11		10				_
Heterogeneity: Chi ² = 0.58, df	'= 1 (P = 0	.45); I²	= 0%				
Test for overall effect: Z = 0.55	5 (P = 0.58	3)					
3.4.4 <37 weeks' (subaroun	data not a	wailah	le)				
Campbell 2006	12	20	.~, २	20	3.8%	4 00 [1 33 12 05]	
Subtotal (95% CI)	12	20		20	3.8%	4.00 [1.33, 12.05]	
Total events	12		3				
Heterogeneity: Not applicable	e						
Test for overall effect: Z = 2.46	6 (P = 0.01)					
Total (95% CI)		388		398	100 0%	1.21 [0 95 1 55]	_
Total events	Q.5	500	81	000	100.070	121[000, 100]	•
Heterogeneity: Chi ² = 12.89 (35 1f= 8 (P =	0.12):1	P= 38%				++
Test for overall effect: $Z = 1.54$	4 (P = 0.12	?) ?)					0.05 0.2 1 5 20
Test for subgroup differences	s: Chi ² = 6	, 42, df=	= 3 (P = 0	.09), I ^z :	= 53.2%		Favours HENC Favours CPAP

Reintubation <7 Days



	HEN	с	CPA	Р		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
3.5.1 <28 weeks							
Collins 2013a	5	30	7	29	8.9%	0.69 [0.25, 1.93]	
Manley 2013	25	83	31	91	36.8%	0.88 [0.57, 1.37]	
Subtotal (95% CI)		113		120	45.6%	0.85 [0.57, 1.26]	
Total events	30		38				
Heterogeneity: Chi ² = 0.19, df	= 1 (P = 0).66); l²	= 0%				
Test for overall effect: Z = 0.81	(P = 0.42)	2)					
3.5.2 28-32 weeks							
Manley 2013	2	69	7	60	9.3%	0.25 [0.05, 1.15]	
Mostafa-Gharehbaghi 2014	2	14	4	13	5.2%	0.46 [0.10, 2.12]	
Liu 2014	4	23	6	19	8.2%	0.55 [0.18, 1.67]	
Yoder 2013	3	55	5	56	6.2%	0.61 [0.15, 2.43]	
Collins 2013a	2	37	1	36	1.3%	1.95 [0.18, 20.53]	\leftarrow
Subtotal (95% CI)		198		184	30.1%	0.51 [0.27, 0.97]	
Total events	13		23				
Heterogeneity: Chi ² = 2.18, df	= 4 (P = 0).70); I 2	= 0%				
Test for overall effect: Z = 2.07	' (P = 0.04	4)					
2 E 2 x 22 weeks							
5.5.5 ≥52 weeks							
Mostata-Gharenbaghi 2014	3	28	4	30	4.8%	0.80 [0.20, 3.28]	
Liu 2014	5	48	(60	1.1%	0.89 [0.30, 2.64]	
Yoder 2013 Subtatal (05% CI)	8	120	(151	8.0% 20.6%	1.34 [0.52, 3.45]	
	4.0	120	4.0	151	20.0%	1.05 [0.50, 1.97]	
l otal events	16	201.12	18				
Teet for everell effect: 7 = 9.14	= Z (P = L),79);1= N	= 0%				
Test for overall effect: $Z = 0.14$	F (P = 0.89	1)					
3.5.4 <37 weeks (subaroup a	lata not a	vailabl	e)				
Campbell 2006	12	20	´	20	37%	4 00 [1 33 12 05]	
Subtotal (95% Cl)	12	20		20	3.7%	4.00 [1.33, 12.05]	
Total events	12		3				
Heterogeneity: Not applicable			Ŭ				
Test for overall effect: Z = 2.48	6 (P = 0.01	D D					
		· /					
Total (95% CI)		459		475	100.0%	0.91 [0.68, 1.20]	
Total events	71		82				
Heterogeneity: Chi ² = 12.90, c	f = 10 (P	= 0.23)	; I² = 22%				
Test for overall effect: Z = 0.70) (P = 0.49	3)					Eavours HENC Eavours CPAP
Test for subgroup differences	: Chi² = 1	0.35, dt	f=3 (P=	0.02), P	² = 71.0%		

Death or BPD



	HEN	С	CPAP			Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
3.1.1 <28 weeks								
Collins 2013a	15	30	18	29	13.9%	0.81 [0.51, 1.27]		
Manley 2013	45	83	45	91	32.6%	1.10 [0.82, 1.46]	_	
Subtotal (95% CI)		113		120	46.5%	1.01 [0.79, 1.29]		
Total events	60		63					
Heterogeneity: Chi ² = 1.25, df: Test for overall effect: Z = 0.08	= 1 (P = 0 (P = 0.94	1.26); I² 4)	= 20%					
3.1.2 28-32 weeks								
Mostafa-Gharehbaghi 2014	1	14	3	13	2.4%	0.31 [0.04, 2.61]	←	
Manley 2013	6	69	12	60	9.7%	0.43 [0.17, 1.09]	• • • · · · · · · · · · · · · · · · · ·	
Liu 2014	11	23	11	19	9.1%	0.83 [0.47, 1.47]		
Collins 2013a	16	37	16	36	12.3%	0.97 [0.58, 1.64]		
Yoder 2013	12	55	13	58	9.6%	0.97 [0.49, 1.95]		
Subtotal (95% CI)		198		186	43.2%	0.78 [0.57, 1.08]		
Total events	46	500.17	55					
Test for overall effect: Z = 1.50	= 4 (P = 0 (P = 0.13	1.50); if 3)	= 0%					
3.1.3 >32 weeks								
Mostafa-Gharehbaghi 2014	Ο	28	Ω	30		Not estimable		
Yoder 2013	6	52	9	61	6.3%	0.78 (0.30, 2.05)		
Liu 2014	10	48	6	60	4.0%	2.08 [0.82, 5.32]		
Subtotal (95% Cl)		128		151	10.3%	1.29 [0.67, 2.48]		
Total events	16		15					
Heterogeneity: Chi ² = 2.04, df:	= 1 (P = 0).15); I ^z	= 51%					
Test for overall effect: Z = 0.77	(P = 0.44	4)						
Total (95% CI)		439		457	100.0%	0.94 [0.78, 1.14]	-	
Total events	122		133					
Heterogeneity: Chi ² = 8.42, df:	= 8 (P = 0).39); i ²	= 5%					
Test for overall effect: Z = 0.63	(P = 0.53	3)					Favours HFNC Favours CPAP	
 Test for subgroup differences; 	: Chi² = 2	.48, df=	= 2 (P = 0	.29), I²:	= 19.5%			

Pneumothorax



Study or subgroup	HFNC	CPAP	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H,Fixed,95% Cl		M-H,Fixed,95% Cl
Collins 2013	0/67	1/65		12.9 %	0.32 [0.01, 7.80]
Liu 2014	1/71	2/79		16.0 %	0.56 [0.05, 6.00]
Manley 2013	1/152	4/151		34.0 %	0.25 [0.03, 2.20]
Mostafa-Gharehbaghi 2014	1/42	3/43		25.1 %	0.34 [0.04, 3.15]
Yoder 2013	0/107	1/119		12.0 %	0.37 [0.02, 9.00]
Total (95% CI)	439	457	-	100.0 %	0.35 [0.11, 1.06]
Total events: 3 (HFNC), 11 (CPAP)					
Heterogeneity: $Chi^2 = 0.25$, df = 4	$(P = 0.99); I^2 = 0.0$)%			
Test for overall effect: $Z = 1.86$ (P =	= 0.062)				
Test for subgroup differences: Not a	applicable				
			0.01 0.1 1 10 100		
			Favours HFNC Favours CPAP		

Nasal Trauma





Conclusions

- High Flow can be used effectively and safely as post-extubation support
- Rescue CPAP should be available
- Care should be taken with the most preterm infants (particularly <26 weeks)

HF TO **'WEAN' FROM CPAP** IN PRETERM INFANTS

HF To 'Wean' From CPAP

- Only 2 small RCTs with conflicting results
- No difference in successful weaning from CPAP
- HF use may result in longer durations of respiratory support and supplemental oxygen
- Previous studies have demonstrated the quickest way to wean CPAP is the 'cold turkey' approach

Using HF to 'wean' from CPAP is discouraged

HF vs. CPAP/NIPPV AS PRIMARY SUPPORT FOR PRETERM INFANTS

HF As Primary Support: Issues With Current Data

- Only about 450 preterm infants in RCTs
 No extremely preterm infants
- Data are from trials that are small/pilot studies, subgroups, interim analyses

Nasal High Flow as Primary Respiratory Support for Preterm Infants - an international, multi-centre, randomised, controlled, non-inferiority trial

Calum Roberts, Louise Owen, Brett Manley, Dag Helge Frøisland, Susan Donath, Kim Dalziel, Margo Pritchard, David Cartwright, Clare Collins, Atul Malhotra, and Peter Davis for the HIPSTER Trial Investigators





Australian Government

Patients – Inclusion Criteria

- Infants born at 28 to 36+6 weeks' gestation
- No previous endotracheal ventilation or surfactant
- Decision by the attending clinician to commence or continue non-invasive respiratory support after initial stabilisation/resuscitation



Australian Government



Patients – Exclusion Criteria

- Urgent requirement for intubation and ventilation
- Already meeting specified 'treatment failure' criteria
- Known major congenital anomaly or pneumothorax
- Had already received ≥4 hours of CPAP treatment



Australian Government



Intervention Group – High Flow

- Initial flow 6-8 litres per minute
- Fisher & Paykel 'Optiflow Junior' or Vapotherm 'Precision Flow' devices
- Cannulae sized as per manufacturers instructions
- Maximum flow 8 litres per minute



Australian Government



Control Group – CPAP

- Initial pressure 6-8 cm of water
- Mechanical ventilator, underwater 'bubble' system, or variable-flow device
- Short binasal prongs or nasal mask
- Maximum pressure 8 cm of water



Australian Government



Primary Outcome

• Treatment failure within 72 hours after randomisation



Australian Government



Treatment Failure Criteria

- An infant receiving maximal support (High Flow 8 litres per minute or CPAP 8 cm of water) and one or more of:
 - FiO₂ ≥0.40
 - pH ≤7.20 plus pCO2 >60 mm Hg (8 kPa) on arterial or capillary blood gas, after ≥1 hour of allocated treatment
 - >1 apnoea requiring positive pressure ventilation in 24 hours, or ≥6 requiring intervention in 6 hours
- Infants requiring urgent intubation and ventilation were considered to have treatment failure



Australian Government



Recruitment

- Recruitment began on May 27, 2013
- After review of primary outcome data for the first 515 infants, the data safety monitoring committee recommended the trial be stopped
- Recruitment ceased on June 16, 2015, at which time 583 infants had been randomised
- 564 infants were eligible to be included in analysis



Australian Government



Primary Outcome

Treatment failure within 72 hours of randomisation



High Flow

VS



CPAP



Australian Government



Primary Outcome

Treatment failure within 72 hours of randomisation

High Flow		CPAP					
71/278 25.5%	VS	38/286 13.3%					
Risk difference for treatment failure with							
High Flow, 12.3% , 95% confidence interval,							
5.8 to 1	L8.7% (P	<0.001)					



Australian Government



Intubation

within 72 hours of randomisation

High Flow		CPAP					
43/278 15.5%	VS	33/286 11.5%					
Risk difference for intubation with High							
Flow, 3.9% , 95% confidence interval, -1.7							
to 9	.6% (P=C).17)					



Australian Government



Secondary Outcomes

- No difference in BPD, death, or most other important outcomes
- HF infants received median 1 additional day of respiratory support
- CPAP infants more likely to have pneumothorax while on allocated support, but not overall
- CPAP infants more likely to have nasal traum



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Conclusions

- High Flow therapy results in a significantly higher rate of treatment failure than CPAP, when used as primary support for preterm infants with respiratory distress
- Use of primary High Flow with 'rescue' CPAP results in no difference in intubation rate or adverse outcomes



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Conclusions

- Increasing experience and enthusiasm
- BUT
- Uncertainty remains about safety, efficacy and optimal flow rate
- Available information does not support HFNC as a current "Standard of Treatment" for noninvasive respiratory support

Practice Points Based on Opinion & Evidence

- Selection of patients
- Optimal flow
- Weaning
- Failure criteria
- Prong size & devices
- Further research

Suggested Reading

- Manley BJ, Owen LS. High-flow nasal cannula: Mechanism, evidence and recommendations. Seminars in Fetal & Neonatal Medicine:2016;21:139-145
- Nasal high-flow therapy for primary respiratory support. Robert et al. NEJM Sept 2016.