

1 A Comparison of Nasal Trauma in Preterm Infants Extubated to Either Heated Humidified High Flow
2 Nasal Cannulae or Nasal Continuous Positive Airway Pressure

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15 Abstract

16 The objectives of this study were (i) to devise a nasal trauma score for preterm infants receiving non-
17 invasive respiratory support, (ii) to compare the incidence of nasal trauma in preterm infants < 32
18 weeks gestation randomised to either Nasal Continuous Positive Airway Pressure (NCPAP) or Heated
19 Humidified High Flow Nasal Cannulae (HHHFNC), in the first 7 days post extubation and (iii) to
20 assess the effect of two different nasal dressings in those assigned to NCPAP.

21 We randomly assigned preterm ventilated infants to receive Vapotherm® HHHFNC or NCPAP post
22 extubation. Infants receiving HHHFNC were treated with Sticky Whiskers® and infants receiving
23 NCPAP received either Sticky Whiskers® or Cannulaide® nasal dressings. Bedside nursing staff
24 scored 6 sites on each infant's nose for: erythema, bleeding or ulceration. Scores were recorded three
25 times daily for the first 7 days post extubation. The sum of these 21 scores was used as the summary
26 measure of nasal trauma.

27 The mean nasal trauma score for infants assigned HHHFNC was 2.8 (SD 5.7) compared to 11.7 for
28 NCPAP (SD 10.4), $p < 0.001$. There was no difference in mean trauma score between infants on NCPAP
29 assigned Sticky Whiskers® 14.4 (SD 12.5) or Cannulaide® 9.5 (SD 7.3), $p = 0.06$.

30 *Conclusion:* HHHFNC resulted in significantly less nasal trauma in the first 7 days post extubation
31 than NCPAP, was most significant in infants < 28 weeks of gestation. The use of protective dressings
32 was not associated with decreased nasal trauma for infants on NCPAP.

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36 Keywords: Nasal trauma, NCPAP, Highflow nasal cannulae

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38 Abbreviations:

39 HHHFNC Heated Humidified High Flow Nasal Cannulae

40 NCPAP Nasal Continuous Positive Airway Pressure

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43 Introduction

44 Preterm infants are at high risk of developing pressure ulcers due to immature skin, exposure to
45 medical devices, nutritional deficiencies and exposure to ambient humidity. Fifty per cent of pressure
46 ulcers in neonates were reported to be associated with the use of medical equipment and devices [16].

47 A pressure ulcer is defined as a localised injury to the skin and/or underlying tissue as a result of
48 pressure [14]. A number of skin assessment tools are available for adult and paediatric intensive care
49 populations [1], however there is no standardised classification of pressure ulcers specifically for
50 preterm infants.

51 The most commonly reported pressure affected area in preterm infants is the nose [6] and is associated
52 with the use of Nasal Continuous Positive Airway Pressure (NCPAP). NCPAP facilitates extubation,
53 but can cause nasal trauma irrespective of the device used [17]. The incidence of NCPAP associated
54 nasal trauma in the neonatal population ranges from 15-100% [4-6,12]. Risk factors for developing
55 nasal pressure ulcers in this population are: gestation of < 32 weeks, birth weight of <1500g and
56 duration of NCPAP > 5 days [5]. The majority of nasal trauma resolves spontaneously when NCPAP is
57 discontinued. However, it can lead to permanent disfigurement and long term functional sequelae
58 [5,9,15,].

59 Nasal dressings are used in preterm infants receiving NCPAP with an aim of minimising nasal trauma
60 [4,5, 7]. These may either provide a direct barrier e.g. hydrocolloid applied to the septum and/or nares,
61 or secure the prongs to maintain a gap between the nasal septum and prongs. However, there are
62 limited safety and efficacy data to support their use.

63 Heated Humidified High-Flow Nasal Cannulae (HHHFNC) are increasingly being used as an
64 alternative to NCPAP in preterm infants despite the paucity of clinical evidence to support this
65 practice. HHHFNC prongs are generally shorter and narrower than those used in NCPAP and do not
66 form a seal with the nares. They are commonly perceived to cause less nasal trauma and be better
67 tolerated when compared with NCPAP but the incidence of nasal trauma associated with their use is
68 uncertain.

69 We undertook this study firstly to devise a nasal trauma score for preterm infants receiving non-
70 invasive respiratory support and secondly to compare the incidence of nasal trauma in preterm infants <

71 32 weeks gestation randomised to either NCPAP or HHHFNC in the first 7 days post-extubation and
72 assess the effect of two different protective nasal dressings in those assigned to NCPAP.

73 The respiratory outcomes of this trial are reported separately [3].

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75 Methods

76 This is a substudy of preterm infants enrolled in a randomised controlled trial to compare HHHFNC
77 and NCPAP post-extubation [3]. Infants were eligible for the study if they were born at < 32 weeks of
78 gestation, required endotracheal intubation and positive pressure ventilation and were considered ready
79 for extubation by the clinical team. Infants with suspected upper airway obstruction, congenital airway
80 malformations or major cardiopulmonary malformations were excluded. This single centre study was
81 approved by the Human Research Ethics Committee of the Mercy Hospital for Women, Melbourne,
82 Australia and performed in accordance with the 1964 Declaration of Helsinki. Informed written
83 consent was obtained from parents prior to study commencement. Infants were randomised to
84 VapoTherm[®] HHHFNC with Sticky Whiskers[®] (VapoTherm Inc, Stevensville, MD, USA, Beevers
85 Manufacturing & Supply, McMinnville, OR, USA) or NCPAP via Hudson[®] binasal prongs (Hudson
86 Respiratory Care Inc, Temecula, CA, USA) with either Sticky Whiskers[®] or Cannulaide[®] (Beevers
87 Manufacturing & Supply, McMinnville, OR, USA). A random number sequence was generated using
88 STATA Statistical Software (Release 10.0. College Station, TX: Stata Corp, 2010), and the
89 randomisation sequence was stratified by gestational age into <28 weeks and 28.0-31.6 weeks
90 gestation. A variable block size was used for treatment allocation. Sequentially numbered, sealed
91 opaque envelopes containing the treatment allocation were opened immediately prior to extubation. A
92 clinical trials exemption number (CTN 015/2008) was obtained from the Therapeutics Goods
93 Administration as commercially manufactured hydrocolloid protective dressings were not available in
94 Australia at the time of this study.

95 A nasal trauma scoring chart was modified from Kaufman [10] (Appendix) and tested for precision .

96 The inter-rater reliability was tested using 6 observers who independently scored the noses of 5 preterm
97 infants. The bedside nursing staff scored 6 sites on each infant's nose for: erythema, bleeding,
98 ulceration or skin tear. Nasal trauma scores were recorded three times daily for the first 7 days post-
99 extubation. The sum of these 21 scores was used as the summary measure of nasal trauma.

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101 Statistical Analysis

102 The sample size required to show a difference in nasal trauma between devices was difficult to estimate
103 due to the paucity of previous data. This was therefore a convenience sample using a randomised
104 controlled trial powered for a primary respiratory outcome. The single measures intraclass correlation
105 coefficient was calculated to assess the reliability of the nasal trauma score. Analysis was by intention
106 to treat. Mean values between the 2 groups were analysed by Student's paired t-test. All statistical
107 analyses were performed using STATA Statistical Software: (Release 10.0. College Station, TX: Stata
108 Corp, 2010).

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110 Results

111 The intraclass correlation coefficient for the nasal trauma score was 0.64 (95% CI 0.26, 0.94).
112 We randomised 132 preterm infants < 32 weeks gestation to receive either HHHFNC (n=67) or
113 NCPAP (n=65) post-extubation. The baseline demographic characteristics of enrolled infants were
114 similar between groups with the exception of sex (Table 1). There were more males in the NCPAP
115 group 41 (63%) compared to 33 (49%) of those assigned HHHFNC. The study flow chart for infants in
116 each group is shown in Figure 1. All infants randomised to HHHFNC were allocated Sticky Whiskers[®].
117 In the NCPAP group 32 were allocated Sticky Whiskers[®] and 33 Cannulaide[®]. Seven infants assigned
118 to HHHFNC and 8 in the NCPAP group were reintubated in the first week post-extubation for
119 respiratory failure. Thirteen (20%) infants assigned to NCPAP (7 Sticky Whiskers[®] and 6 Cannulaide[®])
120 were changed to HHHFNC due to nasal trauma in the first 7 days post-extubation. These infants had a
121 mean nasal trauma score of 22 (SD 10.1) compared to a mean score of 7.4 (SD 6.7) in those who
122 remained on NCPAP (p<0.001).

123 There was a significant difference in the nasal trauma score between the two modes of respiratory
124 support. The mean nasal trauma score for infants assigned HHHFNC was 2.8 (SD 5.7) compared to
125 11.7 for NCPAP (SD 10.4) p<0.001. There was no difference in mean trauma score between infants
126 on NCPAP assigned Sticky Whiskers[®] 14.4 (SD 12.5) or Cannulaide[®] 9.5 (SD 7.3), p=0.06.

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128 Discussion

129 This study has shown that the nasal trauma score developed specifically for preterm infants showed
130 good inter-rater reliability with the intraclass correlation coefficient 0.64 (95% CI 0.26,0.94) indicating
131 moderate-strong agreement between observers.

132 Importantly, the use of HHHFNC post-extubation was associated with significantly less nasal trauma
133 than NCPAP. Furthermore, there was no difference in the nasal trauma score between infants assigned
134 two different protective dressings in the NCPAP group. These findings have important implications for
135 the care of preterm infants receiving respiratory support.

136 Currently, there is no nasal trauma score designed specifically for preterm infants. Fischer et al [5]
137 reported 91% of non-blanching erythematous pressure areas resolved spontaneously and did not
138 progress. However the same authors reported that 78% of partial thickness dermal erosions were
139 preceded by a non-blanching erythematous phase. In the nasal trauma score developed for this study
140 we elected to use a cumulative score in order to capture the natural history of these pressure areas as a
141 research tool. Further development of this nasal trauma score into a clinical tool to allow clinicians to
142 identify when nasal trauma has reached a critical threshold would be useful for the implementation and
143 evaluation of pressure reducing strategies.

144 Our study identified a significant difference in the mean nasal trauma score between infants receiving
145 HHHFNC with Sticky Whiskers[®] and those receiving NCPAP with either Sticky Whiskers[®] or
146 Cannulaide[®]. The use of HHHFNC post-extubation was associated with significantly less nasal
147 trauma than NCPAP. The smaller dimensions of HHHFNC compared to NCPAP prongs are likely to
148 be a major factor in the reduction of nasal trauma seen in the HHHFNC group. HHHFNC are tapered
149 from the base to the tip, they are narrower and shorter than NCPAP prongs and should not occlude
150 more the 50% of the nares. NCPAP is however dependent upon achieving a seal between the prongs
151 and nares so pressure effects are almost inevitable. Humidification of inspiratory gases is important for
152 respiratory mucosal integrity. It has been the improvement of humidification systems that has allowed
153 the development of HHHFNC. One in-vitro study reported that the humidity delivered by HHHFNC
154 (Vapotherm[®]) was significantly greater than the humidity delivered during NCPAP, 83% (SD 3.1)
155 versus 76% (SD 0.81), $p < 0.001$ at flows of 3-8 L/min [2]. The effect of this difference on clinical
156 outcomes such as nasal trauma is currently unknown.

157 Our study also identified that there was no difference in the nasal trauma score between infants
158 assigned two different protective dressings in the NCPAP. We elected to compare the two NCPAP

159 dressings firstly to allow direct comparison of HHHFNC and NCPAP using the same fixation device
160 (Stickywhiskers[®]) and to evaluate the efficacy of the barrier effect of Cannulaide[®] for infants on
161 NCPAP. Cannulaide[®] cannot be used for infants on HHHFNC as a leak between cannulae and nares
162 must be maintained. A third NCPAP group with no protective/ fixation dressings would have been
163 desirable but would have resulted in 3 small groups and reduced study power. Review of study centre
164 data demonstrated there was no difference in the mean nasal trauma score between infants assigned
165 protective dressings in this trial and the mean nasal trauma score from 53 infants without protective
166 dressings receiving NCPAP prior to trial commencement, 11.7 (SD 10.4) and 8.4 (SD 8.9) respectively,
167 $p=0.08$. This is in contrast to the findings of Gunzlemez et al., who reported a significant reduction in
168 nasal injury when silicon gel dressings were applied [7]. Nasal dressings are used extensively in
169 clinical practice for infants on NCPAP [4,17] but the findings of our study do not support their routine
170 use. Safety concerns have been raised regarding their use. If infants require emergency intermittent
171 positive pressure via resuscitation masks, the dressings can prevent an adequate mask seal and rapid
172 removal of the adhesive dressing can also result in skin breakdown [8]. Despite the fact we have
173 demonstrated that HHHFNC was associated with less nasal trauma than NCPAP there is likely to be a
174 subset of the preterm population who will require the positive distending pressure that only NCPAP
175 can provide. Protective dressings may have a role in limiting progression of nasal pressure injury in
176 those infants who require NCPAP but this needs to be further evaluated in a large randomised
177 controlled trial.

178 Damage to nasal mucosa may contribute to rates of unexplained septicaemia in the preterm population
179 [13]. Nosocomial sepsis places a significant burden on the infant and the healthcare system. Each
180 episode of nosocomial sepsis is estimated to cost 10 000 USD and increase the length of stay by 5.2
181 days [11]. The association of nasal trauma and nosocomial infection needs to be studied further in
182 large randomised controlled trials.

183 We acknowledge there are limitations to this unblinded study. The sample size was calculated for a
184 primary respiratory outcome and excluded infants who only received non-invasive respiratory support.
185 Thirteen infants (20%) in the NCPAP group changed to HHHFNC in the first 7 days post-extubation
186 because of nasal trauma. The nasal trauma resolved with the transition to HHHFNC. Five infants in the
187 HHHFNC group changed to NCPAP due to apnoea and these infants accounted for the majority of the
188 nasal trauma observed in the HHHFNC group. There was no ulceration or severe lesions seen in infants

189 who received HHHFNC exclusively. While these crossovers are likely to have diluted the treatment
190 effect, the observed difference in nasal trauma between groups was clinically and statistically
191 significant.

192 In conclusion, HHHFNC resulted in significantly less nasal trauma in the first 7 days post extubation
193 than NCPAP. The use of protective dressings was not associated with decreased nasal trauma for
194 infants on NCPAP. Further large randomised controlled trials are required to study the association
195 between nasal trauma and nosocomial sepsis and to evaluate the role of protective nasal dressings for
196 infants on NCPAP.

197

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206 References

- 207 1. Baharestani MM, Ratliff CR. Pressure ulcers in neonates and children: An NPUAP white paper. *Adv*
208 *Skin Wound Care* 2007, Apr;20(4):208, 210, 212, 214, 216, 218-20.
209
- 210 2. Chang GY, Cox CA, Shaffer TH. Nasal cannula, CPAP, and high-flow nasal cannula: Effect of flow
211 on temperature, humidity, pressure, and resistance. *Biomed Instrum Technol* 2011;45(1):69-74.
212
- 213 3. Collins CL, Holberton JR, Barfield C, Davis PG. A Randomised Controlled Trial to Compare
214 Heated Humidified High Flow Nasal Cannulae with Nasal Continuous Positive Airway Pressure Post-
215 extubation in Premature Infants. *J Pediatrics* 2013, May: 162 (5):949-954
216
- 217 4. do Nascimento RM, Ferreira AL, Coutinho AC, Santos Veríssimo RC. The frequency of nasal injury
218 in newborns due to the use of continuous positive airway pressure with prongs. *Rev Lat Am*
219 *Enfermagem* 2009;17(4):489-94.
220
- 221 5. Fischer C, Bertelle V, Hohlfeld J, Forcada-Guex M, Stadelmann-Diaw C, Tolsa JF. Nasal trauma
222 due to continuous positive airway pressure in neonates. *Arch Dis Child Fetal Neonatal Ed* 2010,
223 Nov;95(6):F447-51.
224
- 225 6. Fujii K, Sugama J, Okuwa M, Sanada H, Mizokami Y. Incidence and risk factors of pressure ulcers
226 in seven neonatal intensive care units in japan: A multisite prospective cohort study. *Int Wound J* 2010,
227 Oct;7(5):323-8.
228
- 229 7. Günlemez A, Isken T, Gökalp AS, Türker G, Arisoy EA. Effect of silicon gel sheeting in nasal
230 injury associated with nasal CPAP in preterm infants. *Indian Pediatr* 2010, Mar;47(3):265-7.
231
- 232 8. Helou S, Birenbaum HJ, Blue D, Pane MA, Marinkovich GA. The velcro mustache:a potential
233 barrier to effective bag-and-mask ventilation in neonates on Nasal cpap: two care reports. *Respir Care*
234 2011, Jul;56(7):1040-2
235
- 236 9. Jatana KR, Oplatek A, Stein M, Phillips G, Kang DR, Elmaraghy CA. Effects of nasal continuous
237 positive airway pressure and cannula use in the neonatal intensive care unit setting. *Arch Otolaryngol*
238 *Head Neck Surg* 2010, Mar;136(3):287-91.
239
- 240 10. Kaufman D, Zanelli S, Walsh B, Hicks T. Evaluation of a nasal break-down scoring system for
241 premature infants requiring CPAP [abstract]. *Respir Care E-PAS2007*:61390.
242 www.abstracts2view.com/pasall/. Accessed on 1/11/12
243
- 244 11. Leroyer A, Bedu A, Lombrail P, Desplanques L, Diakite B, Bingen E, et al. Prolongation of
245 hospital stay and extra costs due to hospital-acquired infection in a neonatal unit. *J Hosp Infect* 1997,
246 Jan;35(1):37-45
247
- 248 12. Robertson NJ, McCarthy LS, Hamilton PA, Moss AL. Nasal deformities resulting from flow driver
249 continuous positive airway pressure. *Arch Dis Child Fetal Neonatal Ed* 1996, Nov 1;75(3):F209-12.
250
- 251 13. Rønnestad A, Abrahamsen TG, Medbø S, Reigstad H, Lossius K, Kaaresen PI, et al. Septicemia in
252 the first week of life in a norwegian national cohort of extremely premature infants. *Pediatrics* 2005,
253 Mar;115(3):e262-8.
254
- 255 14. Pressure ulcer prevention quick reference guide; 2010. www.npuap.org Accessed 1/11/12
256
- 257 15. Smith LP, Roy S. Treatment strategy for iatrogenic nasal vestibular stenosis in young children. *Int J*
258 *Pediatr Otorhinolaryngol* 2006, Aug;70(8):1369-73.
259
- 260 16. Willock J, Harris C, Harrison J, Poole C. Identifying the characteristics of children with pressure
261 ulcers. *Nurs Times* 2005;101(11):40-3.2.
262

263 17. Yong SC, Chen SJ, Boo NY. Incidence of nasal trauma associated with nasal prong versus nasal
264 mask during continuous positive airway pressure treatment in very low birthweight infants: A
265 randomised control study. Arch Dis Child Fetal Neonatal Ed 2005, Nov;90(6):F48.
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268 Figure 1: Study Flowchart for infants assigned to HHHFNC or NCPAP in the first 7

269 days post-extubation

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311 Infants Eligible for the Study

179 did not Undergo Randomisation
 73 were not approached
 19 died or were transferred prior to extubation
 27 clinicians were unwilling to randomise
 39 recruitment suspended due to HHHFNC circuit recall
 21 declined

132 Underwent Randomisation

67 Assigned HHHFNC + Sticky Whiskers®

281

32 Assigned NCPAP + Sticky Whiskers®

33 Assigned NCPAP + Cannulaide®

7 reintubated

7 reintubated

1 reintubated

287

5 changed to NCPAP for apnoea

6 changed to HHHFNC for nasal trauma

7 changed to HHHFNC for nasal trauma

289

55 continue HHHFNC + Sticky Whiskers®
291
292

19 continue NCPAP + Sticky Whiskers®

25 continue NCPAP + Cannulaide®

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294

295 Table 1: Baseline characteristics of infants at randomisation.

	HHHFNC N=67	NCPAP N= 65	
Nasal dressing	HHHFNC Sticky Whiskers [®] N=67	NCPAP Sticky Whiskers [®] N=32	NCPAP Cannulaide [®] N=33
Male n (%)	33 (49)	20 (63)	21 (64)
Birthweight g mean (SD)	1123 (317)	1100 (394)	1109 (361)
Completed Weeks of Gestation mean (SD)	27.9 (1.9)	27.5 (2.2)	27.8 (1.8)
Singleton n (%)	51 (76)	27 (84)	26 (79)
Antenatal Corticosteroids n (%)	59 (88)	29 (91)	29 (88)
Surfactant n (%)	66 (99)	32 (100)	32 (97)
1 min Apgar Score median (IQR 25th-75th)	5 (3-7)	5 (4-6)	6 (4-6)
5 min Apgar Score median (IQR 25th-75th)	7 (6-8)	8 (6-8)	8 (7-9)

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298 **Appendix : Nasal Trauma Score Chart**

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Score																					
Date																					
Shift	A	P	N	A	P	N	A	P	N	A	P	N	A	P	N	A	P	N	A	P	N
	M	M		M	M		M	M		M	M		M	M		M	M		M	M	
Internal Nare	L																				
	R																				
External Nare	L																				
	R																				
Philtrum																					
Septum																					
Total Score																					

301

302

Score

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0= normal

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1= pink/red

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2= bleeding/ ulcer/ scab

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3= skin tear

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