A study of the effect of nasal modes of ventilation on the incidence of gastro-oesophageal reflux in preterm neonates

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ABSTRACT

BACKGROUND

Nasal modes of respiratory support cause variable amounts of gastric dilatation which may increase gastro-oesophageal reflux (GER) in preterms. To compare the incidence of GER in nasally ventilated, preterm babies with controls (babies not on ventilation). Type of study: A prospective, observational comparative study.

METHOD

Twenty-three preterm babies of gestational age 28–36 weeks and weight ranging between 1,000 g and <2,500 g on either nasal continuous positive airway pressure (nCPAP) or nasal intermittent positive pressure ventilation (nIPPV) were assessed for GER. They were compared with controls not on ventilation some of who were test babies when off ventilation (subgroup A) and some were unrelated babies not on ventilator but matched for gestational age and weight with test babies (subgroup B). All babies were subjected to continuous, oesophageal pH monitoring with dual sensor (upper and lower oesophageal) catheters. Reflux index (RI) was calculated as the percentage of study time the lower oesophageal pH was <4. Primary outcome was the RI in the test and controls groups. Secondary outcome was the temporal relation of the reflux with symptoms if any. Numerical data were shown as mean with standard deviation and statistical comparisons were done using the χ^2 -test, Fischer test, and *t*-test wherever applicable.

RESULTS

The RI was higher in ventilated babies as compared to the control group, particularly in the subgroup A, where test babies formed their own controls. Grade IV reflux (7 cases) was seen only in the ventilated babies. There was no difference in the incidence of GER in babies on nCPAP as compared with nIPPV. Grade IV reflux could not be reliably predicted by RI alone. No definite temporal relation between episodes of reflux and symptoms could be determined in this study.

CONCLUSION

There is an increase in GER in preterms on nasal modes of ventilation. A combination of upper (pharyngeal) and lower oesophageal sensors are

preferred to a single lower oesophageal sensor when assessing GER by oesophageal pHmetry in neonates.

MJAFI 2012;68:12–15

Key Words: CPAP; gastro-oesophageal reflux; nasal ventilation; preterm

INTRODUCTION

Gastro-oesophageal reflux (GER), the involuntary passage of gastric contents into the oesophagus, is not uncommon in preterm babies.¹ These neonates are often put on respiratory support with nasal continuous positive airway pressure (nCPAP) or, more recently, nasal intermittent positive pressure ventilation (nIPPV). These modes of ventilation produce variable amounts of gastric dilatation due to increased gas flow in the pharynx, which may increase GER in these neonates.

Though the overall incidence of GER in preterm babies is 30–50%, the exact incidence of GER in babies on ventilator is not definitely known.^{2,3} Kiciman et al in their study on neonates on CPAP concluded that gastric insufflation and abdominal distension may lead to aspiration secondary to GER.⁴ However, the actual incidence of GER during CPAP and other modes of nasal ventilation have not been adequately studied.⁵ Oesophageal pHmetry is considered to be the present gold standard for the diagnosis of GER in neonates. It is easy to perform and can be done with dual sensor catheters for detecting acid reflux in both the upper and lower oesophagus.⁶ Though simultaneous intra-oesophageal impedance measures non-acid gastro-oesophageal reflux, which is not picked up on oesophageal pHmetry, this is not an easily available diagnostic modality.^{7,8}

MATERIALS AND METHOD

A prospective, observational comparative study was conducted in a tertiary care Neonatal Intensive Care Unit (NICU) on babies on nasal modes of ventilation. The sample size was based on the average incidence of GER in high-risk preterm babies of 40% as seen in other studies. To determine a 20% difference with a significance level of 5% and power of 80%, the sample size was calculated to be at least 20 in each arm (test and control) of the study group. Ethics Committee clearance was obtained and consent was taken in all cases. The study was conducted over a period of 18 months.

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Received: 26.07.2010; Accepted: 28.10.2011
doi: 10.1016/S0377-1237(11)60123-8

Inclusion Criteria

Test group: Consecutive babies admitted to the NICU who were nasally ventilated and had stable blood gases for at least 12 hours formed the test group.

Control group: Ten of the test babies could form their own controls when off ventilation. This could not be done in the remaining 13 babies test babies as 10 of them were shifted from nasal to endotracheal intubation, two died, and one was discharged against medical advice. Hence, for these babies 10 babies not on ventilator but admitted for other reasons and matched for gestational age and weight with these babies, were used as controls. No baby was on oral feeds during the study time (Flowchart 1).

Exclusion Criteria

Extremely low birth weight (ELBW) babies (babies <1,000 g at birth): Babies with birth asphyxia requiring resuscitation and babies with major congenital anomalies were excluded.

Oesophageal pHmetry was done in all babies using single-use neonatal antimony dual sensor pH electrode catheters (MSA 6 Duo-art:922338A, Hersteller) with Gastrograph (Mark 4 MIC, Solotherm, Switzerland). The length of the electrode catheter to

be inserted was measured from angle of mouth to ear lobe plus from ear lobe to xiphisternum. After calibration, this was inserted nasogastrically till a sudden fall of pH to <4 was detected. The catheter was then pulled up till a pH of 4.5–5 was recordable on the gastrograph. This pH denoted the localisation of the lower oesophageal sphincter (LES). The upper sensor would then automatically be at the level of the pharynx. The catheter was fixed firmly to the nose and chin with tape and pH monitoring done for 18–24 hours. During recording, timing of cardio-respiratory symptoms, if any, were recorded. After completion, the study data was downloaded using WinReflux software.

Reflux index (RI) (duration of LES pH <4/total duration of study) was calculated for each case and graded as follows: Physiological (<10%), mild (10–20%), moderate (21–40%) and severe (>40%). Grade IV reflux was diagnosed as any pH <4 detected by the upper sensor placed in the pharynx. Clinically relevant reflux was defined as RI >20% or any reflux detected on pharyngeal sensor (Grade IV reflux).

Analysis

Numerical data was presented as mean ($\pm$ SD). Chi-square test, Fischer test, and paired *t*-test were used wherever applicable.

*(13 babies were taken off nasal ventilation but could not form their own controls due to following reasons: 10 = put on endotracheal intubation, 2 died, 1 discharged against medical advice and hence 10 matched controls had to be included in the study)

Flowchart 1 Cohort flow diagram.

Table 1 Demographic characteristics of the study subgroups.

Characteristics	Subgroup A		P value (paired <i>t</i> -test)	Subgroup B		P value (unpaired <i>t</i> -test)
	Test (n=10)	Control (n=10)		Test (n=13)	Control (n=10)	
Mean gestational age in weeks (SD)	33.8 (3.3)	33.8 (3.3)	NA	35.3 (2.1)	35.8 (2.9)	0.68
Birth weight (g)	2,091 (526)	2,091 (526)	NA	2,210 (543)	2,054 (543)	0.19
Sex (M:F)	2.3:1	2.3:1	NA	1.9:1	1.7:1	0.21

NA: not available.

Table 2 Comparison of reflux index in test and control groups.

Groups	Reflux index (%)	
	Subgroup A Test=10 Control=10	Subgroup B Test=13 Control=10
Test mean (SD)	36.70 (20.59)	31.3 (21.0)
Control mean (SD)	17.43 (17.19)	22.3 (18.5)
Difference (95% CI)	19.27 (9.15, 29.39)	9.0 (-8.23, 26.24)
P value	0.002 (paired <i>t</i> -test)	0.289 (unpaired <i>t</i> -test)

SD: standard deviation.

Table 3 Comparison of gastro-oesophageal reflux in nasal continuous positive airway pressure and nasal intermittent positive pressure ventilation groups.

Reflux index	Numbers		P value
	nCPAP (n=15)	nIPPV (n=8)	
Moderate/severe (RI > 20%)	11	4	0.25
Grade IV reflux	5	2	0.89

nCPAP: nasal continuous positive airway pressure, nIPPV: nasal intermittent positive pressure ventilation, RI: reflux index.

RESULTS

A total of 23 neonates formed the test group. Of these, 10 formed their own controls (subgroup A). The remaining 13 babies were compared with 10 matched controls (subgroup B). There was no significant difference in the demographic characteristics between the test and controls (Table 1).

The RI was significantly higher in the test as compared with the control group in subgroup A (Table 2) and not significantly higher in subgroup B. All babies with Grade IV reflux were in the test group (four in subgroup A and three in subgroup B). No difference was seen in the incidence of reflux between the nCPAP and the nIPPV groups (Table 3).

The sensitivity of RI in predicting Grade IV reflux was 71 % and the specificity was 73 %. The positive predicative value of a RI > 20 in predicting Grade IV reflux was 25 % while the negative predicative value of a RI of < 20 % for ruling out Grade IV GER was 84 % (Table 4).

Table 4 Grade IV reflux compared with reflux index (n=43).

Reflux index	Grade IV reflux present	Grade IV reflux absent
> 20 (moderate/severe)	5	16
≤ 20 (mild)	2	20

A definite relation of timing of GER with the cardiorespiratory event could be established in only one case.

DISCUSSION

A number of studies have shown the incidence of GER in preterm babies to be between 20 % and 50 %, which is 2–3 times higher than in term babies.^{1–3} In our study population of preterm babies we found an incidence of clinically relevant GER (defined as moderate or severe RI (i.e. RI > 20 % or any Grade IV reflux) in 65.22 % (15/23) of nasally ventilated preterm babies (Table 3). Unfortunately we could not use all the babies as their own controls as 13 babies were taken off nasal ventilation could not form their own controls due to following reasons: 10 were put on endotracheal intubation, two died, and one was discharged against medical advice. Hence, 10 matched controls had to be included in the study. Of all the babies on nasal ventilation seven babies were found to have Grade IV reflux (i.e. recording of acid pH detected on upper pharyngeal sensor). In subgroup A (babies who formed their own controls) the mean RI in babies on nasal ventilation was significantly higher as compared to when the same babies were off ventilation. However, in subgroup B (babies who were compared with matched controls) though the test babies had higher RI compared with the controls, this did not reach statistical significance (Table 2). Four test babies in subgroup A and three in subgroup B had Grade IV reflux. These results suggest that nasal modes of ventilation are associated with an increase in GER in preterm babies.

Pradeaux et al in their oesophageal pH recordings on 46 ventilated neonates and subsequently on post-extubation showed no difference in episodes of acidic GER.³ However, Kiciman et al in their study on neonates on CPAP showed that gastric insufflations and abdominal distension increased the chance of aspiration, more so at higher pressure probably due

to reflux.⁴ An animal study done by Wang et al has shown that gastric insufflations were associated with increased GER.⁵ Ku et al failed to establish any relationship between the incidence of GER and gestational age, birth weight, postnatal age or endotracheal ventilator settings.⁹ However, Farhath et al did serial tracheal aspirate for pepsin on fed and unfed mechanically ventilated preterms and found that the former had more number of episodes of microaspirations.¹⁰ This was further increased with methylxanthine therapy. These babies were also more likely to develop bronchopulmonary dysplasia as compared with babies in who no aspiration was detected. In our study 65.22% of babies undergoing nasal modes of ventilation had significant GER and all the babies who had Grade IV reflux were ventilated. However, we could not determine whether these were associated with symptoms. Other workers too have not been able to establish a temporal association between GER and apnoea and desaturation in preterms.¹¹ In our study in only one case could a definite temporal relationship between a reflux episode and a possible symptom (apnoea) be established.

When we analysed the lower oesophageal refluxes with the reflux diagnosed by the upper oesophageal sensor (Grade IV reflux) we found that RI could not reliably predict Grade IV GER. This suggests that dual sensor should be used in neonates being assessed for GER with oesophageal pHmetry. If a single lower sensor is used it is fairly effective in 'ruling out' Grade IV reflux if RI < 20 but is not sensitive in predicting Grade IV reflux if RI > 20. This is important as Grade IV refluxes are more likely to be associated with cardiorespiratory symptoms.

Our study shows that significant GER including Grade IV refluxes do occur more often in preterms on nasal ventilation. In view of the unavoidable differences in the controls the power of the study has decreased. However, though small in sample size this study does point to a trend that needs to be looked into with a better powered study.

Intellectual Contributions of Authors

Study concept: Surg Capt SS Mathai

Drafting and manuscript revision: Surg Capt SS Mathai, Surg Capt KM Adhikari

Statistical analysis: Surg Capt SS Mathai

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CONFLICTS OF INTEREST

This study has been funded by research grants from the O/o DGAFMS, New Delhi.

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