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The first breath during resuscitation of prematurely born infants

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ABSTRACT

Background: The first five initial inflation pressures and times during resuscitation of prematurely born infants are frequently lower than those recommended and rarely result in tidal volumes exceeding the anatomical dead space. Greater volumes were produced when the infant was provoked to inspire by an inflation (active inflation).

Aims: To assess factors associated with a shorter time to the first active inflation.

Study design: Respiratory function monitoring was undertaken during resuscitation, peak inflation pressures (PIP), inflation times and the infant's respiratory activity were simultaneously recorded

Subjects: Infants with a gestational age < 34 weeks requiring resuscitation at birth.

Outcome measures: The relationships of the PIP and inflation time of the first five inflations and first active inflation to the time to the first active inflation.

Results: Recordings from 47 infants, median gestational age of 29 (23-34) weeks, were analysed. The median PIP of the first five inflations was 27 (range 9-37) cmH_2O and inflation time 1.22 (range 0.32 – 4.08) seconds. The median PIP of the first active inflation was 25 (range 19-37) cmH_2O and inflation time 1.35 (0.35-3.67) seconds. The median time to the first active inflation was 7 (range 0 – 50) seconds and was inversely correlated with the PIP (p=0.001) and inflation time (p=0.018) of the first five inflations and the PIP (p=0.001) and inflation time (p=0.008) of the first active inflation.

Conclusion: The magnitude of the inflation pressures and times of the first five inflations inversely correlate with the time to the first breath during resuscitation.

Key words: Resuscitation; preterm infant; Head's paradoxical reflex

Abbreviations: PIP – peak inflation pressure; $ETCO_2$- end tidal carbon dioxide; RFM – respiratory function monitor; CO_2 – carbon dioxide; RCT – randomized controlled trial

INTRODUCTION

Respiratory function monitoring during the initial resuscitation of prematurely born infants has demonstrated that the inflation pressures and times delivered are variable (1) and frequently lower than those recommended (2), resulting in expiratory tidal volumes less than the anatomical deadspace (1). Expired tidal volumes, however, were significantly greater if the infant inspired during the inflation (1).We use the term “active inflation” for the occurrence of an infant’s inspiration occurring during a positive pressure inflation (1). In a subsequent study, in the presence of minimal leak (<10%), expiratory tidal volumes were significantly higher both for an initial sustained (two to three seconds) inflation and subsequent inflations that coincided with spontaneous breathing (3). Indeed, one study (4) found that a sustained lung inflation was only successful when accompanied by an inspiratory effort by the infant, that is larger tidal volumes were produced and establishment of a larger fraction of the FRC gain. End tidal carbon dioxide ($ETCO_2$) levels have also been shown to be significantly higher with an active inflation (5, 6).

Head demonstrated that if vagal conduction was blocked, rapid inflation, instead of producing apnoea, resulted in stronger and more pronounced diaphragmatic contraction (7). This was named Head’s paradoxical reflex and has been suggested to be the mechanism by which the first functional residual capacity appears. Hoskyns et al investigated the respiratory reflex responses to resuscitation in 21 preterm infants requiring endotracheal resuscitation at birth (8). They found that despite mean inflation pressures of 27.3 cmH_2O, inspiratory tidal volumes were often less than 4.4 ml/kg ie less than twice the anatomical dead space (8). When, however, Head’s paradoxical reflex was stimulated, inspiratory volumes exceeded 4.4 ml/kg on 14 occasions compared to only four when the reflex was not stimulated. The first active inflation (1), we suggest is a manifestation of Head’s paradoxical reflex, which is more frequent if there is low lung compliance (9). Hence, we hypothesized that the time to the first active inflation would be influenced by the initial inflation pressures and times of the first five inflations, the initial pressure and time of the first active inflation, the infant's gestational age and whether they had been exposed to antenatal steroids. The aim of this study was to determine if those factors were significantly associated with the time to the first active inflation, as such information could be used to improve the efficacy of resuscitation.

METHODS

Respiratory function monitoring recordings made during the resuscitation of infants born less than 34 weeks of gestational age born at Kings College Hospital NHS Foundation Trust between 2012-2014 were examined. This group of infants were targeted as they are more likely to require resuscitation than more mature, prematurely born infants. Ethical approval was given for the respiratory function monitoring by the Outer North London Ethics Committee. The Committee required written parental consent only for the analysis of the data, consent was obtained when the mother had been transferred to the postnatal ward.

Resuscitation protocol

Clinicians taking part in the resuscitations were all trained in newborn life support. As per the perinatal unit's policy, they were encouraged to follow the Neonatal Life Support guidelines (2) that is to use inflation pressures of 20cm H_2O and a positive end expiratory pressure of 5 cmH_2O, ie a peak inflation pressure (PIP) of 25 cmH_2O for the first five inflations each of which was to be maintained for 2 to 3 seconds. The inflation pressures were then to be increased if chest movement was considered to be inadequate by the clinical team. The clinicians had access to the "in real" time respiratory function monitoring outputs, but these were introduced as part of a research study, hence clinicians were encouraged to undertake resuscitation according to their newborn life support training. Positive pressure ventilation was delivered by a t-piece device (Neopuff Infant resuscitator, Fisher & Paykel Healthcare, Auckland, New Zealand). Infants were usually resuscitated via a facemask, but were immediately intubated if the infant had a heart rate of less than 60 beats per minute and no respiratory effort as determined by clinical observation.

Monitoring equipment

NM3 respiratory profile monitors (RPM) (Philips Respironics, Pennsylvania, USA) were used. The monitor was connected to a Dell Latitude Laptop with customised Spectra software Version 3.0.1.4 (Grove Medical, London, UK). The NM3 has a combined pressure, flow, tidal volume and carbon dioxide (CO_2) sensor (dead space 0.8ml). The sensor was placed between the t-piece device and mask or endotracheal tube. The NM3 monitor is automatically calibrated for flow, pressure and CO2 according to the factory-stored calibration in the monitor. According to the manufacturer's information, the accuracy of the flow sensor was ±3% and the airway pressure was±2%. The pressure transducer was automatically 'zeroed' to correct for changes in ambient temperature. The clinicians had been trained to use the respiratory function monitor (RFM), which was set up prior to the delivery.

Data collection

The infant's gestational age and whether they had been exposed to antenatal steroids were determined by review of the medical notes.

Analysis

The recordings were examined to identify the infant's first breath (Figure 1), in all cases the infant's first breath coincided with an inflation (active inflation). The time from commencement of resuscitation to the first active inflation was determined, as were the PIP and inflation time of the first five inflations and the first active inflation.

Recordings were excluded from the analysis if:

(i) the infant had breathed prior to the onset of resuscitation

(ii) there was a large leak, defined as a difference between the inspiratory and expiratory tidal volumes of at least 30% likely making identification of the first active inflation inaccurate

(iii) the initial endotracheal tube had been misplaced and the infant required reintubation

(iv) there was no active inflation during the recording

Statistical analysis

Differences between infants whose recordings were and were not analysed were assessed for statistical significance using Mann Whitney U-test or Chi squared test as appropriate. Strengths of correlations were assessed by calculating Pearson's correlation coefficients. Whether antenatal exposure was related to the time to the first inflation was assessed using the Mann Whitney U-test. Data which were not normally distributed were log transformed as necessary for the analysis. Statistical analysis was carried out using SpSSC version 22, IBM, USA.

RESULTS

One hundred and eighty eight traces were available for analysis, 141 were excluded: the infant had breathed before resuscitation (n=72), large leak (n=49), misplaced endotracheal tube (n=3) or no active inflation (n=17). The 47 infants from whom recordings were analysed did not differ significantly from those whose recordings were not analysed (Table 1). The median time to the first active inflation was 7 (range 0-50) seconds. The median PIP and median inflation time of the first five inflations were significantly longer if an active inflation occurred during the first five inflations than if it did not (Table 2). The time to the first active inflation inversely correlated with the peak inflation pressures ($p = 0.001$) and the inflation time ($p = 0.018$) of the first five inflations (Figure). The time to the first active inflation inversely correlated both with the PIP ($p=0.001$) and the inflation time of the first active inflation ($p=0.008$). There were no significant correlations with either gestational age or antenatal steroid exposure and the time to the first active inflation

DISCUSSION

We have demonstrated that the time to the first active inflation was significantly shorter in infants resuscitated with higher peak inflating pressures and longer inflation times during the first five inflations. In addition, we have shown that the inflation pressures and times of the first active inflation were significantly associated with the time to first active inflation. Our results suggest that the recommended (2) pressures and times of the first five inflations during resuscitation of prematurely born infants are more likely to provoke a Head's paradoxical reflex. After cutting the vagi, Head described a stage during which inflation of the lungs resulted in an inspiratory effort (7). We, as others (8) suggest the first inspiration taken by an infant which coincides with a positive pressure inflation is a manifestation of Head's paradoxical reflex. This reflex has been shown to be important in preserving lung compliance with a role in reopening partially collapsed airways (10).

We have previously reported that an inflation time of at least 1.5 seconds during initial resuscitation of prematurely born infants did not produce clinically relevant increases in expiratory tidal volumes (11). In that study, however, active inflations were excluded as we wished to assess the effects of different pressures and inflation times per se on tidal volume exchange and it is not possible to determine the magnitude of the infant's contribution during active inflations. A systematic review of the results of randomised controlled trials (RCTs) of sustained inflations versus positive pressure inflations at birth (12), although not finding any reductions in BPD or death, demonstrated that sustained inflations were associated with a reduced requirement for subsequent mechanical ventilation. Whether the different inflation times influenced the efficacy of resuscitation as evidenced by a shorter time to the first active inflation, however, was not investigated in the studies included in the meta-analysis.

The time to the first active inflation did not significantly correlate with either gestational age or exposure to antenatal steroids. We had presumed very immature infants and those not exposed to antenatal steroids would be more likely to have non-compliant lungs and hence Head's paradoxical reflex more often provoked (12). More than 70% of the infants included in this study, however, had been exposed to antenatal steroids, which likely reduced our ability to detect any effect of either antenatal steroid exposure or gestational age.

This study has strengths and some weaknesses. We analysed the results of detailed respiratory function monitoring recordings made during resuscitation. A number of recordings were excluded from the analysis, but comparison of infants who were and were not included in the analysis did not reveal any significant differences in their demographics, hence we feel our results are generalizable. The study was only possible because the clinicians recruiting the prematurely born infants often did not always follow the guidelines (2), so it was possible to examine the effects of a range of inflation pressures and times as has been previously reported (1). This occurred despite the clinicians involved having undertaken approved training.

In conclusion, we have demonstrated a significant inverse correlation between the time to the first breath (active inflation) and inflation times and pressures. Our data suggest respiratory function monitoring may be considered essential to guide resuscitation at birth, in particular the use of positive pressure inflations and sustained inflations. Our data further argue for more intensive training to further ensure the recommendations (2) for the first five inflations are followed as this might improve the efficacy of resuscitation by reducing the time to the first breath.

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Conflict of interest: None to declare

Contributor statement

CH analysed the recordings; PB and VM undertook the data collection; ADM and AG designed the study. All authors have approved the final article.

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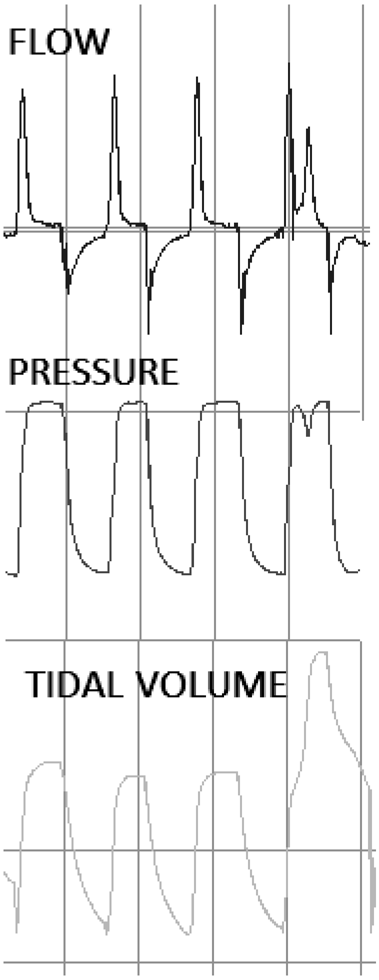
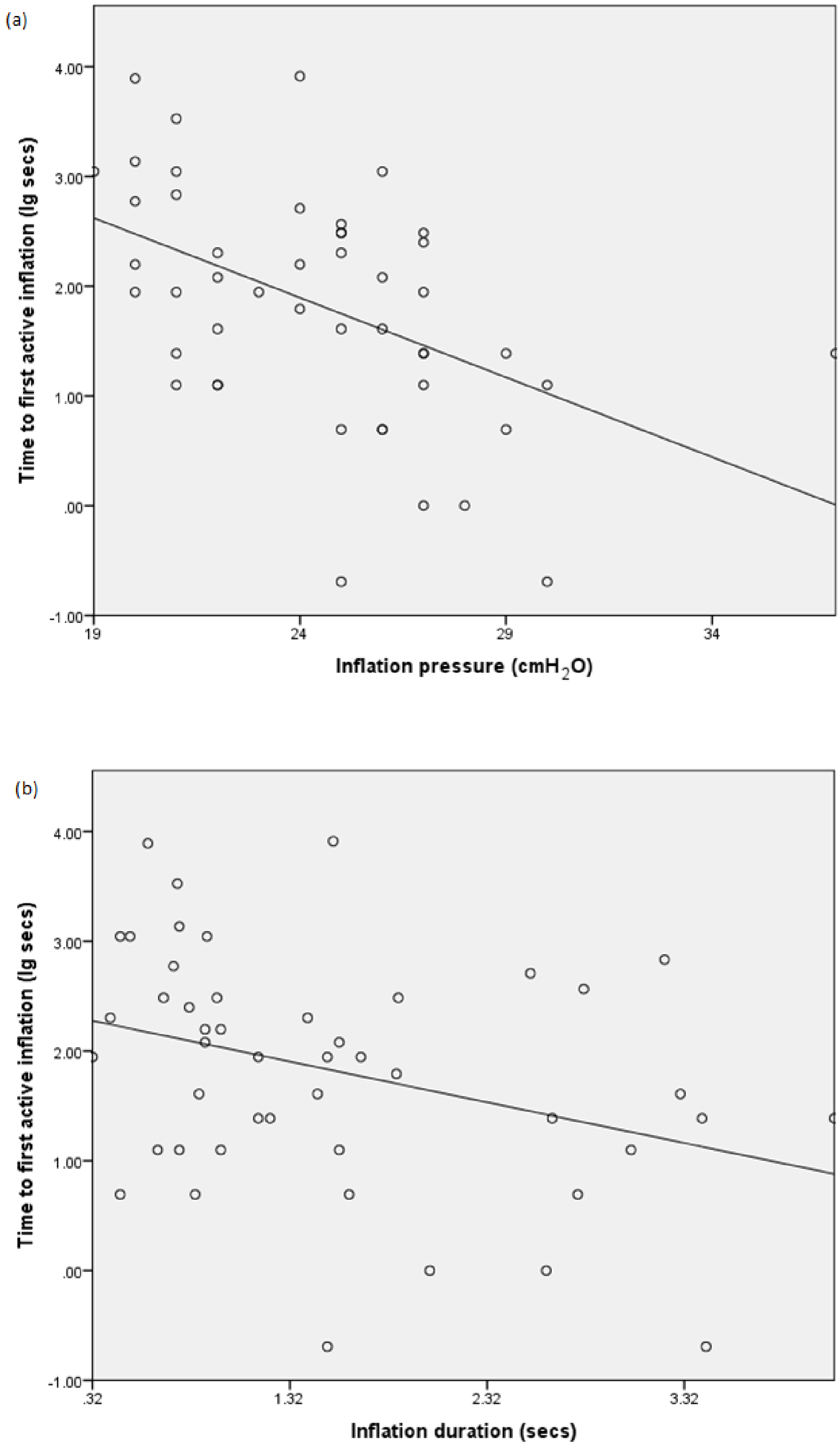
FIGURE LEGEND

Figure 1:



Recording of the flow, pressure and tidal volume. An active inspiration is shown on the fourth inflation by the negative deflection in the inflation pressure trace and the double peak in the flow trace. The active inspiration is associated with an increased tidal volume.

Figure 2:



(a)
Time to first active inflation (lg secs)
4.00
3.00
2.00
1.00
.00
-1.00
19
24
29
34
Inflation pressure (cmH2O)
(b)
Time to first active inflation (lg secs)
4.00
3.00
2.00
1.00
.00
-1.00
.32
1.32
2.32
3.32
Inflation duration (secs)

Relationship between the time to the first active inflation and (a) the peak inflating pressures (PIP) and (b) the inflation times

Regression lines are shown

(a) r = -0.15 PIP + 5.38

(b) r = -0.37 inflation time + 2.39

Table 1: Demographics by analysis status

The data are demonstrated as median (range) or n (%)

	Analysed	Not analysed
N	47	141
Gestational age (weeks)	29 (23-34)	31 (23-34)
Birth weight (kg)	1.230 (0.484-2.170)	1.330 (0.570-2.826)
Males	23 (49%)	84 (60%)
Caesarian section	22 (47%)	71 (50%)
Antenatal steroids	36 (77%)	111 (79%)

Table 2: Inflation pressures and times of the first five inflations according to whether the first active inflation occurred during the first five inflations or not

Data are presented as median (range)

	Active inflation in the first five inflations		
	Yes	No	p value
N	32	15	
Inflation pressure (cmH_2O)	25 (20-37)	21 (19-27)	0.003
Inflation time (sec)	1.6 (0.46-4.08)	0.8 (0.32-1.54)	<0.001

HIGHLIGHTS

Respiratory function monitoring was undertaken during the resuscitation of prematurely born infants, the pressures and inflation times were simultaneously recorded with the infant's respiratory activity.

The magnitude of the pressure and time of the first five inflations inversely correlated with the time to the first breath