Respiratory Muscle Strength in Healthy Infants and those With Surgically Correctable Anomalies

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Summary. Assessment of respiratory muscle strength provides important diagnostic and prognostic information. Normative data in healthy, term infants is, however, limited. Surgically correctable birth defects, congenital diaphragmatic hernia (CDH) and abdominal wall defects (AWD), commonly have impaired diaphragm function. The study aims were to obtain normative data for respiratory muscle strength in healthy, term born infants at birth and at 6 weeks postnatal age (PNA) and to investigate the influence of growth and maturation on inspiratory muscle strength in CDH/AWD infants. Maximal inspiratory (cPimax) and expiratory (cPemax) pressures during crying were measured at birth in 67 healthy, term born infants (mean (SD) gestational age (GA) 39.4 (1.7) weeks) and reassessed in 27 at 6 weeks PNA. cPimax and functional residual capacity (FRC) (22.3 (4.2) ml/kg) were also measured in 23 infants with AWD/CDH (mean (SD) GA 36.9 (2.1) weeks) and reassessed in 16 at median (range) 6.5 (1.5–15) months PNA. In healthy infants, mean (SD) cPimax was 88.8 (19.33) cmH_2O and cPemax 61.8 (13.5) cmH_2O at birth, increasing significantly at followup to 100.9 (15.2) cmH_2O ($P < 0.05$) and 82.6 (19.4) cmH_2O ($P < 0.001$) respectively. Mean (SD) cPimax was significantly lower (47.5 (22.4) cmH_2O, $P < 0.0001$) in AWD/CDH infants compared to healthy infants at birth but had increased significantly to 88.1 (27.6) cmH_2O ($P < 0.0001$) at followup which correlated significantly with increases in FRC ($r^2 = 0.33$, $P = 0.0263$). Infants with AWD and CDH have significantly reduced inspiratory muscle strength compared to healthy term born infants but strength increases markedly in early life. **Pediatr Pulmonol.**

Key words: respiratory muscle strength; maximal inspiratory muscle strength; infant; surgically correctable anomalies; human.

INTRODUCTION

Respiratory muscle strength in neonates can be reduced due to prolonged mechanical ventilation,[1] phrenic nerve injury,[2] sepsis,[3] critical illnesses,[4] and medications.[5] Reductions in respiratory muscle strength can also delay weaning and extubation from mechanical ventilation.[2] Accurate assessment of respiratory muscle strength, therefore, could provide important diagnostic and prognostic information. The availability of normative data for in healthy term infants, however, is limited. We have previously reported values for maximal inspiratory pressure during crying in infants[6] but this was in nine term infants only and obtained without the use of a non-rebreathing valve. A two-way non-rebreathing valve is recommended to improve the accuracy of timing of maximal inspiratory pressure measurements and yields greater values.[7] Normative data generated using the preferred measurement technique in a larger sample are required for comparative purposes.

Congenital diaphragmatic hernia (CDH) and anterior abdominal wall defects (AWD) are common surgically correctable birth defects and are associated with chronic respiratory morbidity. We have previously demonstrated that infants with gastroschisis and congenital diaphragmatic hernia have impaired diaphragm function in the postoperative period.[8] It is not known however, whether there is a gradual improvement in respiratory muscle function or if respiratory muscle weakness remains in such infants, potentially contributing to chronic respiratory morbidity and possible respiratory failure.[9–12]

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Received 14 May 2013; Revised 10 December 2013; Accepted 14 January 2014.

DOI 10.1002/ppul.23007
Published online in Wiley Online Library (wileyonlinelibrary.com).

Infants with CDH and AWD may suffer abnormal antenatal lung growth resulting in reduced lung volume in infancy.[11,13] Although lung volume can directly affect respiratory muscle strength, it is also not known how changes in lung volume with increased postnatal age influence respiratory muscle strength in such patients.

Maximal inspiratory (Pimax) and expiratory (Pemax) pressure, the maximum negative and positive pressures generated during a temporary occlusion of the airway, are the most commonly used measures of inspiratory and expiratory muscle strength respectively. In infants, as the respiratory efforts produced during crying are considered to be maximal, recording the inspiratory and expiratory airway pressures produced during crying against an airway occlusion provide reproducible measures of inspiratory (cPimax) and expiratory (cPemax) muscle strength.[6,14] A normal or near normal value for cPimax and cPemax can rule out significant respiratory muscle weakness and the requirement for more complex and/or invasive tests. As the tests are simple and easy to apply, serial measurements of cPimax and cPemax could be obtained and used to track respiratory muscle strength.

The aims of this study, therefore, were to obtain normative data for cPimax and cPemax in healthy, term born infants in the newborn period and at 6 weeks postnatal age and to investigate the influence of growth and maturation on any reductions in respiratory muscle strength in infants with CDH/AWD.

MATERIALS AND METHODS

Subjects

Sixty-seven healthy term born infants without respiratory distress or requirement for additional oxygen supplementation were recruited. In addition, 16 infants with anterior abdominal wall defects (gastroschisis and exomphalos) and 7 infants with congenital diaphragmatic hernia were recruited. The study was approved by King's College Hospital NHS Foundation Trust research ethics committee. Infants were studied once informed written consent had been obtained from the parent(s).

ABBREVIATIONS:

CDH	congenital diaphragmatic hernia
AWD	anterior abdominal wall defects
cPimax	maximal inspiratory (cPimax) pressure during crying and expiratory
cPemax	maximal expiratory pressure during crying
GA	gestational age
PNA	postnatal age
FRC	functional residual capacity
HFOV	high frequency oscillatory ventilation
iNO	inhaled nitric oxide
He	helium
O_2	oxygen

All of the infants with surgically correctable anomalies were delivered, underwent surgical repair and received intensive care at King's College Hospital NHS Foundation Trust (Table 1). Two of the infants with CDH and two with gastroschisis received antenatal corticosteroids. None of the infants received caffeine or corticosteroids postnatally. The CDH group comprised seven infants, one of which had a right sided defect. The CDH infants underwent surgery at a median (range) age of 6 days (1–11) following a period of preoperative stabilization. Three infants required high frequency oscillatory ventilation (HFOV) and inhaled nitric oxide (iNO) preoperatively. The median (range) duration of ventilation of the CDH infants was 17 (10–40) days and post-extubation they required supplementary oxygen for a further median (range) of 15 (2–31) days.

The AWD group comprised 16 infants, 13 with gastroschisis and 3 with exomphalos. A thin layer silo was created and staged closure undertaken. The median (range) age at operation was 6 (4–11) days. The AWD infants were ventilated for a median (range) of 2 (1–18) days, no infant required HFOV or iNO. Four infants required supplementary oxygen post-extubation for 1 day.

Equipment

cPimax and cPemax were recorded using a facemask attached to a pneumotachograph to measure airflow (GM Engineering, Kilwinning, UK) placed over the infant's nose and mouth. A two way non-rebreathing valve attached to the distal end of the pneumotachograph allowed occlusion at end expiration (cPimax) or end inspiration (cPemax) (Fig. 1). Airway pressure was measured from a side-port on the pneumotachograph. Differential pressure across the pneumotachograph and airway pressure were measured by differential pressure transducers of the appropriate pressure range (Validyne MP45-1, Validyne, Northridge, CA). The flow and pressure signals were amplified (CD 280 Carrier amplifier, Validyne, Northridge, CA) and recorded and displayed in real time on a computer running an application written using Labview software (National Instruments, Austin TX) with 100 Hz analog to digital sampling (DAQ 16XE-50, National Instruments).

Functional residual capacity was measured in the infants with surgically correctable defects. Lung volume was assessed by measurement of functional residual capacity (FRC) using a helium (He) gas dilution technique and a specially designed infant circuit with a volume of 95 ml.[15] The FRC system (Equilibrated Biosystems, Inc., Series 7700, Melville, NY) contained a rebreathing bag filled with a mixture of He and oxygen (O_2), connected to a three-way valve and face mask from which the infant breathed. Actuation of the valve, at end-expiration, connected the patient to the rebreathing bag.

TABLE 1— Individual Patient Demographics and Details Concerning the Respiratory Condition of the CDH and AWD Infants

Patient	Diagnosis	GA (weeks)	BWT (g)	Antenatal steroids (Y/N)	Caffeine (Y/N)	Diuretics (Y/N)	Postnatal steroids (Y/N)	Nitric oxide (Y/N)	HFOV (Y/N)	Ventilation (days)	Supplementary oxygen (days)	PNA at surgery (days)
1	Exomphalos major	38	2,748	N	N	N	N	N	N	18	0	7
2	Exomphalos major	38	2,840	N	N	N	N	N	N	18	1	5
3	Exomphalos small	39	3,315	N	N	N	N	N	N	1	0	1
4	Gastroschisis	36	1,980	N	N	N	N	N	N	1	1	4
5	Gastroschisis	34	1,596	N	N	N	N	N	N	3	0	6
6	Gastroschisis	37	1,890	N	N	N	N	N	N	1	0	7
7	Gastroschisis	34	2,342	Y (2×)	N	N	N	N	N	4	0	5
8	Gastroschisis	38	2,590	N	N	N	N	N	N	1	0	9
9	Gastroschisis	37	2,095	N	N	N	N	N	N	2	0	9
10	Gastroschisis	38	3,180	N	N	N	N	N	N	4	0	7
11	Gastroschisis	39	2,810	N	N	N	N	N	N	3	0	5
12	Gastroschisis	39	2,400	N	N	N	N	N	N	1	0	4
13	Gastroschisis	38	3,380	Y (1×)	N	N	N	N	N	1	0	4
14	Gastroschisis	35	1,946	N	N	N	N	N	N	2	1	11
15	Gastroschisis	36	2,200	N	N	N	N	N	N	14	1	6
16	Gastroschisis	37	2,926	N	N	N	N	N	N	2	0	6
17	CDH left side	37	2,770	N	N	N	N	Y	Y	22	2	1
18	CDH left side	34	1,754	Y (2×)	N	N	N	N	N	16	28	6
19	CDH left side	40	3,515	N	N	N	N	N	N	10	4	4
20	CDH left side	38	2,825	N	N	Y	N	Y	Y	40	31	11
21	CDH left side	39	3,630	N	N	N	N	Y	Y	17	15	7
22	CDH left side	33	2,245	N	N	N	N	Y	Y	19	21	8
23	CDH right side	36	2,975	Y (2×)	N	N	N	N	N	16	15	4

CDH, congenital diaphragmatic hernia; Y/N, Yes/No response, if Yes number of doses given were appropriate; GA, gestational age; BWT, birthweight; HFOV, high frequency oscillatory ventilation; PNA, postnatal age.

The change in He concentration against time was displayed in real time on a flat panel display. Rebreathing of the He/O_2 gas mixture was continued until equilibration of He within the system occurred. The FRC was corrected for oxygen consumption (7 ml/kg/min)[16] and BTPS conditions. The FRC was expressed as the mean of paired measurements within 10% of each other and related to body weight. The coefficient of repeatability of FRC measurements in spontaneously breathing infants is 3.9 ml/kg[17] with a median FRC in term infants of 30 ml/kg (range 24–36).[11]

Oxygen saturation was monitored continuously during each study using an Ohmeda Biox 3740 pulse oximeter with an Ohmeda Flex II reusable probe.

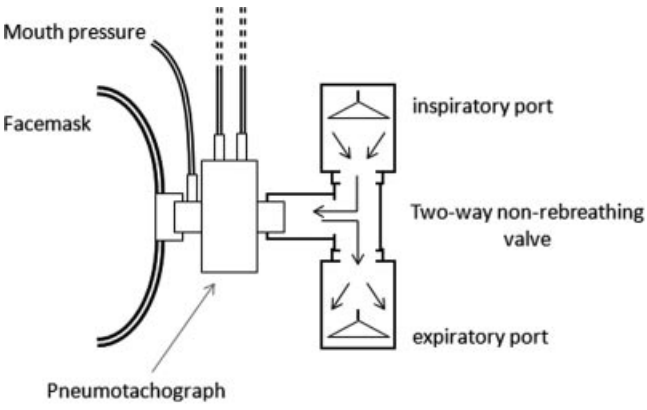

Fig. 1. Diagrammatic representation of the equipment used to measure cPimax and cPemax. The inspiratory port on the two way non-rebreathing valve was occluded during the preceding expiration when measuring cPimax. The expiratory post was occluded during the preceding inspiration when measuring cPemax.

Protocol

The infants were studied in the supine position at least 1 hr after a feed. To measure respiratory muscle strength the facemask with the pneumotachograph and two way non-rebreathing valve were held firmly over the infant's nose and mouth during crying. To measure cPimax the inspiratory arm of the valve was occluded during the preceding expiration as indicated by a crying effort. To measure cPemax, the expiratory arm of the valve was occluded during the preceding inspiration. Use of the two way non-rebreathing valve in this way ensured correct timing of the occlusion at the start of either inspiration or expiration as appropriate. The timing of the occlusions was determined by observation of the real time display of the flow signal. The occlusion was maintained for at least 5–8 inspiratory efforts as experience from previous studies indicates that the maximum inspiratory effort

would normally have occurred during this period.[15] At least three sets of occlusions were performed. If inspiratory/expiratory pressure was continuing to increase after the third period of occlusion, further sets of occlusions were performed until the investigator was confident a maximum effort had been performed. From the series of occlusions cPimax and cPemax were determined as being the largest negative and positive pressures generated. Only cPemax manoeuvres with a plateau pressure of at least 1 sec were accepted for subsequent analysis.[14] We have previously demonstrated that the coefficient of repeatability of cPimax was 5.6 cmH_2O and cPemax was 6.2 cmH_2O.[6] FRC was then measured after a suitable period of time had elapsed (at least 30 min).

TABLE 2— Demographics and Respiratory Muscle Strength at Birth for the Healthy Term Born, CDH and AWD Infants

	Healthy	CDH	AWD
Number	67	7	16 (13 gastroschisis)
Gestational age (weeks)	39.4 (1.7)	36.6 (2.6)	37.1 (1.66)
Birthweight (kg)	3.24 (0.68)	5.33 (1.73)	2.52 (0.54)
FRC (ml/kg)		27.2 (3.3)	24.1 (3.7)
cPimax (cmH_2O)	88.8 (19.3)	29.0 (16.1)	55.6 (20.1)
cPemax (cmH_2O)	61.8 (13.5)		

All data presented as mean (SD). CDH, congenital diaphragmatic hernia; AWD, abdominal wall defect; FRC, functional residual capacity; cPimax, maximal inspiratory pressure during crying, cPemax, maximal expiratory pressure during crying.

Statistical Analysis

On testing, data were found to be normally distributed and are expressed as mean (SD) except for time of measurement of cPimax post-surgical repair of defect which is expressed as median (range). The lower range of normal for cPimax and cPemax were calculated by subtracting the SD of the mean multiplied by 1.65 from the group mean values. Change in respiratory muscle strength between birth and followup was assessed using paired *t* tests and comparisons between the healthy and the AWD/CDH infants was assessed using un-paired *t* tests. cPimax and cPemax were also expressed per kg bodyweight to examine the effect of postnatal growth and maturation. The strength of relationships between maximal respiratory pressures and age, birthweight and lung volume were assessed using Pearson's correlation analysis. All data were analyzed using GraphPad Prism software (ver 5.00 for Windows, GraphPad Software, San Diego CA).

RESULTS

Sixty-seven healthy term born infants were recruited (Table 2) and studied at a mean (SD) postnatal age of 1.6 (1.4) days. The mean (SD) cPimax was 88.8 (19.3) cmH_2O and the mean (SD) cPemax was 61.8 (13.5) cmH_2O. There was no correlation between respiratory muscle strength and birthweight (Fig. 2). The lower range of normal was determined as 56.9 cmH_2O for cPimax and 39.5 cmH_2O for cPemax.

cPimax and cPemax were reassessed in 27 infants at 6 weeks postnatal age. In this group both cPimax and cPemax had increased significantly (day 1 cPimax 89.7 (20.8) cmH_2O vs. week 6 100.9 (15.2) cmH_2O, $P < 0.05$; day 1 cPemax 60.8 (14.6) cmH_2O vs. week 6 82.6 (19.4) cmH_2O, $P < 0.001$) (Fig. 3). Mean (SD) bodyweight increased significantly between measurements (3.39 (0.66) kg vs. 4.85 (0.68) kg, $P < 0.001$). There was a significant fall in mean (SD) cPimax/kg (27.9 (9.0) cmH_2O vs. 21.1 (3.6) cmH_2O) but no change in mean (SD) cPemax/kg (18.6 (5.9) cmH_2O vs. 17.2 (4.1) cmH_2O) between day 1 and followup, suggesting a disproportionate increase in weight relative to cPimax whereas there was a proportional increase in bodyweight and expiratory muscle strength. There were no

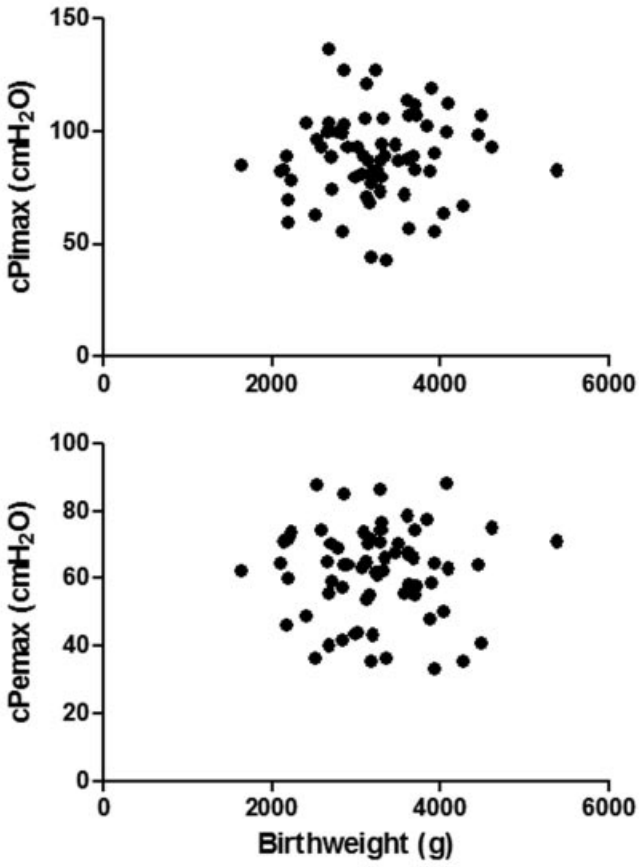

Fig. 2. Relationships of birthweight to maximal inspiratory (cPimax) and expiratory (cPemax) pressure during crying in 67 term born infants measured at birth.

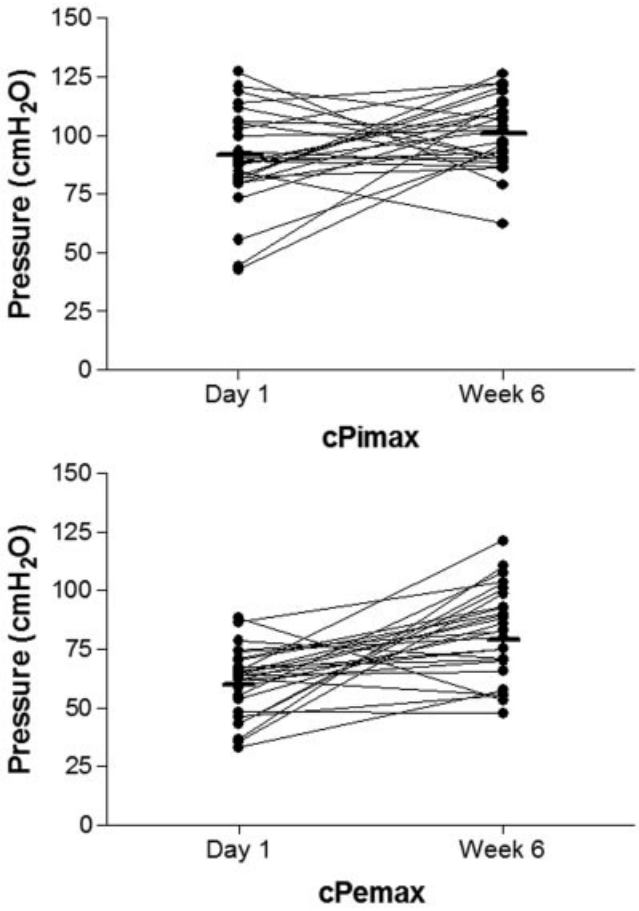

Fig. 3. Maximal inspiratory (cPimax) and expiratory (cPemax) pressure during crying in 27 healthy term born infants measured at birth and at 6 weeks. Short lines represent the mean value for the group.

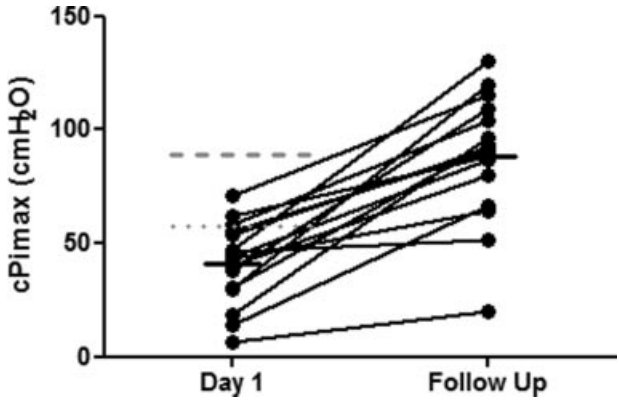

Fig. 4. Cohort of 16 AWD/CDH infants measured after surgery and then at followup. Short lines represent the mean value for the group. Broken gray lines represent mean maximal inspiratory pressure during crying (cPimax) measured in term born infants at birth and the lower limit of normal based on these data.

statistically significant differences in any variable between the group as a whole and the 27 infants who were measured on two occasions.

Sixteen infants with AWD and seven infants with CDH were recruited and cPimax measured postoperatively (Tables 1 and 2). Surgical repair of the defect was performed at a median (range) postnatal age of 6 (1–11) days (Tables 1 and 2). Measurements of cPimax were performed following post-operative convalescence of approximately 2 weeks. Gestational age was significantly lower in both the AWD ($P < 0.001$) and CDH ($P < 0.01$) infants and the birthweight significantly lower in the AWD infants ($P < 0.001$) compared to the healthy term born infants (Table 2). Mean (SD) cPimax was significantly lower in the AWD ($P < 0.001$) and CDH ($P < 0.001$) infants compared to the healthy term born infants (Table 2). In the AWD infants, cPimax was significantly correlated with gestational age ($r^2 = 0.35$, $P = 0.016$), birthweight ($r^2 = 0.49$, $P = 0.002$) and FRC ($r^2 = 0.33$, $P = 0.023$) while in the group as a whole cPimax and cPimax/kg correlated significantly with FRC ($r^2 = 0.38$, $P = 0.002$ and $r^2 = 0.31$, $P = 0.006$ respectively).

Sixteen of the 23 infants with surgically correctable anomalies (6 CDH) were measured at followup, which occurred at a median (range) age of 6.5 (1.5–15) months. cPimax increased significantly from birth (41.2 (17.7) cmH_2O) to follow up (88.1 (27.6) cmH_2O, $P < 0.0001$; Fig. 4). Mean cPimax in the 16 AWD/CDH infants was significantly lower ($P < 0.0001$) compared to cPimax measured in the 67 healthy infants in the perinatal period. When measured postoperatively, only six of the whole cohort of 23 AWD/CDH infants had inspiratory muscle strength in the normal range for healthy infants born at term (Fig. 4). The rate of increase in cPimax in the AWD/CDH (1.88 (4.6) cmH_2O/week) infants was not significantly different from the rate of change in the healthy term born infants (2.8 (2.0) cmH_2O/week) across the first 6 weeks of life. Functional residual capacity increased significantly between birth and followup in the AWD/CDH infants (21.5 (4.5) ml/kg vs. 29.5 (4.3) ml/kg $P < 0.0001$). The increase in cPimax in the AWD and CDH infants correlated significantly with the increase in FRC from birth to followup ($r^2 = 0.33$, $P = 0.0263$; Fig. 5).

DISCUSSION

This study has obtained normative data for cPimax and cPemax in healthy term born infants and demonstrated that respiratory muscle strength was not related to birthweight in healthy term born infants. Both cPimax and cPemax did, however, increase significantly during the first 6 weeks of life. Inspiratory muscle strength was significantly lower in infants with AWD and CDH compared to controls immediately following surgical correction of the abnormality. Subsequently cPimax

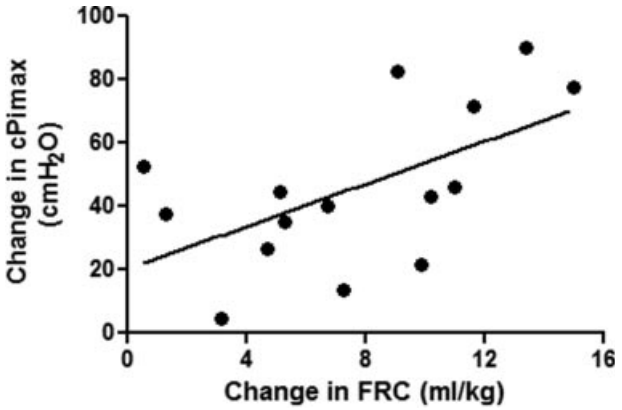

Fig. 5. Relationship between change in functional residual capacity (FRC) and change in maximal inspiratory pressure during crying (cPimax) in the 16 AWD/CDH infants measured at birth and at followup ($r^2 = 0.33$, $P = 0.0263$).

increased over the first months of life. The rate of increase in muscle strength in infants with CDH and AWD was not different from that observed in healthy term born infants. The increase in lung volume correlated with the increases in cPimax in the CDH and AWD infants.

In adults maximum respiratory pressures are measured from a maintained pressure plateau.[18] In infants, while cPemax is measured from the expiratory pressure plateau sustained over 1 sec, cPimax is measured from the maximum instantaneous peak in negative inspiratory pressure.[6,14] Measuring cPimax from a peak rather than a plateau pressure results in little difference in the values obtained.[19] Although lung mechanics and lung volume were not formally assessed in the healthy infants, none had any respiratory problems at birth or in the intervening weeks between hospital discharge and follow-up and there were no limitations associated with pressure transmission across the lung to the to the airway opening. The face mask covered the nose and mouth reducing compliance of the cheeks.

Maximal respiratory pressures were measured using a two-way non-rebreathing valve which simplifies the measurement by ensuring correct timing of airway occlusion and invariably results in higher values for cPImax and cPemax being obtained.[7] Occlusion of the appropriate arm of the two way non-rebreathing valve selectively permits expiration during cPimax measurement and inspiration during cPemax measurement, such that respiratory efforts occur from progressively lower lung volumes during cPimax and progressively higher lung volumes during cPemax. Such changes in lung volume result in increased force generation due to improvements in the length–tension relationship of respiratory muscles[20,21] and increasing contributions from the passive elastic recoil pressure of the lung and chest wall.[22] In our previous study,[6] we used a complete occlusion method which prevented both inspiration and expiration. Such differences in the measurement techniques could explain the lower cPimax and cPemax values reported previously.[6] It should also be noted that cPimax and cPemax in the earlier study were based on only nine term born infants. Furthermore, unlike our previous study[6] no relationship was observed between respiratory muscle strength and birthweight. The absence of such a relationship was, most likely, a consequence of our current study population consisting of healthy, term born infants.

The study by Shardonofsky et al.[14] reported values for mean (SD) cPimax (118 (21) cmH_2O) and cPemax (125 (35) cmH_2O) in excess of those in the current study. The study by Shardonofsky did, however, contain a range of ages up to 3.76 years. Mean cPimax reported for our term born healthy infants was similar to that observed in adult life.[23] The high inspiratory pressures have been attributed in part to the Laplace relationship[24] such that in infants, the thin muscles with intrinsically lower force generating capacity can produce high pressures because of the smaller radius of curvature of the chest wall and diaphragm.

In contrast to cPimax, cPemax was substantially lower than that observed in adult life.[23] This pattern of lower expiratory muscle strength in infancy and childhood has also been observed previously.[14,21,24] Cook et al.[24] found Pemax was approximately 75% of the adult value in children with a mean (range) age 8.7 (6.7–9.8) years and Gaultier and Zinman[21] observed that adult values for Pemax were not achieved before 11 years of age. Shardonofsky et al.[14] found cPemax in infants to be considerably lower than adult values despite cPimax being in the normal range for adults. They also observed a slight but positive correlation of cPemax with body weight. It is not clear, however, why cPemax in contrast to cPimax, is less in infants compared to adults. It has been postulated that expiratory muscle contraction may be submaximal during crying efforts or that differences are due to reduced expiratory muscle mass in infancy.

cPimax and cPemax did, however, increase significantly by the followup measurement performed at 6 weeks of age. Our results emphasize that if the severity of an infant's respiratory muscle weakness is to be appropriately assessed, their results must be compared to normative values for their age. Such a developmental pattern of respiratory muscle strength has been observed previously.[14,25] Muscle mass increases with somatic growth and maturation and mean cross sectional area of all muscle fibers increases postnatally.[26] There are also increases in respiratory drive, maturation of the neuromuscular junction, respiratory muscle conditioning, ossification of the rib cage and reduced chest wall compliance[27] that occur with increasing postnatal age that

in combination with increasing muscle mass could explain the increases in both cPimax and cPemax over the first 6 weeks of life. It is possible, also, that the infants had a more vigorous cry when older such that measuring respiratory muscle strength using a unidirectional valve, that allowed changes in lung volume to occur, would put the respiratory muscles at a better mechanical advantage and allow greater force production. Interestingly though, when corrected for body weight, cPimax/kg decreased from day 1 to followup at 6 weeks, while cPemax/kg did not change appreciably between assessments. Such changes indicate proportional increases in expiratory muscle strength relative to bodyweight. Progressive increases in lung and chest wall recoil that occur during postnatal life,[24,28] changes in abdominal muscle recruitment and contributions from individual expiratory muscles,[29] or differences in the antagonistic activity of the diaphragm[30] could explain the relative reductions in cPemax at birth and its subsequently greater increases in the first weeks of life.

cPimax was significantly lower in the AWD and CDH infants compared to the healthy term born infants. We have previously reported no significant differences in cPimax, between AWD or CDH infants and gestational age matched controls[8] suggesting maturation at birth is a significant factor in determining inspiratory muscle strength. The timing of follow-up in the AWD/CDH infants was variable, and hence no direct comparison to cPimax in the healthy term born infants was appropriate. Substantial increases in cPimax were, however, observed in the AWD and CDH infants over the period of follow-up such that most of the AWD/CDH infants were able to produce cPimax values approaching those observed in healthy infants.[14] Such improvements in respiratory muscle strength support the results of Scott et al.[25] who observed no difference in crying transdiaphragmatic pressures between infants with surgically repaired AWD and CDH when measured at 4 months PNA and compared to healthy age matched infants.

Lung hypoplasia and reduced FRC are characteristic of CDH[13] and commonly observed in AWD[11] and are most likely a consequence of impaired antenatal lung growth. In the group of CDH and AWD patients as a whole, cPimax and cPimax/kg correlated significantly with FRC. Gaultier and Zinman[21] demonstrated that Pimax was directly related to vital capacity in children, hence the improvements in cPimax observed in the followup cohort of CDH and AWD infants most likely reflect overall lung growth. cPimax is the product of the pressures generated by the respiratory and accessory respiratory muscles. Transdiaphragmatic pressure (Pdi) production is highly dependent not only on lung volume but also thoraco-abdominal configuration.[31] Zinman and Gaultier[32] observed in children that changes in thoraco-abdominal configuration that would be expected to place the diaphragm at a mechanical advantage were countered by an opposite effect on the other inspiratory muscles. Studies in adults have shown a decrease in Pimax in C1 quadriplegic patients when the lungs were passively inflated altering the length tension relationship of the accessory muscles.[33] Although we did not measure thoraco-abdominal configuration in the CDH and AWD patients, it is feasible that improvements in this and also lung volume alongside changes in respiratory muscle bulk and composition, rib cage mechanical efficiency, diaphragm configuration and increases in the size of the zone of apposition may have occurred with maturation leading to increased cPimax.

It is possible that the reduction in cPimax in the CDH and AWD infants on day 1 compared to followup was due to respiratory muscle disuse atrophy associated with mechanical ventilation and/or atrophy related to poor nutrition. The infants were, however, studied once extubated and breathing spontaneously. Surgery, particularly thoracic and upper abdominal, can affect respiratory muscle function but the effect is transitory.[34] None of the AWD and CDH infants were hypercapnic or hypoxic or had any electrolyte or metabolic disturbances.

A number of factors including prolonged mechanical ventilation,[1] phrenic nerve injury,[2] sepsis,[3] critical illnesses,[4] and medications[5] can result in reductions in respiratory muscle strength in neonates. Such reductions can compromise respiratory function and necessitate prolonged invasive and noninvasive ventilatory support. Measurement of respiratory muscle strength can, therefore, provide important diagnostic and prognostic information. The current study provides normative values for cPimax and cPemax from a population of 67 healthy term born infants which can be used for comparative purposes. Cut off values for cPImax and cPemax were calculated to allow interpretation of measurement results by subtracting 1.65 SD from the means of this normal population. This definition is accepted for creating cut off values and defining abnormality. A low value for cPimax or cPemax suggests the patient is weak, while normal or near normal value can rule out significant respiratory muscle weakness and the requirement for more complex and/or invasive tests as well as informing clinical management. As measurements of cPimax and cPemax are simple and easy to apply, serial measurements can be also obtained and used to track changes in respiratory muscle strength.

In summary, this study has presented normative data for inspiratory and expiratory muscle strength in healthy term born infants. Respiratory muscle strength was not related to birthweight and increased significantly during the first 6 weeks of life. Infants with AWD and CDH have significantly reduced cPimax when compared to healthy term born infants following surgical correction of the abnormality, however, cPimax does improve over the first

months of life. The increase in inspiratory muscle strength correlated to increases in lung volume.

ACKNOWLEDGEMENTS

A.G. is a National Institute of Health Senior Investigator.

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