Original Article

موضوع أصيل

RESPIRATORY SUPPORT ADEQUACY FOR VERY LOW BIRTH WEIGHT INFANTS POST EXTUBATION

كفاءة الدعم التنفسي للولدان بوزن ولادة منخفض جداً بعد سحب الأنبوب الرغامي

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ملخص البحث

هدف البحث: دراسة العوامل المتعلقة بفشل تجربة سحب الأنبوب الرغامي للولدان بوزن ولادة منخفض جداً.

طرق البحث: دراسة راجعة لملفات الولدان ذوي وزن الولادة المنخفض جداً، ممن أدخلوا وحدة العناية المركزة للخدج وحديثي الولادة في مستشفى توام، واحتاجوا إلى تهوية آلية عن طريق أنبوب رغامي في الفترة بين كانون الثاني 2011 وحتى الشهر نفسه من العام 2018.

النتائج: تمت دراسة العوامل المؤثرة أثناء الحمل، قياسات التهوية الآلية، نتائج غازات الدم قبل وبعد ساعتين من سحب الأنبوب الرغامي وعيار الفوسفور في المصل في الأسبوع الثاني بعد الولادة. شملت الدراسة 446 من الولدان بعمر حملي أقل من 32 أسبوعاً أو بوزن ولادة أقل من 1500 غ. توجه القصة الحملية قرار سحب الأنبوب الرغامي تبعاً للأسابيع الحملية. في الأسابيع الحملية (21+4 و26+6) يترافق فشل تجربة سحب الأنبوب الرغامي مع جنس المولود الذكر، ارتفاع الحاجة للأكسجين >0.30 بعد التجربة، ارتفاع مستوى غاز ثنائي أكسيد الكربون >55 ملم زئبق بعد التجربة، مظهر الزجاج المغشى في صورة الصدر الشعاعية عند التجربة الأولى، القناة الشريانية واسعة القطر، الدرجات المنخفضة والعالية من النزف داخل البطينات، بينما يترافق نجاح التجربة مع الإنتظار حتى انخفاض حاجة الأوكسجين الى (0.25)، مستوى ضغط نهاية الزفير PEEP في المستوى 6-7 سم.ماء. أما في الأسابيع الحملية (27-29+6) فيترافق فشل تجربة سحب الأنبوب الرغامي مع ارتفاع الحاجة للأكسجين >0.30 بعد التجربة، انخفاض مستوى pH في تحليل غازات الدم (6.9-7.24)، الدرجات العالية من النزف داخل البطينات، بينما يترافق نجاح التجربة مع الانتظار حتى انخفاض حاجة الأوكسجين إلى 0.21، مستوى ضغط نهاية الزفير PEEP بين 6-7 سم.ماء بعد التجربة. في الأسابيع الحملية (30-32) يترافق فشل تجربة سحب الأنبوب الرغامي مع ارتفاع الحاجة للأكسجين >0.30 بعد التجربة، انخفاض مستوى pH في غازات الدم (6.9-7.24)، انخفاض مستوى أوكسجين الدم دون 20-40 ملم. زئبق، القناة الشريانية واسعة القطر، بينما يترافق نجاح التجربة مع الانتظار حتى انخفاض حاجة الأوكسجين إلى 0.25، زمن الشهيق >0.38 ثانية قبل التجربة. يحدد العمر الحملي عدد جرعات العلاج بعامل التوتر السطحي اللازمة لضمان نجاح تجربة سحب الأنبوب الرغامي. يترافق فشل تجربة سحب الأنبوب الرغامي مع انخفاض مستوى الفوسفور في المصل.

الإستنتاجات: تختلف العوامل الإنذارية المحددة لفشل تجربة سحب الأنبوب الرغامي باختلاف الأسابيع الحملية. قد تساعد النتائج السابقة الطبيب المعالج في اتخاذ قرار سحب الأنبوب الرغامي في الوقت المناسب لتقليص الشدة المرافقة لفشل التجربة. نشجع المتابعة بإجراء أبحاث لاحقة مع حجم عينه أكبر لدراسة العوامل الإنذارية الثانوية لفشل تجربة سحب الأنبوب الرغامي.

ABSTRACT

Objective: *Study of risk factors related to extubation trial failure for very low birth infants.*

Methods: *Retrospective study analyzing records of very low birth weight infants "VLBW", who were admitted to neonatal intensive care unit in Tawam Hospital and intubated, January 2011 till January 2018.*

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Results: *The study analyzed antenatal risk factors, ventilation parameters, blood gas results prior and two hours post extubation trial, phosphorus level at 2nd week of life, 446 patients <32 weeks GA, or < 1500 g birth weight were included. Extubation trial for each GA group is enlighted by Antenatal history for best results. For GA (21+4-26+6) weeks, extubation failure is associated with male gender, post extubation FIO2 level >0.30, high PCO2 level above 55 mm.hg post extubation, ground glass appearance on chest XR at extubation trial, large PDA, low and advanced grade intraventricular hemorrhage. While extubation success is associated with deferring extubation until FIO2 requirement level is low to the level of (0.25), positive end expiratory pressure (PEEP) level range of (6-7) cm water. For GA groups (27-29+6), extubation failure is associated with post extubation FIO2 level >0.30 low PH level (6.9-7.24) post extubation, advanced intraventricular hemorrhage IVH grade (3 and 4), while extubation success is associated with deferring extubation until FIO2 requirement is low to the level of (0.21), and post extubation positive end expiratory pressure (PEEP) level range (6-7) cm.water. For GA group (30- 32w), extubation failure is associated with post extubation FIO2 level >0.30, low PH level (6.97.24-) post extubation, low PO2 (20-40) mm.Hg post extubation, large PDA, while success is associated with deferring extubation until FIO2 requirement is low to the level of (0.25 and inspiratory time >0.38 seconds before extubation). For safe extubation, number of surfactant treatment doses are guided by GA group. Low phosphorus level is associated with extubation failure.*

Conclusions: *Risk factors for extubation trial failure are different between GA groups. Associated risk factors may guide physician to predict the result of extubation trial and reduce exposure to failure. Follow up research studies on larger sample size are needed to analyze secondary risk factors.*

INTRODUCTION

Antenatal steroids and early use of nasal continuous positive airway pressure (NCPAP) have significantly improved outcomes of very low birth weight infants with respiratory distress syndrome,[1,2] but intubation with ventilator support is still required and the optimal timing of extubation remains unclear. Nearly two thirds of prematures born at less than 29 week gestation require mechanical ventilation during NICU stay.[3]

Acute complications, and bronchopulmonary dysplasia (BPD), adverse neurodevelopmental outcomes, related to mechanical ventilation and endotracheal intubation in extreme preterm infants[4,5] are encouraging physicians to extubate infants as early as possible. Short-term (less than 7 days) mechanical ventilation itself is known to be a cause of rapid diaphragmatic dysfunction, and long-term ventilation (more than 12 days) is also associated with failure of normal pulmonary growth and maturation.[6]

But still 40% of mechanically ventilated ELBW infants require re-intubation following extubation.[7] Failure of extubation has been associated with higher mortality rates, increased length of hospital stay, and longer ventilation days.[8,9]

Mode of ventilation that converts electrical activity of diaphragm into proportionally assisted and synchronized breath is known as neutrally adjusted ventilatory assist (NAVA).[6] Infants inform the neonatologist of what support they need, directing both the timing and depth of their breath pattern.[10] NIV NAVA can provide synchronized post extubation ventilatory support as measured by decreased PCO2 in premature infant.[11] NAVA appears to work well in neonates, but if NAVA makes a difference in outcomes in this population, has not been established so far.[10]

METHODS

In this study we evaluate the rate and predictors of extubation failure in very low birth weight infants. Retrospectively we analyzed all VLBW preterm infants who were admitted to our neonatal intensive care unit (NICU) and intubated from January 2011 till January 2018. Risk factors, ventilation parameters, blood gas results prior and 2 hours post extubation trial were analyzed. We defined extubation failure as need for re-intubation within 5 days due to attending physician assessment of clinical status and blood gas reports.

1580 shot of surfactant were recorded 2011-2018, given to 761 patients in NICU, as some patients require 1st, 2nd, 3rd or 4th doses of surfactant. 457 patients were <32 weeks GA, or <1500 g birth weight. Eleven patients were excluded for congenital anomaly, 446 patients were included. 132 out of 446 didn't experience an extubation trial till end of 14 days of life. Statistical analysis was conducted using IBM SPSS Statistics version 20. Categorical variables were compared using nonparametric Chi-square test. Patients grouped to GA (21+4-23+6, 24-26+6, 27-29+6,30-32), and merged both tiny groups if sample size was small and ignored by the analytic system. Extubation results in (success, fail) and we added (not fit for extubation till end of 14 days of life) to failure group for perinatal analysis. Continuous variables were analyzed using general linear modelof nonparametric ANOVA test.

1st trial extubation (till 14 days of life): 314 out of 446 patients had undergone a 1st trial of extubation after assessment of clinical stability by attending physician. (before completing 14 days after birth). 222/314 (70.7%) patients succeeded 1st trial extubation (success was defined as passing 5 days without re-intubation). 92/314 (29.29%) Patients failed 1st trial extubation (needed re-intubation within 5 days post extubation).

2nd trial extubation (considered only within 7 days of life to observe patients over the next 5 days): 34/92 Extubated post 1st week, were excluded. 15/92 patients were not fit for extubation till 14 days of life. 43/92 patients had undergone 2nd trial of extubation (within 7 days of life). 29/43 patients succeeded 2nd trial of extubation. 14/43 patients failed 2nd trial of extubation.

3rd trial extubation (considered only within 7 days of life to observe patients over the next 5 days): 12 patients were not fit for extubation within the first 7 days of life, excluded. 3 patients had undergone 3rd trial extubation within 1st week. Two patients succeeded 3rd trial of extubation. One patient failed 3rd trial of extubation.

RESULTS AND DISCUSSION

Our study is done in one center where the team has almost the same clinical practice guide. It is a unique study for the number of infants included in the analysis and the design that revealed specific predictors for extubation trial for each GA group in different lung development stage. The following is a discussion for each analyzed parameter.

Prenatal steroid: Steroid treatment was grouped into (no steroid given or unknown, steroid given), then subgrouped into (1 dose or 2 doses comparison). Timing of each dose was not clear in patient's records. Mild significant association between antenatal steroid and extubation success was noticed for GA 27-29+6 weeks. The association ismild with a single dose and less with 2 doses. Linear by linear, χ^2 (2, n=507) =4.73, p-value=0.023, cramer's V 0.155. Linear by linear, χ^2 (1, n=338)=3.62, p-value=0.042, Cramer's V 0.160. The unrecorded cases may underestimate the effect of steroid.

Small for GA: Size for GA grouped into (small for GA-below 10th centile on Fenton growth chart, adequate for GA). Adequate sized GA group (30-32) weeks, have moderate association with extubation success than small for GA. Pearson's Chi-square, χ^2 (1, n=495)=6.5, Fisure's exact test, p-value=0.039, Cramer's V 0.232.

Large for GA: Is not related to extubation trial. Size for GA grouped into (large for GA-above 90th centile on Fenton growth chart, adequate for GA). Pearson's Chi-square, χ^2 (1, n=491) =0.009, Fisure's exact test, p-value=0.578.

Gender: Sex grouped into (male, female). Male gender of GA (21+4 to 26+6) weeks has moderate association with extubation failure. No difference in association for other GA groups. Pearson's Chi-square, χ^2 (1, n=507) =7.8, 0.02, 0.11. p-value=0.005, cramer's V 0.204, p-value=0.49, p-value=0.46, respectively.

Surfactant doses: Number of surfactant doses were determined by physician opinion and clinical needs. Patients who died at 1st day of life were excluded. The test was performed on 4 levels to test the cut off statistically significant doses for each GA. Extubation results grouped into (success, fail). No association exists between extubation trial and all doses of surfactant for (21+4 to 23+6) weeks. Linear by linear association, χ^2 (1, n=60, 70, 70) =3, 1.3, 1.3, p-value is 0.157, 0.317,

0.317, respectively. GA (21+4-23+6) weeks are at canalicular stage of fetal lung development, and has no surfactant production. All doses of surfactant were not enough to make a statistical difference in extubation trial. The immature lung and ventilation dependence are the causesof failure and surfactant was not enough alone to be the treatment of choice to prevent extuabtion failure. We noticed a significant association between extubation success and 2 doses of surfactant given to GA group (24-26+6) weeks, before 1st extubation trial or one dose before both trials. Linear by linear association, χ^2 (1, n=60,70)=5.7, 6.5, p-value is 0.019, 0.010 respectively. Less significant extubation success association was observed for GA group (24-26+6) weeks when 3 accumulative doses of surfactant were given before the 1st trial of extubation or over several trials. Linear by linear association, χ^2 (1, n=60 and 70)=4, 6, 5.9, p-value is 0.031, 0.015 respectively. GA group (24-26+6) weeks are at saccular lung maturity stage, where surfactant is detected in fetal amniotic fluid, and 2 doses of surfactant are enough to compensate for surfactant deficiency and make a statistical significant association with extubation success. One or two doses of surfactant given before the 1st trial of extubation or later for GA group (27-29+6) weeks result in accumulative significant association with extubation success. Linear by linear association, χ^2 (1, n=363, 314, 363)=13.46, 14.6, 13.4, p-value is 0.0002, 0.0001, 0.0002 respectively. While the 3rd does not make a difference in extubation trial. GA group (2729-+6) weeks is in fetal saccular lung maturity stage with increase in surfactant production more that the previous GA group. One dose is enough to make a significant statistical difference in extubation trial, and further doses are not statistically needed. Statistical significant association between extubation success and 1 dose, then accumulative 2, 3 doses of surfactant, was observed for GA group (30-32) weeks. Linear by linear association, χ^2 (1, n=363)=4.98, 5.8, 16.5, p-value is 0.026, 0.016, 0.00004. GA group (30-32) weeks normally produce more surfactant than the previous GA groups, and in case of deficiency, the accumulative doses are association with extubated trial success. Extra factors causing surfactant deficiency in GA group (30-32) weeks, need to be studied further.

Gestational diabetic status GDM: Is not related to extubation trial. Mothers grouped into (no GDM or unknown, GDM). Pearson's Chi-square, χ^2 (1, n=507)= 2, p-value=0.09. Unknown cases may affect results.

Chorioamnionitis: Is not related to extubation trial. Mother's status before delivery estimated clinically and grouped into (no chorioamnionitis or unknown, chorioamnionitis). Pearson's Chi-square, χ^2 (1, n=507)=1.1, Fisher's exact test, p-value=0.198. The unrecorded cases may under-estimate the infectious status association, and the follow up histologic chorioamnionitis was not recorded.

Pre-labor ruptured membrane PROM: Mother's status (no PROM or unknown, PROM >18 hours). For GA (21+4-26+6) weeks, (no PROM group) is associated with extubation failure in all GA groups. Pearson's Chi-square, χ^2 (1, n=507)=9.3, p-value=0.002. cramer's V 0.346.

Caffeine treatment: Is not related to extubation trialfor all GA groups. Pearson's Chi square, χ^2 (1, n=363) =2.3 Fisher's exact test, p-value=0.089.

Phosphorous level PO4: PO4 level at the second week of life (less than 1.8 mmol/L, above 1.8 mmol/L). Low PO4 level for GA (24-26+6) weeks was strongly associated with extubation failure, and mildly associated for GA (27-29+6) weeks. Pearson's Chi-square, χ^2 (1, n=299)=7.1, 4.3. p-value=0.007, 0.036. cramer's V 0.305, 0.176 respectively. While no association observed for GA groups (21+4-23+6, 30-32). Pearson's Chi-square, χ^2 (1, n=299) =1.2, 3.5. p 0.42, 0.06.

Day of life at 1st intubation: Is not related to extubation trial. Day of life at 1st intubation (intubated in delivery room, any time later). Pearson's Chi-square, χ^2 (1, n=359) =0.09, 1.1, 0.08. p-value is 0.76, 0.29, 0.77, respectively. All GA groups (21+4-23+6) patients were intubated at delivery room for respiratory failure.

Ventilation mode before extubation: Is not related to extubation trial for all GA groups. Mode before extubation trial (NAVA, conventional ventilation +/- volume targeted ventilation, PSV). For NAVA mode of ventilation Pearson's Chi-square, χ^2 (1, n=338)=0.67, Fisher's exact test, p-value=0.24.

For conventional ventilation modes, whether Volume targeted setup was applied or not.Pearson's Chi-square, χ^2 (1, n=169)=0.119 Fisher's exact test, p-value=0.442. For PSV (pre-extubation mode) mode. Pearson's Chi-square, χ^2 (1, n=338)=0.71 Fisher's exact test, p-value=0.238.

Ventilation peak inspiratory pressure (PIP) level before extubation: Is not related to extubation trial. PIP level was determined by attending physician between 828- cm H_2O, median 18.8 cm.H_2O, mode 20 cm.H_2O. One-way ANOVA F (2, 250)=0.71, p-value=0.49.

Ventilation positive end-expiratory pressure (PEEP) level before extubation: Range of PEEP level was determined by attending physician between 58-cm.H2O. No relation was noticed between High PEEP ≥ 6 cm.H_2O ventilation or low PEEP <6 cm.H2O before extubation and extubation trial for all GA groups. Pearson's Chi-square, χ^2 (1, n=330)=0.56 Fisher's exact test, p-value=0.26.

Ventilation rate before extubation: Rate of ventilation was determined by attending physician 20-60/min, "mode 40/min". No relation is noticed between high ventilation rate (41-60/min) or low ventilation rate (20-40/min) before extubation and extubation trial for all GA groups. Pearson's Chi-square, χ^2 (1, n=287) =0.89 Fisher's exact test, p-value= 0.21.

Fraction of inspired oxygen FIO2: Mode of FIO2 before extubation was 0.21. The level at which patient was extubated, was determined by physician assessment. Significance was checked at 2 levels, 0.21 then 0.25. FIO2 supply reduced to 0.21 before extubation has mild association with extubation success for GA group (27-29+6) week. Linear by linear association, χ^2 (1, n=334)=4.84. p-value=0.028.

FIO2 supply reduced to 0.25 before extubation had strong association with extubation success for GA group (21+4- 26+6,30-32) weeks. Linear by linear association, χ^2 (1, n=334)=9, 17.84. p-value is 0.003, 0.000026.

Inspiratory time before extubation (IT): IT before extubation was determined by physician, (0.20-0.86) second. Mode 0.38 second. IT grouped into (0.20-0.33, 0.33-0.37, 0.38-0.4, 0.4-0.86) second. Short IT group (0.2-0.33, 0.33-0.37) sec has no relation with extubation trial, longer IT group (0.38-0.4, 0.4-0.86) sec has no relation with extubation trial. Comparison between (0.20-0.37, 0.38-0.86) sec was significant for GA group (30-32) weeks, IT >0.38 sec before extubation was associated with less extubation failure and more success. Pearson's Chi-square, χ^2 (1, n=162)=5.23, Fisure's exact test, p-value= 0.04. cramer's V 0.324.

As the longer IT group (0.4-0.86) sec act the same as IT group (0.38-0.4) sec, and RDS management requires lower possible range for IT, we recommend starting with IT in the range (0.38-0.4) sec as an adequate support for safe ventilation and extubation trial.

Patient's respiratory rate before extubation (RR): Is not related to extubation trial. RR observed in the range (20-99)/min, mode 50/min. RR grouped into (20-40, 40-70,70-99)/min. Pearson's Chi-square, χ^2 (1, n=168)=0.01, 0.043, Fisure's exact test, p-value is 0.53, 0.5. Patients who are tachypnic may still succeed extubation trial, as well as patients with normal to variably slow breathing patients.

Neurally adjusted ventilatory assist NAVA level before extubation: Is not related to extubation trial. NAVA level mean 1.5 (0.8-3) cm.H2O/μV. Level of NAVA for extubation trial was determined by attending physician. One-way ANOVA F(1,48)= 0.012, p-value=0.91.

Electrical activity of the diaphragm (Edi):

Edi max: Is not related to extubation trial. Edi max mean 8.77 (2.9, 14) μV. One-way ANOVA F (1, 29)= 1.6, p-value=0.2.

Edi min: Is not related to extubation trial. (Edi min) mean 1.36 (0.3, 5.5) μV. One-way ANOVA F (1, 29)= 1.15, p-value=0.29.

Blood gas PH before extubation: Is not related to extubation trial. PH mean 7.33(7.0-7.57). One-way ANOVA F (2, 348)=0.52, p-value=0.59.

Blood gas PCO2 before extubation: Is not related

to extubation trial. Mean PCO2 41 (9.2-69) mm.Hg. One-way ANOVA F (2, 348) =0.42, p-value=0.65.

Blood gas PO2 before extubation: Is not related to extubation trial. Mean PO2 49.4 (21.5-144) mm.Hg. One-way ANOVA F (2, 348)=1.7, p-value=0.16.

Blood gas HCO3 before extubation: Is not related to extubation trial. Mean HCO3 21.38 (9.7-34) mEq/L. One-way ANOVA F (2, 348)= 0.27, p-value=0.75.

Blood gas BE before extubation: Is not related to extubation trial. Mean BE -3.98 (-15.3 to +6). One-way ANOVA F (2, 348)=1.3, p-value=0.82.

Blood gas HB before extubation: Is not related to extubation trial. Mean HB 14.5 (7.3-24) g/dl. One-way ANOVA F (2, 346) =0.953, p-value=0.38.

Blood gas LAC before extubation: Is not related to extubation trial. Mean LAC 2.82 (0-12.7) mmol/L. One-way ANOVA F (2) =0.289, p-value=0.749.

Post extubation ventilation mode: Is not related to extubation trial. Post extubation mode (continuous positive airway pressure CPAP, non invasive NAVA ventilation "NIV NAVA", non-invasive ventilation). Pearson's Chi-square, χ^2 (1, n=350)=0.26, 2.87. p-value is 0.87, 0.23 for GA (21+4-26+6, 27-29+6), respectively. Pearson's Chi-square, χ^2 (1, n=258)=1.304, 2.27, 3. Fisher's Exact Test, p-value is 0.315, 0.126, 0.1 for GA (30-32) weeks on 3 steps comparison of 2 modes per each test.

Ventilation PIP post extubation: Is not related to extubation trial. Post extubation PIP level mode 8 cm.H_2O. PIP grouped into (5-8, 9-30) cm.H_2O. Pearson's Chi-square, χ^2 (1, n=233)=2.7. Fisher's Exact Test, p-value=0.067.

Ventilation PEEP post extubation: Low Post extubation PEEP level (less than 6, 6-7) cm.H_2O. No difference in association exists between post extubation PEEP and extubation trial for all GA groups. Pearson's Chi-square, χ^2 (1, n=313)=0.417. Fisher's Exact Test p-value=0.314.

High post extubation PEEP level (6-7, 8-10) cm.H_2O. Post extubation PEEP level (6-7) cm.H_2O is associated with extubation success for GA (21+4-26+6, 27-29+6). This association is not significant for GA group (30-32) week. Pearson's Chi square, χ^2 (1, n=114) =4.47, 4.86. p-value is 0.042, 0.028. Cramer's 0.415, 0.273. Pearson's Chi-square, χ^2 (1, n=114)=1.79. Fisher's Exact Test p-value=0.208, respectively.

Ventilation FIO2 post extubation: Post extubation FIO2 level mode 0.21, grouped into (0.21-0.30,0.31-0.90). Significant association between FIO2 level >0.30 and extubation failure is observed for all GA groups. Pearson's Chi-square, χ^2 (1, n=356) =6.78, 9.71, 13.6. p-value=0.009, 0.003. Cramer's 0.318, 0.234. Fisher's Exact Test p-value= 0.004, respectively.

Ventilation rate post extubation: Is not related to extubation trial. Post extubation ventilation rate (15-30, 31-60). Pearson's Chi-square, χ^2 (1, n=221) =0.87, 2.2. p-value is 0.26, 0.1. χ^2 (1, n=221)=1.29. Fisher's Exact Test p-value is 0.21, respectively.

Post extubation ventilation inspiratory time (IT): Is not related to extubation trial. (IT) was determined by attending physician by clinical assessment, IT mean 0.40 (0.30-0.59) sec. One-way ANOVA F (2, 47)=1.8, p-value=0.175.

Post extubation neurally adjusted ventilatory assist NAVA level: Is not related to extubation trial. NAVA mean 1.74 (0.5-3.7) cm.H2O/μV. One-way ANOVA F (1, 60) =0.009, p-value=0.925.

Post extubation electrical activity of the diaphragm (Edi) Edi max: Is not related to extubation trial. Edi max recorded from observational measurements. Edi max mean 7 (2.8-12) μV. F(1, 18) =0.245, p-value=0.629.

Edi min: Is not related to extubation trial. Edi max recorded from observational measurements. Edi max mean 1.4 (0.25-) μV. F(1, 18) =0.001, p-value=0.997.

Post extubation blood gas-pH: Post extubation pH level mode 7.3, grouped into (6.9-7.24, 7.25-7.34, 7.35-7.55). Low pH level noticed to be associated with extubation failure for GA groups (27-29+6, 30-32).

Pearson's Chi-square, χ^2 (1, n=285)=5. p-value=0.025. Cramer's 0.192. Pearson's Chi-square, χ^2 (1, n=285) =10.27. Fisher's Exact Test p-value=0.015, respectively, while low pH level has no relation with extubation trial for GA (21+4-26+6). Pearson's Chi-square, χ^2 (1, n=285) =2.9. p-value=0.085. High pH level has no relation with extubation trial for all GA. Pearson's Chi-square, χ^2 (1, n=314) =3.9, 2, 0.39. Fisher's Exact Test p-value is 0.05, 0.11, 0.45.

Post extubation blood gas-PCO2: PCO2 level post extubation mode 42 mm.Hg, PCO2 grouped into (19-34 ,35-54, 55-86) mm.Hg. High PCO2 level above 55 mm.Hg is associated with extubation trial failure for GA (21+4-26+6). Pearson's Chi-square, χ^2 (1, 308) =6.61, p-value=0.01, Cramer's 0.329. Physician decided to re-intubate patients (trial failed) selectively at this level of PCO2, and we have noticed no association between PIP, ventilation Rate and extubation trial, therefore giving a chance for ventilation setting adjustment to reduce PCO2 level by increasing PIP, rate of ventilation may not be helpful to turn the trial result into success.

Post extubation ventilation rate grouped into (15-31,30-60)/min. No relation exists between PCO2 post extubation and post extubation ventilation Rate for all GA groups. F (2, 218)=1.59, p-value=0.206. Post extubation PCO2 mean was compared by general linear model test to check relation with patient's respiratory rate for post extubation failure group for all GA groups. At failure we grouped patient's respiratory rate into (0-30, 31-60, 61-100)/min. No relation exists between PCO2 post extubation and patient's respiratory rate at failure for all GA groups. F (2, 108)=0.39, p-value=0.677. We conclude that ventilation rate and patient's respiratory rate at failure have no association with PCO2 level post extubation, and extra factors need to be studied further. No relation between high PCO2 and extubation trial for (27-29+6, 30-32). Pearson's Chi-square, χ^2 (1, n=308)=1.81, 1.33, p-value=0.142, Fisher's exact test p-value= 0.321. No relation exists between low PCO2 and extubation trial for all GA groups. Pearson's Chi square, χ^2 (1, n=322) =0.22, 1.82, 0.016. Fisher's exact test p-value=0.6, p-value=0.127, Fisher's exact test p-value=0.68. Low PCO2 is not a predictor for extubtion trial success. Pearson's Chi-square, χ^2 (1, n=308) =1.81, 1.33, p-value=0.142, Fisher's exact test p-value=0.321. No relation exists between low PCO2 and extubation trial for all GA groups. Pearson's Chi-square, χ^2 (1, n=322) =0.22, 1.82, 0.016. Fisher's exact test p-value=0.6, p-value=0.127, Fisher's exact test p-value=0.68. Low PCO2 is not a predictor for extubtion trial success.

Post extubation blood gas-PO2: PO2 level post extubation mode 40 (18-127) mm.Hg, grouped into (20-40, 41-70, 71-145) mm.Hg. No relation exists between low PO2 post extubation and extubation trial for GA groups (21+4-26+6, 27-29+6). Pearson's Chi-square, χ^2 (1, n=320)=3.7, 0.89. p-value is 0.54, 0.76. Low PO2 post extubation is associated with extubation failure for GA (30-32) week. Pearson's Chi-square, χ^2 (1, n=320) =5.3, p-value=0.021. Cramer's 0.225. No relation exists between high PO2 post extubation and extubation trial for all GA groups. Pearson's Chi-square, χ^2 (1, n=206) =0.71. p-value=0.25.

Post extubation blood gas-HCO3: Is not related to extubation trial. HCO3 level post extubation grouped into (10-18, 18.1-25, 25.1-36) mEq/L. For metabolic Pearson's Chi-square, χ^2 (1, n=334)=2.78, Fisure's exact test, p-value=0.07. For no metabolic alkalosis Pearson's Chi-square, χ^2 (1, n=308)=0.73, 0.12,1.1. Fisure's exact test, p-value is 0.31, 0.48, 0.34.

Chest XR at failure: CXR was done for all patients who failed extubation trial to check ETT tip position. The major finding for all GA groups was ground glass appearance 60%, 51.6%, 87.5% for GA group (21+4-26+6, 27-29+6, 30-32). CXR at failure grouped as reported into (non-ground glass appearance, significant ground glass appearance). A 3 way Chi-square test was performed to examine the relation between times of extubation failure (1, 2) and CXR findings post extubation failure for all GA groups. Significant association exists between significant ground glass appearance and 1st trial failure, non-ground glass appearance and 2nd extubation failure for GA group (21+4-26+6), while no association for other more mature GA groups (27-29+6, 30-32). Pearson's Chi-square, χ^2 (1, n=119) =6.66, 1.8, 0.15 Fisher's exact test p-value is 0.02, 0.16, 0.87, respectively. At 1st trial extubation for GA group (21+4-26+6), we recommend to study

the efficacy of performing CXR before extubation trial to guide extubation decision. At 2nd trial failure for GA group (21+4-26+6), CXR cleared of ground glass appearance but trial may still fail of other reasons.

Times extubation: Times of extubation (1^{st},2^{nd}, 3^{rd}). No relation exists between 2^{nd} time of extubation and extubation trial result for all GA groups. Pearson's Chi-square, χ^2 (1, n=357) =0.192, Fisher's exact test, p-value=0.391. No relation exists between 3^{rd} time of extubationand extubation trial for GA (27-29+6, 30-32) groups. Pearson's Chi-square, χ^2 (1, n=257) =0.169, Fisher's exact test, p-value=0.551.

Extubation day: Extubation day (within 2 days of life, later). No relation exists between timing of 1st extubation and extubation trial for GA groups (27,6+29-32-30). Pearson's Chi-square, χ^2 (1, n=352)=0.855, Fisher's exact test, p-value=0.21.

For GA (21+4-23+6, 24-26+6) extubation day (within 7 days of life, later). No relation between timing of extubation and extubation trial for all tiny GA groups. Pearson's Chi-square, χ^2 (1, n=68)=0.009, Fisher's exact test, p-value=0.56.

Day of failure: GA group do not predict day of failure post extubation trial. On-way ANOVA F (2, 104) =0.78, p-value=0.457.

Air leak syndrome: Is not related to extubation trial. Air leak (no air leak, air leak syndrome till 14 days of life [PIE + tension pneumothorax]). Pearson's Chi-square, χ^2 (1, n=451) =3.1, 1.56, 4.5. Fisher's exact test, p-value is 0.062, 0.215, 0.183.

Patent Dductus Arteriosus PDA: PDA (tiny PDA and no treatment needed, large significant PDA requiring treatment). No relation exists between PDA and extubation trial for GA groups (27-29+6). Pearson's Chi-square, χ^2 (1, n=436) =2.7. p-value=0.09. Significant association between large PDA and extubation failure is observed for GA group (21+4-26+6, 30-32). Pearson's Chi-square, χ^2 (1, n=436) =8.24, 5.9. p-value=0.004 Fisher's exact test p-value=0.029.

Intra ventricular hemorrhage IVH: IVH grade (no IVH, low grade 1and 2, advanced grade 3 and 4). Low grade IVH is associated with extubation failure group for GA group (21+4-26+6). No relation exists between low grade IVH and extubation trial for GA groups (27-29+6, 30-32). Pearson's Chi-square, χ^2 (1, n=394) =8.2, 0.75, 1.17. p-value is 0.004, 0.38, Fisher's exact test, p-value=0.24, respectively.

A significant association exists between advanced IVH grade and extubation failure for GA groups (21+4-26+6, 27-29+6). Pearson's Chi-square, χ^2 (1, n=349) =11.9, 8.2. [p=0.001, Cramer's 0.353], Fisher's exact test, p=0.011, respectively. While no relation exists for GA (30-32). Pearson's Chi square, χ^2 (1, n=349) =0.172. Fisher's exact test, p=0.854.

Do times extubation increase IVH rate? No relation exists between low grade IVH and extubation times for all GA groups. Pearson's Chi-square, χ^2 (1, n=302) =0.385, Fisher's exact test, p=0.37. No relation exists between advanced grade IVH and extubation times for all GA groups. Pearson's Chi-square, χ^2 (1, n=340) =0.12, 3.4, 1.51. Fisher's exact test, p-value is 0.49, 0.06, 0.23.

CONCLUSIONS

Risk factors for extubation trial failure are different between GA groups. Associated risk factors may guide physician to predict the result of extubation trial and reduce exposure to failure. Accurate documentation of antenatal history helps to increase the significance of risk factors association. Follow up research studies on larger sample size are needed to analyze secondary risk factors.

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