Original Article

Success and failure of extubation in premature newborns up to 32 weeks of gestational age

Sucesso e falha de extubação em recém-nascidos prematuros até 32 semanas de idade gestacional

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ABSTRACT | INTRODUCTION: The benefits of mechanical ventilation in preterm infants are complemented by successful extraction. **OBJECTIVE:** To evaluate ventilatory and gasometric parameters before extubation and to identify possible factors that may contribute to the endotracheal extubation decision in preterm infants up to 32 weeks. **METHODS:** This is a prospective observational study. The study sample was selected in a non-probabilistic way. Preterm infants with a gestational age of up to 32 weeks and invasive mechanical ventilation for at least 24 hours were included. Exclusion criteria were newborns with malformations, heart disease, and those transferred to other hospitals before the first elective extubation. Weaning and extubation followed the protocol of the Neonatal Intensive Care Unit (NICU) (presence of regular spontaneous breathing with a cough reflex, FiO2 <40% to maintain 90% saturation; inspiratory pressure between 15-18 cmH2O; RR = 15 to 20 ipm; pH> 7.25 mmHg and PaCO2 <50 mmHg). The newborn was followed up to 7 days after extubation. **RESULTS:** 20 preterm newborns were included, in 75% of the cases intubation was due to neonatal respiratory distress syndrome. Of the total sample, 40% were unsuccessful. In the logistic regression, it was observed that the inspired oxygen fraction (p = 0.03) and the mean airway pressure (p = 0.03) showed significance as a predictor of extubation. The time of use of invasive mechanical ventilation was not statistically significant (p = 0.06) for the evaluated result. **CONCLUSION:** In this study, ventilatory and blood gas parameters did not influence the success or failure outcome. However, these data associated with the patient's condition can help guide and schedule safer extubation.

KEYWORDS: Infant, premature. Extubation. Mechanical ventilation. Intensive care units, neonatal. Premature birth. Extubation failure.

RESUMO | INTRODUÇÃO: Os benefícios da ventilação mecânica em neonatos prematuros se complementam com o sucesso na sua retirada. **OBJETIVO:** Avaliar os parâmetros ventilatórios e gasométricos pré extubação e identificar possíveis fatores que possam contribuir na decisão da extubação endotraqueal em recém-nascidos prematuros até 32 semanas. **MÉTODOS:** Trata-se de um estudo prospectivo, de caráter observacional. A amostra do estudo foi selecionada de forma não probabilística. Foram incluídos prematuros com idade gestacional até 32 semanas, e em ventilação mecânica invasiva por no mínimo 24 horas. E os critérios de exclusão foram recém-nascidos com malformações, cardiopatias e os transferidos para outros hospitais antes da primeira extubação eletiva. Os dados sobre o diagnóstico clínico, dados vitais, parâmetros da ventilação mecânica e gasometria arterial, registrado em uma ficha elaborada pelos pesquisadores e coletados diariamente, uma vez por dia desde o primeiro dia de ventilação mecânica invasiva até o momento de retirada do tubo endotraqueal, sendo o recém-nascido acompanhado até 7 dias após a extubação. O desmame e a extubação seguiu o protocolo da Unidade de Terapia Intensiva Neonatal (UTIN) (presença de respiração espontânea regular e com reflexo de tosse, FiO2 < 40% para manter saturação 90%; pressão inspiratória entre 15 – 18 cmH2O; FR=15 a 20 ipm; pH > 7,25 mmHg e PaCO2 < 50 mmHg). **RESULTADOS:** Dos 20 recém-nascidos prematuros incluídos no estudo, 14 eram do sexo masculino, a média de idade gestacional foi de 28,9± 2,12 semanas e a média do peso ao nascimento foi 1069,5g ± 375,5. Em 75% dos casos, a intubação foi devido à síndrome do desconforto respiratório neonatal. Do total da amostra, 40% apresentaram. Não houve diferença significativa entre os grupos sucesso e falha na extubação, quanto aos dados ventilatórios e gasométricos analisados pré e pós extubação (p>0,05). Na regressão logística, observou-se que a fração inspirada de oxigênio (p= 0,03) e a pressão média de vias aéreas (p= 0,03) apresentaram significância como preditor para extubação. O tempo de uso da ventilação mecânica invasiva não apresentou significância estatística (p=0,06), para o desfecho avaliado. **CONCLUSÃO:** Neste estudo, os parâmetros mínimos ventilatórios como FiO2 e MAP se relacionam diretamente com o sucesso da extubação, bem como estar atento às condições clínicas do paciente auxiliam a equipe a nortear o desmame e programar uma extubação mais criteriosa e segura.

PALAVRAS-CHAVE: Recém-nascido prematuro. Extubação. Ventilação mecânica. Unidades de terapia intensiva neonatal. Nascimento prematuro. Falha na extubação.

Introduction

Prematurity is currently considered a public health problem, and one of the main risk factors for neonatal morbidity and mortality[1]. According to the World Health Organization (WHO) is considered a premature newborn that baby that is born before complete 37 weeks of gestation age[2], can be classified according to gestational age in extremely premature (< 28 weeks), moderate premature (28 to 31+6 weeks) and late preterm birth (32 to 36+6)[3].

One of the main complications that affect the premature newborn is respiratory distress syndrome, which is a disorder caused by pulmonary immaturity and a small amount of surfactant, that compromises alveolar integrity, hindering normal gas exchange. Neonatal respiratory distress syndrome occurs at birth or shortly after birth, before 24 hours of life and increases in severity during the first 48 hours of life[4], and is the most common cause of admission to the Neonatal Intensive Care Unit (NICU)[5]. The incidence of neonatal respiratory distress syndrome is higher as gestational age decreases[4,6], ranging from 21,3% to 56,9% according to the literature[7,8].

Thus, it is common for a premature newborn, especially the extremely premature, to need invasive ventilatory support to maintain adequate ventilation and oxygenation after birth[9]; about 89% of extremely low birth weight premature babies are ventilated in the first days of life[10]. However, prolonged use of invasive ventilatory support, as well as poorly adjusted parameters, can cause lung injuries such as pneumothorax, interstitial pulmonary emphysema, and bronchopulmonary dysplasia[11,12], the latter being the main complication of prolonged use of invasive mechanical ventilation.

Thus, one of the challenges for the multi-professional team is to reduce the time of invasive mechanical ventilation, preventing both complications related to the use of mechanical ventilation, as well as the failure of extubation and reintubation[13]. Interventions that decrease exposure to invasive mechanical ventilation and result in successful extubation have long-term benefits[14]. Successful extubation is defined as not requiring reintubation during a predetermined time window, but in premature infants, this observation window can vary from 12 hours to seven days[14].

The hypothesis that guided the research was that the ventilatory parameters used in mechanical ventilation influence early weaning and the success of extubation. Thus, the objective of this study was to evaluate the ventilatory and gasometric parameters before extubation and to identify possible factors that may contribute to the decision of endotracheal extubation in premature newborns up to 32 weeks of gestational age.

Methods

This is a prospective, observational study. The research was approved by the Research Ethics Committee with human beings of the institution where the research took place under opinion number 2.836.816 (CAAE 91754318.6.0000.0096). The study was carried out at the Neonatal Intensive Care Unit - NICU of a tertiary teaching hospital. Data collection took place from December/2018 to July/2019. Parents signed the Free and Informed Consent Form to participate in the study.

Inclusion criteria were premature newborns with a gestational age up to 32 weeks, of both sexes, and in invasive mechanics for at least 24 hours. Exclusion criteria were newborns with malformations, heart disease, and those transferred to other hospitals before the first elective extubation. The study sample was selected in a non-probabilistic manner.

Data on clinical diagnosis, vital data, mechanical ventilation parameters, and arterial blood gases, were recorded in a form prepared by the researchers and collected daily, once a day, in the morning, from the first day of invasive mechanical ventilation to the moment extubation. Follow-up was carried out for 7 days after extubation, with only the first elective extubation considered for the study.

The criteria for weaning and extubation were defined according to the studied NICU protocol, being eligible for extubation the newborn with regular spontaneous breathing and with cough reflex, a fraction of inspired oxygen less than 40% to maintain 90% saturation, inspiratory pressure between 15 - 18 cmH2O, respiratory rate of 15 to 20 inspirations per minute, pH lower 7.25 mmHg and PaCO2 lower 50 mmHg, which follows the recommendations of the Brazilian

Consensus on Mechanical Ventilation (23). Despite the existence of a protocol for weaning at the NICU where this study was carried out, no readiness test was used to guide the extubation of preterm infants, always respecting the gasometric and ventilation parameters mentioned above, in addition to the clinical and hemodynamic conditions. of the newborn, as well as the clinical judgment of the medical team.

Extubation success was considered when the newborn remained 7 days without the need for endotracheal reintubation, maintaining adequate saturation and clinical stability (Figure 1).

Figure 1. Diagram of the study design
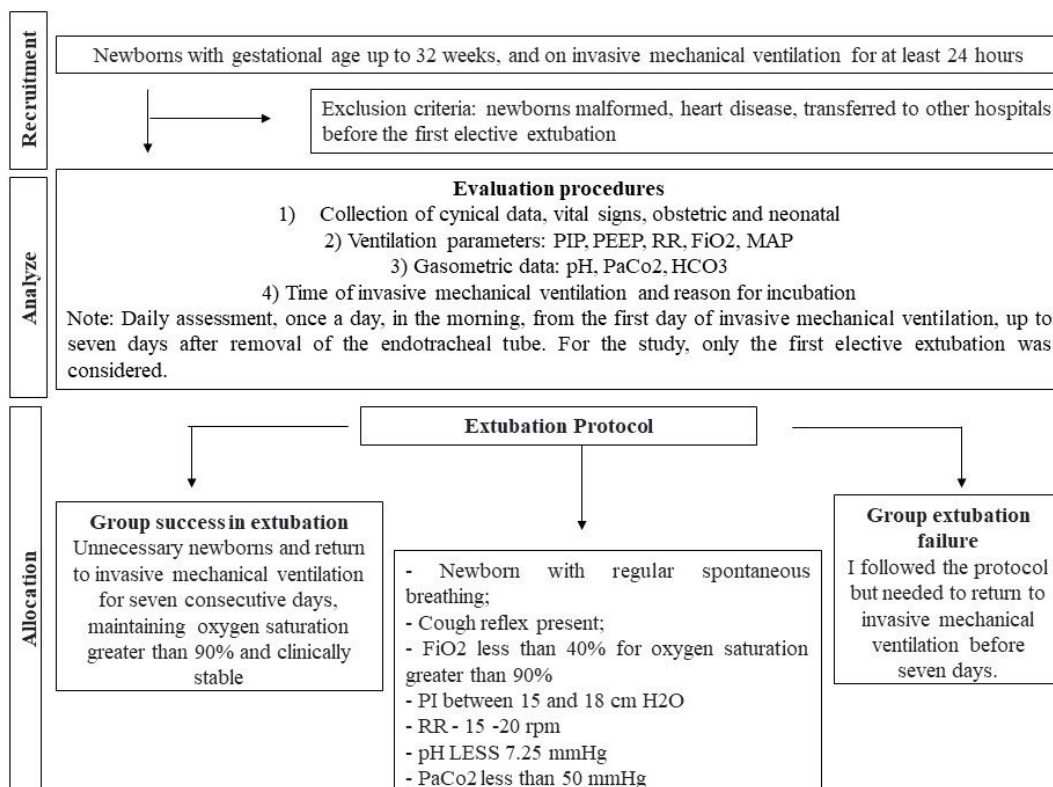
The collected data were tabulated in a Microsoft Excel® spreadsheet. Data analysis was performed using descriptive analysis techniques to characterize the sample using measures of central tendency and dispersion (mean and standard deviation) for continuous variables. The statistical software JASP was used for data analysis. Student's t-test was used to compare the continuous variables in the success or failure groups, with $p < 0.05$ being considered significant.

After the statistical analysis using means and standard deviation, a logistic regression model was fitted where the data were analyzed using Software R 3.6.1 and RStudio 1.2.1335. In the logistic regression model, the outcome of the study was the response variable, in this case, success or failure of extubation, for this we used the package MASS v. 7.3-51.4 and caret v. 6.0-84, resulting in a final model with the variables mean airway pressure and inspired oxygen fraction, significant at 5% and significant invasive mechanical ventilation time at 10%.

Results

During the data collection period, 43 premature newborns up to 32 weeks of gestational age were admitted to the NICU. Of these, 11 died before the first extubation, two premature newborns were transferred to another hospital before the first elective extubation, and 10 premature newborns did not require invasive ventilatory support during hospitalization. The study sample consisted of 20 premature newborns up to 32 weeks of gestational age. Of these, 12 (60%) had extubation success and 8 (40%) had extubation failure. Failed newborns were reintubated within 144 hours after extubation.

Of the 20 premature newborns included in the study, 14 were male, the average gestational age was 28,9 ± 2,12 weeks and the average birth weight was 1069,5g ± 375,5. As for the score of apgar in the fifth minute, 6 newborns were classified with a score between 4 and 7, and 14 above 7. When separated by the success and failure group in extubation, newborns had similar characteristics. The mothers of newborns in the study used corticosteroids during prenatal care. Invasive mechanical ventilation was indicated for 15 premature newborns (75%) due to respiratory distress syndrome, data are shown in table 1.

Table 1. General characteristics of newborns according to the groups' success and failure in extubation n = (20)

	Success Group (n=12)		Failure Group (n=8)		
	Mean	SD	Mean	SD	P value
GA WEEK	28,83	± 2,12	28,87	±1,45	0,96
GAC	29,91	±2,15	29,62	±1,50	0,74
BW	1094,5	±375,5	1031,8	±272,6	0,69
HR	154,6	±15,4	150,5	±21,24	0,61
RR	49,33	±13,98	44,25	±13,25	0,42

Note. Student's t-test; GA: gestational age; GAC: corrected gestational age at the time of extubation; BW; Birth Weight; HR: Heart rate; RR: Respiratory rate

All premature newborns received non-invasive ventilation in the nasal intermittent positive pressure (NIPPV) after extubation. The causes of extubation failure in the studied group were: apnea 4 (50%), gastrointestinal complications / infections 2 (25%), atelectasis 1 (12,5%), and surgical procedure / exams 1 (12,5%). They occurred between the first 24 hours and 144 hours after extubation, as shown in Figure 2.

Figure 2. Graph of the moment of extubation failure according to causes
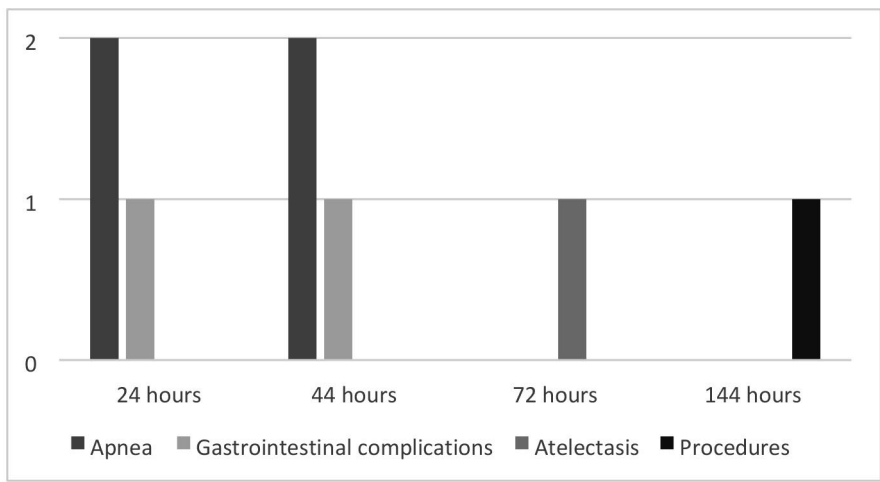
All premature newborns were extubated following the weaning protocol for mechanical ventilation of the NICU at the study site. There was no significant difference between the success and failure in extubation groups, regarding the gasometric data analyzed before and after extubation (Table 2).

Table 2. Pre- and post-extubation blood gas data of newborns in the success and failure extubation groups n = (20)

	Success Group (n=12)		Failure Group (n=8)		P value
	Mean	SD	Mean	SD	
pH pre	7,36	±0,07	7,40	±0,107	0,34
pH post	7,36	±0,065	7,32	±0,092	0,32
PaCO2 pre	36,15	±6,48	31,50	±10,42	0,23
PaCO2 post	36,48	±6,68	39,98	±12,48	0,45
HCO3 pre	20,70	±2,37	21,73	±2,03	0,33
HCO3 post	20,85	±1,54	19,82	±1,68	0,19

Note. Student's t-test.

According to the logistic regression model, it was observed that the mean airway pressure (MAP) and the inspired oxygen fraction (FiO2) were significant in the successful outcome, indicating that the lower these parameters, the greater the chance of success for extubation (Table 4). The IMV time was 5.9 days, varying between one and twenty, the mean MAP was 7.72 (± 0.77) and the mean FiO2 was 0.25 (± 0.05).

Table 3. Logistic Regression Analysis of variables n = 20

	OR	CI 95%	p Value
IMV time	6,33	6,15-5,24	0,06
MAP	1,03	3,34-3,17	0,03
FiO2	1,86	2,98-1,25	0,03

Note: IMV: invasive mechanical ventilation; FiO2: fraction of inspired oxygen; MAP: mean airway pressure; OR: Odds ratio; CI: Confidence Interval

Discussion

Due to the particularities of premature newborns, several authors have sought the definition and establishment of objective criteria, which can assist in the weaning and safe extubation of these premature newborns through readiness tests[15,16]. Although most of these tests have good sensitivity to predict extubation success, they have low specificity[17]. The parameter reduction is a common practice in NICU[17,18]. The results of the study are in line with what the world literature brings, that the neonatal patient's weaning is still surrounded by doubts and challenges.

In the present study, the extubation failure rate was 40%, in agreement with previously published data, which vary between 23 and 40%[18,19]. Therefore, it is important that weaning and elective extubation are well planned, thus preventing the adverse effects of prolonged invasive mechanical ventilation as well as possible complications related to reintubation. Gestational age and low birth weight are variables that can contribute to the failure or failure of extubation[16]. In this study, no difference was observed concerning the success and failure of extubation groups in relation to birth weight and gestational age.

In a study carried out in France, where preterm newborns under 32 weeks were evaluated, differences between the success and extubation failure groups were observed in relation to the parameters pH, PaCO2, positive inspiratory pressure and positive expiratory pressure[21]; however, in this study there was no statistically significant difference in relation to ventilatory and gasometric parameters. This is possibly justified by the use of the standardized weaning protocol for invasive mechanical ventilation. Although no significant difference was observed between the success and failure groups, the literature shows that gas data such as pH, PaCO2 and HCO3 can be used as parameters to predict extubation success in the neonatal population[16,20].

During invasive mechanical ventilation, one of the controlled parameters is the inspired fraction of oxygen, which in high concentrations is harmful to the newborn. Hyperoxia can lead to lung inflammation, alveolar injury, progressive lung damage and death[22]. When logistic regression was performed, it was observed that premature newborns who needed a lower fraction of inspired oxygen to maintain adequate peripheral oxygen saturation during weaning from invasive mechanical ventilation had a higher rate of success in extubation[23,24]. These results are in line with other published data, which demonstrated that the inspired oxygen fraction greater than 40% before extubation is associated with a higher risk of failure[9,23].

Other factors that were related to the successful outcome of extubation were the variables mean airway pressure and time of invasive mechanical ventilation. The time of invasive mechanical ventilation can lead to asynchrony between the patient and the ventilator, as well as prolonged periods of invasive mechanical ventilation can cause damage to the airways and subglottic stenosis[24,25].

All premature newborns evaluated in this study were extubated and subjected to non-invasive ventilation, which has been associated with a higher rate of extubation success, as it helps maintain the airways open during spontaneous breathing[26]. As the protocol of the service, the non-invasive modality of choice was ventilation with nasal intermittent positive pressure (NIPPV), with all extubated newborns placed in this mode. According to Sant'Anna, this modality can also be used when premature newborns fail with the use of nasal CPAP, in an attempt to prevent reintubation[27].

As limitations of this study, we can mention that only data from the first elective extubation were used, the complications related to unplanned extubations and the small sample size were not considered; this is probably justified by the limited time for data collection.

Conclusion

Minimum ventilatory parameters such as FiO2 and MAP are directly related to extubation success, as well as being attentive to the patient's clinical conditions helping the team to guide weaning and schedule a more careful and safer extubation. Further studies are needed to deepen the theme.

Author contributions

Jurkevicz R. participated in the conception and design of the study, data acquisition, data analysis and interpretation and article writing. Andreazza MG participated in the conception and design of the study, data interpretation, statistical analysis and article writing. Oliveira ALS participated in the design of the study and article review. Galo RBS participated in the design of the study, data analysis and interpretation, statistical analysis and article writing. Gomes EO participated in the design of the study, data acquisition and article review.

Competing interests

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, the manuscript preparation, statistical analysis, etc.)

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