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THE CONSEQUENCES OF FAILING ELECTIVE NONINVASIVE RESPIRATORY SUPPORT AS COMPARED TO IMMEDIATE INTUBATION: A POPULATION STUDY OF VERY LOW BIRTH WEIGHT NEONATES

NIEPOWODZENIE WENTYLACJI NIEINWAZYJNEJ VS ELEKTYWNA INTUBACJA OD URODZENIA – PORÓWNANIE WYNIKÓW LECZENIA; BADANIE POPULACYJNE U NOWORODKÓW Z BARDZO MAŁĄ URODZENIOWĄ MASĄ CIAŁA

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Abstract

Introduction: *Elective noninvasive respiratory support has become common. However, many neonates fail this procedure and they may require intubation.*

The aim *of this study was to determine the relative outcome of very low birth weight neonates who failed noninvasive respiratory support compared to those that were initially intubated and mechanically ventilated.*

Material and methods: *We accessed the database of every neonate who received respiratory support in 18 hospitals in the central region of Poland and examined the records for a 7-year period. The evaluation encompassed 1667 neonates with very low birth weight who were potential candidates for elective noninvasive respiratory support. Three prospective primary outcome measures were assessed using logistic regression to control for differences in baseline risk. We also examined the length of respiratory support corrected for EGA.*

Results: *After controlling for significant baseline factors, we found that there was no statistically significant difference in mortality, severe retinopathy of prematurity (ROP) or severe bronchopulmonary dysplasia (BPD) between infants failing noninvasive respiratory support and those electively intubated. However, their mortality and severe ROP were significantly higher than in those successfully treated with noninvasive respiratory support. Additionally, there was no difference in the length of mechanical ventilation or the length of all respiratory support between those that failed noninvasive support and those that were electively intubated.*

Conclusion: *Our study suggests that in those preterm infants who are at a higher risk of failing noninvasive ventilation there is no compelling reason to administer elective intubation and mechanical ventilation immediately after birth. It seems that efforts should rather be made towards the implementation of the optimal non-invasive respiratory support.*

Key words: noninvasive ventilation, preterm infants, treatment outcome, retrospective study

Streszczenie

Wstęp: *Nieinwazyjna wentylacja stała się powszechną metodą wspomagania oddychania u nowo-rodków. Jednakże nie u wszystkich pacjentów jest ona skuteczna i konieczne jest jednak ich zaintubowanie.*

Cel: *Celem naszych badań było porównanie wyników leczenia grupy noworodków z bardzo małą urodzeniową masą ciała (very low birth weight VLBW), u których wentylacja nieinwazyjna była nieskuteczna z grupą noworodków VLBW intubowanych bezpośrednio po urodzeniu i wentylowanych mechanicznie.*

Materiał i metody: *W 18 szpitalach centralnego regionu Polski zebrano dane o każdym dziecku, które w okresie 7 lat otrzymało wsparcie oddychania. Analizie poddano 1667 noworodków z bardzo małą urodzeniową masą ciała, u których po urodzeniu istniała konieczność zastosowania wsparcia oddechowego. Metodą regresji logistycznej oceniano trzy pierwotne punkty końcowe. Dodatkowo analizowano długotrwałość stosowanego wsparcia oddechowego.*

Wyniki: *Nie było różnic istotnych statystycznie w długości stosowanego wsparcia oddechowego między grupą noworodków intubowanych po nieskutecznym wsparciu nieinwazyjnym a intubowanymi elektywnie bezpośrednio po urodzeniu i wentylowanymi mechanicznie. Wykazano, po skontrolowaniu istotnych czynników wyjściowych, brak różnic w śmiertelności oraz występowaniu ciężkiej retinopatii wcześniaczej i ciężkiej dysplazji oskrzelowo-płucnej między obiema grupami. W obu powyższych grupach śmiertelność i występowanie ROP było istotnie wyższe niż w grupie skutecznie leczonej od urodzenia wsparciem nieinwazyjnym.*

Wnioski: *Nasze badanie wykazuje, że w grupie noworodków przedwcześnie urodzonych z podwyższonym ryzykiem niepowodzenia wentylacji nieinwazyjnej nie ma istotnych powodów do planowej intubacji i wentylacji mechanicznej bezpośrednio po urodzeniu. Dla poprawy wyników leczenia należy optymalizować nieinwazyjne wspomaganie oddychania.*

Słowa kluczowe: wentylacja nieinwazyjna, noworodki przedwcześnie urodzone, wyniki leczenia, badanie retrospektywne.

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BACKGROUND

Noninvasive respiratory support of neonates was first reported in 1971 [1]. The use of elective noninvasive respiratory support had become quite common by the last decade [2, 3] and encompassed both continuous and biphasic positive airway pressure. The aggregate of related randomized controlled trials has now confirmed the safety and effectiveness of noninvasive respiratory support and rescue surfactant as a more useful method in comparison to elective surfactant and mechanical ventilation [4]. We also reported that the increased use of noninvasive ventilation in Poland led to decreased neonatal mortality [5].

Some focus has been placed on the selection of appropriate candidates for elective noninvasive respiratory support [6-9], though no general guidelines have evolved. There is a consensus that infants that fail elective noninvasive respiratory support and are subsequently intubated have poorer outcomes. While a few studies support this [8, 10], there is a paucity of evidence to suggest that these infants would have been better off having been initially intubated and managed with invasive ventilation.

We previously developed a database of the baseline parameters, the course of treatment and outcome for every infant requiring respiratory support in the central region of Poland over a 7-year period [5].

AIM

To determine the relative outcome of very low birth weight (VLBW) neonates who failed noninvasive respiratory support compared to those that were electively intubated and mechanically ventilated.

MATERIAL AND METHODS

In collaboration with the Noninvasive Respiratory Support Group of the Polish Neonatal Society, a program was developed to capture the course of treatment and outcomes of all the neonates requiring respiratory support in 18 hospitals in the central region of Poland [5]. The project, including a publication of its analyses, was approved by the Ethics Committee of each of the participating centers. The database collected over a 7- year period includes the demographics, respiratory care and neonatal outcomes of every neonate requiring respiratory support in the region. It straddles the adoption of new guidelines calling for expanded use of noninvasive ventilation. Our definition of respiratory support did not include supplemental oxygen or high-flow nasal support, but rather only invasive or noninvasive ventilation. The latter included nasal continuous and biphasic continuous airway pressure [NCPAP] delivered either with Infant Flow (CareFusion, Yorba Linda California) or ventilator based NCPAP. The median year of this study was 2004. The data were collected by means of careful chart reviews conducted by clinicians at each hospital. Once submitted to the coordinating center, data were carefully reviewed for completeness and illogical responses. This was accomplished through rule-based data flagging and also by manual review. Clinical monitors adjudicated apparent problems in addition to conducting site visits to clarify and audit the data.

Of the 5551 infants requiring respiratory support in our database, 2002 had birth weights of 1500 grams or less. Of these, 335 were excluded from the analysis, because they were felt to be poor candidates for elective noninvasive respiratory support based on low Apgar scores. Of the 335 infants who were excluded, nearly all, i.e. 285, had been electively intubated. Thus, the population that was analyzed comprised 1667 VLBW infants. Of these 55% were electively intubated and invasively ventilated and the rest were electively managed with noninvasive respiratory support. Noninvasive respiratory support failure and subsequent intubation occurred in 21%. The population analyzed thus comprised three groups: noninvasive respiratory support successes (589), noninvasive respiratory support failures (161) and elective intubations (917).

To select the population to be analyzed for this study, the cases of all the neonates with a birth weight of 1500 grams or less were identified. Clearly, neonates that were not spontaneously breathing or were moribund were not appropriate candidates for elective noninvasive ventilation. To address this, we excluded neonates that had a 1-minute Apgar score of 1 or less or a 5-minute Apgar score of 3 or less. Infants that were initially intubated for the administration of surfactant and extubated within 2 hours of birth and then managed noninvasively were categorized as elective noninvasive support. Noninvasive failure was defined as subsequent intubation and mechanical ventilation.

We prospectively identified three primary outcome measures. The first was mortality at discharge. The other two were severe BPD (bronchopulmonary dysplasia) and severe ROP (retinopathy of prematurity) among survivors. Severe ROP was defined as the need for laser therapy. Severe BPD was defined as the need for 0.30 inspired oxygen, or continued respiratory support at 36 weeks post conceptual age. Severe BPD was selected due to its being associated with significant long-term morbidity. We hypothesized that the outcomes of infants who failed noninvasive respiratory support would be no worse than those electively intubated, after controlling for baseline risk factors.

We developed a separate logistic regression model to control for baseline risk for each of the three outcomes. Twelve baseline parameters were evaluated as risk factors (estimated gestational age (EGA), birth weight, small for gestational age), elective surfactant (first two hours of life), gender, outborn delivery, Apgar 1, Apgar 5, C-Section, singleton birth, gestational diabetes, and antenatal steroids). Each model was constructed using backward stepwise logistic regression of these 12 potential risk factors. The only risk factors that were statistically significantly related to the dependent variable (primary outcome) were retained in each of the three models. Following the development of the risk model, the tricotomous respiratory support category variable was added, with its p-value indicating significance among the 3 categories. Differences between pairs of the three were then evaluated with the risk model. When the differences were significant, the Relative Risk (RR) was calculated based on the Odds Ratio (OR) and nominal incidence rates for the two in order to help interpretation.

The Pearson chi-square test was used to evaluate differences in categorical variables for treatment groups. Analysis of Variance (ANOVA) was used to evaluate differences among continuous variables for the three treatment groups. Differences between two of the three were evaluated using the post hoc Least Squares Difference test.

For all the statistical analyses a $p<0.05$ was considered statistically significant.

RESULTS

Table I presents a summary of the baseline status for each of the three categories. There were marked differences among the three groups. What is of note is a slight, but statistically significant difference in the birth-weight and maturity. Of more clinical relevance, and likely associated with the selection of the mode of elective support, were statistically significant differences in such factors as the use of prenatal steroids, outborn delivery, Apgar scores and use of surfactant within 2 hours of birth.

The outcomes for each of the 3 treatment categories are summarized in table II. There were marked, clinically relevant, statistically significant differences among the groups for most of these parameters. While the statistics is not shown in the table, the infants who successfully managed with noninvasive respiratory support experienced significantly decreased severe BPD ($p<0.001$), severe ROP and shorter respiratory support. There were no differences in the length of mechanical ventilation or total length of respiratory support between those electively intubated and those failing noninvasive respiratory support.

Table III identifies the baseline risk factors that were found to be statistically significantly related to the three clinical outcomes: mortality, severe retinopathy of prematurity and severe bronchopulmonary dysplasia. Birth weight and EGA were significant risk factors for all the three outcomes. In addition, five other risk factors were statistically significant for mortality (SGA, Apgar 5, elective surfactant, antenatal steroids, and outborn status). For severe ROP in survivors one other risk factor, i.e. C-section, was statistically significant. For severe BPD among survivors, two other risk factors were statistically significant, i.e. antenatal steroids, and being outborn.

After controlling for these significant baseline variables, the difference in mortality persisted among the three groups. However, the difference in mortality between noninvasive respiratory support failures and elective intubation did not persist. In contrast, patients with noninvasive respiratory support success had a markedly lower risk of mortality than patients with failures ($p<0.001$, RR=0.27) and than those initially intubated ($p<0.001$ RR=0.32). After controlling for significant baseline variables, the difference in the incidence of severe ROP among the 3 groups was diminished. The difference in risk between noninvasive respiratory support

Table I. Characteristics of neonates in the study groups regarding selected clinical and demographic parameters.

Tabela I. Charakterystyka noworodków w badanych grupach pod względem wybranych parametrów demograficznych i klinicznych.

	NRS Success ***(NIW powodzenie)***	**NRS Failure** ***(NIW niepowodzenie)***	**Elective MV** ***(Elektywna MW)***	**p-value:NRS Success vs. NRS Failure (*p-value NIW powodzenie vs. NIW niepowodzenie)***	**p-value:NRS Success vs. MV (p-value NIW *powodzenie vs. MW)***	**p-value:NRS Failure vs. MV (p-value: *NIW niepowodzenie vs. MW)***
	[A]	**[B]**	**[C]**	**[p value: A vs. B]**	**[p value: A vs. C]**	**[p value: B vs. C]**
n	589	161	917	-	-	-
Weight (kg) *Masa ciała (kg)*	1.19 (.25)	1.11 (.26)	1.04 (.27)	=0.001	<0.001	=0.001
EGA [hbd] *Wiek płodowy [tydzień ciąży]*	30.0 (2.6)	28.7 (2.6)	28.0 (2.6)	<0.001	<0.001	=0.001
SGA (%) *Hipotrofia wewnątrzłonowa (%)*	30	25	28	ns	ns	ns
Gender (% female) *Płeć (%żeńskiej)*	52	45	46	ns	ns	Ns
Singleton (%) *Ciąża pojedyncza (%)*	77	83	82	ns	ns	Ns
C-Section *Cięcie cesarskie*	65	62.	59	ns	ns	ns
Gestational Diabetes (%) *Cukrzyca ciężarnej (%)*	3.6	1.9	3.2	ns	ns	ns
Antenatal steroids (%) *Sterydy prenatalne (%)*	49	63	51	=0.002	ns	=0.013
Outborn (%) *Urodzone poza ośrodkiem (%)*	11	26	20	<0.001	<0.001	ns
Apgar 1 min	5.9 (2.6)	6.0 (2.6)	4.6 (2.6)	ns	<0.001	<0.001
Apgar 5 min	7.1 (1.7)	7.0 (1.8)	5.9 (1.8)	ns	<0.001	<0.001
Early surfactant (%) *Wczesna podaż surfaktantu (%)*	10	12	22	ns	ns	ns

Abbreviations *(skróty)*:
NRS – noninvasive respiratory support *(NIW – nieinwazyjne wsparcie oddechowe)*
MV – elective intubation and invasive ventilation *(MW – elektywna intubacja i wentylacja inwazyjna)*
Table description *(opis tabeli)*:
Continuous data are presented as mean (standard deviation). The p value reflects the difference among the 3 groups, determined by ANOVA or chi-squared, as appropriate.
Dane ciągłe są prezentowane w postaci średniej (odchylenia standardowego). Wartość p przedstawiono jako wynik testu analizy wariancji lub chi-kwadrat.

Table II. The clinical characteristics of neonates in the study groups.
Tabela II. Charakterystyka kliniczna noworodków w badanych grupach.

		NRS Success *(NIW powodzenie)*	**NRS Failure** *(NIW niepowodzenie)*	**Elective MV** *(Elektywna MW)*	**p-value: NRS Success vs. NRS Failure (p-value)** *(NIW powodzenie vs. NIW niepowodzenie)*	**p-value: NRS Success vs. MV (p-value)** (*NIW powodzenie vs. MW*)	**p-value: NRS Failure vs. MV (p-value):** (*NIW niepowodzenie vs. MW*)
All patients *(wszyscy pacjenci)*		**[A]**	**[B]**	**[C]**	**[p value: A vs. B]**	**[p value: A vs. C]**	**[p value: B vs. C]**
	n	589	161	917	-	-	-
	Any surfactant (%) *Podaż surfaktantu (%)*	10	37	53	<0.001	<0.001	<0.001
	PDA Treated (%) *Leczenie przetrwałego przewodu tętniczego (%)*	5.6	14	17	<0.001	ns	ns
	Pneumothorax (%) *Odma opłucnowa(%)*	1.2	9	6	<0.001	<0.001	ns
	Death (%) *Zgon (%)*	3.2	12	19	<0.001	<0.001	=0.034
Among survivors *(tylko pacjenci, którzy przeżyli)*	Length MV (weeks PCA) *Długość MW (wiek postkoncepcyjny)*	-	29.9(2.4)	29.6(2.7)	-	-	=0.030
	Length RS (weeks PCA) *Długość wsparcia oddechowego (wiek postkoncepcyjny)*	33.3(5.3)	40.4(10.4)	39.6(14.7)	<0.001	<0.001	ns
	Severe BPD (%) *Ciężka dysplazja oskrzelowo-płucna(%)*	5.4	9.2	12	ns	<0.001	ns
	Severe ROP (%) *Ciężka retinopatia wcześniaków (%)*	4.4	15	12	<0.001	<0.001	ns

Abbreviations *(skróty)*:
NRS – noninvasive respiratory support *(NIW – nieinwazyjne wsparcie oddechowe)*
MV – elective intubation and invasive ventilation *(MW – elektywna intubacja i wentylacja inwazyjna)*
Severe ROP is defined as the need for laser treatment. *(Ciężka etinopatia wcześniaków jest określana jako wymagajaca laseroterapii.)*
Severe BPD as the need for 0.30 FiO2 or respiratory support at 36 weeks PCA. *(Ciężka dysplazja oskrzelowo-płucna – jako konieczność stosowania biernej tlenoterapii co najmniej 30% lub jakiegokolwiek wsparcia oddechowego w 36 tygodniu wieku postkoncepcyjnego)*
Table description (opis tabeli):
Continuous data are presented as mean (standard deviation). The p value reflects the difference among the 3 groups, determined by ANOVA or chi-squared, as appropriate.
Dane ciągłe są prezentowane w postaci średniej (odchylenia standardowego). Wartość p przedstawiono jako wynik testu analizy wariancji lub chi-kwadrat.

Table III. Analysis of the prevalence of clinical failures.
Tabela III. Analiza częstości występowania niepowodzeń klinicznych.

	Mortality *Umieralność*	**Severe ROP** *Ciężka retinopatia wcześniaków*	**Severe BPD** *Ciężka dysplazja oskrzelowo-płucna*
EGA *Wiek płodowy*	<0.001	<0.001	<0.001
Birth weigh *Urodzeniowa masa ciała*	<0.001	=0.030	<0.001
Small for GA *Za mały w stosunku do wieku płodowego*	=0.006	ns	ns
Early surfactant *Wczesna podaż surfaktantu*	=0.041	ns	ns
Outborn *Urodzony poza ośrodkiem*	=0.037	ns	<0.001
Apgar 5 min *Ocena wg skali Apgar*	<0.001	ns	ns
Cesarean Section *Cięcie cesarskie*	ns	=0.014	ns
Antenatal steroids *Sterydoterapia prenatalna*	=0.010	ns	=0.002

Small for GA body weight below 10 pc for age *(Za mały w stosunku do wieku płodowego – masa ciała poniżej 10 percentyla dla wieku*
GA gestational age *(wiek płodowy)*
Early surfactant – in the first two hours after birth *(Wczesna podaż surfaktantu – w pierwszych dwóch godzinach po urodzeniu)*
Abbreviations *(skróty)*:
EGA – estimated gestational age *(szacowany wiek płodowy)*
Severe ROP is defined as the need for laser treatment *(Ciężka etinopatia wcześniaków jest określana jako wymagająca laseroterapii.)*
Severe BPD as the need for 0.30 FiO2 or respiratory support at 36 weeks PCA *(Ciężka dysplazja oskrzelowo-płucna – jako konieczność stosowania biernej tlenoterapii co najmniej 30% lub jakiegokolwiek wsparcia oddechowego w 36 tygodniu wieku postkoncepcyjnego)*

failures and elective intubations was not statistically significant. Those neonates who were successfully treated with noninvasive respiratory support had less risk of severe-ROP than those electively intubated (p=0.042, RR=0.66) and those that failed (p=0.012 RR=0.48). After controlling for significant baseline variables, the differences in the incidence of severe BPD among the 3 groups disappeared (tab. IV).

DISCUSSION

We evaluated a population of 1667 VLBW infants felt to have been candidates for elective noninvasive ventilation to determine if there were consequences of delayed intubation associated with noninvasive ventilation failure. It is our belief that the present report is the first one comparing infants failing elective noninvasive respiratory support with those electively intubated. We found that after controlling for baseline risk factors, there were no significant consequences of noninvasive failure and subsequent delayed intubation. We evaluated mortality and, for those who were survivors, severe ROP, severe BPD as well as length of support. Mortality, severe ROP and severe BPD, controlling for baseline risks, were comparable. The length of respiratory support and mechanical ventilation, and adjusting for EGA, were also nearly identical.

Other authors have reported comparisons of noninvasive respiratory support success and failure. In line with our expectations, after controlling for baseline risks, we found that those neonates who successfully managed with noninvasive respiratory support, compared to the ones electively or subsequently intubated, had markedly lower mortality and also less severe ROP. We also found that the incidence of severe BPD seen among the three groups was fully explained by the baseline risk factors. In the population we analyzed this is not surprising. From an observational study of extremely preterm infants (32 weeks EGA or less), Dargaville et al. recently reported on the outcome of those who failed NCPAP, as compared to those that succeeded [10]. They found an increase in BPD, major morbidities and mortality associated with NCPAP failure, but only among those infants who were 28 weeks EGA or less. However, their analysis of mortality and morbidity did not control for baseline risk factors. A recent meta-analysis of randomized comparisons of NCPAP and elective intubation found a trend suggesting reduced mortality associated with elective NCPAP, reduced BPD and reduced severe ROP [4]. However, only the combined variable of death or BPD was lower in a statistically significant way. The trials in this meta-analysis all included only infants of lower maturity than those in our evaluation. We identified birth weight and

Table IV. Evaluation of relative risk of clinical failure in three compared groups of respiratory support.
Tabela IV. Ocena ryzyka względnego niepowodzeń klinicznych w trzech porównywanych grupach wsparcia oddechowego.

	p-value	**OR (95% CI)** ***Iloraz szans (95% przedział ufności)***	**RR** ***Ryzyko względne***
Mortality *Umieralność*	<0.001	-	-
NRS Failure/MV *NIW niepowodzenie/MW*	0.964	1.01 (1.77-.58)	na
NRS Success/MV *NIW powodzenie/MW*	<0.001	.27 (.46-.16)	.32
NIV Success/Failure *NIW powodzenie/niepowodzenie*	<0.001	.25 (.12-.51)	.27
Severe ROP *Ciężka retinopatia wcześniaków*	0.094	-	-
NRS Failure/MV *NIW nieskuteczna/MW*	0.098	1.59 (.92-2.7)	na
NRS Success/MV *NIW powodzenie/MW*	0.042	.60 (.37-.98)	.66
NIV Success/Failure *NIW powodzenie/niepowodzenie*	0.012	.42(.21-.83)	.48
Severe BPD *Ciężka dysplazja oskrzelowo-płucna*	0.884	-	-
NRS Failure/MV *NIW niepowodzenie/MW*	0.653	.86(.45-1.66)	na
NRS Success/MV *NIW powodzenie/MW*	0.903	.97(.61-1.53)	na
NIV Success/Failure *NIW powodzenie/Niepowodzenie*	0.975	.80(.31-1.66)	na

Abbreviations *(skróty)*:
NRS – noninvasive respiratory support *(NIW – nieinwazyjne wsparcie oddechowe)*
MV – elective intubation and invasive ventilation *(MW – elektywna intubacja i wentylacja inwazyjna)*
Severe ROP is defined as the need for laser treatment *(Ciężka etinopatia wcześniaków jest określana jako wymagajaca laseroterapii.)*
Severe BPD as the need for 0.30 FiO2 or respiratory support at 36 weeks PCA *(Ciężka dysplazja oskrzelowo-płucna – jako konieczność stosowania biernej tlenoterapii co najmniej 30% lub jakiegokolwiek wsparcia oddechowego w 36 tygodniu wieku postkoncepcyjnego)*
Table description *(opis tabeli)*:
OR is Odds Ratio and RR the Relative Risk. CI is confidence Interval.
OR – iloraz szans, RR – ryzyko względne, CI – przedział ufności

EGA as significant risk factors in our risk model for each of the three outcomes, which is consistent with the findings of these two studies.

It is not clear to what degree outcomes are driven by baseline risk rather than the success or failure of elective noninvasive respiratory support. Our data suggest that that failure has its consequences when compared to successful noninvasive respiratory support, but not to elective intubation. Timing the decision of when to intubate might also be an important factor. Whether morbidity is associated with the physiological perturbations of failure (e.g. pneumothorax, poorer gas exchange) or the consequences of eventual intubation and its inherent risks, is, however, uncertain. Several authors have reported that increasing FiO2 requirements in response to noninvasive respiratory support is a predictor of eventual noninvasive respiratory support failure [7, 10]. We believe more research is needed to identify the optimum criteria for failure of noninvasive respiratory support and the corresponding appropriate time for subsequent intubation.

However, it should be remembered that adverse events associated with tracheal intubation are still common in neonatal intensive care units [11].

Some work suggests that differences in the effectiveness of noninvasive respiratory support are associated with elements of management. Buzzella et al. reported from a randomized trial that increased success was associated with a strategy of higher nominal NCPAP pressures [12]. Others have reported on the differences in the effectiveness associated with the type of device [9, 13, 14]. The mode of support is also believed to be important. Ramanathan et al. recently reported results from a randomized trial comparing

NCPAP and NIPPV, finding the latter more effective [15]. However, another larger trial of more diverse devices did not confirm this conclusion [16]. While all these variations are evident, we further suggest that optimizing noninvasive respiratory support management (mode, pressures and perhaps devices) and reducing treatment failure might result in better relative outcomes. However, much work needs to be done to evaluate optimum strategies, before careful comparisons of these factors can be undertaken.

Our study has limitations. It is a population study and not data from a randomized comparison. A project of the latter kind would be needed to compare specific noninvasive respiratory support populations, strategies and failure criteria. To address the natural selection of our population, we controlled for relevant risks associated with 12 baseline parameters. Other factors not available to us might have yielded different results. We also used initial Apgar scores to exclude infants less appropriate for noninvasive respiratory support. A different threshold, and thus a different population, might yield different results. Finally, the conditions of prenatal practice in Poland 10 years ago, most notably the limited use of surfactant and also the lower utilization of antenatal steroids, might have an effect on the applicability of our findings.

CONCLUSIONS

There is nothing in this study to suggest outcomes could have been markedly improved if more neonates were intubated electively. This information is definitely directly projectable to healthcare systems which are in the process of developing prenatal practices. We also believe that it has important implications in areas with more developed practices. Most importantly, it highlights the importance of considering baseline risk when evaluating the outcomes associated with delayed intubation. In addition, we suggest that more emphasis, in both research and clinical practice, needs to be placed on improving the management of noninvasive respiratory support. This includes not only the refined use of support pressure and perhaps the expanded use of biphasic noninvasive respiratory support and noninvasive positive pressure ventilation, but also optimal noninvasive respiratory support failure criteria.

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