ORIGINAL ARTICLE

Paediatric ventilation treatment of acute lung injury in Nordic intensive care units

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Background: Treatment of acute respiratory distress syndrome (ARDS) in children is largely based on extrapolated knowledge obtained from adults and which varies between different hospitals. This study explores ventilation treatment strategies for children with ARDS in the Nordic countries, and compares these with international practice.

Methods: In October 2012, a questionnaire covering ventilation treatment strategies for children aged 1 month to 6 years of age with ARDS was sent to 21 large Nordic intensive care units that treat children with ARDS. Pre-terms and children with congenital conditions were excluded.

Results: Eighteen of the 21 (86%) targeted intensive care units responded to the questionnaire. Fifty per cent of these facilities were paediatric intensive care units. Written guidelines existed in 44% of the units. Fifty per cent of the units frequently used cuffed endotracheal tubes. Ventilation was achieved by pressure control for 89% vs. volume control for 11% of units. Bronchodilators were used by all units, whereas steroids usage was 83% and surfactant 39%. Inhaled nitric oxide and high frequency oscillation were available in 94% of the units. Neurally adjusted ventilator assist was used by 44% of the units. Extracorporeal membrane oxygenation could be started in 44% of the units.

Conclusion: Ventilation treatment strategies for paediatric ARDS in the Nordic countries are relatively uniform and largely in accordance with international practice. The use of steroids and surfactant is more frequent than shown in other studies.

Editorial comment: what this article tells us
The present study shows that ventilation treatment strategies for acute respiratory distress syndrome in children in Nordic intensive care units are relatively uniform and in accordance with international recommendations. Albeit, only in 44% of the units have written guidelines for the ventilation treatment and some differences were found in the provision of intensive care for children between Nordic institutions.

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Table 1 ARDS criteria according to Berlin definition.

Timing	Within a week of a known insult or new or worsening respiratory symptoms		
Chest imaging	Bilateral opacities – not fully explained by effusions, lobar/lung collage or nodules		
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload		
	Need objective assessment (echocardiography) to exclude hydrostatic oedema if no risk factor present		
	Mild	Moderate	Severe
Oxygenation	$200 < PaO_2/FiO_2 \leq 300$ with PEEP or CPAP ≥ 5	$100 < PaO_2/FiO_2 \leq 200$ with PEEP ≥ 5	$PaO_2/FiO_2 \leq 100$ with PEEP ≥ 5

ARDS, acute respiratory distress syndrome; CPAP, continuous positive airway pressure in cmH_2O; FiO_2, fraction of inspired oxygen; PaO_2, partial pressure of arterial oxygen; PaO_2/FiO_2, oxygen ratio in mmHg; PEEP, positive end-expiratory pressure in cmH_2O.

Acute pulmonary injury is characterised by inflammation and hypoxaemia. The American-European Consensus Conference agreed upon the definitions of acute lung injury (ALI) and the more serious acute respiratory distress syndrome (ARDS).[1] The diagnostic criteria for acute onset of lung injury are hypoxaemia, bilateral opacities on chest imaging and respiratory failure that is not explained by heart failure. These diagnostic criteria have been widely adopted by clinicians and used in studies and for the collection of epidemiological data. However, the revised Berlin definition (2012) introduced mild, moderate and severe ARDS as the only categories and this is suggested to be a more accurate definition (Table 1).[2] The Berlin definition is valid for both adult and paediatric populations.[2,3]

In recent decades, there has been a shift towards lung-protective ventilation strategies with low tidal volumes (TVs) and lowered peak inspiratory pressure. The shift in strategy was undertaken in response to the ARDS Network Study, which demonstrated a reduced mortality in adults, when using such approaches.[4] The treatment of children with ARDS relies largely upon knowledge extrapolated from the adult population, although some paediatric studies and protocols do exist.[5–7]

There are variations in the treatment of paediatric ARDS between units and probably between individual clinicians.[8] Homogeneous international guidelines for the treatment of paediatric ARDS would be beneficial. However, the complexity of ARDS makes it challenging to define common and valid treatment principles, specifically for the paediatric population. Moreover, it is challenging to conduct clinical trials in children with ALI for several reasons. The incidence of ARDS is less than 3/100,000 < 16 years of age.[9] Patient enrolment is difficult due to high parental refusal rates, generally ranging from 27% to 53%.[10,11] Clinical trials in paediatric ARDS would also require long-term participation of many centres in order to conduct a randomised controlled trial (RCT) of acceptable quality.[10] Nevertheless, it is utterly important to increase our knowledge and improve the treatment of paediatric ARDS, which is a serious condition with a high mortality that ranges between 30% and 35%.[9,12]

The aim of the present study was to explore ventilation treatment strategies for children with ARDS in the Nordic countries of Finland, Sweden, Norway and Denmark, and to determine the extent to which these are consistent with international practice.

Materials and methods

Intensive care units (ICUs) in the Nordic countries of Finland, Sweden, Norway and Denmark were surveyed. No patient data were involved, and the need of acceptance by the respective Ethics Committees was waived. In October 2012, a questionnaire was sent once by mail to the heads of the department of 21 different units that provide respiratory support for children. These ICUs are responsible for the treatment of children with ARDS in a total population of approximately 25 million people in the study area. Each unit was requested to answer the questionnaire collectively in order to determine the standard treatment approach for that unit. The aim of the questionnaire was to explore the treatment strategies that were used for children with ALI or ARDS, who had previously been healthy and who were aged between 1 month (full term) and up to 6 years of age. In the present investigation,

we refer to ALI and ARDS cases as ARDS only, according to the newly revised Berlin definition. Children younger than 1 month of age were not included in the study to exclude lung defects that were related to birth and congenital abnormalities. The upper age limit was set to delineate between children and adults. The questionnaire included issues that covered different ventilation modes, pressure and volume limits; the use of high-frequency oscillatory ventilation (HFOV), administration of inhaled nitric oxide (iNO), prone position and extracorporeal membrane oxygenation (ECMO); and other adjuvant treatment modalities. The ICUs were instructed to compare the treatment of 1-year-old patients to those of 6-year-old patients with ARDS and state which airway pressures and TVs they use for these two age groups before changing treatment strategies. The results are descriptive.

Results

Eighteen of the 21 (86%) ICUs responded to the questionnaire they had been sent. Fifty per cent of respondents were paediatric intensive care units (PICUs). Only eight (44%) ICU (three PICUs and five mixed ICUs) had written guidelines for the standard treatment of paediatric ALI patients. Anaesthesiologists were in charge of the paediatric patients in 10 (56%) of the ICUs, and paediatricians were in charge in three (17%) ICUs. Anaesthesiologists together with paediatricians managed five (27%) ICUs (Table 2).

Nine (50%) of the ICUs frequently used cuffed endotracheal tubes (ETT), whereas five (27%) ICUs never used cuffed tubes. The use of cuffed ETT was more frequent in the ICUs run by anaesthesiologists (Table 2).

The most commonly used ventilation mode was pressure controlled/supported (PC/PS), which was reported by 16 (89%) of the ICUs. Two units (11%) used volume-controlled (VC) ventilation. Neurally adjusted ventilatory assist (NAVA) mode was regularly used in four (22%) of the ICUs in the Nordic countries, whereas 10 units (56%) never used NAVA.

Inhaled NO and HFOV were available at 17 (94%) of the ICUs whereas ECMO was only available at eight (44%) ICUs (Table 3). When conventional ventilation was not enough, 13 (72%) ICUs attempted HFOV as the first alternative, 2 (11%) ICUs attempted iNO before HFOV and 2 (11%) ICUs immediately transported the patient to another hospital. One ICU was excluded because of insufficient answer to this question.

Table 2 Characteristics of the participant intensive care units.

Country	ICU	Specialists in charge	Treat only children	Written guidelines	Use cuffed ETT
Denmark	Copenhagen	Anaesthesiologists and paediatricians	No	No	Always
	Odense	Anaesthesiologists	No	Yes	Never
	Aarhus PICU*	Anaesthesiologists	Yes	No	Regularly
	Aarhus NICU	Paediatricians	Yes	No	Never
Sweden	Gothenburg	Anaesthesiologists	Yes	Yes	Sometimes
	Lund	Anaesthesiologists	Yes	No	Always
	Stockholm	Anaesthesiologists	Yes	Yes	Sometimes
	Uppsala	Anaesthesiologists	Yes	Yes	Regularly
	Umeå	Anaesthesiologists and paediatricians	No	No	Never
Norway	Bergen	Anaesthesiologists and paediatricians	No	Yes	Never
	Oslo-Rikshospitalet	Anaesthesiologists	No	Yes	Regularly
	Oslo-Ullevål	Paediatricians	Yes	No	Regularly
	Stavanger	Anaesthesiologists	No	Yes	Regularly
	Tromsø	Anaesthesiologists and paediatricians	No	Yes	Never
	Trondheim	Anaesthesiologists	No	No	Regularly
Finland	Helsinki	Anaesthesiologists	Yes	No	Always
	Turku	Anaesthesiologists and paediatricians	No	No	Sometimes
	Oulu	Paediatricians	Yes	No	Sometimes

*In Aarhus, children younger than 2 years of age with acute respiratory distress syndrome were treated in NICU and older children in PICU. ETT, endotracheal tubes; ICU, intensive care unit; NICU, neonatal intensive care unit; PICU, paediatric intensive care unit.

Steroids were used in 15 (83%) of the ICUs, and they reported a wide variation in type and dose of steroid (betamethasone, methylprednisolone, dexamethasone and hydrocortisone). Surfactant (Curosurf 100–200 μg/kg) was used in seven (39%) ICUs. Sixteen (89%) ICUs used the prone position when treating paediatric patients with ARDS.

The maximal positive end-expiratory pressure (PEEP), TVs and peak pressure used prior to changing treatment strategy are shown in Table 4. When treating 1-year-old patients and 6-year-old patients with ARDS, 12 (67%) ICUs used the same maximal PEEPs for all children irrespective of age, 5 (27%) ICUs used higher maximal PEEPs in the 6-year-old children and no ICU reported using a lower maximal PEEP in 6-year-old children. One ICU was excluded because it did not treat the youngest children. Maximal PEEPs that lay between 10 and 15 cmH_2O were reported by 13 (72%) ICUs, maximal PEEPs of less than 10 cmH_2O were reported by two (11%) ICUs and maximal PEEPs of more than 15 cmH_2O were reported by three (17%) ICUs. One ICU answered 'no limit'.

Table 3 The use of alternative treatment strategies.

Intervention (%)	Always	Regularly	Sometimes	Never
NAVA	None	22	22	56
iNO	None	None	94	6
HFOV	None	None	94	6
ECMO	None	None	44	56
Prone position	None	None	89	11
Steroids	None	None	83	17
Surfactant	None	None	39	61

ECMO, extracorporeal membrane oxygenation; HFOV, high-frequency oscillation; iNO, inhaled nitric oxide; NAVA, neurally adjusted ventilator assist.

Eleven (61%) ICUs used the same maximal peak pressure in all children irrespective of age, whereas six (33%) ICUs used higher maximal peak pressure in the 6-year-old children. One ICU was excluded because it did not treat the youngest children. The most commonly used maximal peak pressure, reported by 14 (78%) ICUs, was between 30 and 35 cmH_2O. One (5.5%) ICU used a maximal peak pressure of less than 30 cmH_2O, and another ICU used a maximal peak pressure in excess of 35 cmH_2O, stating 'no limit'. Two ICUs were excluded because of incomplete answers.

Thirteen (72%) ICUs ventilated all children with similar TVs, irrespective of age, two (11%) ICUs used higher TVs in 6-year-old children and another two ICUs used lower TVs in children six years of age. One ICU was excluded because it did not treat the youngest children.

Twelve (67%) ICUs always ventilated children with TVs between 6 and 8 ml/kg, four (22%) ICUs sometimes used TVs less than 6 ml/kg and two (11%) ICUs sometimes used TVs in excess of 8 ml/kg.

Discussion

The present survey demonstrated that current ventilation treatment strategies of paediatric ARDS are relatively uniform among the Nordic countries studied and are largely consistent with international practice. We found that 44% of the ICUs had written guidelines for ventilation. Our findings also revealed that the dominant ventilation mode was PC/PS, the target TV usually lay between 6 and 8 ml/kg with variations that ranged from 5 to 10 ml/kg and the most commonly reported maximal peak pressure before changing ventilation strategy was between 30 and 35 cmH_2O. We found a higher use of steroids and surfactant compared with international prac-

Table 4 Mechanical ventilation parameters.

PEEP		TV		Peak pressure	
Maximal values (cmH_2O)	ICU (%)	Maximal values (ml/kg)	ICU (%)	Maximal values (cmH_2O)	ICU (%)*
< 10	11	< 6	22	< 30	5.5
10–15	72	6–8	67	30–35	78
> 15	17	> 10	11	> 35	5.5

*11% incomplete answers. ICU, intensive care unit; PEEP, positive end-expiratory pressure; TV, tidal volume.

tice. Differences in treatment were independent of country, except for surfactant, which was not used in Norway. The use of cuffed ETTs was more frequent in the ICUs run by anaesthesiologists compared with paediatricians.

A similar pattern of ventilation strategies used in paediatric ARDS was reported by other studies.[8,10] Santschi et al. investigated 59 PICUs in 12 countries in North America and Europe (referred to as the PALIVE study) and reported that PC was used in 43%, pressure regulated volume control in 28.2% and VC in 26.6% of the patients with ARDS.[8] There is insufficient evidence in the literature to recommend one ventilation mode over another.[10,13]

In the present survey, 12 (67%) ICUs used a target TV of 6–8 ml/kg whereas only two (11%) ICUs used TVs in excess of 8 ml/kg. These findings are consistent with the reported 8.3 ± 3.3 ml/kg mean TV in the PALIVE study,[8] 8.0 ml/kg used in Australian and New Zealand PICUs,[9] 8.1 ml/kg reported by a Canadian group[6] and the 7.1 ± 1.5 ml/kg reported by a Finnish group.[7] Santschi et al. also found that the majority of paediatric intensivists used TVs in the 5–8 ml/kg range.[14] However, data obtained from the practice sites revealed that more than 25% of paediatric patients were ventilated with TVs in excess of 10 ml/kg and that high positive inspiratory pressure levels were often tolerated.[14]

Adult guidelines for mechanical ventilation strategies in ARDS recommend to keep the plateau airway pressure 30 cmH_2O or less.[15] The maximum acceptable peak pressure before changing ventilation strategy in our survey was in the range of 30–35 cmH_2O for 14 (78%) of the ICUs, which was also shown by Santschi and colleagues.[14] Both plateau pressure and peak pressure can be used in this context, but plateau pressure can be difficult to measure when using uncuffed ETT. Eleven (61%) ICUs used the same maximal peak pressure in all children and did not report any age-dependent difference.

Thirteen (72%) Nordic ICUs accepted maximum PEEP values within the 10–15 cmH_2O range, although wider differences were observed as one unit accepted a maximum of 20 cmH_2O and another unit reported a maximum of only 7 cmH_2O. The same maximal PEEP values were also found by Santschi and colleagues.[14] PEEP is recommended in respiratory support to avoid the collapse of the alveoli, but there are no definitive recommendations regarding PEEP values in paediatric ARDS treatment. Khemani and Newth suggested that future paediatric ARDS practice will focus on 'higher PEEP and lower TV (peak pressure)'.[10]

Cuffed ETT reduce the tube exchange rate, improve reliable lung function, improve capnography monitoring and do not increase morbidity among children with longer ventilator demands.[16–18] We found that cuffed ETT were always or regularly used in 50% of the ICUs. The PALIVE study reported cuffed ETT usage in 62.9% of the patients.[8]

In the present study, NAVA was used regularly or occasionally in 44% of the ICUs. A recent study on NAVA usage in paediatric intensive care patients found that NAVA enhanced oxygenation at lower airway pressures and reduced the use of sedatives during longer periods of treatment compared with standard ventilation.[19]

All but one Nordic ICU had access to iNO and HFOV in our study. Previous studies found no benefits of iNO on survival or duration of mechanical ventilation.[20,21] Even so, oxygenation may improve and iNO is used as rescue therapy in severe respiratory conditions.[22] In the PALIVE study, iNO was used in 12.7% of children with ARDS.[8] HFOV with small TVs is, theoretically, the ideal lung-protective ventilation approach to use for ARDS. However, there is not enough evidence to conclude that HFOV reduces mortality or long-term morbidity in paediatric ARDS.[23]

The use of steroids in paediatric ARDS in our survey was reported by 83% of the ICUs, which was significantly higher than that reported in the PALIVE study.[8] The most frequent drug was methylprednisolone, but hydrocortisone and dexamethasone were also used. Two meta-analyses in adults that included studies of different doses of corticosteroids indicated that corticosteroids usage possibly worsens the outcome.[24,25] However, another meta-analysis that reviewed only the use of low-dose corticosteroids (methylprednisolone 0.5–2.5 mg/kg/day) showed improved morbidity and mortality outcome in ARDS without adverse reactions.[26] We are not aware of any RCTs that advocate the use of steroids in children with ARDS.

Surfactant was used in 39% of the paediatric ICUs in our study. No Norwegian ICU used sur-

factant in children with ARDS. The PALIVE study reported that surfactant was only given to 4.2% of the children.[8] The efficacy of exogenous surfactant therapy in children and adolescents with ARDS is debatable. A multicentre randomised blinded trial indicated improved oxygenation and reduced mortality for surfactant usage.[27] However, another study found that beneficial effects of surfactant are uncertain and its use cannot routinely be recommended in paediatric ARDS.[28]

We found that 89% of the Nordic ICUs used the prone position. Curley reported that the use of the prone position for children with ALI improved oxygenation, but found that it did not significantly increase ventilator-free days.[29] A multicentre RCT on adults with severe ARDS reported that the prone position significantly improved the outcome by substantially decreasing the 28-day and 90-day mortality.[30]

All ICUs in our study that responded to our questionnaire reported using bronchodilators (β-agonists) in paediatric ARDS. Santschi et al. showed that a great proportion of paediatric intensivists used adjunctive treatments (iNO, prone position, steroids, surfactant, ECMO, β-agonists), when the patients' condition worsened.[8]

The present study is the first assessment of ventilation treatment strategies used for paediatric ARDS in the Nordic countries. Our response rate was 86%. We chose to survey the larger ICUs and not every hospital that could conceivably treat children with ARDS in the Nordic countries. It is reasonable to assume that the findings of this study provide an adequate picture of current ventilation treatment practice of paediatric ARDS in Finland, Sweden, Norway and Denmark. Our questionnaire did not aim to explore the characteristics of the participating ICUs such as the details of their guidelines. Moreover, no information was sought about the assessment of patients or treatment data including which patients received steroids, surfactant, HFOV, ECMO or iNO and when they received them. We assume therefore, that there can be further differences between the units that are not revealed by the present study's questionnaire.

Conclusion

This survey found that the current ventilation treatment strategies used for paediatric ARDS in the Nordic countries were relatively uniform and largely consistent with international practice. Lung protective ventilation strategies that circumvent increased alveoli shear stress and ventilator-associated lung injury were prominent in all the units that responded. Differences in treatment are independent of country, except for surfactant usage, which was eschewed in Norway. The usage of steroids and surfactant were higher in the most of the Nordic ICUs surveyed compared with that reported by international studies. An area of possible future improvement is the more frequent use of cuffed ETT.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1. Paediatric ventilation treatment of acute lung injury in Nordic intensive care units.