Effective Neurally Adjusted Ventilatory Assist (NAVA) Ventilation in a Child With Jeune Syndrome

Gianluca Cosi, MD,[a] Giulia Genoni, MD,[b] Alice Monzani, MD,[b] Barbara Pilan, MD,[a] Maria Lavrano, MD,[b] Federica Ferrero, MD[a]

Jeune syndrome (asphyxiating thoracic dystrophy) is a rare skeletal dysplasia mainly characterized by dystrophy of the thoracic cage. Neurally adjusted ventilatory assist (NAVA) is a respiratory support in which pressure assistance is provided in proportion to and synchronous with the electrical activity of the diaphragm. We present the case of a 4-month-old infant with asphyxiating thoracic dystrophy and respiratory failure successfully ventilated with NAVA. In this case, NAVA improved patient–ventilator synchrony, reducing endotracheal secretion and gastric overdistention. The reduction of breathing effort and the improvement in enteral feeding tolerance and weight gain made the patient eligible for thoracic surgical correction.

Jeune syndrome (asphyxiating thoracic dystrophy [ATD]) is a rare autosomal recessive skeletal dysplasia. It is characterized by a small, narrow chest, limb shortness, and associated congenital abnormalities with a high neonatal mortality (60%–80%) resulting from respiratory failure.[1]

Neurally adjusted ventilatory assist (NAVA) is a respiratory support that is triggered by the electrical signal of the diaphragm. Pressure assistance is provided in proportion to and synchronous with the electrical activity of the diaphragm (EAdi), and its amount is adjustable by the operator via an amplification factor called NAVA level.[2]

We present a case of the successful application of NAVA to an infant with ATD.

CASE REPORT

A female neonate was born by vaginal delivery at 41+3 weeks gestation, as the fourth and last child to healthy, consanguineous (first cousins) Egyptian parents. Her sister (their first child) died at 4 months of age from respiratory failure due to ATD. Prenatal ultrasound at 20+5 weeks gestational age showed short femoral and a small thorax. At birth, the patient's weight was 2.850 kg (3rd–10th percentile), length was 46 cm (<3rd percentile), and head circumference was 35 cm (50–75th percentile). Physical examination revealed a small chest and short extremities. Skeletal radiographs showed a narrow thorax with a cardiothoracic ratio of 0.81, short and horizontally oriented ribs (Fig 1A), a typical trident appearance of the acetabular margins, and shortened femoral bones.

A homozygous mutation in the WDR60 gene (variant c.1703-3T>A), which is pathogenic of ATD, was found.

The patient was discharged at the age of 1 month, oxygen dependent. At the age of 4 months (weight, 3.250 kg) she was readmitted to our ICU for aspiration pneumonia and

abstract

[a]*Neonatal and Pediatric ICU, Maggiore della Carità Hospital, Novara, Italy; and* [b]*Division of Pediatrics, Department of Health Sciences, University of Piemonte Orientale, Novara, Italy.*

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Address correspondence to Giulia Genoni, Division of Pediatrics, Department of Health Sciences, University of Piemonte Orientale, Corso Mazzini 18, 28100 Novara, Italy. E-mail: genonigiulia@gmail.com

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severe respiratory failure. Chest radiograph showed diffuse bilateral pulmonary infiltrates (Fig 1B). Arterial blood gas (ABG) analysis showed carbon dioxide retention (pH, 7.27; $PaCo_2$, 80.5 mm Hg) and severe hypoxemia (Pao_2, 30 mm Hg, pulse oxygen saturation [Spo_2], 80%). Because of lung hypoplasia and restrictive lung impairment, high-frequency oscillatory ventilation with SensorMedics 3100A (CareFusion, San Diego, CA) was started with a fraction of inspired oxygen (Fio_2) of 0.80, a mean airway pressure of 15 cm H_2O, an amplitude of 34 cmH_2O, and a frequency of 10 Hz. However, ventilation was difficult due to the extreme discomfort of the patient with considerable need for high dose sedation.

On hospital day (HD) 6, because respiratory parameters were low (Fio_2, 0.30; mean airway pressure, 10 cm H_2O) with normal ABGs, Spo_2, and vital parameters, the first attempt of extubation was made, but the child was immediately reintubated for severe dyspnea and desaturation. Ventilatory support was resumed with synchronized intermittent mandatory ventilation (SIMV) plus volume guarantee mode using a Servo-I ventilator (Maquet, Solna, Sweden) with the following settings: Fio_2 0.40; 4 cm H_2O positive end-expiratory pressure (PEEP); 15 cm H_2O pressure support; 26 cm H_2O peak inspiratory pressure (PIP); tidal volume 6 mL/kg (range, 6–10 mL/kg); minimum mandatory rate, 30 breaths per minute. The mandatory rate was adjusted to maintain normal $PaCo_2$ while the patient's spontaneous respiratory rate was 40 to 55 breaths per minute. At this stage, the patient was agitated, with heavy endotracheal secretions and frequent desaturations, and required high-dose sedation (dexmedetomidine, maximum dose: 1.5 μg/kg per hour; morphine, maximum dose: 30 μg/kg per hour; midazolam, maximum dose: 2 μg/kg per minute); despite a minimal daily administration of enteral feeding through a nasogastric tube, she showed significant gastric residual volumes, vomit, and gastric overdistension (Fig 1C). Notably, despite the fact that the child was receiving parenteral nutrition, no weight gain was observed at that time.

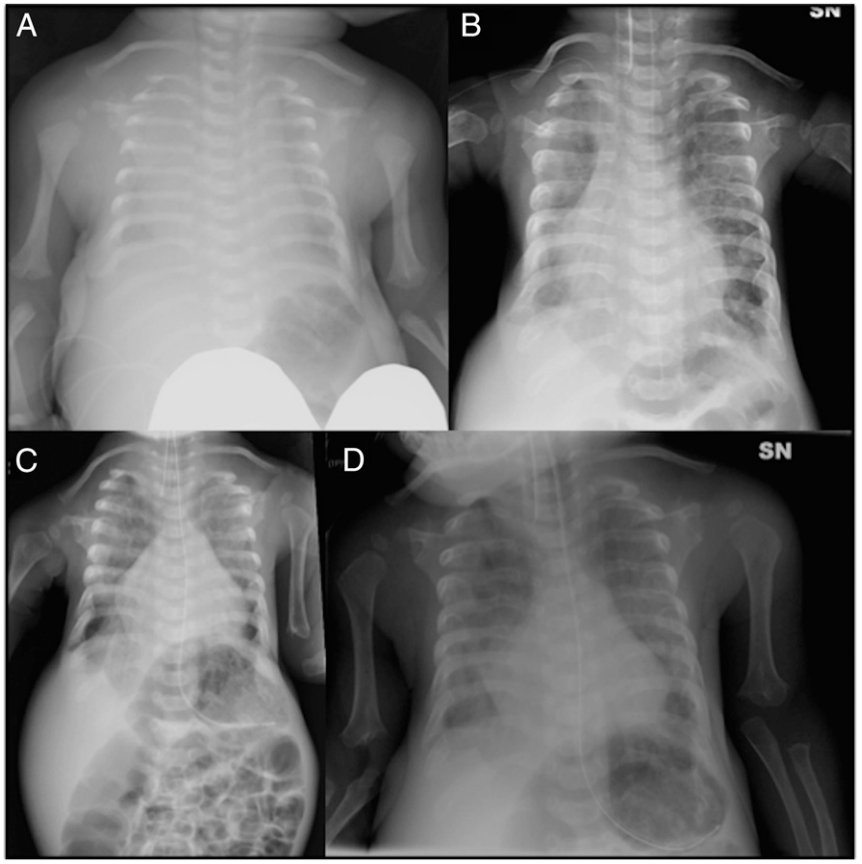

FIGURE 1
The patient's chest radiographs: A, soon after birth, showing skeletal features of ATD (narrow thorax, short, horizontally oriented ribs); B, diffuse bilateral pulmonary infiltrates on HD 1, ventilation mode: high-frequency oscillatory ventilation; C, evident gastric overdistension on HD 6, ventilation mode: SIMV plus volume guarantee; and D, resolution of gastric overdistension on HD 10, ventilation mode: NAVA.

On HD 10, we decided to switch to NAVA. The NAVA catheter was placed, and the correct positioning was confirmed. Using the dedicated "NAVA preview" window of the ventilator, the starting NAVA level of 1 cm $H_2O/\mu V$ was titrated to match the same PIP (26 cm H_2O) delivered in SIMV, reaching a maximum value of 1.5 cm $H_2O/\mu V$; the peak pressure limit was 40 cm H_2O, and PEEP and Fio_2 were the same as in SIMV (Fig 2). Maintaining the manufacturer's default setting, the trigger threshold was 0.5 μV above the minimal EAdi, and the ventilator cycled off when the EAdi signal decreased to 70% of EAdi peak value. Apnea time was 10 seconds, and back-up ventilation was set to match the pre-NAVA ventilator settings. Within 2 to 12 hours after starting NAVA, we observed a dramatic decrease in inspiratory pressure (PIP, 15 cm H_2O) with a reduced requirement for oxygen (Fio_2, 0.30) and a higher (40–65 breaths per minute) and more variable respiratory rate; tidal volume increased with high breath by breath variability (6–8 mL/kg), and Eadi peak was maintained within the range of 5 to 15 μV.

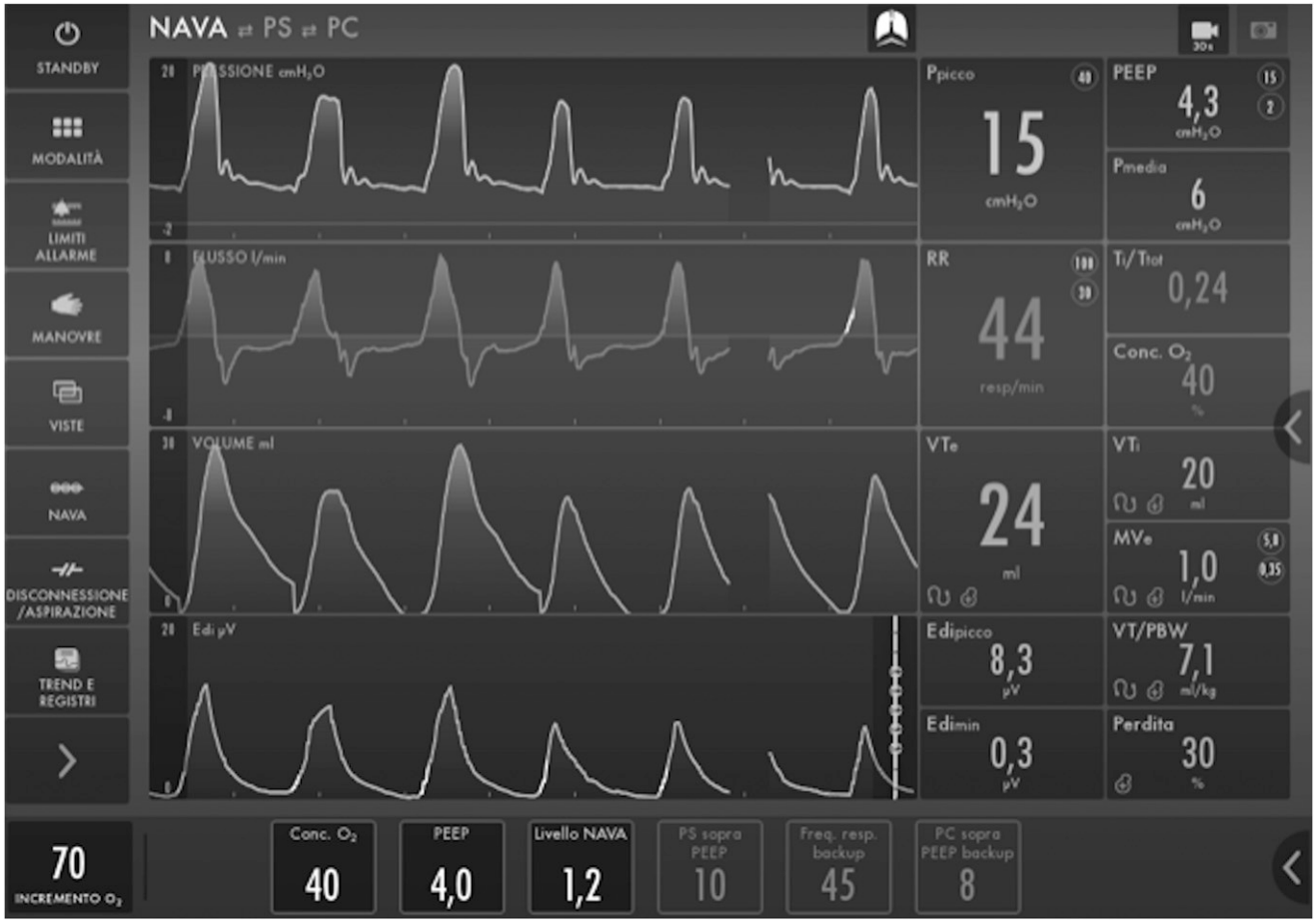

FIGURE 2
NAVA ventilator monitor after 2 hours of NAVA ventilation (HD 10).

The child's breathing became much more harmonious and smoother, endotracheal secretions, desaturations, and vomit decreased, and a resolution of gastric overdistension was noted after 2 to 6 hours (Fig 1D). Sedation was quickly reduced (in about 24 hours, sedation was decreased to: dexmedetomidine, maximum dose: 1.0 µg/kg per hour; morphine was gradually reduced to a maximum dose of 15 µg/kg per hour; midazolam, maximum dose: 1 µg/kg per minute) and suspended after 4 days (HD 14).

On HD 14, a gastrostomy tube was placed and enteral nutrition with a preterm formula (80 kcal/100 mL) was started and well tolerated. After 2 days (Fio_2, 0.27, NAVA level, 1.0 cm H_2O/µV), the second attempt of extubation was made.

The respiratory conditions of the child immediately worsened and she was reintubated and ventilated with NAVA. In light of the failure of several extubation attempts and of the chest anatomy, a tracheostomy was made. NAVA was continued (Fio_2, 0.25; NAVA level, 0.5–1.0 cm H_2O/µV), ABGs, Spo_2, and vital parameters maintained normal values, and ventilatory assist was comfortable and synchronous with spontaneous respiratory efforts of the patient without the need for sedation over time.

The adequate unload of respiratory muscles and the lessened fatigue, associated with good enteral nutrition, which provided about 130 kcal/kg per day with a volume intake of 160 mL/kg per day, allowed a satisfactory weight gain (15 g/day) permitting, after 55 days of hospitalization (weight 3.940 kg), the transfer of the patient to the referral Center of Pediatric Thoracic Surgery for surgical correction of thoracic dystrophy.

DISCUSSION

ATD is a heterogeneous, multiorgan disease that sees the dystrophy of the thoracic cage as the main defect with a consequent wide spectrum of respiratory dysfunctions and pulmonary complications.[1] In the most severe form, the disease can be fatal during the neonatal period for intractable respiratory failure, or it can be characterized by the development of progressive respiratory failure within the first years of life with recurrent

pulmonary infections representing the main cause of death in up to 80% of children.[1,3] Patients become mechanical ventilation–dependent and often need tracheostomy.[1,3] In addition, gastrostomy is often necessary because of persistent feeding difficulties with insufficient weight gain.[1,3] Surgical correction of thoracic dystrophy is suggested in the attempt to arrest the progression of the irreversible respiratory failure.[3,4]

Hemodynamic, metabolic, and ventilator stability, such as regular weight gain, are challenging in these patients, but they represent indispensable preoperative requirements.

In several recent studies, NAVA has been safely used, for short time periods, in children and neonates, showing positive effects on ventilatory patterns, mainly ascribed by the authors to improved patient–ventilator synchrony.[5–7]

Consistent with this data, during NAVA, our patient showed normal vital signs, gas exchange, and oxygen saturations, with an immediate decrease of Fio_2 and PIP, sustained over time.[5–7] Tidal volume increased with higher breath by breath variability, supporting the concept that NAVA allows the patient to improve tidal volume, despite reducing PIP[7] and without increasing PEEP, thus avoiding lung hyperinflation.[8] The patient's breathing became easier and smoother with harmonious chest movements, and her respiratory rate increased, showing a higher variability.[9] Keeping in mind the multifactorial features of the underlying lung disease in ATD, combining lung hypoplasia with consequent restrictive lung function impairment, ciliopathy, and malacic airways, these data suggest that NAVA delivers a ventilatory support tailored to the patient's respiratory needs and ventilatory pattern, optimizing the breathing performance and unloading respiratory muscles. The improved comfort made possible a rapid reduction and suspension of sedation.

The mutation in the WDR60 gene found in our patient, as previously described, can be ascribed to skeletal ciliopathies, which show a defect in primary cilium function.[10] We also found a reduction of endotracheal secretion, which was possibly related to a NAVA positive effect on mucociliary clearance potentially due to a reduction of inflammation in the airways and lungs.

As previously described, by improving the synchrony between ventilator trigger/cycle off and spontaneous inspiration/exhalation of the patient and reducing leaks and air swallowing around the uncuffed endotracheal tube or tracheostomy, the gastric overdistension decreased with a consequent reduction of regurgitation and vomit episodes.[11]

Finally, satisfactory weight gain was possible during NAVA as a result of the resumption of adequate enteral feeding, together with the reduction of energy and oxygen consumption. Notably, in our patient, NAVA was safely and effectively used for a long time period (over 1 month).

CONCLUSIONS

To our knowledge, this is the first case of an ATD patient effectively and safely ventilated by NAVA mode.

Despite the severity and complexity of lung disease, NAVA succeeded in reducing respiratory muscle fatigue as a result of increased patient–ventilator synchrony and allowed, at the same time, an improvement in enteral feeding tolerance and weight gain, which made the patient eligible for the corrective intervention of thoracic surgery.

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ABBREVIATIONS

ABG: arterial blood gas
ATD: asphyxiating thoracic dystrophy
EAdi: electrical activity of the diaphragm
Fio_2: fraction of inspired oxygen
HD: hospital day
NAVA: neurally adjusted ventilatory assist
PEEP: positive end-expiratory pressure
PIP: peak inspiratory pressure
SIMV: synchronized intermittent mandatory ventilation
Spo_2: pulse oxygen saturation

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