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Use of the EIS (Electrical Impedance Segmentography System) in Less-Invasive Surfactant Administration (LISA) in New-Borns Suffering from Respiratory Failure

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EIS; Respiratory failure; Newborn; LISA

1. Abstract

1.1. Background and Aims: Electrical Impedance Segmentography System simultaneously detects transthoracic impedance changes, which are directly proportional to the amount of gas volume in the lung, allowing regional and dynamic monitoring of pulmonary ventilation in real time. It is a complementary technique to the most common methods used in the context of respiratory failure in the new-born. We want to demonstrate how a simple, non-invasive, free of radiation bedside monitoring method can provide us extemporaneous feedback about the ventilatory condition of the new-born suffering from respiratory failure and treated with surfactant administration, even before the aid of an X-ray is required.

1.2. Methods: We designed a retrospective, observational study which included new-borns, suffering from respiratory distress syndrome or transient tachypnoea, who received surfactant administration with LISA method. All patients underwent EIS, that monitors the impedance across four quadrants of the lung with 10 electrodes. For each patient, the percentage changes in the impedance of each lung quadrant were analysed, during and after five the administration of the surfactant, visible within an image of a virtual lung provided by the instrument.

1.3. Results: After the LISA procedure, there was a rapid improvement in SaO2, a reduction in FiO2 levels and an increase in the percentage of impedance, therefore an increase of the ventilation of the lung quadrants. The improvement in pulmonary ventilation was confirmed by bedside x-ray. EIS allows continuous visual and quantitative monitoring of regional lung ventilation.

1.4. Conclusions: The main advantage of the EIS method is the immediate visual assessment of changes in pulmonary ventilation, especially during therapeutic maneuvers. This method can provide us information about on the ventilatory condition of the new-born undergoing LISA even before the aid of an X-ray is required. The latter only supplies with instant assessments of respiratory mechanics which, by nature, can vary significantly in short periods. Thanks to its technical characteristics the EIS may represent a reliable tool for dynamic monitoring lung recruitment and optimizing ventilation.

2. Introduction

Electrical Impedance Segmentography (EIS), a rather new technique, is a method that allows to evaluate new- borns with respiratory failure, as well as to study lung physiology. Respiratory Failure (RF) is a significant problem seen in the preterm and term infants admitted to neonatal intensive care units, although management has improved over time and survival rates have increased. Respiratory Distress Syndrome (RDS) is the most common cause of respiratory failure in preterm infants, also in moderate-to-late pre-terms [1], caused by surfactant deficiency. In term or near-term infants, acute respiratory failure is usually a result of meconium aspiration syndrome, sepsis, pneumonia, transient tachypnea, primary pulmonary hypertension. In past years, an invasive approach to ventilation was used in children with respiratory failure, but this resulted in short-term lung damage and long-term bronchodysplasia. The use of the surfactant is the most important therapeutic measure in new-borns with respiratory failure. Nowadays there is a more pragmatic approach in the management of distress. Indeed, the administration of the surfactant is based on the clinical assessment of respiratory work and oxygen requirement in the early stage [2]. The new protocols recommend early surfactant use together with early Continuous Positive Pressure (CPAP) and advise against invasive mechanical ventilation. The purpose of efforts on improving respiratory failure management is to increase survival and minimize adverse effects [3]. In the last decade, the method of administration of the surfactant has also changed for spontaneously breathing babies. From the bolus administration of endotracheal surfactant during mechanical ventilation (INSURE technique, Intubate-SURfactant-Extubate) we have moved to less invasive approaches. The most used is the administration of the surfactant by means of a catheter inserted into the trachea with the new-born in spontaneous breathing on continuous positive airway pressure (LISA technique, less invasive surfactant administration) [4]. Many studies show that LISA reduces the need for mechanical ventilation [5] and possible neonatal complications such as intraventricular haemorrhages and bronchodysplasia, especially in very pre-term neonates [6-8]. In late pre-term infants the benefit of LISA on the prevention of chronic lung diseases is lower, however its use in this population is still recommended, [2] because it is less invasive than previous techniques and because it reduces the time of ventilation [7-10].

EIS, although not yet a very widespread and standardized technique, is certainly complementary to other methods and has recently received much interest from research and clinical routine as a reliable means to optimize respiratory function [11]. The primary purpose of EIS is to detect regional impedance changes simultaneously in the upper and lower, right, and left sides of the chest and main ventilatory parameters. In this paper we analyse EIS, a valid system for continuous monitoring of lung volumes and ventilation distribution of new-borns undergoing surfactant administration. We want to demonstrate how a simple, safe, and non-invasive bedside monitoring method can provide us information about on the ventilatory condition of the new-born undergoing LISA even before the aid of an X-ray is required. The latter only supplies with instant assessments of respiratory mechanics which, by nature, can vary significantly in short periods.

3. Objectives

We used EIS to determine its applicability as a monitoring tool to control regional lung ventilation. The primary objective of our study was to analyse the parameters deriving from EIS monitoring infants in Neonatal Intensive Care Units, suffering from respiratory failure, and treated with surfactant using the LISA technique. Furthermore, our aim is to evaluate how the real-time results provided by the EIS can be complementary to the use of chest X-rays, accelerating the identification of any type of complication and allowing immediate therapeutic manoeuvres, improving the quality of care.

4. Materials and Methods

We designed a retrospective, observational study which included all new-borns referred to Neonatal Intensive Care Unit (NICU) of the AOU Policlinico G. Rodolico-San Marco of Catania from 1 January 2019 to 31 December 2020, who received surfactant administration with LISA method under monitoring of EIS. The local university Ethics Committee approved the study, and all measurements were performed according to the Declaration of Helsinki.

We included infants with gestational age between 31 and 38 weeks with early respiratory failure, defined by the requirement for non-invasive ventilatory support during the first 24 hours after birth. Enrolled patients present respiratory conditions such as respiratory distress syndrome and transient tachypnoea of the new-born. All new-borns with severe asphyxia at birth (Apgar 0-3 at 5 minutes, pH <7 from umbilical cord and BE> 12mEq/L), congenital malformations, phrenic palsy, maternal infection, and those who had needed endotracheal intubation were excluded.

Enrolled patients required non-invasive ventilation, such as NCPAP (Nasal Continuous Positive Airway Pressure), SNIPPV (Synchronized Nasal Intermittent Positive Pressure Ventilation) or NIPPV (Nasal Intermittent Positive Pressure Ventilation). Due to demanding hard work of breathing and the need for a FiO_2> 30%, patients were subjected to surfactant administration via the LISA technique [2, 5], consisting in the administration of surfactant through a thin catheter inserted into the vocal cords maintaining non-invasive ventilation. In order to reduce the noxious stimulus non-pharmacological techniques, such as containment holding, swaddling and, where appropriate, administration of sucrose, were used, not sedative or analgesic drugs [12]. A score according to the Neonatal Infant Pain Scale (NIPS) [13] was recorded for each patient during the procedure. All neonates underwent chest X-Ray before and after LISA administration. For each patient, we evaluated the amount of FiO_2 and SaO_2 before the administration of the surfactant and five minutes after the LISA.

Maternal, pregnancy and delivery characteristics were recorded, as well as ventilatory supports used, duration of ventilation, number of surfactant doses, complications during hospitalization and length of hospitalization, as shown in Table 1.

All patients studied underwent EIS which monitors the impedance across four quadrants of the lung before, during and after five minutes the administration of the surfactant, using a commercially available device for clinical use. In order to monitor the electrical impedance, in the frontal region of the chest an electrode was applied to the centre of the sternum as a reference axis and the other 4 electrodes are placed on the chest in 4 regions (i.e., upper right, upper left, lower right and lower left). In the dorsal plane the other 5 electrodes were positioned in a specular way to the front ones. For added convenience the device has butterfly electrodes which entails combining the four external and one central electrode, as shown in Figure 1.

The duration of the examination was set at a minimum of 40 minutes from the administration of the surfactant. During the recording using the option to set markers on the touch screen of the computer, we documented episodes such as movements, crying, manipulations and the exact moment in which the surfactant with the LISA technique was administered. The real-time user interface of EIS system shows a virtual lung image with the percentage changes in the impedance of each quadrant. The percentage changes in the air flow were analysed, before and after five minutes from the administration of the surfactant (See table 2) – which was visible within an image of a virtual lung provided by the instrument. By ideally dividing the virtual lung into four quadrants, we considered the recruitment of lung regions after LISA for each patient, as shown in Figure 2.

Statistical analysis was performed using paired student t-test. P-values below 0.05 were considered statistically significant. Analysis of the dependent variables "SpO2", "FiO2", "upper right quadrant (UR)", "lower right quadrant (LR)", "upper left quadrant (UL)" and "lower left quadrant (LL)" were performed with a 1-tailed paired t-test comparing the two values ("SpO2_pre" vs "SpO2_post"; "FiO2_pre" vs "FiO2_post"; "UR_pre" vs "UR_post"; "LR_pre" vs "LR_post"; "UL_pre" vs "UL_post"; "LL_pre" vs "LL_post") for each patient. Assumption of normality was performed with K-S test. Alpha was 0.05. We also correlated the value of FiO2 with the percentage of impedance of the four quadrants after the administration of surfactant, assuming as a weak correlation index between 0 and 0.3, a moderate correlation coefficient between 0.3 and 0.7 and a correlation index strong between 0.7 and 1.

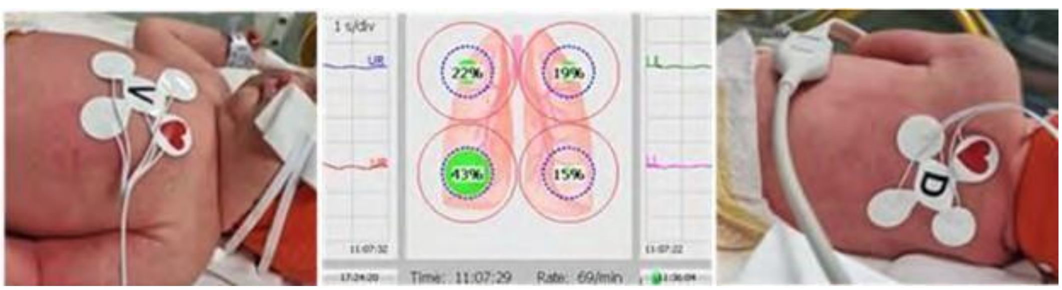

Figure 1: Butterfly electrodes placed on the ventral and dorsal planes of the thorax. Electrical Impedance Segmentography showing the ventilation pattern in four quadrants of the lung overtime.

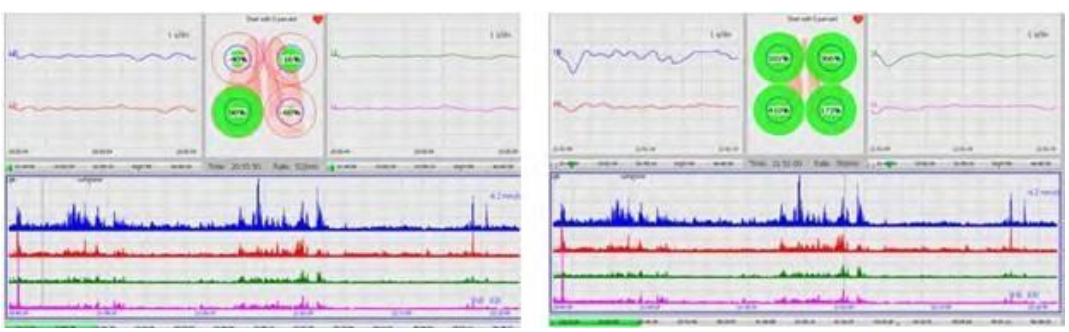

Figure 2: The real-time user interface of EIS system shows impedance values obtained before (a) and after (b) surfactant administration.

5. Results

A total of 10 neonates were included in the study, mostly female. The gestational age is on average of 34 ± 2,3 weeks. Their weight at birth was between 1460 g and 2655 g, with an average of 1895 ± 366,5 g. We observed that most of the pregnancies were twins (70%) and that 60% of the women received antenatal corticosteroids treatment (mostly two doses). Cesarean section occurred in all cases. All children had an Apgar score of 7,2 ± 0,63 at 5 minutes and 8,5 ± 0,52 at 10 minutes. The common causes of respiratory failure were respiratory distress syndrome, more common in infants of younger gestational age, and transient tachypnoea of the new- born. Caffeine prophylaxis soon after admission was administered in all patients at a loading dose of 20 mg / kg followed by maintenance of 5-10 mg / kg / day [2], [14]. All infants, except two of them, received only one dose of surfactant at 200 mg/kg and in none of patients side effects occurred. Enrolled children had a medium NIPS score of 4 ± 1,05. The medium duration of ventilation was 7,3 ± 2,26 days and days in hospitalization was 21.6 ± 9.64 days. Details of the data collected are showed in Table 1.

In all patients, immediately after the LISA procedure, there was a rapid improvement in SaO2 with a reduction in FiO2 levels. In enrolled patients EIS allowed continuous visual and quantitative monitoring of regional lung ventilation. Prior to surfactant administration, 60% of infants had only one vented quadrant, 30% of patients vented only two quadrants, and 10% of cases did not vent any lung quadrant. After five minutes from surfactant administration, we evaluated the recruitment of the virtual lung regions and the percentages of the impedance. Among the children who had only one ventilated, 33% of them had complete opening of 3 lung quadrants, while 50% of them showed opening of all 4 quadrants and 17% of them had opening of only one quadrant pulmonary. As for infants who had two ventilated quadrants, in 66% there was no recruitment of other lung regions, while in 33% of them had opening of only one quadrant. Finally, in the infants who did not have an air exchange, ventilation of one lung lobe was obtained.

Table 1: Characteristics of the patients studied by electrical impedance tomography (EIS)

N° Male/Female	7-Mar
GA	34 ± 2,3 weeks
N° Delivery (TC)	10-Oct
N° Twin birth	10-Jul
N° Antenatal steroids	10-Jun
APGAR	7,2 ± 0,63/ 8,5 ± 0,52
BW	1895 ± 366,5 g
N° RDS/TTN	2-Aug
N° NCPAP	10-May
N° NIPPV	10-Feb
N° SNIPPV	10-Mar
Days of ventilation	7,3 ± 2,26 days
Days in hospital	21.6 ± 9.64 days

GA: gestational age; BW: birth weight; RDS: respiratory distress syndrome; TTN: transient tachypnoea of the new-born

The analysis of the paired t-test of SpO2 [t (9) = - 14,182; p <0.001] and FiO2 [t (9) = 9,494; p <0,001], showing a higher score for “SpO2_post” and “FiO2_pre” than for “SpO2_pre” (85,10 ± 0,994) and “FiO2_post” (25.20 ± 0.917). There is also a significant difference between the two measurements of percentage of impedance of: UR [t (9) = -5,415; p <0,004], showing a higher score for “UR_post” than for “UR_pre” (16,5 ± 7,644); LR [t (9) = -3,165; p <0,006], showing a higher score for “LR_post” than for “LR_pre” (11,9 ± 8,502); UL [t (9) = -3,364; p <0,001], showing a higher score for “UL_post” than for “UL_pre” (22 ± 9,391); LL [t (9) = -3,429; p <0,004], showing a higher score for “LL_post” than for “LL_pre” (6,1 ± 4,218). Table 2 shows the percentage of saturation and FiO2 and the percentage of regional impedance before and after LISA.

The correlation between the value of FiO2 and the percentage of impedance of each of the four quadrants after the administration of surfactant was found to be moderate (the correlation index for all quadrants is greater than 0.3).

Control X-Rays were performed in each patient after surfactant administration. An improvement in pulmonary ventilation was confirmed by bedside x-ray. The use of EIS anticipated what was subsequently confirmed by the chest X-Ray.

Table 2: Percentage of saturation, FiO2 and regional impedance before and after surfactant administration for all patients.

	Pre ± SD	Post ± SD	DF	P value
SpO2 %	85.10 ± 0,994	95,5 ± 0,428	-14.182	<0,001
FiO2 %	48,5 ± 2,892	25.20 ± 0,917	9,494	<0,001
UR %	16,5 ± 7,644	52,6 ± 14,809	-5,415	<0,004
LR %	11,9 ± 8,502	37,6 ± 11,290	-3,165	<0,006
UL %	22 ± 9,391	70,1 ± 9,7	-3,364	<0,001
LL %	6,1 ± 4,218	41,2 ± 12,09	-3,429	<0,004

DS: standard deviation; DF: degrees of freedom

6. Discussion and Conclusion

Respiratory failure can cause decreased tidal volume and Functional Residual Capacity (FRC) and requires respiratory assistance. Chest X-Ray, respiratory function monitors, transcutaneous blood gas monitoring, capnography and blood gas analysis are the most used tools to understand the evolution of the respiratory picture of new-borns at NICU [15, 16]. In studies and in clinical practice, monitoring of respiratory function in new-borns admitted in the neonatal intensive care units uses various radiation-free imaging technologies

[15, 17], including lung ultrasound [2, 18], electrical impedance tomography (EIT) [19-22], and segmentography (EIS) [5].

Bedside lung ultrasound is a reliable and useful diagnostic and predictive tool for common neonatal respiratory diseases and a guide to invasive interventions [23]. Many studies have demonstrated the accuracy of lung ultrasound in infants with respiratory distress [24-26], finding sensitivity and specificity superior to clinical diagnosis and chest x-ray [27]. However, its application in the respiratory field is not widespread and routine in neonatal intensive care.

Electrical Impedance Tomography (EIT), using paired electrodes (16 up to 32 electrodes) positioned around the chest circumference, provides real-time images lung composition by simultaneous injection and measurement of electric alternating currents [19]. EIT using reconstruction algorithms, quantifies the impedance differences caused by pathological processes. Electrodes can be integrated into belts or placed individually with equal spacing.

The great limitation of this technique is the placement of many electrodes at equal distances around the small chest of critically ill neonates, the poor resolution and the few validation studies [15].

On the other hand, in the EIS only 10 electrodes are applied to monitor the electrical impedance. We placed surface electrodes on the chest in the upper and lower region on the left and right and in the sternal area as a reference axis, in the ventral and dorsal area. From the regions into which we ideally divided the lung it is possible to obtain the impedance shift. Impedance measurement allows to monitor global and regional lung ventilation in both spontaneously breathing and mechanically ventilated babies [17].

The principle behind EIS is that biological tissue creates a specific resistance, i.e., a bioelectric impedance, against electrical oscillations, influenced by the volume of gas, blood, liquids and cellular integrity. Since the lung has a rather low electrical conductivity, the impedance is directly proportional to the amount of gas volume in the lung [19, 28].

Simple, non-invasive, free of radiation, it is a complementary technique to the most common methods used in the context of respiratory problems in the new-born. This technique allows not only global but also regional and dynamic monitoring of pulmonary ventilation in real time. This offers extemporaneous feedback on many therapeutic measures and guarantees a more careful management, guiding all therapeutic adjustments [29]. By continuously monitoring the four lung quadrants with ten small electrodes, it allows to detect volume changes in many therapeutic measures: changing the ventilation mode, correct positioning of the endotracheal tube, recruitment manoeuvres, lung aspiration, pneumothorax drainage, the administration of surfactant and so on [22, 30].

To date, there are not many studies on the use of EIS in clinical practice. Durlak [31] used impedance segmentography in a series of children with bronchopulmonary dysplasia who underwent pulmonary function tests after bronchodilator. Recently, Brandt et al., used EIS to compare impedance in two different ventilation techniques in children admitted to intensive care [32].

Betta et al. [33], in a case report of a new born with respiratory distress syndrome and pulmonary atelectasis treated with surfactant, anticipated what we assert in this study. EIS is useful for monitoring respiratory course and therapeutic adjustments.

In our study EIS was applied as a tool to perform continuous measurements during LISA in critically ill children. During the procedure the measurement of the electrical impedance segmentography was recorded, which allowed us to see the improvements in real time. All children undergoing LISA achieved an improvement in ventilatory parameters in terms of increased saturation and reduced need for oxygen. Thanks to monitoring with the EIS, after the administration of surfactant, all patients achieved an increase in the percentage of impedance, therefore an increase of the gas volume in the lung. The impedance is directly proportional to the amount of gas volume in the lung. In our patients the percentage of impedance after LISA has always increased, even in the quadrants already ventilated before the administration of the surfactant. Our study design allowed us to conclude that surfactant administration in all cases, even when there is no recruitment of other lung regions, improves lung gas exchanges. Using the lung image provided by the instrument screen it was possible to visualize an increase in the ventilated lobes. The main advantage of the EIS method is the immediate visual assessment of changes in pulmonary ventilation, especially during therapeutic manoeuvres, such as the administration of surfactant.

The goal of our study is to report the valuable utility of EIS in respiratory failure. Thanks to its technical characteristics the EIS can represent a reliable tool for dynamic monitoring of lung recruitment and optimizing ventilation according to the needs and characteristics of the individual patient, avoiding damage to the already widely compromised lung.

Out study contains at least two main limits. The study involved a small series of cases, mostly twins, and we could not guarantee reliability on impedance measurement as there may be movement or manipulation artifacts and malposition of electrodes, especially because children weighing less than 3 kg.

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