# Effects of Endotracheal Intubation and Surfactant on a 3-Channel Neonatal Electroencephalogram

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**Objective** To evaluate the effects of surfactant administration on the neonatal brain using 3-channel neonatal electroencephalography (EEG).

**Study design** A prospective cohort of 30 infants had scalp electrodes placed to record brain waves using 3-channel EEG (Fp1-O1, C3-C4, and Fp2-O2). Sixty-second EEG epochs were collected from a 10-minute medication-free baseline, during premedication for endotracheal intubation, at surfactant administration, and at 10, 20, and 30 minutes after surfactant administration for amplitude comparisons. Oxygen saturation and heart rate were monitored continuously. Blood pressure and transcutaneous carbon dioxide were recorded every 5 minutes.

**Results** Eighteen of 29 infants (62%) exhibited brain wave suppression on EEG after surfactant administration ($P \leq .008$). Four of those 18 infants did not receive premedication. Nine infants exhibited evidence of EEG suppression during endotracheal intubation, all of whom received premedication before intubation. Five infants had EEG suppression during endotracheal suctioning. Oxygen saturation, heart rate, and blood pressure were not independent predictors of brain wave suppression.

**Conclusion** Eighteen of 29 intubated infants (62%) had evidence of brain wave suppression on raw EEG after surfactant administration. Nine patients had evidence of brief EEG suppression with endotracheal intubation alone, a finding not previously reported in neonates. Intubation and surfactant administration have the potential to alter cerebral function in neonates. *(J Pediatr 2012;161:252-7)*.

Endotracheal surfactant administration has been shown to reduce neonatal mortality and improve lung function in infants with respiratory distress syndrome.[1] After being approved by the US Food and Drug Administration in 1990, surfactant replacement is now routinely used in most neonatal intensive care units for infants with respiratory distress syndrome, meconium aspiration syndrome, and other etiologies.[2] Infants with respiratory distress syndrome and meconium aspiration syndrome typically exhibit a significant improvement in pulmonary mechanics along with improved chest radiography findings shortly after surfactant administration.[3] However, delivery of surfactant via an endotracheal tube (ETT) has been associated with cerebroelectrical depression as recorded by single-channel amplitude-integrated electroencephalography (aEEG).[4-7] The duration of aEEG changes after surfactant administration have been reported to be as short as 10-20 minutes by Skov et al[5] and as long as 24 hours by van den Berg et al[6]; in both of those studies, surfactant was administered as a single bolus via an ETT. The etiology of the changes in electrical brain wave activity occurring with surfactant administration is unclear, and there are no published long-term studies on neurodevelopmental outcomes.

ETT placement in newborns is known to be a painful procedure and is also associated with adverse physiological effects including bradycardia,[8,9] alterations in blood pressure (BP),[10,12-15] and increased intracranial pressure.[11,16] Furthermore, surfactant administration is known to be associated with changes in cerebral blood flow velocity,[5,17,18] BP,[5,18] oxygen saturation measured by preductal pulse oximetry ($SpO_2$),[5] and carbon dioxide measured transcutaneously ($TcCO_2$).[7] The objective of the present study was to use 3-channel electroencephalography (EEG) to further characterize the effects of surfactant administration and related procedures on the neonatal brain.

## Methods

A prospective cohort of 30 infants (24 preterm and 6 full term) who were admitted to the University of California San Diego's Infant Special Care Center and who underwent endotracheal intubation and/or surfactant administration were studied using 3-channel EEG between December 2009 and December 2010. The University's

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| aEEG | Amplitude-integrated electroencephalography |
| BP | Blood pressure |
| EEG | Electroencephalography |
| ETT | Endotracheal tube |
| $SpO_2$ | Oxygen saturation measured by pulse oximetry |
| $TcCO_2$ | Transcutaneous carbon dioxide |

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Institutional Review Board approved the study, and previous informed consent was obtained from a parent of each enrolled infant.

Any newborn in the Infant Special Care Center who required surfactant administration and was not emergent was a candidate for this study, including infants previously intubated and on ventilatory support. Each infant was studied only once during surfactant administration. Infants with a facial or airway anomaly that could interfere with ventilation or intubation, the need for emergent intubation, known chromosomal abnormality, congenital brain abnormality, or intraventricular hemorrhage grade III or greater were excluded. No infant had received antiepileptic drug therapy or was receiving a continuous narcotic infusion while participating in the study.

Heart rate and $SpO_2$ data were collected continuously, and BP and $TcCO_2$ were recorded every 5 minutes. For infants without a BP transducer in place, BP was obtained by oscillometry and recorded every 5 minutes until completion of the study. A data acquisition system (BioPac Systems, Goleta, California) recorded analog physiological data. Analog signals from the oximeter (Radical; Masimo, Irvine, California) were analyzed using AcqKnowledge software (BioPac Systems), which linked them in time. For pulse rate and $SpO_2$, the exact duration of any change from baseline, with medians, means, maxima, and minima, were calculated and stored for subsequent analysis using PROFOX software (PROFOX Associates, Escondido, California). BP, $TcCO_2$, and demographic data were recorded by a staff member (a registered nurse, registered respiratory therapist, pediatric resident, or neonatal fellow). Blood gas analysis was not performed for this study.

### EEG Monitoring and Analysis

Once the clinical team decided to intubate and/or provide surfactant administration to an enrolled patient, a modified neonatal 3-channel EEG (Fp1-01, C3-C4, and Fp2-O2) montage was used to record continuously before, during, and after surfactant administration. Raw EEG brain wave activity data were collected with the Bio-Logic digital EEG data collection system (Bio-Logic Systems, Mundelein, Illinois). Scalp electrodes were placed according to the International 10-20 System by a single neonatology fellow previously registered with the American Board of Registration of Electroencephalographic and Evoked Potential Technologists. Electrode impedance levels were kept below 10 kΩ. Low-pass and high-pass filters were set at 1 Hz and 70 Hz, respectively. The 60-Hz notch filter was not engaged. The 3-channel montage used in this study records EEG activity from both hemispheres and has been validated as comparable to routine 9-channel neonatal montage in seizure detection.[19]

A 10-minute baseline EEG recording was obtained before the administration of any medication or surfactant. EEG recordings were made continuously throughout each study and continued for at least 30 minutes after completion of surfactant administration or until the EEG returned to near baseline values. A single child neurologist (R.H.) qualitatively analyzed EEG data for changes in amplitude, frequency, and seizure activity. For quantitative EEG analysis, the median amplitude in microvolts over a 60-second epoch from the start of the recording (baseline), during premedication, at surfactant administration, and at 10, 20, and 30 minutes after surfactant administration was selected and analyzed using Persyst Insight II EEG software (Persyst Development, Prescott, Arizona). Median EEG amplitudes were collected from all EEG channels for a comparison of values before and after surfactant administration.

### Surfactant and Intubation Procedure

In our neonatal unit, surfactant therapy involved either Survanta (beractant; Abbott Nutrition, Columbus, Ohio) or Curosurf (poractant alfa; Cornerstone Therapeutics, Cary, North Carolina) administered as an intratracheal suspension via ETT. Survanta was given at a dose of 4 mL/kg via ETT. If a repeat dose was necessary, it was given 6 hours after the initial dose. The standard dose of Curosurf was 2.5 mL/kg via ETT, with a repeat dose of 1.25 mL/kg/dose every 12 hours if necessary to increase fraction of inspired oxygen. After confirmation of ETT placement, a 5 Fr multi-access catheter (Ballard, Roswell, Georgia) was placed inline to the ventilator and was connected to the ETT for surfactant administration. Infants were given half the aliquot of surfactant in each lung. The attending neonatologist and/or neonatal fellow/neonatal nurse practitioner chose the type of surfactant used at the time of intubation.

The current standard of care for elective endotracheal intubation in our neonatal unit includes the use of a combination of premedication agents, including a short-acting muscle relaxant. Oxygen is administered via a flow-inflating resuscitation bag, with the fraction of inspired oxygen adjusted to maintain saturation at $\geq$95% and <100% before endotracheal intubation, followed by atropine (20 $\mu$g/kg) to prevent vagolytic response and a narcotic for pain management. Fentanyl (2 $\mu$g/kg) and then cisatracurium (up to 200 $\mu$g/kg) were given 1 minute before endotracheal intubation. Intubation was performed by an attending neonatologist, neonatal fellow, pediatric intern/resident, or neonatal nurse practitioner using the appropriate-sized laryngoscope and ETT. Proper ETT placement was confirmed with a Pedi-Cap colorimetric qualitative $CO_2$ detector, (Nellcor, Pleasanton, California) and/or chest auscultation and radiography. All endotracheal intubation attempts were limited to 30 seconds, including the duration of intubation. Brief endotracheal suctioning via a Ballard Multi-Access Catheter connected to 100-mmHg wall suction was performed before surfactant administration.

### Statistical Analyses

Minimum, maximum, mean, median, and SD amplitudes from all EEG channels were collected before and after surfactant administration. Data are expressed as median voltage of amplitude in microvolts. The Wilcoxon matched-pair signed rank test was used for quantitative data analysis. Statistical