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DIVISIÓN DE ESTUDIOS DE POSGRADO E INVESTIGACIÓN  
SECRETARÍA DE SALUD  
INSTITUTO NACIONAL DE PEDIATRÍA**

**“Study Of The Physiology Of Nasal CPAP In An Animal  
Model And Clinical Impact Analysis In Newborns With  
Respiratory Distress”**

**TRABAJO DE INVESTIGACION  
QUE PRESENTA LA**

**DRA. FLOR EMILIA ABINADER NUÑEZ  
PARA OBTENER EL TÍTULO DE  
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**DR. LUIS MARTIN GARRIDO GARCIA  
TUTOR**



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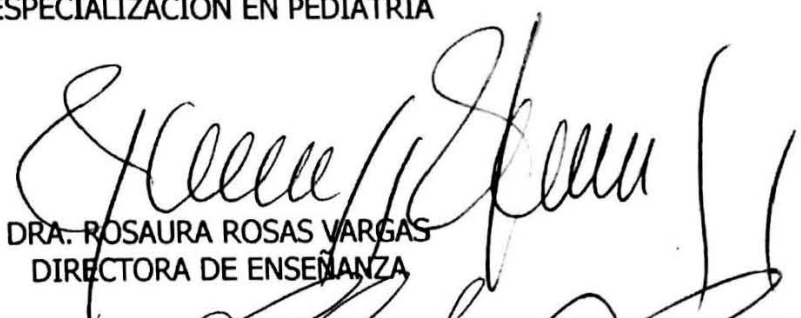
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**TESIS DE ESPECIALIDAD**

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And Clinical Impact Analysis In Newborns With Respiratory  
Distress”**



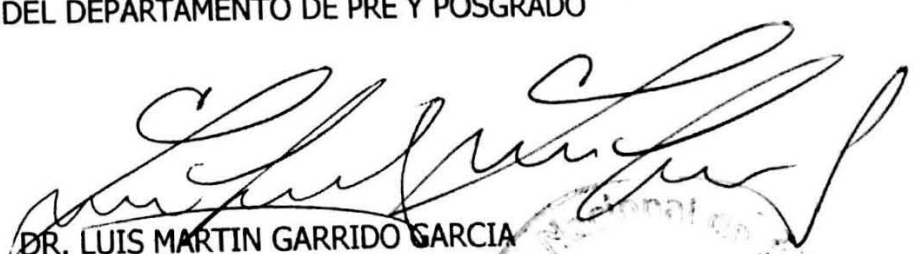
DR. ALEJANDRO SERRANO SIERRA  
PROFESOR TITULAR DEL CURSO DE  
ESPECIALIZACION EN PEDIATRIA



DRA. ROSAURA ROSAS VARGAS  
DIRECTORA DE ENSEÑANZA



DR. LUIS MARTIN GARRIDO GARCIA  
JEFE DEL DEPARTAMENTO DE PRE Y POSGRADO



DR. LUIS MARTIN GARRIDO GARCIA  
TUTOR DE TESIS



# **Study Of The Physiology Of Nasal CPAP In An Animal Model And Clinical Impact Analysis In Newborns With Respiratory Distress**

A Orozco- Gutiérrez, A D Martínez-Oñate, A T Castillo, M Pineda-Leyte, A S Martínez, E N Abinader, C R Alcocer-Arreguin, R C Gil

## **Keywords**

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## **Abstract**

Background: The continuous positive airway pressure (CPAP) is used to treat respiratory failure in infants with excellent results, pneumothorax occurs from 1.4% to 10.3% of children and mortality varies between 6.5% and 48%. We reported a study in pigs to determine if the cough and nasal seal affect these results. We reported a study in pigs to determine if the cough and nasal seal affect these results.

Method: 4 pigs were anesthetized and their intrabronchial pressure was measured by applying CPAP with sealed and unsealed prongs. Then cough was caused and the intrabronchial pressure changes were measured. Results: With CPAP unsealed disappears negative inspiratory pressure and the average pressure in the airway (MAP) increases. By using sealed CPAP the findings would increase. Then cough was caused and the intrabronchial pressure changes were measured.

Results: With CPAP unsealed disappears negative inspiratory pressure and the average pressure in the airway (MAP) increases. By using sealed CPAP the findings would increase. By using CPAP sealed the findings would increase.

With the cough, the CPAP without seal decreases all pressures, with seal the PE increases and the PI is more negative. In either case the measurement of the

external pressure CPAP detected intrabronchial changes. In either case the measurement of the external pressure CPAP detected intrabronchial changes.

Conclusions: The nasal CPAP with leakage increases the PI and eliminates the negative expiratory pressure, decreasing the alveolar collapse, cough increases the negative pressure and probably cause barotrauma The nasal seal increases the PI and PMVA, increasing the oxygen diffusion gradient and improving oxygenation

With cough the pressures increase the risk of barotrauma. Monitoring in children and does not detect the intrabronchial changes of pressure in the airway.

## Introduction

The continuous positive airway pressure (CPAP) has been used since 1971, when Gregory and his colleagues showed that CPAP endotracheal with a bag of anesthesia improved oxygenation and reduced mortality in preterm infants with respiratory distress syndrome subsequently different devices and strategies were developed to provide it [1-5].

In the following years, the mechanical ventilation replaced CPAP as the most common form of ventilatory support until it practically fell into disuse, was not until 1989 that Dr. Avery published a classic study by mentioning that the use of CPAP generated a lower risk of injury Chronic lung ventilation compared to mechanical ventilation, this ventilation technique was reintroduced in the treatment of these children. [6-10].

In recent years, acceptance of CPAP has increased and various articles evaluating the efficacy and safety of the procedure have been reported [11-23].

Despite the widespread use of nasal CPAP there are few studies on the physiological bases [24,25] and little is known about the variables that affect the response of patients [26]. This lack of physiological knowledge has led to very different clinical outcomes that have tried to standardize developing a large number of devices for daily treatment of neonates [27-30].

Despite the variety of available interfaces for applying CPAP [31,32] nasal prongs are the most common method and the general consensus is that they should be as broad as possible to reduce resistance and fit comfortably without air leaks or damage tissue [33].

However, there are some gray areas in their application [34-37]. It is generally accepted that to deliver intra points of pressure CPAP of bubble is represented by the depth of immersion of the expiratory tube [38-40]. However, Chilton and Brooks and De Paoli reported that pharyngeal pressure is reduced by approximately 50% in infants with open mouth [41,42].

Khan and Cols found that airway pressure during CPAP is variable and depends on the interaction of the depth of immersion and flow [43]. Another concern regarding

the use of nasal CPAP is the presentation of pneumothorax as an often complication without a clear cause and tested from this accident [44].

We have not found any studies that measured the pressure changes associated with crying or hiccups, these events are common in children with CPAP and produce elevations on intrathoracic pressure in combination with treatment may be a perfect combination to cause pneumothorax.

Pneumothorax frequency associated with the use of CPAP in children with respiratory distress often varies from a low of 1.6% to 10.3% and the reported mortality is as low as 6.5% up to 48% in children with severe respiratory distress without any documented explanation for this variability [6,7,10,16,20,22,35,45,46].

The COIN study [45] and the SUPPORT study [46] two randomized controlled clinical trials have shown that CPAP can be used in young infants with high success rates, but have presented discrepancies in the risk of pneumothorax, COIN trial showed a high incidence of pneumothorax (9%) while the SUPPORT study reported a frequency of 6.8%. This was attributed to the fact that the COIN essay utilizes a CPAP of 8 cms. H<sub>2</sub>O opposed to a CPAP of 6 cms. H<sub>2</sub>O used in the SUPPORT essay.

In 2010 we initiated a line of research trying to better understand the physiology of CPAP and achieve increased safety of the procedure, first we developed a mechanical simulator to study the physiology of CPAP and its response to common phenomena such as coughing and crying this study showed that nasal seal and common physiological phenomena have an impact on intrabronchial pressure, which affects the safety and efficacy of the procedure [48]. The study in animals intends to corroborate the findings of work in the simulator and provide a basis for further clinical studies.

## **Hypothesis**

The hypothesis is that the hermetic seal of the nasal passages with nasal prongs modifies airway pressure by increasing the diffusion gradient and may experience increases or decreases during physiological phenomena such as crying or opening the mouth.

## **Materials and Methods**

Surgical preparation.

We used 4 Yorkshire pigs with 6 days of birth weight of 2,500 grs. were anesthetized with acepromazine (0.75 mg/kg intramuscular) and sodium pentobarbital (6 mg/kg). On sedated pig was applied 2% lidocaine and a tracheotomy was performed by placing a catheter in the secondary bronchus and measuring the intrabronchial pressure using an aneroid manometer. Performing 20 measurements for each variable in each pig.

We measured basal pressure of the animal spontaneously breathing, nasal CPAP tipped leaking and sealed and then the measurements were repeated causing coughing.

Nasal CPAP was applied with pressure of 7 cms. H<sub>2</sub>O using prongs sized to the nares of the pig and measured pressure in the system with a pressure gauge at the entrance of the prongs with the same system used in CPAP treatment in Children.

In all cases we measured ventilatory pressure for 20 cycles (inspiration and expiration), we obtained the average inspiratory and expiratory pressure in every situation, the average pressure was obtained by subtracting the average of the inspiratory pressure to the average of the expiratory pressure.



## Results

Basal Determination without CPAP.

The average inspiratory and expiratory pressure in the bronchus without CPAP was (10/-10.29 cms. H<sub>2</sub>O) and remained stable. The average pressure was 0.29.

Coughing increased the expiratory pressure (12.93 cms. H<sub>2</sub>O) and inspiratory (-6 cms. H<sub>2</sub>O), the average pressure was raised to 6.93.

Measuring the pressure in the system CPAP was stable varying from 2.5 cms. H<sub>2</sub>O inspiration to 7.5 cms. H<sub>2</sub>O expiration.

Nasal CPAP with unsealed ends

The average inspiratory and expiratory pressure in the bronchus with air leaking on nasal prongs in the nostrils was (9.70/0 cm. H<sub>2</sub>O) range (0/12 and stable), with cough expiratory pressure was maintained but increased negative inspiratory pressure (9.85/-15 cms. H<sub>2</sub>O), the average pressure decreased to -6.15.

We should mention that the range of negative inspiratory pressure was -10 to -20 cms. H<sub>2</sub>O.

Nasal CPAP with sealed edges

The average inspiratory and expiratory pressure with prongs without air leak through nostril was the 12.29/-2.5 cms. H<sub>2</sub>O, the average pressure rose to 9.79 cms. H<sub>2</sub>O.

The range of negative pressure during inspiration was from 0 to -5 cms. H<sub>2</sub>O.

Cough with inspiratory and expiratory pressure was 16/-19 cms. H<sub>2</sub>O and the average pressure was -2.4 cms. H<sub>2</sub>O.

The range of negative pressure during inspiration was from -19 to -20 cms. of water.

The pressure in the measurement system of CPAP was stable at 2.5 cms. H<sub>2</sub>O inspiration to 7.5 cms.

**Table 1**

Pressure Intrabronchial without CPAP, CPAP with and without nasal seal and changes provoked by cough.

Pressure in H <sub>2</sub> O cms.	Basal without CPAP	Nasal CPAP unsealed prongs	Nasal CPAP sealed prongs
Without Cough.			
Expiratory Pressure	10.29 (10/12)	9.70 (8 to 12)	12.29 (12 to 14)
Inspiratory Pressure.	-10 (-8 / -12)	0 (0)	2.5 (0-5)
Average pressure (pE-pl)	0.29	9.7	9.79
Variation in cms. H <sub>2</sub> O			
Expiratory		-0.59	2
Inspiratory		10	7.5
Average		9.41%	9.5
External pressure measured			
Expiratory	7.5	7.5	7.5
Inspiratory	2.5	2.5	2.5
With Cough			
Expiratory Pressure	12.93 (10-20)	8.85 (8-10)	16.6 (15-18)
Inspiratory Pressure	-6 (-8 to -12)	-15 (-10 to -20)	-19 (-18 to -20)
Average pressure (pE-pl)	6.93	-6.45	-2.4
Variation in cms. H <sub>2</sub> O			
Expiratory		-4.08	3.67
Inspiratory		-9	13
Average		-13.8	-9.33
External pressure measured			
Expiratory	7.5	7.5	7.5
Inspiratory	2.5	2.5	2.5

## Analysis

The average pressure on the airway is increased 9 times when using nasal CPAP with both sealed edges and leaking edges. This increases the alveolar-arterial oxygen gradient that explains the improvement of children with respiratory distress. Expiratory pressure remains almost unchanged and the inspiratory pressure loses its negativity becoming neutral (0) in the case of leaking edges and positive (2.5) when using sealed edges, so with CPAP it lowers the alveolar collapse reducing the need for exogenous surfactant and bronchopulmonary dysplasia.

Under normal conditions (without CPAP) while coughing the average pressure increases and becomes positive increasing from 0.29 to 6.93, the expiratory

pressure increases 2.73 and the inspiratory pressure loses 4 cms. H<sub>2</sub>O to rise from -10 to -6 cms. H<sub>2</sub>O. However it remains within relatively narrow ranges.

When using CPAP with or without nasal seal the average pressure becomes negative (-6.45 and -2.4 with seal) probably due to inspiratory flow limitation.

Using CPAP without seal the expiratory pressure decreases in relation to the basal pressure from 12.93 to 8.85 (-33%) by the same flow limitation and by placing the nasal seal increases from 12.93 to 16.6 (28.3%) as the system becomes closed and further allows increments in pressure with the same volume.

The inspiratory pressure with CPAP and cough becomes more negative in the case of CPAP with leak varies from -6 to -9 (50%) with nasal CPAP sealed the negative pressure changes from -6 to -13 (116%) this negative pressure with respect to this calculated flow for a basal pulmonary volume, at a higher volume sued by coughing and found this limited the negative pressure is increased significantly and can be the cause of pneumothorax frequently encountered in clinical practice.

## Discussion

Our work verifies the results obtained by Khan [45] Chilton [39] and De Paoli [40], who demonstrated that the pressure in the airway when employed CPAP is not constant, is influenced by several factors and is not reflected in measuring the pressure in the CPAP circuit. We complement these studies, and we showed that there are secondary pressure changes to common physiological phenomena as cough, events that are common in infants receiving CPAP.

Traditionally, studies have used pressure gauges as close as possible to the nasal cannula as a measure of intrapulmonary pressure [46,47], in agreement with our results from the pressure near the nasal edges is different from the intrapulmonary pressure.

In our study, the use of CPAP with sealed edges increases the pressure and can improve oxygen gradient making the technique more efficient, but when coughing significantly increases the negative pressure, probably by decreasing inspiratory flow and this factor may be causing barotrauma making it more risky.

These intrabronchial pressure changes are not reflected on the gauge system of CPAP, which casts doubt on the effectiveness of surveillance systems of the pressure due to their limited value to prevent acute lung injury by CPAP.

Unexpected increases related to intrabronchial pressure with sealed nostrils and normal physiological events may be an important factor for the wide variability in the results of studies on the efficacy and safety of nasal CPAP and have to be considered in future work on this ventilatory technique.

This study explains the results published in 1973 by Gregory and corroborated in 2009 [11] using tracheal CPAP. In this technique the patient is intubated and connected to a CPAP with an elastic anesthesia bag, which has a high volume that prevents inspiratory pressure to drop and being elastic absorbs pressure surges to maintain alveolar stability and a gradient alveolar-arterial stable.

## **Conclusions**

The use of nasal CPAP has been widely disseminated and has proven an effective procedure for the treatment of premature infants with respiratory distress with an efficacy similar to mechanical ventilation. This is a very well accepted and safe in the treatment of lung diseases.

This study supports our previous findings on a mechanical simulator [48]

The hermetic nasal seal in nostrils either tight ends, secretions or mucosal edema produces unexpected changes in intra bronchial pressure, affecting the efficacy and safety of nasal CPAP. Reducing air leaks the CPAP with nasal seal is more effective. Very young children may need more respiratory support with stable and higher pressures, however the use of nasal CPAP with seal can increase the risk of barotrauma.

In older children or those with less severe lung disease the use of CPAP with leak on nasal edges may be sufficient to maintain respiratory homeostasis and alveolar stability.

Inadvertent changes secondary to nasal seal may explain variability in efficacy and safety results observed in previous studies, and can be influenced by local events routines and uncontrolled (techniques for fixing the points of the same size, edema of the nasal mucosa, nasal bleeding with clots and scabs and cleaning techniques). The hermetic seal on the nostril during the use of nasal CPAP is a factor, which influences the pressure in the airways and should be taken into account during clinical trials to ensure more consistent and reliable results.

Maintaining stable figures in the surveillance system for pressure in the CPAP does not exclude the presence of sudden intrabronchial variations herefore not useful to reduce the risk of barotrauma.

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