

## Incidence of Nosocomial Infection with Nasal Continuous Positive Air Way Pressure Versus Mechanical Ventilation During Treatment of Respiratory Distress in Preterm Neonates

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**Abstract: Objective:** to determine the incidence of nosocomial infections in preterm infants with respiratory distress, if treatment with continuous positive air way pressure (CPAP) compared to treatment with mechanical ventilation (MV). **Patients and Methods:** Sixty premature neonates admitted to the intensive care unit in Al Galaa Teaching Hospital, in their first day of life suffering from respiratory distress, the infants were divided into two groups, 1<sup>st</sup> group include 30 patients supported by CPAP and the 2<sup>nd</sup> group include 30 patients who were supported by mechanical ventilation. Blood cultures and early endotracheal cultures were taken in the 1<sup>st</sup> day of life from the sixty neonates in both groups then another late endotracheal culture was taken from them in the 5<sup>th</sup> day of life. **Results:** 36.67% of patients in the MV group had +ve blood culture and 63.33% had no growth, while in the CPAP group 16.67% had +ve blood culture and 83.33% showed no growth. Early endotracheal cultures showed +ve growth in 63.33% in the MV groups a 23.33% in the CPAP group. (P=0.002), on the other hand late endotracheal cultures showed +ve growth in 36.67% in the MV group and 16.67% in the CPAP group. Klebsiella was the most frequent organism in all +ve cultures. **Conclusion:** The incidence of positive infection in blood cultures and endotracheal cultures is higher in the MV group than in the CPAP group. The incidence of klebsiella among the whole population in the two studied groups was higher in MV group more than in the CPAP group in all the cultures. Within the cases having positive cultures, MV patients needed longer duration on ventilation than patients on CPAP (whether the cultures were taken from the blood or endotracheal).

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**Keywords:** Premature infant, Respiratory distress, cultures, mechanical ventilation, continuous positive air way pressure.

### 1. Introduction

Respiratory distress syndrome (RDS) is the most common cause of respiratory failure and requirement for mechanical ventilation (MV) of newborns. In developing countries, despite facilities for respiratory care of newborn infants, RDS mortality rate and percentage of complications still remain high in comparison to the developed countries (Marraro, 2003).

Mechanical ventilation is a widely used supportive technique in the intensive care units (Greenough *et al.*, 2004). Several forms of external support for respiration have long been described to assist the failing ventilatory pump, and access to lower air ways through tracheostomy or endotracheal tubes had constituted a major advance in the management of patients with respiratory distress. However noninvasive ventilation (NIV) techniques, using patient ventilator interfaces in the form of facial masks, have been designed. (Brochard, 2003). Spontaneous breathing can be supported (CPAP, pressure of volume support ventilation) or ventilation can be totally or partially controlled (volume and

pressure controlled ventilation, synchronized intermittent mandatory ventilation) (Mehta *et al.*, 2004). The early application of nasal continuous positive air way : pressure (NCPAP) reduces the need for subsequent endotracheal intubations, mechanical ventilation, and surfactant therapy. (Merran *et al.*, 2004 and; Subramaniam *et al.*, 2005).

Nosocomial infections are the most common complications encountered in the neonatal intensive care unit (NICU). They are associated with high mortality and prolonged duration of hospitalization in the survivors, contributing to an increased cost of health care (Srinivasan *et al.*, 1998).

The aim of this study was to determine the incidence of nosocomial infections in preterm infants with respiratory distress, if treatment with CPAP compared to treatment with mechanical ventilation.

### 2. Material and Methods

The study was conducted on 60 premature neonates admitted in the intensive care unit in Al Galaa Teaching Hospital, all were admitted in their first day of life and all were suffering from

respiratory distress. The patients were divided into two groups, 1<sup>st</sup> group include 30 patients supported by nasal continuous positive air way pressure (Hamilton Arabella Active Nasal CPAP system blender on bubble CPAP circuit) and the 2<sup>nd</sup> group include 30 patients who were supported by mechanical ventilation (The Bear Cub 750 vs infant ventilator made in USA).

All the neonates were subjected to full history taking including: maternal data and medical records of these neonates were reviewed for the mode of delivery, Apgar score, birth weight (BW), gestational age and thorough physical examination.

#### Investigations included:

1. Investigations conducted according to the need of every case:

- CBC, CRP, serum electrolyte, kidney function, liver function and blood gases.
- Imaging studies as ultrasonography, echocardiography, skeletal survey and CT scan.

2. Blood cultures and early endotracheal cultures were taken in the 1<sup>st</sup> day of life from the sixty neonates in both groups of the study, and then another late endotracheal cultures were taken from them in the 5<sup>th</sup> day of life. Blood cultures were performed using BACTEC Peds blood culture bottles and the BACTEC- 9050 instrument. In our study, we used new sterile endotracheal suction catheter during the technique of sampling. All the cases in our study were under routine care of physiotherapy and suctioning through the endotracheal tube every 3 hours when needed, the suction catheter was changed every time, as we used new sterile one.

All of patients were closely followed up during their period of stay for the progress of the condition including:

- Initial assessment of the original disease and initial cause of admission.
- The outcome, complications and recording the results.

#### Statistical analysis:

Data were entered and analyzed using the Statistical Package for Social Science (SPSS); version 12. Nominal data were expressed as frequency and percentage. Numerical data were expressed as means and standard deviations and were compared using student's t test. Associations were tested using Pearson's correlations. P value less than 0.05 were considered significant.

#### 3. Results

On analyzing the data of the present study we observed that the mean gestational age in the CPAP group was  $33.96 \pm 1.2$  while in the MV group it was  $33.36 \pm 1.4$  with no statistically significant differences between both study groups, also mean body weight on admission and on discharge ( $1.66 \pm 0.37$  and  $1.77 \pm 0.22$  on CPAP group;  $1.78 \pm 0.34$  and  $1.88 \pm 0.26$  on MV group) showed no statistically significant differences between both group. The mean Apgar score at 1<sup>st</sup> min was statistically significant higher in the CPAP group ( $5.1 \pm 1.09$ ) than in MV group ( $4.4 \pm 1.03$ ) while there is no statistically significant differences between the two group as regards Apgar score at 5<sup>th</sup> min. ( $7.96 \pm 0.49$  versus  $7.83 \pm 0.59$  on MV group).

The numbers of siblings, order of delivery in multiple pregnancies and the mode of delivery showed no statistically significant differences between the two groups.

The blood culture results of CPAP group showed that 83.33% had no growth while 16.67% had +ve culture (klebsiella 6.67%, staph. aureus 3.33%, and citrobacter 3.33% and strept. viridans 3.33%). The MV group showed that 63.33 had no growth and 36.67% had +ve culture (klebsiella 16.67, staph. aureus 13.33, strept. viridans 3.33% and candida 3.33%). The +ve blood cultures results were higher in MV group than in CPAP group, but this comparison is statistically insignificant (Table 1).

**Table (1) presentation of the blood culture results in both groups of study**

	Blood culture results						Chi-square	
	CPAP		MV		Total		X <sup>2</sup>	P-value
	N	%	N	%	N	%		
No growth	25	83.33	19	63.33	44	73.33	3.068	0.08
Growth	5	16.67	11	36.67	16	26.67	3.068	0.08
- Klebsiella	2	6.67	5	16.67	7	11.67		
- Staph. aureus	1	3.33	4	13.33	5	8.33		
- Citrobater	1	3.33	0	0	1	3.33		
-Strept. viridans	1	3.33	1	3.33	2	6.67		
- Candida	0	0	1	3.33	1	3.33		

The results of early endotracheal cultures (in the 1<sup>st</sup> day of life) in CPAP group showed no growth on 76.67% and growth on 23.33% of patients (klebsiella 16.67%, coagulase negative staphylococci 3.33% and pseudomonus 3.33%). While MV group showed no growth on 36.67% and growth on 63.33

(klebsiella 43.33%, coagulase negative staphylococci 3.33%, Pseudomonus 3.33%, Acinetobacter 10% and strept. viridans 3.33%). The number of patients showing +ve early endotracheal cultures results is higher in MV group than in CPAP group with statistically highly significant value (Table 2).

**Table (2): The results of early endotracheal cultures (in the 1<sup>st</sup> day of life) in both groups of study.**

	Early Endotracheal cultures						Chi-square	
	CPAP		MV		Total		X2	P-value
	N	%	N	%	N	%		
No growth	23	76.67	11	36.67	34	56.67	9.774	0.002*
Growth	7	23.33	19	63.33	26	43.33	9.774	0.002*
- Klebsiella	5	16.67	13	43.33	18	30.00		
- CO NS	1	3.33	1	3.33	2	3.33		
- Pseudomonus	1	3.33	1	3.33	2	3.33		
- Acinetobacter	0	0.00	3	10.00	3	5.00		
- Strept. Viridans	0	0.00	1	3.33	1	1.67		

The results of late endotracheal cultures (in the 5<sup>th</sup> days of life) in CPAP group showed no growth on 80% and +ve growth on 16.67 of the patients (klebsiella 10%, CONS 3.33% and strept. viridans 3.33%) while in MV group 63.33% of patients showed no growth and 36.67% showed +ve cultures

(klebsiella 23.33%, CONS 3.33%, Pseudomonus 3.33%, Strept. viridans 3.33% and Staph. aureus 3.33%). The results of +ve late endotracheal cultures was higher in the MV group than in the CPAP group but the comparison is statistically insignificant (Table 3).

**Table (3): Presentation of the results of late endotracheal cultures (in the 5<sup>th</sup> day of life) in both groups of study.**

	Late Endotracheal cultures						Chi-square	
	CPAP		MV		Total		X2	P-value
	N	%	N	%	N	%		
No growth	24	80.00	19	63.33	43	71.67	2.815	0.093
Growth	5	16.67	11	36.67	16	26.67	2.815	0.093
- Klebsiella	3	10	7	23.33	10	16.67		
- CO NS	1	3.33	1	3.33	2	3.33		
- Pseudomonus	0	0.00	1	3.33	1	1.67		
- Strept. Viridans	1	3.33	1	3.33	2	3.33		
- Staph.aureus	0	0.00	1	3.33	1	1.67		

NB: one case of CPAP group died before late endotracheal culture was taken.

Table (4): showed the incidence of klebsiella results among the whole population in the two studied groups where it is higher in MV group than the CPAP group in all the cultures but this

comparison is statistically significant only in early endotracheal cultures in 1<sup>st</sup> day of life.

**Table (4): The incidence of Klebsiella results among the whole population in the two studied groups.**

Klebsiella	CPAP/M.V						Chisquare	
	CPAP		MV		Total		X2	P-value
	N	%	N	%	N	%		
Blood culture	2	6.67	5	16.67	7	11.67	1.456	0.228
Early Endotracheal culture	5	16.67	13	43.33	18	30.00	5.079	0.024*
Late Endotracheal culture	3	10.34	7	23.33	10	16.95	1.920	0.166

Comparison between the non infected cases as regard blood cultures, early endotracheal cultures and late endotracheal cultures and their fate in both groups of study showed that the discharged cases in CPAP group are statistically higher than in MV group

as regard no growth results in their blood cultures and early endotracheal cultures (p-value: 0.022 and 0.037 respectively), while it is not significant in the late endotracheal cultures (p-value 0.113) (table 5).

**Table (5): Comparison between the non infected cases as regard blood cultures, early endotracheal cultures and late endotracheal cultures and their fate in both groups of study.**

No growth	FATE										
	CPAP					MV				Chi-Square	
	Discharged		Died			Discharged		Died		X <sup>2</sup>	P-value
	N	%	N	%	N	%	N	%			
Blood cultures	22	88.00	3	12.00	11	57.89	8	42.11	5.218	0.022*	
Early Endotracheal culture (1 <sup>st</sup> day)	20	86.96	3	13.04	6	54.55	5	45.45	4.344	0.037*	
Late Endotracheal culture (5 <sup>th</sup> day)	22	91.67	2	8.33	14	73.68	5	26.32	2.516	0.113	

On the other hand comparison between the infected cases as regard blood culture, early endotracheal cultures and late endotracheal cultures and their fate in both groups of the study showed that

the died cases are higher among MV group than in the CPAP group but this difference is not statistically significant among the cases having +ve growth (Table 6).

**Table (6): Comparison between the infected cases as regard cultures, early endotracheal cultures and late endotracheal cultures and their fate in both groups of study.**

+ve growth	FATE									
	CPAP					MV				Fisher's exact test
	Discharged		Died			Discharged		Died		
	N	%	N	%	N	%	N	%		
Blood cultures	6	80	1	20	6	54.55	5	45.45	0.346	
Early Endotracheal culture (1 <sup>st</sup> day)	6	85.71	1	14.29	11	57.89	8	42.11	0.199	
Late Endotracheal culture (5 <sup>th</sup> day)	4	80	1	20	3	27.27	8	72.73	0.077	

Our results also showed that MV group needed more time on ventilation than the CPAP group and this comparison is statistically significant

whether the patients have negative or positive cultures results (Table 7).

**Table (7) Comparison between the duration on ventilation in relation to the results of cultures in both groups of the study**

Cultures		Duration on Ventilation			T-test	
		N	Mean	SD	T	P-value
-ve blood culture	CPAP	25	7.360	3.581	-2.209	0.033*
	MV	19	13.895	14.259		
+ve Blood culture	CPAP	5	7.600	2.702	-2.377	0.032*
	MV	11	12.818	6.080		
-ve Early Endotracheal culture	CPAP	23	7.565	3.628	-2.390	0.233*
	MV	11	17.000	18.493		
+ve Early Endotracheal culture	CPAP	7	6.857	2.734	-2.412	0.024*
	MV	19	11.474	4.742		
-ve late Endotracheal culture	CPAP	24	6.958	2.274	-3.024	0.004*
	MV	19	10.632	5.387		
+ve late Endotracheal culture	CPAP	5	10.200	6.380	-1.004	0.332
	MV	11	18.455	17.575		

P value < 0.05 were considered significant

#### 4. Discussion

Neonatal respiratory failure consists of several different disease entities, with different pathophysiologies. During the past 30 years technological advances have drastically altered both the diagnostic and therapeutic approaches to newborns requiring mechanical assistance. Treatments have become both patient- and disease-specific. The clinician has numerous choices among the noninvasive and invasive ventilatory treatments that are currently in use (Donn *et al.*, 2003). Concerns about the damaging effects, and expense of conventional mechanical ventilation have led neonatologists to seek new methods of respiratory support for the preterm infant such as non-invasive respiratory support (Millar *et al.*, 2004).

Our study was designed to determine the incidence of nosocomial infections in preterm infants with respiratory distress, if treatment with CPAP compared to treatment with mechanical ventilation.

In our study, the incidence of positive infection in blood cultures, early endotracheal cultures and late endotracheal cultures were higher in MV group more than in the CPAP group. But these comparisons were statistically significant only in the early endotracheal culture. Aurangzeb and Hameed (2003), found that neonatal sepsis is mainly caused by gram-negative organisms, which are developing resistance to commonly used antibiotics. Early onset neonatal sepsis (EOS, occurring in the first 72 hours of life) remains an important cause of illness and death among very low birth weight preterm infants. It was previously reported a change in the distribution of pathogens associated with EOS from predominantly gram-positive to primarily gram-negative organism (Stool *et al.*, 2005).

In our study, blood cultures results in CPAP group were negative in 25 cases, of which 5 patients (20%) showed in early ET cultures colonization by pathogenic gram negative bacilli, 4 cases infected by klebsiella and one by pseudomonas. Two cases had klebsiella, one had staphylococcus aureus, one had citrobacter and one had strept. viridans in blood cultures that was not isolated from ET cultures, suggesting another site for entry of microorganism to blood stream. That means blood cultures were positive in 5 cases that showing no or a different microorganism in early ET cultures.

In MV group; blood cultures results were negative in 19 patients, of them 11 were colonized or infected by different microorganisms in early ET cultures (7 cases infected by klebsiella, 3 cases by Acinetobacter and one by strept. viridans). Klebsiella was isolated from blood cultures of 5 cases. 4 of them did not have klebsiella in early ET cultures and one had blood stream infection, in a patient with

klebsiella in the respiratory tract. Staphylococcus aureus was isolated from blood cultures of 4 cases, all of them did not have staphylococcus aureus in early ET cultures. Strept. viridans and candida were isolated from blood cultures of one case, which did not show candida in the respiratory tract. The total number of cases of the blood stream infection was 11, only one of them showed the same microorganisms in both blood and early ET cultures.

Sanghvi and Tudehope (1997), found that, Gram-negative bacilli (GNB) and coagulase negative staphylococci (CONS) were the most common causes of early onset sepsis and late onset sepsis respectively. Mullett and his colleagues (1998), found that the risk for infection associated with presence of a central venous catheter is the same for each day of exposure (i.e., the same risk on day 5 of presence of the line as on day 30), but the risk associated with ventilatory support increases overtime. Candida sepsis is associated with prolonged antibiotic use before the first episode of nosocomial sepsis and not with birth weight group.

Galanakis *et al.*, (2002), found that, gram-negative bacilli, coagulase-negative staphylococci and streptococci were the most common pathogens: 42%, 34% and 17% respectively. Premature rupture of membranes was the main risk factor for early-onset sepsis and respiratory distress syndrome was the main risk factor for late-onset sepsis. Device use was the major risk factor for acquiring ventilator-associated pneumonia, central venous catheter related blood stream infection and urinary catheter associated urinary tract infection (Van der Kooi, 2007).

In our study, the incidence of Klebsiella results among the whole population in the two studied groups were higher in MV group more than in the CPAP group in all the cultures but this comparison was statistically significant only in early endotracheal cultures in 1<sup>st</sup> day of life.

Abdel-Hady *et al.* (2008), found that extended spectrum beta-lactamase producing Klebsiella pneumoniae is an important cause of nosocomial infections in neonatal intensive care units. The organism gains access to the body either by direct inoculation through breached epithelial surfaces or following aspiration of oropharyngeal organisms (Umeho *et al.*, 2006). Pena *et al.* (2001), demonstrated that klebsiella pneumonia bacteraemia occurring in an epidemic ICU setting is mainly catheter-related.

Klebsiella outbreaks mainly affected premature neonates with intravenous catheters, mechanical ventilation, or both. The high mortality rate was notable. Resistance to multiple antibiotics,

but mainly to broad-spectrum beta-lactam antibiotics, was observed (Ayan *et al.*, 2003).

In our study we found that the number of infected cases decrease between early endotracheal cultures results (in the 1<sup>st</sup> day of life) and the late endotracheal cultures results (in the 5<sup>th</sup> day of life) in both groups of the study.

In comparing the relationship between the blood cultures results versus the fate of patients between both of the study groups in our study, we found that death among MV group is higher than death among CPAP group. These differences were not statistically significant among cases having positive cultures results but statistically significant in cases having negative blood cultures results. On the other hand comparison of the relationship between the early and late endotracheal cultures results versus the fate of patients between both of the study groups we found that death among MV group is higher than death among CPAP group, but these differences were not statistically significant among the cases having positive or negative cultures results.

Benjamin *et al.*, (2004), found that among premature infants, much of mortality experienced in gram-negative rod bacteremia (GNR) is due to infection with pseudomonas rather than enteric GNR. race, the need for mechanical ventilation, and younger post conception age when the blood culture was obtained were also strongly associated with mortality.

In our study we found that in patients having negative cultures results, MV patients needed longer duration on ventilation than patients on CPAP. These comparison were statistically significant whether the cultures were taken from the blood, early endotracheal or late endotracheal. Also, within cases having positive cultures results, MV patients needed longer duration on ventilation than patients on CPAP. These comparisons were statistically significant whether the cultures were taken from the blood, or early endotracheal but not with late endotracheal.

Kneyber *et al.* (2005), observed that, in ventilated infants a low occurrence of concurrent bacterial pulmonary infection, but infants with positive cultures needed prolonged ventilatory support. Couto *et al.* (2006), decided that invasive device use and duration of use continue to greatly influence the development of nosocomial infection in NICUs.

Within the same group, the results of blood and early endotracheal cultures whether positive or negative did not have a statistically significant difference on the duration of ventilation. Cases with positive late endotracheal cultures expressed statistically significant longer duration on ventilation than cases with negative late endotracheal cultures

only in MV group. Also in our study we found that, the patients who died in both groups of the study needed more days on the ventilation than the patients who had been discharged. These comparisons were statistically significant in MV group.

Stoll *et al.* (2002), found that late-onset sepsis remains an important risk factor for death among VLBW preterm infants and for prolonged hospital stay among VLBW survivors.

In conclusion, the present study revealed that nosocomial infections are one of the common complications encountered in the neonatal intensive care unit. The incidence of positive infection in blood cultures and endotracheal cultures results were higher in the MV group than in the CPAP group. The incidence of klebsiella results among the whole population in the two studied groups were also higher in MV group than in the CPAP group in all the cultures within the cases having positive culture results, MV patients needed longer duration on ventilation than patients on CPAP contributing to an increased cost of health care.

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