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Effect of Vitamin D3 (Cholecalciferol) Administration as an Adjuvant Therapy in Preterm Neonates with Respiratory Distress Syndrome

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Abstract

Background: RDS is one of the major problems among newborns and a major reason for increased morbidity and mortality among infants. Preterm babies are the main risk factor for development of RDS. Vitamin D is a steroid hormone that has been known for its important role in regulating body levels of calcium and phosphorus and in mineralization of bone. Since vitamin D deficiency may have a role in several diseases involving the respiratory system as respiratory distress syndrome, we hypothesized that vitamin D3 administration may have a role in improvement of respiratory distress syndrome in preterm neonates.

Aim of Study: It was to evaluate the effect of Vitamin D as an adjuvant therapy in treatment of respiratory distress syndrome.

Patients and Methods: This study was conducted on 60 preterm neonates, their ages ranged between 28 weeks to 36 weeks gestation according to New Ballard Score. They were chosen from those at the Neonatal Intensive Care Unit (NICU), Pediatric department, Tanta University Hospital. They were allocated into three groups (20 each), Group 1 given the traditional therapy of RDS, Group 2 given vitamin D in the low ideal dose (400IU/Day) in addition to the traditional therapy of RDS, Group 3 given vitamin D in the high ideal dose (800 IU/Day) in addition to the traditional therapy of RDS. All preterm neonates were subjected to complete history taking, thorough clinical examination, routine laboratory investigations in addition to serum 25-hydroxyvitamin D by ELISA techniques, chest X-ray at the first 24 hours after delivery. Follow-up of the three groups was done at day 1, 3 and 7 of admission. At Day 21 of Life: Blood samples were taken from the serum of infants again for measuring the serum 25-hydroxyvitamin D level. Data was analyzed by using SPSS.

Results: There was statistical significant increase as regard vitamin D level after treatment in group 3 as compared to group 2 as the difference increase value in group 3 (Mean ± SD=75.719±18.231) was higher than in group 2 (Mean ± SD =43.453±14.728). There was significant improvement in the ABG findings, chest X-ray findings, Down's Score value in group 2,3 but especially in the group 3 of the intake of 800 IU/Day at day seven of admission. There was high statistical significant decrease as regarding the hospital stay duration in group 3 as compared to group 1. There was statistical significant decrease in the morbidity between the three studied groups as group 3 was lower than group 2 and group 2 was lower than group 1. There was no significant difference between all the studied groups as regard the number of died cases.

Conclusion: 25 hydroxy-vitamin D level was found deficient in most cases of RDS in preterm neonates and administration of Vitamin D as an adjuvant therapy in cases of RDS was associated with decreased severity, complications and days of hospital stay in the group that received 800 IU/Day more than the group that received 400 IU/Day.

Key Words: *Respiratory Distress Syndrome – Down's score – 25 hydroxy-vitamin D by ELISA.*

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Introduction

PREMATURE births are responsible for 70% of neonatal mortality, 36% of infant mortality and 25-50% of long-term neurological disabilities. In the last 20 years with the scientific and technological developments observed in the field of neonatology, the survival rate of premature infants has significantly increased [1].

Neonates born before term can have many complications such as respiratory distress syndrome (RDS), intraventricular hemorrhage, necrotizing enterocolitis, bronchopulmonary dysplasia, sepsis, persistent ductus arteriosus and retinopathy [2].

RDS is one of the major problems among newborns and a major reason for increased morbidity and mortality among infants. Preterm babies are the main risk factor for development of RDS [3].

Respiratory distress in the newborn may present as apnea, cyanosis, grunting, inspiratory stridor, nasal flaring, poor feeding, tachypnea and intercostal, subcostal or suprasternal retractions [4].

Vitamin D is a steroid hormone that has been known for its important role in regulating body levels of calcium and phosphorus and in mineralization of bone [я].

Vitamin D deficiency among pregnant women increases the risk of vitamin D deficiency among their off springs [6]. Antenatal vitamin D supplementation increases neonatal 25 (OH) D levels [7].

Serum levels of 25-hydroxyvitamin D are considered the best circulating biomarker of vitamin D metabolic status and reflect contributions from all sources of vitamin D i.e., diet and sun exposure [8].

Animal studies strongly suggest that vitamin D plays a role in lung maturation during the saccular and alveolar stages of lung development late in pregnancy and support earlier observations such as the association of respiratory distress in vitamin D deficient preterm infants (rachitic respiratory distress) [9].

Moreover, in fetal rat lung, vitamin D increases the synthesis and secretion of surfactant lipids and proteins in alveolar type II cells [10].

Patients and Methods

After research ethical committee approval from research center of Tanta University an informed written parental consent was taken from all the participants in this research. This Prospective Case-Control study was conducted on 60 preterm neonates, their ages ranged between 28 weeks to 36 weeks gestation according to New Ballard Score. Cases were chosen from those at the neonatal intensive care unit (NICU), pediatric department, Tanta University Hospital in the period from March 2017 to December 2017.

They were allocated into three groups (20 each), Group 1 given the traditional therapy of RDS (O_2 therapy, assisted ventilation and surfactant therapy), Group 2 given vitamin D in the low ideal dose (400 IU/Day) in addition to the traditional therapy of RDS, Group 3 given vitamin D in the high ideal dose (800 IU/Day) in addition to the traditional therapy of RDS.

Inclusion criteria were: Preterm newborn (<37 weeks gestation) with respiratory distress syndrome admitted to NICU showing clinical signs of respiratory distress e.g. tachypnea, retractions, grunting, cyanosis and chest X-ray findings of respiratory distress syndrome as fine reticulo-granular mottling, ground glass appearance and white Lung.

Exclusion criteria were: Preterm with neonatal sepsis, Newborn with hypoxia, with congenital malformations, with intolerance of feeding, newborn of diabetic mother and full term newborn.

All preterm neonates were subjected to the following:

1- Complete history taking including obstetric history (perinatal, natal and post-natal history) with stress on any medical treatment given during pregnancy and maternal diseases, gestational age and cause of incubation.
2- Thorough clinical examination including assessment of gestational age (GA), weight, length, head circumference, vital measurements (pulse, blood pressure, temperature, respiratory rate and O_2 saturation) and neurological reflexes.
3- Laboratory investigations including complete blood count, c-reactive protein, liver function tests, renal function tests, random blood sugar, serum Na, K, ABG, serum 25-hydroxyvitamin D by ELISA technique. Blood samples were taken form the serum of infants in the first 24 hrs for measuring the serum 25 hydroxy vitamin D level by ELISA kits.
4- Chest X-ray.

Follow-up of the three groups:

At Day 1 , 3 and 7: The groups were evaluated by down's score, arterial blood gases, chest X-ray, hospital stay duration, morbidity & mortality.

At Day 2 1 of Life: Blood samples were taken from the serum of infants again for measuring the serum 25 hydroxy vitamin D level by ELISA kits.

Statistical presentation and analysis of the present study was conducted using the mean, standard deviation, student *t*-test, Chi-square, F-test (ANOVA), Pearson coefficient, Spearman coefficient, Paired *t*-test by IBM SPSS software package version 20. p-value (≤ 0.05) is significant , p-value (>0.05) not significant, p-value (<0.01) is highly Significant.

Results

This table shows : There was no significant difference between all the studied groups as regard the birth weight, length, head circumference, sex and natal history while there was significant increase in performing ceserean section as mode of delivery in comparison to the normal vaginal delivery in all the studied groups.

This table shows: There was statistical significant increase in group 2 as regard vitamin D level

after treatment as compared to before treatment, there was statistical significant increase in group 3 as regard vitamin D level after treatment as compared to before treatment and there was statistical significant increase as regard vitamin D level after treatment in group 3 as compared to group 2 as the difference in group 3 (Mean ± SD=75.719 ± 18.231) was higher than in group 2 (Mean ± SD =43.453± 14.728).

This table shows that: There was no statistical significant difference in the PH value between groups 1, 2 and 3 at day one of admission, there was no statistical significant difference in the PH value between groups 1,2 and 3 at day three of admission, there was statistical significant difference in the PH value between groups 1,2 and 3 at day seven of admission, there was statistical significant increase in the PH value in group 3 as compared to group 1 at day seven of admission, there was no statistical significant difference in the PH value in group 1 between day one, three and seven of admission, there was statistical significant increase in the PH value in group 2 at day seven as compared to day one, there was statistical significant increase in the PH value in group 3 at day three as compared to day one, at day seven as compared to day three and high significant increase in the PH value at day seven as compared to day one.

This table shows that: There was no statistical significant difference in the PaO_2 value between groups 1,2 and 3 at day one of admission, there was no statistical significant difference in the PaO_2 value between groups 1,2 and 3 at day three of admission, there was statistical significant difference in the PaO_2 value between groups 1,2 and 3 at day seven of admission, there was statistical significant increase in the PaO_2 value in group 3 as compared to group 1 at day seven of admission, there was no statistical significant difference in the PaO_2 value in group 1 between day one, three and seven of admission, there was statistical significant increase in the PaO_2 value in group 2 at day three as compared to day one and at day seven as compared to day one, there was statistical significant increase in the PaO_2 value in group 3 at day three as compared to day one, at day seven as compared to day three and high significant increase in the PaO_2 value at day seven as compared to day one.

This table shows that: There was no statistical significant difference in the $PaCO_2$ value between groups 1,2 and 3 at day one of admission, there was no statistical significant difference in the $PaCO_2$ value between groups 1,2 and 3 at day three of admission, there was statistical significant difference in the $PaCO_2$ value between groups 1, 2 and 3 at day seven of admission, there was statistical significant decrease in the $PaCO_2$ value in group 2 as compared to group 1 at day seven of admission and in group 3 as compared to group 1 at day seven of admission, there was no statistical significant difference in the $PaCO_2$ value in group 1 between day one, three and seven of admission, there was statistical significant decrease in the $PaCO_2$ value in group 2 at day three as compared to day one and at day seven as compared to day one, there was statistical significant decrease in the $PaCO_2$ value in group 3 at day seven as compared to day three, high significant decrease in the $PaCO_2$ value at day three as compared to day one and at day seven as compared to day one.

This table shows that: There was no statistical significant difference in the down score between groups 1,2 and 3 at day one of admission, there was no statistical significant difference in the down score between groups 1,2 and 3 at day three of admission, there was statistical significant difference in the down score between groups 1,2 and 3 at day seven of admission, there was statistical significant decrease in the down score in group 3 as compared to group 1 at day seven of admission, there was no statistical significant difference in the down score in group 1 between day one, three and seven of admission, there was statistical significant decrease in the down score in group 2 at day seven as compared to day one, there was high statistical significant decrease in the down score in group 3 at day three as compared to day one, at day seven as compared to day one and at day seven as compared to day three.

This table shows: There was statistical significant difference as regarding the hospital stay between the three studied groups (p-value <0.001), there was statistical significant decrease as regards the hospital stay in group 2 as compared to group 1 (p-value=0.014), there was high statistical significant decrease as regards the hospital stay in group 3 as compared to group 1 (p-value<0.001).

This table shows: There was no statistical significant difference as regards the grades of RDS between the three studied groups at day one of treatment, there was no statistical significant difference as regards the grades of RDS between the three studied groups at day three of treatment, there was statistical significant difference as regards the grades of RDS at day seven of treatment in

group 3 as compared to group 1 ($p2$ value=0.004*), there was no statistical significant difference as regards the grades of RDS in group 1 between day one, three and seven of admission, there was statistical significant difference as regards the grades of RDS in group 2 at day seven as compared to day one (p-value=0.038), there was statistical significant difference as regards the grades of RDS in group 3 at day three as compared to day one (p-value=0.041) and high statistical significant difference at day seven as compared to day one (p-value <0.001).

This table shows: There was statistical significant decrease in the morbidity between the three studied groups as group 3 was lower than group 2 and group 2 was lower than group 1 and the complications were in the form of 2 cases of BPD, 7 cases of pneumothorax and 3 cases of ventilator acquired pneumonia.

Table (1) : Demographic data of the studied groups.

	Groups						Chi-Square or ANOVA	
	Group I		Group II		Group III		X^2 or F	p-value
Sex:								
Male	12	60.00	13	65.00	13	65.00	0.144	0.931
Female	8	40.00	7	35.00	7	35.00		
Natal history:								
Negative	8	40.00	7	35.00	6	30.00	0.440	0.803
Positive	12	60.00	13	65.00	14	70.00		
Mode of delivery:								
CS	11	55.00	12	60.00	18	90.00	6.624	0.036*
NVD	9	45.00	8	40.00	2	10.00		
Birth weight:								
Range	2000–2500		950–2600		800–2800		2.809	0.069
Mean ±SD	2140.000 ± 127.321		1792.500 ± 516.638		1950.000 ± 603.062			
Length:								
Range	35–45		35–45		35-45		0.012	0.988
Mean ±SD	39.400±3.169		39.550±3.017		39.500±3.086			
HC:								
Range	27–32		27–32		27-32		0.022	0.978
Mean ±SD	29.450± 1.468		29.350± 1.565		29.400± 1.501			

Table (2): Vitamin D level before and after treatment in the studied groups.

Vitamin D (ng/ml)	Groups			ANOVA or t-test	
	Group I	Group II	Group III	F or t	p-value
Before ttt:					
Range	11.6–37.5	4.856–32.342	3.5–39.545	0.805	0.452
Mean ± SD	19.923±6.856	16.512±7.887	17.994± 10.434		
After ttt:					
Range	x–x	39.45–100.119	61.651–120.645	–6.353	<0.001*
Mean ± SD	x±x	59.966± 17.207	93.713± 16.380		
Differences:					
Mean ± SD		–43.453± 14.728	–75.719± 18.231		
Paired test:					
p-value		<0.001*	<0.001*		

Table (3): PH values in the studied groups.

PH	Groups			ANOVA		TUKEY'S Test		
	Group I	Group II	Group III	F	*p*-value	I&II	I&III	II&III
Day one:								
Range	7.25–7.5	7.25–7.5	7.25–7.5	0.487	0.617			
Mean ±SD	7.317±0.060	7.325±0.070	7.304±0.068					
Day Three:								
Range	7.25–7.41	7.27–7.41	7.25–7.45	2.025	0.141			
Mean ±SD	7.325±0.054	7.338±0.059	7.362±0.062					
Day Seven:								
Range	7.29–7.41	7.3–7.41	7.33–7.41	4.489	0.016*	0.412	0.012*	0.212
Mean ±SD	7.349±0.053	7.368±0.047	7.392±0.023					
1&3:								
Differences	–0.009±0.046	–0.013±0.056	–0.058±0.078					
Paired test	0.420	0.310	0.004*					
1&7								
Differences	–0.028±0.067	–0.037±0.072	–0.087±0.071					
Paired test	0.100	0.041 *	<0.001 *					
3&7								
Differences	–0.018±0.041	–0.023±0.061	–0.035±0.056					
Paired test	0.095	0.130	0.014*					

Table (4): PaO2 values in the studied groups.

PaO_2	Groups			ANOVA		TUKEY'S Test		
	Group I	Group II	Group III	F	*p*-value	I&II	I&III	II&III
Day one:								
Range	40–68	40–68	40–68	1.341	0.270			
Mean ±SD	50.450±8.745	53.600±8.506	49.300±8.542					
Day Three:								
Range	40–80	45-80	40–80	1.566	0.218			
Mean ±SD	56.100±14.108	63.150±14.061	62.200±12.800					
Day Seven:								
Range	45-77	49-80	50–80	3.234	0.048*	0.490	0.038*	0.352
Mean ±SD	61.706±11.794	66.111±12.966	71.316±9.105					
1&3:								
Differences	–5.650±16.135	–9.550±17.383	–12.900±15.269					
Paired test	0.134	0.024*	0.001 *					
1&7								
Differences	–11.647±12.855	–12.000±17.473	–22.474±13.705					
Paired test	0.078	0.010*	<0.001 *					
3&7								
Differences	–4.118±12.454	–3.500±15.163	–9.263±15.036					
Paired test	0.192	0.341	0.015*					

Table (5): PaO2 values in the studied groups.

PaO_2	Groups			ANOVA		TUKEY'S Test		
	Group I	Group II	Group III	F	*p*-value	I&II	I&III	II&III
Day one:								
Range	32–75	32–75	38–75	1.582	0.214			
Mean ±SD	53.350± 10.747	54.550± 12.137	59.500± 11.839					
Day Three:								
Range	40–75	40–70	32–75	1.813	0.173			
Mean ±SD	52.550± 12.011	49.800± 11.091	45.650± 11.495					
Day Seven:								
Range	38–63	38–50	38–47	8.214	0.001*	0.023 *	0.001*	0.441
Mean ±SD	48.941 ±9.959	42.944±4.988	40.316±2.790					
1 &3:								
Differences	0.800± 10.390	4.750±9.147	13.850± 13.831					
Paired test	0.734	0.031 *	<0.001 *					
1&7								
Differences	3.353 ± 12.728	10.000± 11.530	19.000± 11.363					
Paired test	0.293	0.002*	<0.001 *					
3&7								
Differences	1.941 ±7.318	4.611 ±9.853	6.053± 10.135					
Paired test	0.290	0.063	0.018*					

Table (6): Down score in the studied groups.

Down score	Groups			ANOVA		TUKEY'S Test		
	Group I	Group II	Group III	F	*p*-value	I&II	I&III	II&III
Day one:								
Range	5–9	4–9	4–10	0.392	0.677			
Mean ±SD	6.750± 1.446	6.450± 1.572	6.900± 1.861					
Day Three:								
Range	4–10	3–10	4–9	1.069	0.350			
Mean ±SD	6.350± 1.814	5.800± 1.936	5.550± 1.538					
Day Seven:								
Range	3–10	2–8	2–8	4.755	0.013*	0.055	0.014*	0.861
Mean ±SD	6.235±2.796	4.611 ± 1.614	4.263 ± 1.485					
1 &3:								
Differences	0.400± 1.353	0.650± 1.513	1.350± 1.268					
Paired test	0.202	0.070	<0.001 *					
1&7								
Differences	0.412±2.526	1.667± 1.188	2.632± 1.383					
Paired test	0.511	<0.001 *	<0.001 *					
3&7								
Differences	–0.235±1.480	0.833 ± 1.857	1.105±0.737					
Paired test	0.522	0.059	<0.001 *					

Table (7): Days of hospital stay in the studied groups.

Hospital Stay (days)	Groups			ANOVA		TUKEY'S Test		
	Group I	Group II	Group III	F	*p*-value	I&II	I&III	II&III
Range	4–24	3–16	2–8	11.145	<0.001 *	0.014*	<0.001 *	0.193
Mean ±SD	11.500±6.549	7.350±3.717	4.850±2.007					

Table (8): Radiological grades of RDS in the studied groups.

CXR	Groups								Chi-Square	
	Group I		Group II		Group III		Total			
	N	%	N	%	N	%	N	%	X^2	*p*-value
Day One:										
I	2	10.00	3	15.00	2	10.00	7	11.67	2.510	0.867
II	9	45.00	8	40.00	5	25.00	22	36.67		
III	5	25.00	5	25.00	7	35.00	17	28.33		
IV	4	20.00	4	20.00	6	30.00	14	23.33		
Day Three:										
I	5	25.00	6	30.00	7	35.00	18	30.00	2.674	0.848
II	8	40.00	7	35.00	7	35.00	22	36.67		
III	3	15.00	4	20.00	1	5.00	8	13.33		
IV	4	20.00	3	15.00	5	25.00	12	20.00		
Day Seven:										
I	3	17.65	10	55.56	13	68.42	26	48.15	15.064	p_1 0.105
II	9	52.94	6	33.33	2	10.53	17	31.48		0.020* p^2 0.004*
III	1	5.88	1	5.56	3	15.79	5	9.26		p_3 0.339
IV	4	23.53	1	5.56	1	5.26	6	11.11		
p-value:										
1&3	0.605		0.724		0.053*		0.041 *			
1&7	0.450		0.038*		0.002*		<0.001 *			
3&7	0.723		0.286		0.042*		0.214			

Table (9): Morbidity of the studied groups after treatment (Broncho-Pulmonary dysplasia, pneumothorax, ventilator-acquired pneumonia).

Morbidity	Groups								Chi-Square	
	Group I		Group II		Group III		Total			
	N	%	N	%	N	%	N	%	X^2	*p*-value
No	13	65.00	16	80.00	19	95.00	48	80.00	6.194	0.045*
Yes	7	35.00	4	20.00	1	5.00	12	20.00		
Total	20	100.00	20	100.00	20	100.00	60	100.00		

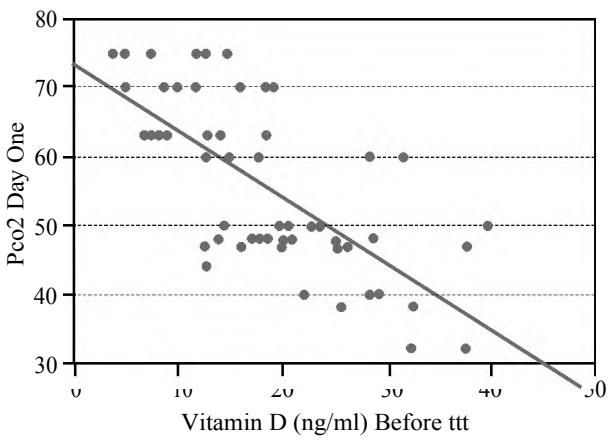

Fig. (1): Significant negative correlation between Vitamin D level before treatment and $PaCO_2$ at day one of admission.

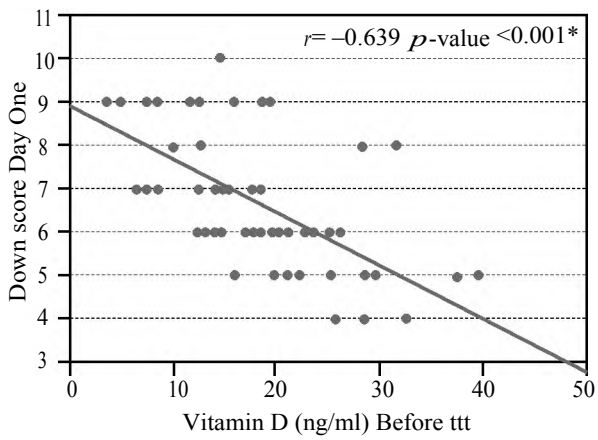

Fig. (2): Significant negative correlation between Vitamin D level before treatment and Down score at day one of admission.

Discussion

In the present study, as regards the mode of delivery, there was significant increase in performing Ceserean section (68.33 %) as mode of delivery in comparison to the normal vaginal delivery (31.67%) in all the studied groups (p-value0.036 <0.05).

This comes in agreement with Heinzmann et al., (2009) **[11]** as they suggested that caesarean section is an additional risk factor of neonatal respiratory distress. Also it Comes in agreement with Anadkat et al., (2012) **[12]** as he studied 895 preterm newborn diagnosed with RDS, 57.2% were delivered by Ceserean section and they defined the cesarean section as an independent predictor of RDS. This also comes in agreement with Qari et al., (2018) **[3]** as their study was conducted on 395 RDS patients and the mode of delivery was Ceserean section in (63.3%) and normal vaginal delivery in (35.6%).

Also in the present study we found that a high percentage of the studied preterm newborns with RDS had either vitamin D deficiency or insufficiency as 25 (41.67%) of the studied patients had serum 25-OHD level at day one below 15ng/ml (Vitamin D deficiency), 15 (25%) of the patients had serum 25-OHD level at day one between 15 -20ng/ml (Vitamin D insufficiency) and 33.3% of the patients had serum 25-OHD level at day one between 20-100ng/ml (normal vitamin D level).

This also comes in agreement with Boskabadi et al., (2018) **[13]** as this study was conducted on 160 preterm infants weighing less than 2000 grams and born at less than 34 weeks' gestation. Serum vitamin D levels were measured in preterm infants without and those with respiratory distress. The prevalence of severe (10ng/ml), moderate (10-20 ng/ml) and mild vitamin D deficiencies were 33.7%, 28.7%, and 17.5% in the control group and the frequencies in preterm infants with respiratory distress were 56.2 %, 32.5 %, 6.2 %, respectively. The frequency of vitamin D deficiencies was significantly higher in the case group (p=0.001).

In a review study in 2015, Lykkedegn et al., (2015) **[10]** reported that vitamin D had positive effects on alveolar type II cells, fibroblast proliferation, surfactant synthesis and alveolarization. These findings support the hypothesis that vitamin D deficiency is a common and modifiable risk factor for BPD and RDS.

As regards the given dose in the present study, Vitamin D3 was given to group 2 as 400 IU/Day & group 3 as 800 IU/Day. This comes in agreement with the recommended dose of Vitamin D by the American Academy of Pediatrics which was 400 IU/Day (Wagner and Greer, 2008) **[14]**. While The European Society for Pediatric Gastroenterology, Hepatology and Nutrition has recommended higher intakes of vitamin D of 800-1000 IU/day for preterm infants, Although this vitamin D intake is likely safe, no data are available for very low birth weight infants and especially infants with birth weight <1000g to assess the safety of providing these vitamin D intakes (Agostoni et al., 2010) **[15]**, (Braegger et al., 2013) **[16]**.

However, Aly and Abdel-Hady (2015) **[17]**, concluded that the upper tolerable intake for healthy full term infants is around 1000IU/day. Upper intake for preterm infants is not known.

Fort et al., (2016) **[18]** undergone randomized controlled trial on 100 infants with gestational age between 23 and 27 weeks demonstrated that the 800IU/d dose of vitamin D supplementation prevented vitamin D deficiency, without toxicity, with concentrations above the desired 25 (OH) D range of 20-60ng/ml in the majority of infants on day 28, giving us the safety to use the 800IU/Day as the high ideal dose.

In the present study, as regards the ABG findings there was a significant improvement in all the parameters in groups 2,3 but especially in the group 3 with the intake of 800IU/Day.

This comes in agreement with Backstrom et al., (1999) **[19]** who compared 39 premature neonates with a gestational age of <33 weeks who received vitamin D at doses 200IU/day or 960 IU/day up to 3 months of age. The number of ventilator days in patients receiving high-dose vitamin D had a significant decrease (0 days versus 4 days (p<0.001) and also, the time required for supportive oxygen therapy was 2 days versus 14 days (p=0.006). In addition, respiratory acidosis was more common in the group receiving low doses of vitamin D.

In the present study as regards the Down Score:

There was significant improvement in the Down Score value in groups 2,3 but especially in the group 3 with the intake of 800IU/Day at day seven of admission, although we found no studies with or against our findings as regards the down score.

In the present study as regards the chest X-ray findings:

There was significant improvement in the chest X-ray findings in groups 2,3 but especially in the

group 3 having the intake of 800 IU/Day at day seven of admission, although we found no studies with or against our findings as regarding the chest X-ray findings.

In the present study we found as regards the hospital stay:

There was statistical significant decrease as regards the hospital stay in group 2 as compared to group 1 (p-value=0.014) and there was high statistical significant decrease as regards the hospital stay in group 3 as compared to group 1 (p value<0.001).

In the present study we found as regards the morbidity which includes the expected complications as (Broncho-Pulmonary dysplasia, pneumothorax, Ventilator-acquired pneumonia): There was statistical significant decrease in the morbidity between the three studied groups as group 3 was lower than group 2 and group 2 was lower than group 1 (p-value=0.045). We found no studies with or against our findings in decreasing the morbidity between our three studied groups with our recommended vitamin D doses intake.

However, we found some studies which proves that the severity of BPD was inversely related to 25-OHD level.

Kazzi et al., (2018) **[20]** conducted a Prospective, observational study on 89 VLBWI (≤ 1250 g). S-25OHD (day one and 21) and respiratory severity score (RSS=FiO2 x MAP) (day one) were examined. Other respiratory morbidities including BPD were compared between infants with S-25OHD ≤ 10ng/ml (deficient) versus >10ng/ml (adequate).

On day one, increasing RSS was inversely related to S-25OHD, trend (p=0.054), Compared to the adequate group, the deficiency group had higher RSS (5.0±2.7 vs 3.6± 1.9), required surfactant therapy more frequently (91% vs 72%) and needed home oxygen therapy more often (48% vs 26%) (p≤0.05), were more likely to develop ventilator-associated pneumonia (p=0.042), required support with mechanical ventilation for a longer duration (p=0.067). Among infants with BPD, the severity of disease was inversely related to S-25OHD, trend (p<0.09).

Conclusion:

Our study concluded that 25 hydroxy-vitamin D level was found deficient in most cases of RDS in preterm neonates and administration of Vitamin D as an adjuvant therapy in cases of RDS was associated with decreased severity, complications and days of hospital stay in the group who received 800 IU/Day more than the group which received 400 IU/Day.

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Conflicts of interest:

No conflicts of interest declared.

Authors' Contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing. All authors have approved the final article work.

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تأثير إعطاء فيتامين (د) كعامل مساعد فى علاج الأطفال حديثى الولادة ناقصى النمو المصابين بمتلازمة الضائقة التنفسية

تساهم الولادة المبكرة بقدر كبير من وفيات الأطفال حديثى الولادة وذلك نتيجة المضاعفات المبكرة والمتأخرة التى تحدث لهذا المرض، متلازمة الضائقة التنفسية هى السبب الرئيسى للأمراض والوفيات فى الأطفال حديثى الولادة ناقصى النمو، أثبتت الدراسات وجود إرتباط بين إنخفاض مستوى ٢٥ هيدروكسى فيتا مين د فى دم الحبل السرى عند الولادة وزيادة خطر الإصابة بأمراض الجهاز التنفسى لاحقاً مثل الربو ومرض الإنسداد الرئوى المزمن.

الهدف من العمل: هو تقييم تأثير فيتامين (د) كعلاج مساعد فى علاج متلازمة الضائقة التنفسية لدى الأطفال حديثى الولادة ناقصى النمو.

المرضى وطرق البحث: أجريت هذه الدراسة على ٦٠ من الأطفال حديثى الولادة نا قصى النمو فى

وحدة العناية المركزة لحديثى الولادة بقسم طب الأطفال ، مستشفى جامعة طنطا وتتراوح أعمادهمبين ٢٨ أسبوعاً إلى ٣٦ أسبوعاً من الحمل بإستخدام مقياس بالارد المعدل New Ballard Score. وتم تقسيم الأطفال إلى ثلاث مجموعات:

المجموعة الإولى: تشمل هذه المجموعة ٢٠ من الأطفال حديثى الولادة ناقصى النمو المشخصون بمتلازمة الضائقة التنفسية وتم إعطائهم العلاج المتعارف عليه للمرض.

المجموعة الثانية: تشمل هذه المجموعة ٢٠ من الأطفال حديثى الولادة ناقصى النمو المشخصون بمتلازمة الضائقة التنفسية وتم إعطائهم فيتامين (د) فى جرعة مثالية منخفضة (٨٠٠ وحدة دولية/يوم) بالإضافة إلى العلاج المتعارف عليه للمرض.

المجموعة الثالثة: تشمل هذه المجموعة ٢٠ من الأطفال حديثى الولادة ناقصى النمو المشخصون بمتلازمة الضائقة التنفسية وتم إعطائهم فيتامين (د) فى جرعة مثالية عالية (٨٠٠ وحدة دو لية/يوم) بالإضافة إلى العلاج المتعارف عليه للمرض. تم إخضاع جميع الحالات إلى ما يلى: تاريخ مرضى شامل، الفحص الإكلينيكى، التحاليل الروتينية بالإضافة إلى نسبة ٢٥- هيدروكسى فيتامين د عن طريق تقنية (ELISA) وأيضاً الأشعة السينية الصدر. تمت هذه الخطوات فى ال ٢٤ ساعة بعد الولادة. تمت متابعة الحالات فى اليوم الأول، الثالث والسابع من دخول الطفل الحضانة. تم قياس مستوى ٢٥- هيدروكسى فيتامين د بالدم مرة أخرى فى اليوم الواحد والعشرين من دخول الطفل الحضانة.

النتائج: تبين وجود فروق إحصائية بمستوى ٢٥- هيدروكسى فيتامين د بالدم بعد العلاج بين المجموعة الثانية والثالثة، حيث تبين وجود إرتفا ع ملحوظ فى مستوى فيتامين د فى المجموعة الثالثة عن المجموعة الثانية، تبين وجود تحسن إحصائى كبير ذات دلالة فى المجموعة الثالثة بعد العلاج من حيث نسبة الغازات بالدم، مقياس دوران (Wown score) تدرج المرض بالأشعة السينية بالصدر فى اليوم السابع بعد بدأ العلاج، تبين وجود إنخفاض إحصائى كبير ذات دلالة من حيث عدد أيام الإقامة بالمستشفى ونسبة المرضية فى المجموعة الثالثة عند المقارنة بالمجموعة الأولى بعد العلاج، تبين عدم وجود فروق إحصائية بين المجموعات الثلاث من حيث عدد الحالات المتوفاه.

الإستنتاج: تبين وجود إنخفاض بمستوى ٢٥- هيدروكسى فيتامين د بالدم فى عدد كبير من الحالات المصابة بمتلازمة الضائقة التنفسية، ساعد إستخدام فيتامين (د) كعامل مساعد فى متلازمة الضائقة التنفسية عند إستخدامه بجرعة ٨٠٠ وحدة دولية باليوم فى إنخفاض شدة المرض، إنخفاض نسبة المضاعفات وتقليل عدد أيام الإقامة بالمستشفى بنسبة أكبر من التى وجدت عند إستخدامه بجرعة ٤٠٠ وحدة دولية باليوم.

التوصيات: ينصح بقياس مستوى ٢٥- هيدروكسى فيتامين د بالدم فى كل الأطفال حديثى الولادة ناقصى النمو المصابين بمتلازمة الضائقة التنفسية. نوصى بالمزيد من الدراسات لتأكيد فاعلية فيتامين د بالجرعات المختلفة عند إستخدامه كعلاج مساعد فى متلازمة الضائقة التنفسية لدى الأطفال حديثى الولادة ناقصى النمو.