

COMPARISON BETWEEN LOW AND HIGH DOSES OF PROPHYLACTIC VITAMIN D IN PREVENTION OF OSTEOPENIA OF PREMATURITY

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Introduction

- Osteopenia of prematurity (OOP) is a term used to describe a reduction in bone mineral content (BMC) of the preterm infant. Its incidence has been steadily increasing with the survival of more premature neonates as a result of advances in neonatal care. The prevalence of metabolic bone disease is inversely associated with birth weight and gestational age. Up to a third of infants weighing less than one kilogram at birth are osteopenic, more so if they are breastfed.
- To develop normally, the skeleton of the fetus requires active materno-fetal transfer of protein, Calcium (Ca) and phosphorus (P). Bone mineralization which occurs predominantly during the third trimester will be inadequate if the fetal increased demands in Ca and P are not met. During pregnancy augmented maternal intestinal absorption and increased skeletal mobilization increase maternal Ca supply to the fetus.
- Factors that impede normal bone mineralization include inadequate postnatal intake of vitamin D, calcium (Ca) and phosphorus (P), extended periods of total parenteral nutrition, and also as a side effect of diuretics and corticosteroids prescribed to these infants. Poor bone mineralization is associated with common neonatal conditions. These include sepsis, bronchopulmonary dysplasia, cerebral pathology, acidosis, necrotizing enterocolitis and cholestasis.
- Depending on the severity of the demineralization, osteopenia can remain clinically silent or, if severe, can cause bone changes in the form of rarefaction, fraying, cupping, subperiosteal new bone formation or even fractures.
- Recommendations for vitamin D supply in preterms are different in Europe and America. The European Society of Pediatric Gastroenterology and Nutrition (ESPGAN) recommend dose of 800-1600 IU/d.(15) The American Academy of Pediatrics (AAP) recommends 200 IU/d.(16) At Alexandria University Maternity Hospital (AUMH) the rate of preterm infants admission is continually increasing reaching more than 50% in the year 2019, and the exact incidence of OOP remains unclear, as a result this study was conducted in an attempt to detect the frequency of OOP and to determine the dose of vitamin D needed to prevent OOP without causing complications associated with hypervitaminosis D in Egyptian infants.

Aim of the work

- In this study the effects of low and high doses of prophylactic vitamin D on biochemical and radiological manifestations of osteopenia of prematurity will be tested.

Methods

- The study was conducted on (80) preterm infants that fulfill the eligibility criteria and delivered at Alexandria University Maternity Hospital (AUMH) whose gestational age was ≤ 32 weeks and birth weight ≤ 1500 g.
- The newborns were randomly divided into two groups using the sealed closed envelope method:
 - Group I (n = 40):** received 200 IU/d vitamin D since they tolerate full enteral nutrition.
 - Group II (n = 40):** received 1600 IU/d vitamin D since they tolerate full enteral nutrition.
 - In the 6th week of age, serum Ca, P, alkaline phosphatase, 25 (OH) vitamin D3 were measured, x-ray of left wrist and a thorough physical examination was carried out.

Results

- This table shows a significantly higher mean serum vitamin D level among patients who received high dose vitamin D (group II) when compared to those who received low dose (group I), with a p value of <0.001 .

Comparison between the two studied groups according to vitamin D level

Vitamin D level (ng/ml)	Group I (n = 40)	Group II (n = 40)	p
Min. - Max.	7.70 - 50.50	21.0 - 127.0	$<0.001^*$
Mean \pm SD.	29.72 \pm 10.25	67.08 \pm 20.81	

t: Student t-test

IQR: Inter quartile range

p: p value for comparing between the studied groups; *: Statistically significant at $p \leq 0.05$

Group I: Low dose (Received 200 IU/d vitamin D)

Group II: High dose (Received 1600 IU/d vitamin D)

- The Table and Figure show a significant positive correlation between vitamin D dose received and vitamin D level, with a p value of <0.001 .

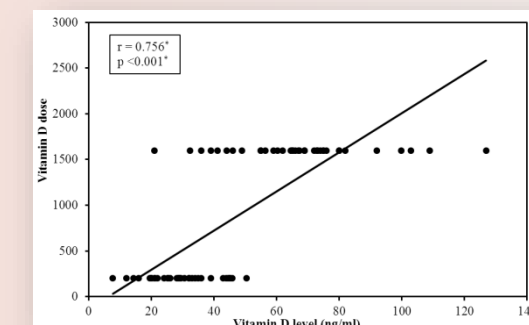
Correlation between Vitamin D dose and Vitamin D level (n=80)

Vitamin D level (ng/ml)	Vitamin D dose	
	r	P
Vitamin D level (ng/ml)	0.756*	$<0.001^*$

*: Statistically significant at $p \leq 0.05$; Group I: Low dose (Received 200 IU/d vitamin D)

Group II: High dose (Received 1600 IU/d vitamin D)

Correlation between Vitamin D dose and Vitamin D level (n=80)



- Wrist x-ray (WXR) findings varied significantly between both groups with group I showing more abnormalities in the x ray findings than group II did with a p value of <0.001 .

Comparison between the two studied groups according to WXR

WXR	Group I (n = 40)		Group II (n = 40)		P
	No.	%	No.	%	
Normal	2	5.0	23	57.5	MCp= $<0.001^*$
Bone rarefaction	21	52.5	15	37.5	
Fraying and cupping and subperiosteal bone formation	14	35.0	2	5.0	
Fracture	3	7.5	0	0.0	

Conclusions

- Prematurity is an important risk factor for neonatal Osteopenia.
- Osteopenia of prematurity was more likely to develop in multiple gestation rather than singleton pregnancies.
- Vitamin D levels showed a direct positive correlation to vitamin D dose, therefore we could assume that patients who receive high vitamin D doses are less likely to develop Osteopenia of prematurity.
- Patients who receive high vitamin D doses are less likely to show radiological abnormalities.
- Complications such as pathological fractures can develop, and may be the first clinical evidence of this condition.
- An important limitation of this study is that we could not correlate radiological Osteopenia, due to unavailability of DEXA scan in our center, with biochemical parameters.