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Research Article

EFFECTIVENESS OF VITAMIN D IN MONITORING OF PEDIATRIC HYPERTENSION: SYSTEMATIC REVIEW AND META-ANALYSIS

Shaimaa. M. Nashat *[1,3], Mohamed. M. Abdelwahab [1], Ehdaa.H. Yalli [2], Renad. A. Felemban [2], Sara. I. Alturkistani [2]
[1]Lecturer of Clinical Pharmacy, College of Pharmacy, Umm Al Qura University, Kingdom of Saudi Arabia
[2]Pharmacy student, College of Pharmacy, Umm Al Qura University, Kingdom of Saudi Arabia
[3]Clinical Pharmacy Department, College of Pharmacy, Umm Al Qura University, El Abedeya Campus 24211, Makkah City, Kingdom of Saudi Arabia
*Corresponding Author Email: smabdelhalim@uqu.edu.sa

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ABSTRACT

The antihypertensive properties of vitamin D include Renoprotective effects, suppression of the renin–angiotensin aldosterone system, direct effects on vascular cells, and effects on calcium metabolism, including prevention of secondary hyperparathyroidism. Low levels of vitamin D are associated with elevated blood pressure (BP) and future cardiovascular events. There has been a recent debate regarding the role of vitamin D deficiency in hypertension based on conflicting epidemiological evidence. Five authors independently searched Medline, Cochrane PubMed, and Medline according to a prespecified protocol for searching about the studies that had assessed the effect of vitamin D supplement on pediatric hypertension in order to map the trends in the evidence of this association. The main end-points were measurements of systolic and diastolic blood pressure. The Total number of forty-eight randomized control trials and case-control studies were reviewed and only nine studies were included in our systematic review study, with a minimum follow-up of 4 months. These eight studies showed a nonsignificant reduction in systolic and diastolic blood pressure in the vitamin D group compared with placebo. We found weak evidence to support a small effect of vitamin D on blood pressure in studies of hypertensive pediatric patients.

Keywords: Renoprotective effects, vitamin D, secondary hyperparathyroidism

INTRODUCTION

The antihypertensive properties of vitamin D include Renoprotective effects, suppression of the renin–angiotensin aldosterone system, direct effects on vascular cells, and effects on calcium metabolism, including prevention of secondary hyperparathyroidism.

Low levels of vitamin D are associated with elevated blood pressure (BP) and future cardiovascular events. There has been a recent debate regarding the role of vitamin D deficiency in hypertension based on conflicting epidemiological evidence. Several trials evaluating the effects of vitamin D supplementation on BP have been conducted with inconsistent results.[1] Few large randomized controlled trials of vitamin D supplementation with primary cardiovascular outcomes have been done, and secondary analyses from other trials have provided little evidence to support an effect of vitamin D supplementation on cardiovascular outcomes [2].

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MATERIALS AND METHODS

Statistical Methods

The Standardized mean difference (SMD) expresses the size of the intervention effect (effect-size) in each study relative to the variability observed in that study. SMD is the mean difference between the two groups divided by the standard deviation of a difference between two random values each from one of two groups. The SMD was used to summarize the effect of vitamin D on systolic and diastolic blood pressure levels by comparing two groups, a study, and a control group. If the SMD is negative, then the vitamin D effect is to decrease systolic and diastolic blood pressure levels, which is a positive effect, and vise-versa. If SMD=0, then there is no effect as this means there is no difference between the two groups.

Heterogeneity

To test homogeneity between studies used in the meta-analysis, (Cochran's *Q*) is used where it is computed by summing the squared deviations of each study's estimate from the overall meta-analytic estimate.

$$I^2 = 100\ \% \times (Q - \mathrm{df})/Q$$

where df=k-1 and k are the no. of studies. I^2 lies between 0% and 100%. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity.

Inclusion Criteria

The total number of forty-eight randomized control trials and case-control studies were reviewed and only ten studies were included in the systematic review study, with a minimum follow-up of 4 months.

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The studies meeting the inclusion criteria were found to be 10 studies. They ranged from the year 2011 to the year 2014. Table (1) presents a summary of the main characteristics of these studies.

The average SMD among studies used in the Meta-analysis was -0.773 which means that results revealed that the use of vitamin D reduces systolic and diastolic blood pressure levels by 0.773. Figure 1 shows the evolution of the effect of Vitamin D on decreasing blood pressure as evident from studies included in the Meta-analysis from the year 2011 to the year 2015. The figure shows that only two studies have considerable effect size while the rest of the studies showed the very small effect which is near zero. Cochran's Q test was insignificant which indicates homogeneity between studies. Also, I^2 index was 0% indicates no observed heterogeneity between studies.

Table 1: Summary of characteristics of studies included in the Meta-Analysis

Authors	Year	Study type	Sample size	Sample description	Conclusions
Muldowney et al.	2011	cross-sectional	195	healthy 20- to 40-year-olds (109 women)	There were interactions between Vitamin D and cardio-metabolic risk factors.[3]
Soliman et al.	2012	prospective	40	Children with mean age 6.6 years	Vitamin D therapy did not have a significant effect on blood pressure.[4]
Forman et al.	2013	prospective, randomized, double-blind, placebo-controlled clinical trial	283	healthy Black population, ages 30–80 years	Three months of oral vitamin D3 supplementation significantly, yet modestly, lowered systolic pressure.[1]
Atabek et al.	2014	Observational	247	obese children and adolescents, 8–16 years of age	Association between low vitamin D status and atherosclerosis independent of traditional risk factors in obese children and adolescents.[5]
Reeves et al.	2014	Cohort observational	43	Mothers and newborns	Low umbilical cord [vitamin D] and [Ca2] may predispose mothers to higher and newborns to lower blood pressures.[6]
Sharma et al.	2014	observational	60	20 normotensive pregnant women, 20 Pregnancy induced hypertension women, 20 healthy non pregnant women	Vitamin D levels were decreased significantly in hypertension patients.[7]
Vimaleswaran et al.	2014	Meta-analysis	35	108 173 individuals from 35 studies	Increased plasma concentrations of 25(OH)D might reduce the risk of hypertension.[2]
Kao et al.	2015	retrospective cross-sectional	229	Patients of children and adolescents attending obesity outpatient clinics age 3-18	Lower serum 25(OH)D levels were associated with higher systolic and diastolic blood pressure.8
Kwon et al.	2015	prospective cohort	205	children, ages 7–9 years	25(OH)D insufficiency is related to metabolic syndrome via the derangement of triacylglycerol. Metabolism and not related to blood pressure.[9]
Masri et al.	2015	retrospective	19	children with idiopathic intracranial hypertension with mean age 6 years	The most common cause of hypertension was vitamin D deficiency.[10]

Table 2: SMD among studies used in the Meta-analysis

No.	Study	Year	SMD	Effect type	**Heterogeneity test**
1	Muldowney et al.	2011	-0.6	Positive	Q=0.68
2	Soliman et al.	2012	-0.5	Positive	
3	Forman et al.	2013	-0.2	Positive	p-value=0.99
4	Atabek et al.	2014	-0.08	Positive	
5	Reeves et al.	2014	-0.9	Positive	I^2=0%
6	Sharma et al.	2014	-2	Positive	
7	Vimaleswaran et al.	2014	-0.09	Positive	
8	Kao et al.	2015	-2.5	Positive	
9	Kwon et al.	2015	-0.6	Positive	
10	Masri et al.	2015	-0.26	Positive	
Total			Mean= -0.773		

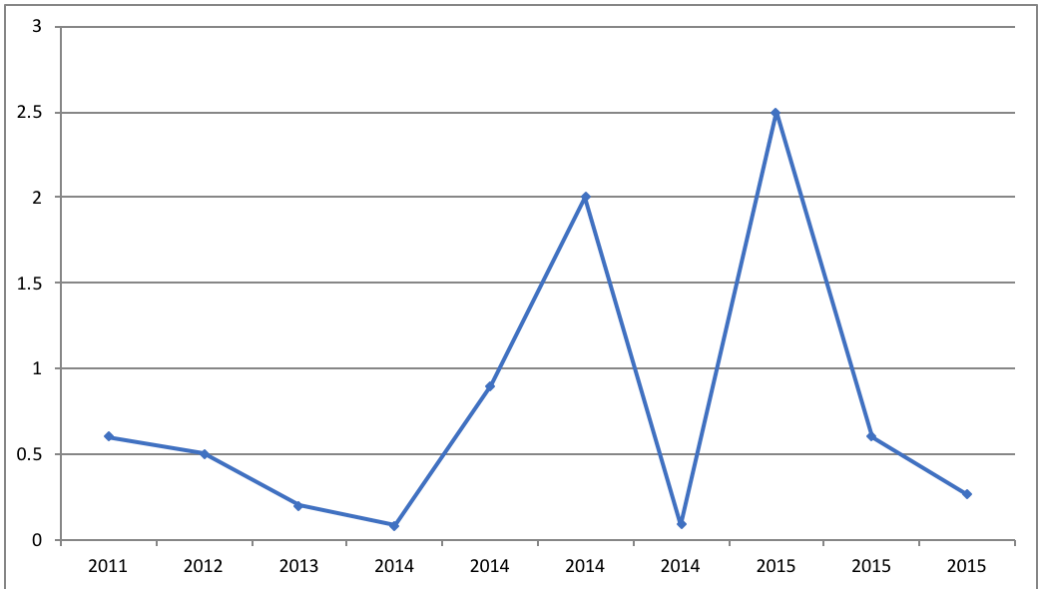

Figure 1: Effect of Vitamin D on decreasing blood pressure in studies included in the Meta-analysis from 2011 to 2015.

DISCUSSION

The present research aimed at exploring the effect of Vitamin D on hypertension and blood pressure levels as evidenced by studies through conducting a systematic review and Meta-analysis. From all the searched databases, ten studies were finally included in the analysis that met the inclusion criteria of a minimum follow-up of 4 months and the availability of blood pressure measurements so that the SMD can be calculated to assess the effect of Vitamin D on blood pressure levels. The ten studies included in the analysis contained 109494 individuals ranging from 6 to 80 years with most of the studies applied to children. Studies contained both genders and different ethnics and races. Studies contained four studies in the year 2014, three in 2015 and one in each year from 2011 to 2013. Studies included three prospective, two retrospective, three observational, one cross-sectional and one Meta-analysis study. Only two studies reported a significant effect, although small, of Vitamin D in decreasing blood pressure. The rest of the studies found the decrease not significant. The effect size in studies ranged from -0.08 to -2.5 where most of the values were near zero with a mean=-0.773 indicating a very little effect of Vitamin D on decreasing blood pressure. There is a need for other studies where a significant effect of Vitamin D is detected so that a recommendation can be made and generalized of using Vitamin D to decrease blood pressure levels.

CONCLUSION

The studies included in the present research showed no significant reduction in systolic and diastolic blood pressure in the vitamin D group compared with placebo. There is a weak evidence to support a small effect of vitamin D on blood pressure in studies of hypertensive pediatric patients as the average effect of Vitamin D on blood pressure levels was only a mean decrease of 0.773 in studies included in the Meta-analysis. Although there was a small decrease in blood pressure due to Vitamin D in the studies included, almost none of them showed that this decrease is significant which makes a generalization of this conclusion not feasible based on these studies.

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