Research Article

Impact of Vitamin D Supplementation in Acute and Chronic Immune Thrombocytopenia in Children.

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Abstract
Introduction: Immune thrombocytopenia (ITP) is the commonest cause of pediatric thrombocytopenia. Vitamin D (VD) is multifunctional hormone that regulates multiple activities in human body especially in immune system. **Aim of the work:** to investigate the role of VD as an immune modulating drug in the treatment of ITP in children. **Patients and Methods:** This cohort study was carried out on 80 patients with ITP. Cases are taken and divided into: Group I: It includes 40 children with acute ITP. They were subdivided into: Group I.A: 20 children will receive VD supplementation & Group I.B: 20 children will not receive VD. Group II: It includes 40 children with chronic ITP. They were subdivided into: Group II.A: 20 children will receive VD supplementation & Group II.B: 20 children will not receive VD. **Results**: VD level was low in all cases. VD supplementation improved platelets count. **Discussion**: VD deficiency may contribute to pathogenesis of ITP. VD supplementation was beneficial for acute and chronic ITP in children. **Recommendation**: Based on the current study we recommend VD assay in all cases of ITP to detect deficiency and give supplementation.
Key Words: ITP: Immune thrombocytopenia, VD: Vitamin D.

Introduction
ITP is an autoimmune disorder characterized by isolated thrombocytopenia (platelet count< 100×10^9/L) caused by immune dysregulation. This dysregulation involves autoantibody production against platelet and megakaryocyte antigens by B-lymphocytes and cytotoxicity by T-lymphocytes (Perera et al., 2016).

Patients and Methods
This cohort study was conducted on 80 patients with ITP. Our patients were taken from hematology unit and clinic in pediatrics department Minia University from August 2018 to February 2019. Cases are taken and divided into:
Group I: It includes 40 children with acute ITP (22 males and 18 females). Their ages ranged from 1 to 10 years. Patients of this group were subdivided into:
Group I.A: 20 children with VD supplementation. & Group I.B: 20 children without VD.

Group II: It includes 40 children with chronic ITP (19 males and 21 females). Their ages ranged from 2 to 11 years. Patients in this group were subdivided into:
Group II.A: 20 children with VD supplementation. & Group II.B: 20 children without VD.
Exclusion criteria: Patients with normal level of vitamin D, rachitic, and delayed motor and mental development and systemic disease that can cause thrombocytopenia.
Inclusion criteria: Diagnostic criteria of ITP according to American society of hematology.

The studied groups were subjected to the following:-

- Careful history taking & General and systemic examinations.
- Laboratory investigations: CBC (using NIHON KOHDEN celltac), ALT,AST, urea, creatinine, (using konelab20i) VD assay (using mini VIDAS)

Results

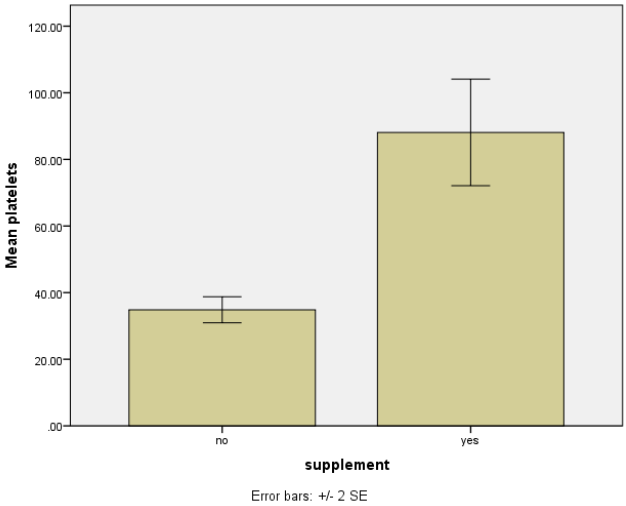

Figure (1) shows difference in platelets count between groups I.A & I.B.

Table (1): Comparison between Platelets count at the end of the study between group II.A & group II.B

	Group II.A (n= 20)	Group II.B (n= 20)	Significance (P value)
Platelets count (x 10^3/µL)	88.1 ± 35.7	34.85± 8.76	0.001*

Age of children ranged from 1.2-11year (mean 6.23± 2.8), their hospital stays ranged from 2-16 days (mean 6.44± 2.56), and disease duration ranged 0.23- 97 months (mean 16.8 ± 20.5). Males represented 51.2% of the studied group while females were 48.8%. Rural patients were 86.3 % of the studied group while 13.8% were from urban area.

Pallor was observed in 19 cases (23.83%), Hemoglobin level ranged from 5.2 to 14gm/dL, Platelets count ranged from 4000- 43000 (mean 16.78± 8.4), most common mucosal bleeding is epistaxis 32.5% then bleeding gums 21.3%, Coomb's test was negative for all cases.

There was significantly strong positive correlation between age of patients and disease duration with P value 0.001.

Mean level of VD in group I was (10.86±2.5) vs. (10.1± 2.1) in group II. The difference was not statistically significant with P=0.15**.** After supplementation, there was a significant increase in VD level in group I.A and group II.A with P value 0.001.

In group I.A and group II.A, Mean platelets number was significantly higher after VD supplementation than before VD with P value 0.001. In group I.B and group II.B, platelets count was significantly higher in the second time, but not similar to increase in platelets with VD supplementation.

There was a significant difference in Platelets count at end of study between group I.A& group I.B and between group II.A & group II.B. Also, There is a significant difference between length of hospital stay in patients received VD and others (P= 0.04).

There is a significant negative correlation between hospital stay and platelets count

(r=0.36-). There is no significant correlation between disease duration and VD level. There were no significant difference between platelets count in males and females (P=0.32).

Discussion

In our study, age of children ranged from 1.2 to 11 years (mean 6.23±2.8) and this is agreed with Weycker et al., (2018).There was a non-significant difference regarding gender of patients. This result is agreed with Aygüneş (2019) but disagreed with Golshan et al., (2016), Čulić et al., (2016) and Arandi et al., (2014). Rural patients were 86.3% of the studied group.

Pallor was noted with 23.8% of patient. Pallor may be acute owing to bleeding or chronic due to iron deficiency or other causes. According to Huscenot et al., (2018), iron deficiency especially if severe can lead to thrombocy-topenia. Petechiae and ecchymosis were present in all cases. This is in agreement with finding of Muninarayan et al., (2019). Coomb's test was negative for all cases. This is agreed by Aygüneş (2019). Correlation between age of patients and disease duration revealed signi-ficant correlation. Makis et al., (2017) agreed with it.

VD was low in all cases without significant difference between acute and chronic. Fattizzo et al., (2016) agreed with deficiency. Lassandro et al., (2019) agreed non-significant difference between acute and chronic. Čulić et al., (2016) reported significant difference between acute and chronic also14.2% of cases had normal VD.

Platelets increased significantly after VD supply. Bockow and Kaplan, (2013) reported similar results. Tham et al., (2018) reported that a small number of patients had an increase in their platelet count with VD replacement. Tham et al., (2018) noticed also a fall in platelet count despite an increase in VD levels.

At the beginning of the study, there was a non-significant difference between platelets count in both acute and chronic groups. Makis et al., (2017) showed that the median platelet count at diagnosis was higher in chronic than acute group.

There were no significant difference between platelets count in males and females, at the beginning and end of the study. This is agreed with Bennett et al., (2017) who reported that gender and platelet count were not significantly correlated with remission.

There is no significant correlation between disease duration and VD level. This is disagreed by Kalbassi et al., (2014) who reported that VD Treatment might diminish recurrence and duration of ITP. Lassandro et al., (2019) reported that VD deficiency does not represent a risk factor for chronic ITP.

Conclusion & Recommendations

Low VD level may contribute to pathogenesis of ITP. VD supplementation caused marked improvement in platelets count. We recommend VD assay for ITP cases at diagnosis. VD supplementation is essential for deficient cases. Further studies for accurate dosing and duration of VD.

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