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A study on the effect of vitamin d supplementation on primary dysmenorrhea: A prospective case control study

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Abstract

Dysmenorrhea is a common problem among women of reproductive age group. The aim of this study is to investigate the effect of vitamin D supplementation in treatment of primary dysmenorrhea. A study was conducted on 60 women with primary dysmenorrhea and vit D deficiency referred to our OPD. Eligible women were randomly selected into treatment and control groups (30 in each group). Individuals in the treatment group received 50 000 IU oral vit D and the control group received placebo weekly for eight weeks. After two months of treatment, there was a significant difference in serum vit D concentration between the two groups ($p < 0.001$). Pain severity decreased in treatment group after eight weeks of treatment. There was a significant difference in pain intensity between the two groups after eight weeks of treatment. A weekly dose of (50 000 IU) oral vit D supplementation for eight weeks in patients with primary dysmenorrhea could improve pain intensity.

Keywords: Dysmenorrhea, supplementation, vitamin D

Introduction

Dysmenorrhea is a common Gynecological problem in reproductive age women. Primary dysmenorrhea is characterised by cramping pain in lower abdomen associated with menstruation without any evident disease or pathology [1]. The prevalence of dysmenorrhea among reproductive women in India ranging between 56% to 78%. The difference in the prevalence rate of dysmenorrhea in various studies is probably due to the weather condition of each region [2]. Dysmenorrhea affects quality of women's life negatively and even limits their activity in severe cases [3]. Dysmenorrhea begins following the release of prostaglandins from endometrial cells Therefore, suppression of prostaglandin synthesis or function has been the main therapeutic target in treatment of dysmenorrhea [4]. Till now, different strategies and treatments including non-steroidal anti-inflammatory drugs (NSAIDs), contraceptives, herbal extracts, and supplements have been used for management of menstrual pain. Vitamin D is a steroid hormone, which is mainly (80–90%) synthesized in the skin by sunlight exposure and its small remaining portion is obtained from the diet and supplements. Vit D and vit D receptor (VDR) are involved in calcium (Ca) homeostasis, bone mineralization, and different metabolic pathways in human as well as modulation of reproductive processes in women and men [5]. Endometrium is a target of vit D and 1 α OH is expressed in the human uterus. It has been shown that vit D reduces production of prostaglandins [6]. This study is aimed at evaluating the effect of vit D supplementation on primary dysmenorrhea.

Materials and Methods

This prospective case-control study was conducted on women with primary dysmenorrhea referred to our OPD for the period of one year 2020 to 2021. After obtaining written informed consent, 60 patients aged 18 to 35 years old adult females attending our OPD with primary dysmenorrhea will be enrolled for the study.

Patients with primary dysmenorrhea aged 18–30 years, having at least four recent consecutive painful periods the past six months, bleeding of 3–7 d were included in the study. Those taking contraceptives within the past two months, using intrauterine device or drugs containing Ca or vit D within the past six months, smoking and history of renal stones, granulomatous disease, hyperparathyroidism, and any malignancy were excluded.

At the same time, before enrollment in the study, secondary causes of dysmenorrhea were ruled out by uterine and ovarian sonography.

Eligible patients were included in the study consecutively and randomly allocated into two groups of treatment and control by block randomization. Individuals in the treatment group (30patients) received 50 000 IU oral vit D pearl once per week after food and the control group received identical placebo (30 patients) with the same manner for eight weeks.

The researchers assessed vit D levels, pain severity (by using VAS score based on history) and the use of NSAIDS at the base line after 8 weeks of treatment. VAS is a 0-10 scale pain rank with zero indicating no pain, and 10 indicating severe pain.

Patients will be followed up for the next 2months and asked to fill in the VAS score at the end of 2 months after vitamin D supplementation. Also vitamin D3 levels were rechecked for their 25(OH) vitamin D3 levels at the end of 2months.

Statistical Analysis

The collected data were compiled and will be subjected to statistical analysis using statistical package for social services (SPSS) version16.

Results

Of the sixty dysmenorrhea women 70 percentage were found to have vit D deficiency among the vitamin D supplemented group At the start of the study mean vitamin D level was around 17.45±10.43 VAS score was 8.8±0.997 NSAID usage was around 96% 2 months after administering the drug, mean vitamin D level was 41.93 ±10.21 VAS score was 2.967±1.098 NSAID usage reduced to 11%.

Among the placebo group, At the start of the study, mean vitamin D level was around 19.10, VAS score was 8.90±0.845, NSAID usage was 93.3%, After giving placebo drug, mean vitamin D level was 19.74, VAS score was 8.27±0.69, NSAID usage was 93.3% at the end of 2nd month there was no difference in placebo group.

Table 1: Demographic characteristics of two study groups

Variable	Vitamin D group Mean±SD	Placebo group Mean±SD	'p' Values
Age	21.3±1.765	21.667±2.264	0.487
BMI	22±2.084	21.6±1.884	0.478
Menarche age	12.401±1.102	12.333±1.184	0.825

Table 2: Mean Vitamin Level at Different Period

Vitamin D level	Base line		2 months		Base line vs 2 months	
	Mean	SD	Mean	SD	p value	
No vitamin	16.167	7.874	17.453	9.22	0.563	Not Significant
Vitamin	16.873	7.244	41.933	9.67	< 0.001	Significant
P	0.719 Not significant		< 0.001 Significant			

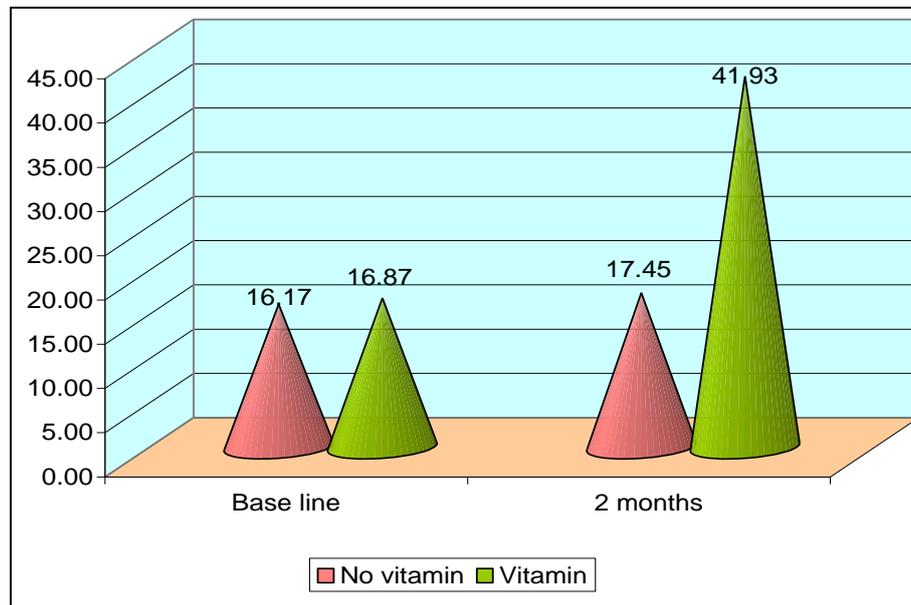


Fig 1: Show the comparsion of vitamin D Level base line vs 2 months

Table 3: Comparison of Mean Vas Score

VAS score	Base line VAS		2 months	
	Mean	Sd	mean	sd
No vitamin	8.9	0.845	8.267	0.691
Vitamin	8.8	0.997	2.967	1.098
t	0.419		22.371	
p	0.677		<0.001	

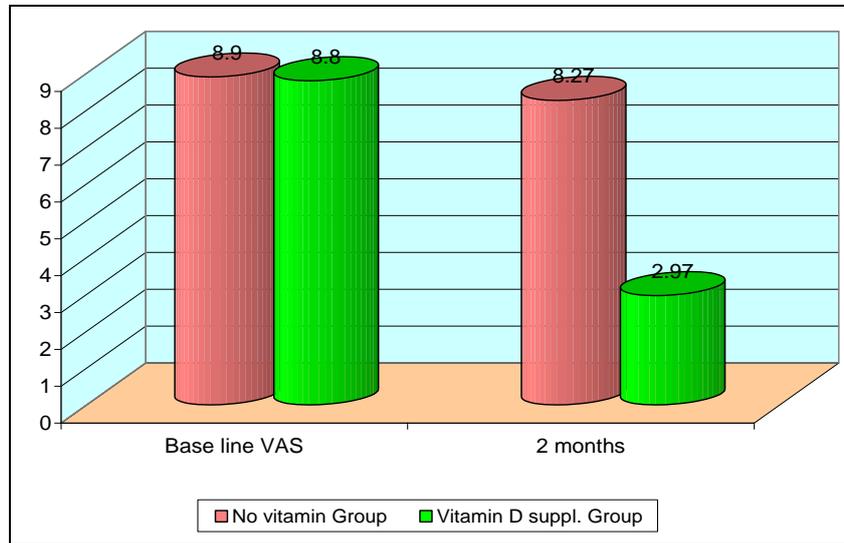


Fig 2: Comparison of men vas score

Table 4: Comparison of NSAIDS Usage

NSAIDS usage	NSAIDS usage baseline		usage at 2nd month	
	No Suppl.	Vit suppl. given	No Suppl.	Vit suppl. given
Yes	28	28	28	3
No	2	2	2	27

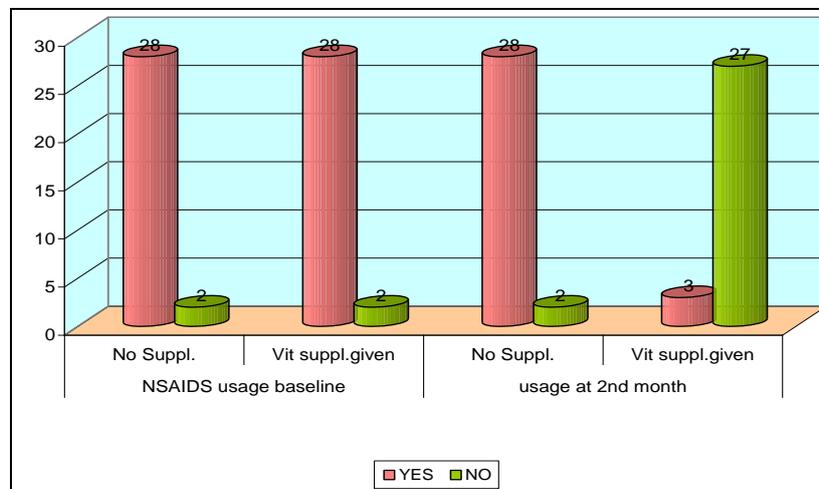


Fig 3: NSAIDS comparison

Discussion

This prospective interventional study was conducted by enrolling and following up of 60 patients who were diagnosed with dysmenorrhoea in the Department of Obstetrics and Gynaecology in our OPD, who have been evaluated for baseline Vitamin-D levels and following supplementation and were analyzed for correlation with the pain perception.

Total of 60 patients are divided into two groups of 30 each. Group A had no supplementation of Vit D and Group B had taken Vitamin D3 supplementation.

Age distribution of the participants which ranged from 18 to 35 years. Mean age of Group A is 21.67 and Group B is 21.3. No significant difference between both groups. P value is 0.487 Not significant.

Based on height and weight of the individual patients, their Body Mass Index (BMI) was calculated using Quetelet's index and they were categorized as underweight, normal weight and overweight/obesity based on these values.

No significant difference between both groups regarding BMI

BMI 21.63 in Group A and 22.1 in group B, p value is 0.478 Not significant.

The age of onset of menarche among the study participants and it ranged from 13 to 16 years. The average age of menarche onset was 12.3 ± 1.187 years in group A and 12.4 ± 1.10 in group B. No significant difference of both groups. The menarche onset and its distribution with the stage of adolescence. Majority of these females had their menarche in the early adolescence stage (96.5%) and only few developed during mid-adolescence (3.5%). No significant difference between mean age of menarche for both groups.

The average levels of Vitamin-D were 17.45 ± 9.22 ng/ml at baseline which rose to 41.93 ± 9.67 at 2 months. This difference was found to be statistically significant as tested using a nova test and p-value <0.001.

The pain perception during dysmenorrhoea was computed by Visual Analog Scale (VAS) score and compared between the groups that were Vitamin-D not taken group and vit D3 taken groups at baseline. The average VAS score of former group (8.9

± 0.85) were comparable with the later group (8.8 ± 0.99) and the difference was not found to be statistically significant as shown by Independent t-test ($P > 0.05$).

The pain perception by Visual Analog Scale (VAS) score was compared between the groups that were Vitamin-D not taken and vit d3 taken groups post-intervention. The average VAS score of former group after 2 months (8.27 ± 0.69) were comparable with the later group (2.97 ± 1.09) and this difference was found to be statistically significant as shown by Independent t-test ($P < 0.05$).

The comparison of VAS score for dysmenorrhoea before and after Vitamin-D supplementation. The pain score lowered (2.96 ± 1.09) at 2 months with Vitamin-D supplementation as compared from the baseline pain score (8.8 ± 0.99) and this difference was found to be statistically significant as revealed by paired t-test ($P < 0.001$).

The quantitative association between the Vitamin-D levels before and after intervention with the pain perception during dysmenorrhoea. The Spearman's rho correlation coefficient was used for this quantitative analysis. It was observed that increase in Vitamin-D levels following 2 months of Vitamin-D supplementation was negatively correlated with VAS pain score ($P < 0.05$) whereas no association was found between these two variables before intervention.

The significant relationship between NSAID usage for Vitamin-D supplementation and non supplementation group p value is < 0.001 . Of all those who have used NSAID ($n=28$) for dysmenorrhoea symptoms at baseline, those who became non-users post-intervention were significantly higher as compared to the sustained NSAID users. In Vit D3 supplementation group, Only 3 cases needed NSAID usage after 2 months. This association was statistically significant on applying McNemar's Chi-square test ($P < 0.05$).

In our study, after treatment, serum concentration of vit D in treatment group increased from deficiency level to sufficient level but did not reach to high levels. In our study, by increase in vit D concentration pain intensity reduced significantly after treatment. This may indicate that higher levels of vit D may cause more reduction in pain severity^[7].

As all of patients in our study had vit D deficiency, we could not comment on the effect of vit D supplementation in the treatment of primary dysmenorrhea in those with sufficient vit D concentration. Therefore, yet it remains unknown if dysmenorrhea pain would be improved with vit D supplementation in women with normal baseline serum levels of vit D.

Vit D acts through different mechanisms in improving dysmenorrheal pain in endometrium; in endometrium it reduces expression of cyclooxygenase-2 and consequently reduces prostaglandin production, up-regulates 15-hydroxyprostaglandin dehydrogenase, increases prostaglandin inactivation, regulates the expression of prostaglandin receptor, and consequently reduces pain intensity. Vit D may also act through its anti-inflammatory effects^[8].

Small sample, short duration of treatment, and follow-up are the main limitations of our study.

Future randomized controlled clinical trials with greater sample size, longer duration of treatment, and different doses of vit D as a maintenance dose and longer follow-up period are required to confirm the efficacy of vit D in treatment of primary dysmenorrhea.

Conclusion

Based on the study findings, it seems that vit D supplementation

with a weekly dose of 50 000 IU for eight weeks could improve pain intensity and decrease the need for using NSAID in patients with primary dysmenorrhea and vit D deficiency^[9].

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