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# Cholecalciferol for Primary Dysmenorrhea in a College- aged Population- A Clinical Trial

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## ABSTRACT

Primary dysmenorrhea is the most common gynecological complaints among adolescents. The purpose of the present study is to evaluate the effect of vitamin-D in reduction of pelvic pain in women suffering primary dysmenorrhea. This double blind randomized clinical trial was performed on women suffering from primary dysmenorrhea. For case group (n=27), vitamin-D was prescribed as a single dose of 300 000IU starting 5 days before the beginning of menstruation, for three consecutive cycles. For control group (n=27), a Placebo was prescribed. Pain severity was evaluated using Visual Analogue Scale (VAS). There was a reduction of the pain score in the first month for both groups (mean score of 5.3±2.24 for group-A and 5.21±2.35 for group-B). In the next two months pain reduction continued for group-A, but for group-B pain scores grows higher than the first month. Independent student t-test showed that pain score was significantly lower in group-A than group-B after beginning of therapy in the second and third month (P= 0.023 and 0.001 respectively). There was no significant difference between two groups in the level of vitamin-D in follicular and luteal Phase. Vitamin-D causes significant pain reduction in primary dysmenorrhea that due to its safety can be a simple treatment for this problem.

**Key words:** Pain Severity, Pelvic Pain, Primary Dysmenorrhea, Vitamin-D, Cholecalciferol

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## 1. INTRODUCTION

Primary dysmenorrhea is the most common gynecological complaints among adolescents. Conventional treatments include nonsteroidal anti-inflammatory drugs and hormonal contraceptives, but complementary and alternative medicine is a growing area of interest (1). According to the Consensus Guideline (2), primary dysmenorrhea is a crampy, suprapubic pain that begins between several hours before and a few hours after the beginning of menstruation. According to the Consensus Guideline (2), primary dysmenorrhea is a crampy, suprapubic pain that begins between several hours before and a few hours after the beginning of menstruation. Primary dysmenorrhea is a crampy, suprapubic pain that begins between several hours before and a few hours after the beginning of menstruation. Primary dysmenorrhea is a condition of recurrent, painful cramp of lower abdomen during menstruation in absence of any

pathological conditions in pelvis. This condition is often accompanied by; nausea, vomiting, diarrhea, headache, back pain, dizziness, asthenia and insomnia (2, 3). The prevalence of dysmenorrhea ranges from 60 to 93 percent among adolescent females (4-7). Although primary dysmenorrhea is not a life threatening condition and it does not cause organic dysfunction, but it can results in limitation of daily, social and physical activity (5-8). Thus Non-steroidal anti-inflammatory drugs (NSAIDs) and hormonal contraceptives are used as medication therapy (9, 10). Recently a single study which was conducted by Lascoet.al (11), suggested that a single high dose of cholecalciferol maybe efficient in treatment of primary dysmenorrhea. According to this data and as vitamin-D deficiency is common in Iranian population; we aimed the present study in order to reevaluate the effects of medication therapy with vitamin-D on primary dysmenorrhea.

## 2. MATERIALS AND METHODS

This study was a double-blinded clinical trial, which was conducted during November 2012 and May 2013, in Kermanshah University of medical sciences, Kermanshah, Iran. The study protocol generally was based on Lascoet.al's (11) study and was approved by ethics committee of the obstetrics and gynecology department in Imam Reza Hospital (affiliated to Kermanshah University of medical sciences).

$$n = \frac{Z^2 \cdot P(1-P)}{d^2} \quad (1)$$

All collected data was recorded and patients were treated according to the ethical guidelines of medical research. Prior to the beginning of the study, all patients were informed about the aims and procedures. Participation in this study was voluntary and the patients were free to withdraw the project whenever they wanted. Furthermore, the identity of research participants was protected, since the data files were anonymous and all names were omitted.

### 2.1. Patient enrolment

Fifty seven Iranian students, aged between 18 to 30 years old were recruited in the study. Patients' sampling method was convenience and they were allocated randomly in 2 groups, each containing 27 participants, by giving them a code (A or B) via a concealed, sealed, opaque envelope (code A as case group and code B as control one). Patients were enrolled in the study if they had following criteria: single and sexually inactive, aged between 18 to 30 years old, their menstrual cycles lasted 21 to 35 days with menstruation lasting 3 to 7 days, experienced at least 4 painful periods of their past 6 menstrual cycles, no consumption of any kind of medications including oral contraceptives, vitamin D and calcium, normal abdomino pelvic sonography in the past 6 months. Moreover patients were not permitted in the study if they had any history of pervious abdomino pelvic surgery or abnormality, history of any kinds of pelvic infection, history of abdominal pain except during their periods, history of psychological disease or consumption of psychological medication, history of hyper menorrhoea or abnormal bleeding, history of alcohol consumption or cigarette smoking, history of gastrointestinal disease such as peptic ulcer and history of long duration stressful situations.

### 2.2. Treatment and measurements

At the beginning of study serum level of 25-hydroxy vitamin-D3 was measured, analyzed and recorded using Chemiluminescenc method, with Diasorin Liaison machines (Saluggia, Italy), with a normal range of 30-100 ng/ml, for all participants. Case group or group-A received a single high dose of oral cholecalciferol (300 000 IU), 5

days before beginning of their next menstrual cycle, for 3 months and at the same time control group or group-B received placebo. Both vitamin-D pearls and placebo were formulated by Zahravi Drug Company, Iran, and were in the same shape, smell and size. Medications were wrapped in concealed pockets and randomly were given to the patients so that both patients and researchers were blind and did not know who would receive which medication. Moreover patients were free to use mefenamic acid if their pain did not ameliorate, but they had to record it in a sheet.

### 2.3. Outcomes

Primary outcome of this study was severity of abdominal pain which was measured by a visual analog scale (VAS). Patients marked their pain intensity on a 100 mm ruler based on VAS, one month before start of treatment and then monthly until 3 months later. Pain intensity was categorized as mild (less than 40 mm), moderate (40-80 mm) and sever (more than 80 mm). Secondary outcome was use of NSAID during the study.

### 2.4. Statistical Analysis

Numerical variables were described using the mean and standard deviation (SD). Independent student T-test was used to compare means of numerical variables between two groups. And in order to analyze within group analysis of VAS scores paired T-test was conducted.

## 3. RESULTS AND DISCUSSION

Age distribution, pain severity and body mass index (BMI) were same in the two groups and there was no significant difference between two groups in terms of family history of dysmenorrhoea and education level. Also there was no significant difference in use of NSAIDs between two groups however; group-B used NSAID more than group-A people. Moreover mean level of vitamin-D was  $7.28 \pm 3.64$  in group-A and  $6.28 \pm 2.77$  in group-B which was not significantly different. Pain score was high in both groups at baseline, with mean VAS of  $7.13 \pm 1.85$  in group-A and  $7.38 \pm 1.56$  in group-B (no significant difference was seen,  $P=0.58$ ). Then there was a reduction of the score in the first month for both groups (mean score of  $5.3 \pm 2.24$  for group-A and  $5.21 \pm 2.35$  for group-B). In the next two months pain reduction continued for group-A (mean scores of  $3.97 \pm 1.9$  and  $3.77 \pm 1.77$  respectively), but for group-B pain scores grows higher than the first month (mean scores of  $5.24 \pm 2.27$  and  $5.55 \pm 2.02$  respectively). Independent student T-test showed that pain score was significantly lower in group-A than group-B after beginning of therapy in the second and third month ( $P= 0.023$  and  $0.001$  respectively). Furthermore Within group analysis with paired student T-test revealed significant differences between pain scores in-group-A. So that mean VAS scores at the end of first, second and the third month were significantly lower than the baseline. Also mean pain scores at the end of second and the third month was

significantly lower than the first month (all P-values was less than 0.001). But there was no significant difference between VAS scores at the end of third month in comparison with the second month (P= 0.13). Moreover in group-B, mean scores at the end of first, second and the third month was significantly lower in comparison to the baseline (all P-values< 0.001). We divided baseline scores

of VAS in to two set, less than 7 and more or equal to 7, then analyzed the difference of pain reduction in third month and the baseline in this two set. In the case of VAS $\geq$  7, pain reduction was greater in the two groups and the reduction in group-A was significantly more than group-B with the P-value of <0.001. (Figure 1 & Figure 2).

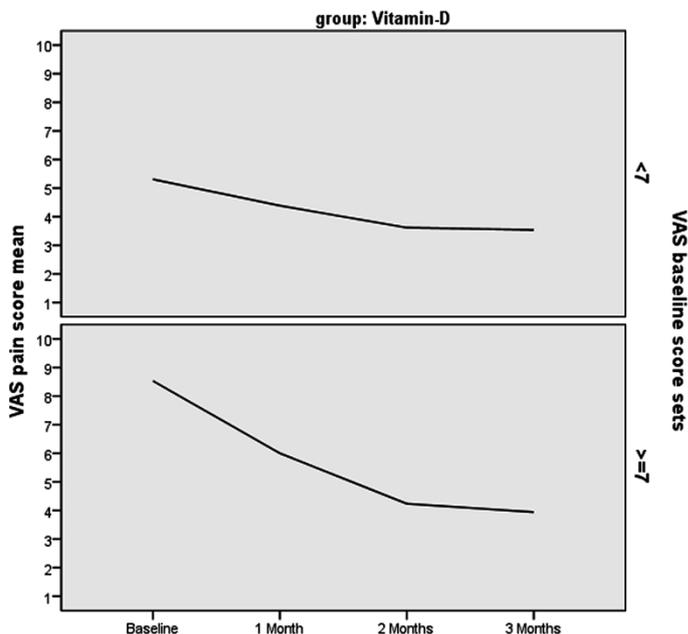


Figure 1. Changes in mean pain score of vitamin-D treated group (group-A) over 3 months of study

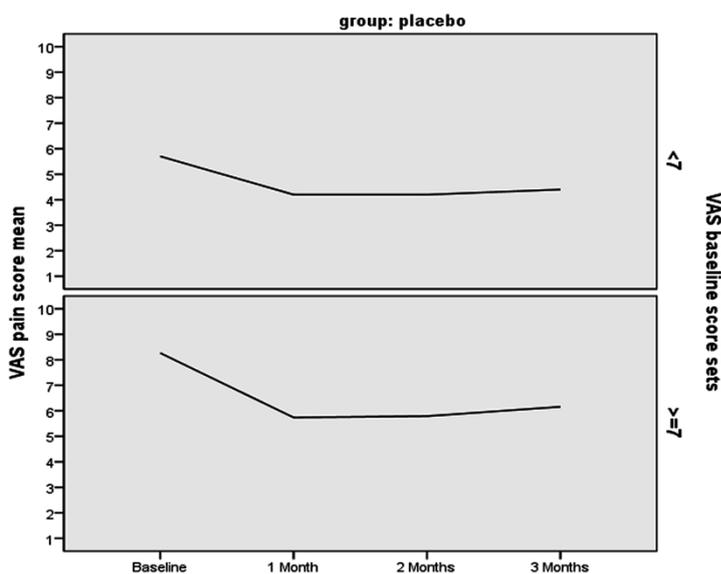


Figure 2. Changes in mean pain score of placebo treated group (group-B) over 3 months of study.

In the present study, we investigate the effect of single high dose of oral cholecalciferol on patients with primary dysmenorrhea. This study was performed based on study of Lasco et.al (11). Also our findings are consistent with their findings and support this idea that use of cholecalciferol in patients with dysmenorrhea can reduce their pain. In our study although use of NSAID in group-B

was higher than group-A, which received vitamin-D, the difference was not significant and this finding was in contrast with Lasco et.al findings which demonstrated that patients who received cholecalciferol did not use NSAIDs. However this controversy can be explained by race differences and the people different pain threshold. Besides, in a cross sectional study which was conducted by

Bertone-Johnson ER et.al between 2006 and 2008 in United States, the effect of High dietary intake of vitamin D on premenstrual syndrome (PMS) was assessed. In this study no relationship was found between vitamin-D levels in late luteal phase and PMS but they suggested a possibility of an inverse association between intake of vitamin D and overall menstrual symptom severity (12). On the other hand, vitamin-D deficiency is a common problem in Iranian population. A study which was conducted in 2001 by Endocrinology & Metabolism Research Center (EMRC) in Tehran, Iran, showed that Vitamin-D deficiency has a high prevalence in Tehran. In this study prevalence of severe, moderate and mild vitamin-D deficiency was reported 9.5%, 57.6%, and 14.2% respectively (13). Therefore, as it was expected, we detected low levels of 25-hydroxy vitamin-D3 in both groups of participants and the average level was 6.76ng/ml.

#### 4. CONCLUSION

In conclusion, our study showed that cholecalciferol as a safe and easy treatment can be used to reduce pain in primary dysmenorrhea and also can limit use of NSAIDs.

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#### AUTHORS CONTRIBUTION

This work was carried out in collaboration among all authors.

#### CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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