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Does Preoperative Vitamin D Level Effect Acute Postoperative Pain After Hip Arthroplasty Surgery

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Abstract

Objective: 25-OH Vitamin D is well known that has an important role in the perception of pain. Vitamin D insufficiency is important health problem all over the world. Most of the research related to vitamin D and pain is about chronic pain. In this study, it was investigated whether there is an association between Vitamin D levels and acute postoperative pain.

Methods: Preoperative Vitamin D levels were measured in patients who underwent elective hip replacement. Patients undergoing spinal anesthesia were administered patient-controlled analgesia (PCA). Patients whose pain assessment was performed with the postoperative visual analog scale (VAS), the time of initial analgesic administration, the number of analgesic needs, the number of bolus opioid use and additional NSAID use were evaluated.

Results: It has seen that a negative correlation between the vitamin D values and postoperative VAS scores. It was determined that patients with low vitamin D had earlier postoperative first analgesic administration time. It was also determined that as the vitamin D values decreased, the number of bolus opioids and total analgesic requirements used was higher.

Conclusion: In postoperative pain, low preoperative vitamin D level caused an increase in VAS scores and analgesic need and patients have low vitamin D also had earlier analgesic administration time.

Keywords: 25-OH Vitamin D, acute postoperative pain, hip arthroplasty, VAS

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INTRODUCTION

25-Dihydroxyvitamin D3 (25-OH Vitamin D) plays an important role in the pathophysiology of critical diseases and acute stress conditions. It also has important role in defense against pathogens, immunomodulation, and skeletal muscle function (1,2). Vitamin D insufficiency is important health problem all over the world, and it has been shown that low Vitamin D levels are associated with bad consequence in hospitalized patients (3,4). Vitamin D deficiency is present in more than half of all hospitalized patients and it is associated with muscle weakness, especially much more in the proximal muscle groups (5,6). There are clinical studies on hypovitaminosis D on many systems such as the musculoskeletal system, respiratory system, and cardiovascular system, but it is seen that the number of studies on this subject is low, especially on surgical patients. Most of these studies are related to specific issues and situations such as postoperative cardiac morbidity, postoperative infection, or the period after liver transplantation (7-9). Malnutrition and vitamin deficiencies are common among geriatric patients undergoing elective orthopedic surgery and are known to be independent risk factors for postoperative side effects (10). It is well known that Vitamin D has a significant role in the perception of pain and Vitamin D deficiency is associated with higher opioid use in patients with chronic pain syndromes and cancer. Studies have found that vitamin D levels are lower than normal in patients with pain (11,12). Hip arthroplasty surgery is one of the most frequently performed surgery in orthopedics practice and postoperative pain is one of the most important factors that impair patient comfort after surgery. It's known that postoperative pain delays mobilization and recovery. In this study, we aimed to examine the effect of preoperative vitamin D values on postoperative pain levels after hip arthroplasty.

METHODS

This prospective study was approved by the local Ethics Committee (Ordu University, 2017/116-118, Ordu, TURKEY) and patient consent forms was obtained from all patients. The study included 53 patients in the ASA I-III (American Society of Anesthesiologists risk score) group over the age of 18, who will undergo elective hip replacement surgery due to coxarthrosis. The probability sampling method (simple random sample) was used. Patients that were on vitamin D treatment, who had used analgesics in the previous 24 hours, patients who could not be reached, patients that have used opioids for a long period, and those with any neuromuscular disorder were excluded from the analysis. When the patients came to the operating room, electrocardiography, pulse oximetry, and noninvasive blood pressure monitoring were performed. Venous cannulation was performed on the appropriate side of the dorsum of the hand, and a 5 ml blood sample was taken and sent to the laboratory for vitamin D measurement. Then, 0.9% isotonic NaCl infusion was started through the opened venous access. After these procedures, following appropriate field sterilization and covering, 0.5% hyperbaric bupivacaine (Marcaine Spinal Heavy) was applied to patients in a sitting position by using a 25 gauge spinal needle from the L3-4 interval; spinal anesthesia was applied with 3 mL-15 mg. The sensory block was evaluated with the pinprick test, while the motor block was evaluated with the Bromage scale (0: Can move the leg, foot, and knee easily, 1: Knee and foot

movements are normal, but cannot lift the leg straight, 2: Cannot flex the knee, 3: Cannot move the foot and knee) Surgery was allowed when the sensory block level was T10 and the Bromage scale was 3. At the end of the surgery, the PCA device prepared with tramadol HCL was attached and the loading dose was administered to the patients who were taken to the postoperative recovery unit before being sent to the room (Tramadol PCA Protocol: Loading dose 50 mg, bolus dose 20 mg, lockout time 20 minutes and basal infusion dose 10 mg/hour). VAS values were recorded by the visual analog scale at postoperative 30th minute, 1st, 2nd, 4th, 6th, 8th, 12th, and 24th hours for pain assessment. Dexketoprofen trometamol 50 mg was administered intravenously to patients with a VAS value of 4 and above during postoperative follow-up. Patients' time of first analgesic administration, the total number of analgesic needs, the number of PCA bolus opioid use, and the number of additional NSAID use were recorded. The study was completed in a double-blind manner by ensuring the patient and the researchers evaluating the pain were not aware of the vitamin D level. The primary output measurements of this study are VAS scores, vitamin D level and the total number of analgesic needs.

Sample Size and Power Analysis

At least 52 patients with low and high levels of vitamin D were calculated as an alpha value of 0.05 and power 80% (13).

Vitamin D analysis:

Cobas Vitamin D assay: 25-OH Vitamin D (electrochemiluminescence binding assay) on the Roche Cobas e601 instrument. Elecsys uses a competitive immunoassay for the detection of total vitamin D (25-OH).

Statistical Analysis

For vitamin D values, the Shapiro Wilk test was used to check normality assumption in terms of values such as demographic data, time of first analgesic administration, and the total number of analgesic needs. Differences in vitamin D values in terms of analgesic requirement time, the total number of analgesic needs, and time of first analgesic administration were evaluated using the student's t-test and Mann-Whitney U test. The Chi-Square test was used for qualitative data comparison and Pearson correlation analysis was used to evaluate data correlation. Statiscal significance level was accepted as $p<0.05$. All statistical calculations were made in SPSS 20.0 (for Windows; SPSS Inc., Chicago, IL, USA) statistics package program.

RESULTS

A total of 53 patients, 19 female, and 34 males, were included in our study. The mean age of the patients was 61.25±9.83 for women, and 59.94±10.42 for men. In Table 1, the mean age, vitamin D and PTH values of the patients participating in the study as well as the mean duration of the regional block, the duration of the surgery, and the time of first analgesic administration are shown. The mean vitamin D values of the patients were 14±67 µg / L and it was statistically significantly lower in women (12.04±4.69, p=0.004, Table 2). It was determined that the sensory block ending time was longer in male patients (p=0.027, Table 2). It was determined that female patients needed analgesic earlier than male patients (p=0.006, Table 2). Female patients had higher VAS values than men (p=0.041, p=0.035,

p=0.013, p=0.021, Table 3). Also, the total number of analgesic needs needed and the number of additional NSAID use was higher in women than men (p=0.008, P=0.007, Table 3). In our study, we determined that as the vitamin D values of the patients decreased, the sensory block ending time also shortened (p=0.000, Table 4). In addition, it was observed that there was a negative correlation between the vitamin D values of the patients and their VAS scores (p=0.000, p=0.000, p=0.000, p=0.048, p=0.000, Table 4). It was observed that patients with low vitamin D levels had earlier first analgesic administration time (p=0.001, Table 4).

Table 1. Age, Vitamin D, PTH values, durations of regional blockade, surgery and first analgesic administration time of all patients

	Mean	Std. deviation	Min.	Max.
Age (year)	**61,25**	**9,83**	**38**	**78**
Vitamin D (µg/L)	**14,67**	**5,04**	**6,43**	**25,18**
PTH (pg/ml)	**39,17**	**20,20**	**7,31**	**94,22**
Time to reach T10 of sensory block (min)	**4,26**	**1,19**	**2**	**6**
Time to reach Bromage 3 (min)	**6,75**	**1,07**	**5**	**9**
Surgery duration (min)	**57,92**	**5,41**	**50**	**75**
Sensory block end time (min)	**156,89**	**13,84**	**135**	**190**
First analgesic administration time (min)	**115,57**	**11,42**	**90**	**140**

Table 2. Age, Vitamin D, PTH values, durations of regional blockade, surgery and first analgesic administration time in female and male patients

	Female	Male	P
Age (year)	63,58 ± 8,45	59,94 ± 10,42	P>0,05
Vitamin D (µg/L)	12,04 ± 4,69	16,13 ± 4,68	P=0,004*
PTH (pg/ml)	34,51 ± 16,96	41,78 ± 21,61	P>0,05
Time to reach T10 of sensory block (min)	4,32 ± 1,10	4,24 ± 1,25	P>0,05
Time to reach Bromage 3 (min)	6,53 ± 1,02	6,88 ± 1,09	P>0,05
Surgery duration (min)	58,16 ± 5,82	57,79 ± 5,25	P>0,05
Sensory block end time (min)	151,32 ± 11,76	160,00 ± 14,08	P=0,027*
First analgesic administration time (min)	109,47 ± 12,00	118,97 ± 9,67	P=0,006*

Statiscal significance level was accepted as p<0.05

Table 3. VAS scores, total number of analgesic needs, PCA bolus opioid use and additional NSAID use in female and male patients

	Female	Male	P
Postoperative 30th min VAS score	0	0	P>0,05
Postoperative 1st hour VAS score	2	0	P=0,041*
Postoperative 2nd hour VAS score	6	5	P=0,035*
Postoperative 4th hour VAS score	4	4	P>0,05
Postoperative 6th hour VAS score	5	5	P=0,013*
Postoperative 8th hour VAS score	4	4	P>0,05
Postoperative 12th hour VAS score	3	3	P>0,05
Postoperative 24th hour VAS score	2	2	P=0,021*
Total number of analgesic needs	2	1	P=0,008*
Number of PCA bolus opioid use	1	0	P>0,05
Number of additional NSAID use	1	1	P=0,007*

Statiscal significance level was accepted as p<0.05

It was also determined in our study that as the Vitamin D values of the patients decreased, the number of bolus opioid and total analgesic requirements used was higher (p=0.000, Table 4). In our study, a statistically significant negative correlation was found between vitamin D values and VAS values at postoperative 1st and 6th hours in female patients (p=0.018, p=0.020, Table 5). In addition, as the vitamin D values increased, it was observed that the number of bolus opioid and total

analgesic needs decreased (p=0.001, p=0.025, Table 5). In male patients, a negative correlation was found between vitamin D values and postoperative VAS scores (p=0.012, p=0.001, p=0.020, p=0.001, Table 6). In addition, it was determined that as vitamin D values increased in male patients, the time of first analgesic administration was also prolonged (p=0.036, Table 6).

Table 4. Correlation of age and vitamin D values in all groups

		Sensory block end time	Postop. 1st hour VAS	Postop. 2nd hour VAS	Postop. 4th hour VAS	Postop. 6th hour VAS	Postop. 8th hour VAS	Postop. 12th hour VAS	Postop. 24th hour VAS	First analg. admin. time	Total analgesic needs	PCA bolus opioid use	Add. NSAID use
Age	r value	-0,024	0,115	0,035	-0,039	-0,165	-0,336 *	-0,003	0,054	0,125	-0,006	0,103	-0,099
	p value	>0,05	>0,05	>0,05	>0,05	>0,05	0,014 *	>0,05	>0,05	0,371	0,968	0,465	0,479
Vit D	r value	0,585 **	-0,519 **	-0,548 **	-0,22	-0,554 **	-0,273 *	-0,265	-0,567 **	0,452 **	-0,658 **	-0,579 **	-0,202
	p value	0,000	0,000	0,000	>0,05	0,000	0,048	>0,05	0,000	0,001	0,000	0,000	0,147

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 5. Correlation of age and vitamin D values in female patients

		Sensory block end time	Postop. 1st hour VAS	Postop. 2nd hour VAS	Postop. 4th hour VAS	Postop. 6th hour VAS	Postop. 8th hour VAS	Postop. 12th hour VAS	Postop. 24th hour VAS	Total analgesic needs	PCA bolus opioid use
Age	r value	-0,411	0,289	0,027	0,224	-0,280	-0,119	0,175	0,082	-0,061	0,283
	p value	0,081	0,231	0,911	0,357	0,245	0,628	0,473	0,739	0,804	0,240
Vit D	r value	0,535*	-0,535*	-0,399	0,073	-0,527*	-0,252	-0,155	-0,363	-0,511*	-0,720**
	p value	0,018	0,018	0,091	0,765	0,020	0,298	0,526	0,127	0,025	0,001

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 6. Correlation of age and vitamin D values in male patients

		Sensory block end time	Postop. 1st hour VAS	Postop. 2nd hour VAS	Postop. 4th hour VAS	Postop. 6th hour VAS	Postop. 8th hour VAS	Postop. 12th hour VAS	Postop. 24th hour VAS	Total analgesic needs	PCA bolus opioid use	First analg. admin. time
Age	r value	0,172	-0,025	-0,026	-0,217	-0,273	-0,509**	-0,158	-0,021	-0,101	-0,018	0,451**
	p value	0,331	0,890	0,883	0,218	0,119	0,002	0,372	0,907	0,571	0,919	0,007
Vit D	r value	0,501 **	-0,426*	-0,536 **	0,003	-0,396*	-0,112	-0,149	-0,560**	-0,719**	-0,532**	0,361*
	p value	0,003	0,012	0,001	0,988	0,020	0,528	0,399	0,001	0,000	0,001	0,036

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

Vitamin D deficiency is an important cause of concern for human health. Especially the elderly people are at high risk for deficiency (6,14). In our study, the average vitamin D values of our patients were found to be below our reference laboratory

values of 20-32 µg/L and were significantly lower in women (12.04±4.69) compared to men (16.13±4.68). Our study has resulted in a similar way in this respect with studies in the literature showing a higher rate of moderate vitamin D insufficiency in women (15-17). Low vitamin D levels in the body are known to be associated with many diseases such as osteoporosis, heart disease, and type I diabetes (18). Vitamin D has a major role in the perception of pain. Low level of Vitamin D has been associated with headache, abdominal pain, back pain, musculoskeletal pain, and fibromyalgia. Pain pathways associated with hormonal, immunological, and neuronal changes are affected by vitamin D levels (11,12,19). Inadequate treatment of postoperative pain delays patient recovery. Although the importance of effective pain control is acknowledged, 70% of patients still complain of moderate or severe pain after surgery (20). Hip arthroplasty is associated with high degree postoperative pain. Effective postoperative pain management leads to early recovery and reduces hospital stay (21,22). In our study, it was found that there was a negative correlation between the vitamin D values of our patients and the postoperative VAS scores at the 1st, 2nd, 6th, 8th, and 24th hours, and the VAS score increased as the vitamin D level decreased. The effect of gender differences on clinical pain conditions is well known. In many studies, it has been found that women have more severe pain than men and consume more morphine in the postoperative period (23,24). Female patients have a higher incidence of pain than men in terms of acute pain as well as chronic pain (25). Similarly in our study, it was seen that the female patients needed analgesic earlier than male patients, and female patients had higher VAS values than men at the 1st, 2nd, 6th, and 24th hours postoperatively. In the analysis performed in patients who underwent major surgical interventions by Kim et al., it was found that patients with low vitamin D levels had both 1.7 days more opioid use in the postoperative period compared to patients with adequate 25-OH vitamin D levels and found that they used a higher dose of analgesic equivalent to a high morphine milligram (26). There is an independent relevance between low vitamin D level and hospitalization of older adults. Nawabi et al. (27) reported that preoperative low vitamin D levels cause negative consequences after hip arthroplasty, and therefore, studies on vitamin D, which is a relatively basic and inexpensive method to correct, would be useful. In the study of Mak et al., (28) on 218 patients over 65 years with hip fracture, it was reported that the postoperative pain levels evaluated with the Verbal Rating Scale (VRS) were found to be lower in patients with high baseline levels. Also in our study, we found that patients with low vitamin D levels had higher VAS scores. In our study there was a negative correlation between the vitamin D values of our patients and their VAS scores at the postoperative 1st, 2nd, 6th, 8th, and 24th hours, and the VAS score increased as the vitamin D level decreased. In addition, the duration of the first analgesic administration was determined earlier in patients with low vitamin D levels than patients with high vitamin D levels. The study of Xu et al. conducted on 360 patients who underwent lumbar spine surgery, showed that patients with high serum vitamin D levels had better results in terms of postoperative VAS scores. Researchers stated that severe pain scores were among the significant

predictors of vitamin D deficiency (29). In our study, when we evaluated it in terms of analgesic needs, we found that as the vitamin D values of our patients decreased, the number of bolus opioid and total analgesic needs was higher. In pain management, recent findings of vitamin D-mediated prostaglandin E2 inhibition provide a reliable mechanical explanation for the role and mechanism of vitamin D in pain management (30). In the geriatric age group, musculoskeletal pain due to osteomalacia may be due to the formation of a spongy matrix beneath the periosteal membranes caused by demineralization. Expansion of this collagen matrix causes throbbing bone pain (31). Vitamin D deficiency is associated with musculoskeletal pain refractory to drugs (32). These kinds of findings are important in pain medicine because they indicate that vitamin D deficiency is potential comorbidity with pain. Chriss Wall et al. reported that there are a number of modifiable factors, such as anemia, malnutrition, and vitamin D deficiency, that increase the risk of postoperative complications following arthroplasty, and that optimizing these factors in the preoperative period may reduce the risk of adverse outcomes (33). It is known that vitamin D deficiency is observed more frequently in female patients and that there is a positive relationship between this deficiency and various nonspecific bone pain, especially in female patients (16,34). Also in our study, the vitamin D levels of our female patients were statistically significantly lower than those of men. It was also observed that female patients needed analgesic earlier than male patients. Although the total number of analgesic needs needed and the number of additional NSAID use is still not clearly explained in women compared to men, the relationship between vitamin D and pain is still not clearly explained, but it is thought that the most likely mechanism of vitamin D to reduce pain is through its anti-inflammatory effect. Adequate vitamin D levels lead to less inflammation and lower inflammatory cytokine and prostaglandin levels (30). As is known, one of the most important elements of patient comfort after surgery is undoubtedly pain reduction. In our study, there was a negative correlation between vitamin D values and postoperative VAS scores in patients who underwent hip arthroplasty, and patients with low vitamin D values were found to need analgesics earlier. There are also publications in the literature investigating the relationship between low vitamin D levels and high pain scores and reporting that there is no relationship between these two conditions. Bose et al. evaluated the relationship between vitamin D levels and the time-weighted pain scores and whole opioid usage in their analysis of the data of 185 patients with bariatric surgery but reported that they could not find a relationship between preoperative vitamin D levels and postoperative pain scores / opioid consumption in these patients (35). Lee et al. reported that as vitamin D levels decreased in patients with neuropathic pain, pain intensity increased according to the McGill pain questionnaire (MPQ) and VAS scores, and with vitamin D supplementation in both VAS and MPQ there was significant decrease in pain scores of -48.5% and -39.4%, respectively. (36). Low vitamin D level has been associated with poor outcomes, such as long-term hospital stay after hip arthroplasty surgery and measures of quality of life (37). Anna Lee et al. showed that patients with low vitamin D levels in patients who underwent knee arthroplasty had higher

postoperative pain scores. The researchers also stated that the postoperative persistent pain scores for the period 3 months after surgery were also significantly higher in patients with insufficient vitamin D levels. According to results of this study, preoperative hypovitaminosis D has been observed as a risk factor for moderate to severe persistent pain (11). Vitamin D deficiency in geriatric patients is a dominant poor factor for postoperative side effects. Meyer et al. discovered that patients with vitamin D deficiency were more likely to have poor postoperative outcomes in a study on patients who had undergone elective orthopedic surgery. Re-operation rates and hospital readmission rates were observed to be higher in these patients (10). In a study conducted by Heidari et al. (34) on 276 patients with pain in different parts of the skeletal system, found a positive relationship between non-specific pain such as leg pain, arthralgia, rib pain, and low vitamin D levels (<20 ng/ml). Larrosa et al. (38) evaluated parameters such as fracture type, comorbidities, and osteoporosis history in 324 hip fracture patients in their study, and reported that patients who received vitamin D supplements had less severe fractures in fracture grading. Again, several randomized controlled studies in the literature have shown that addition of vitamin D make better pain management and leads to a significantly lower pain score in patients with chronic pain as compared to placebo (39). The main limitation of this study is that the vitamin D levels of the patients were always measured in the same season and another limitation is that the patients VAS scores were evaluated only rest time.

CONCLUSION

In our study, low vitamin D levels in patients who underwent hip arthroplasty surgery were found to be associated with an increase in VAS score, earlier analgesic requirement, and an increase in the amount of total analgesic and bolus opioids used. Considering the frequency of hip arthroplasties in the geriatric population and that this age group is in the high-risk group for D hypovitaminosis, the importance of early diagnosis and treatment of low vitamin D levels becomes evident. It is obvious that any additional medication required for the patient's various needs during the postoperative period will result in additional costs. Considering correctable factors in the preoperative period, especially when it comes to analgesic consumption, can be considered as a safe and low-cost method to overcome these and similar problems. Given the positive effects of vitamin D on bones, muscles, and general health, we believe it is critical to conduct vitamin D screening tests at appropriate intervals determined by health policies and to supplement vitamin D care, especially for individuals in the geriatric age group.

Ethics Committee Approval: This prospective study was approved by the local Ethics Committee (Ordu University, 2017/116-118, Ordu, TURKEY).

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