The Effect of Preoperative 25-Hydroxy Vitamin D Supplement and Surgical Site Infection

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Received: 26 Apr. 2022; Accepted: 08 Dec. 2022

Abstract- Surgical site infection (SSI) is one of the most important complications of surgery and is known in quality improvement programs as a very important indicator for evaluating the performance of surgeons and hospitals. In recent studies, interesting effects for vitamin D such as antimicrobial effects, wound healing, immune regulation, etc. have been considered and the effectiveness of this vitamin on the above has been proven in laboratory environments and animal models. Therefore, the present study was designed and performed to evaluate the effect of vitamin D tablets before surgery on surgical site infection in patients referred to Shariati Hospital. This study was performed as a randomized controlled trial (RCT) on 200 patients who underwent surgery in Shariati Hospital in Tehran and in the general surgery department between 1397 and 1398. Patients were randomly assigned to two groups of 100 persons, including intervention and control. In all patients, vitamin D levels were measured and recorded 15 days before surgery. The intervention group included patients who received 2 tablets of fifty thousand units of vitamin D seven to ten days before the operation. The second group also included patients who did not undergo any intervention and only in order to maintain blindness of the same size and simultaneously with the first group. They received a placebo. Finally, all patients were followed at intervals of one, three, seven and thirty days after surgery and then compared to the extent of infection at the site of surgery and other desired variables. In this study, 200 persons with a mean age of 47.78 years were examined. 57.5% (115 persons) were female and the rest were male. Overall, 19 (9.5%) of the patients studied underwent surgery at the site of follow-up within one month of follow-up (14 in the control group and 5 in the intervention group). Detection between the two groups was observed in terms of infection (P=0.030). In general, based on the results of the analysis, in the present study, there was a statistically significant relationship between surgical site infection with low serum vitamin D level, increase in the number of hospital days, female gender, wound classification, ASA class of patients and vitamin D consumption before surgery. (P<0.05). The results of this study showed that there is a significant relationship between surgical site infection and consumption of edible vitamin D as well as serum vitamin D levels before surgery so that vitamin D deficiency can be considered as an independent risk factor for infection. Hospitals were considered, including surgical site infections. Therefore, performing preoperative tests as well as performing the required interventions can be very effective in improving this index and reducing surgical site infections.

Acta Med Iran 2023;61(1):36-42.

Keywords: Vitamin D tablets; Surgical site infection; Risk factors; Surgical site infection (SSI)

Introduction

Surgical Site Infection SSI (Surgical Site Infection) is one of the most common and serious complications in surgical patients, which increases mortality, complications, hospitalization time and the cost (1-2).

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Infection of the surgical site occurs in 2-5% of patients after external abdominal surgery (such as thorax surgery, orthopedics and neurosurgery) and occurs in more than 20% of patients undergoing intra-abdominal surgery (3-5).

Due to the potentially dangerous consequences of surgical site infection despite antibiotic prophylaxis, it may be necessary to identify the risk factors. Surgical site infection (SSI) is one of the most important and costly complications of surgery and is known in quality improvement programs as a very important indicator for evaluating the performance of surgeons and hospitals (6-9). Therefore, finding new methods to improve this index is an important and attractive topic in scientific societies. Recent studies have focused on the dramatic effects of vitamin D, such as antimicrobial effects, wound healing, immune regulation, cell growth, maintaining the integrity of intestinal mucosa, and the impact on diabetic wounds of course animal models have been proven these effects (10).

Although some of these studies have looked at the potential effects of this vitamin in reducing nosocomial infections and surgical site infections, so far, a comprehensive study has been able to show the relationship between the location of infections in general surgeries (and not just specific types) determining the vitamin (11-13). Despite advances in surgical techniques and the pathogenesis of infection, surgical wounds have been widely used and prophylactic antibiotics have been widely used. It is one of the most common nosocomial infections in patients with infectious diseases, leading to an increase in morbidity and mortality (14). According to the CDC, there are 500,000 surgical wounds in the United States each year, with the average length of hospitalized wound infection increasing to 7.5 days and costing the United States about $ 130 million to $ 845 million annually (15,16).

Therefore, due to the high prevalence of vitamin D deficiency in Iran and other countries and the potential effects of this deficiency which cause increasing the rate of infection at the surgical site and lowering the quality indicators of hospital services, it is necessary to study in this field. If the relationship between vitamin D intake and reduction of nosocomial infections, especially surgical site infections, can be clarified, a big step can be taken in reducing its potential costs to the health system and the risks facing patients. Therefore, the present study was designed and conducted to investigate the relationship between pre-operative vitamin D intake and surgical site infection.

Materials and Methods

The present study is a randomized clinical trial (RCT) study conducted over a two-year period at Shariati Hospital in Tehran. For this purpose, at first all patients who underwent elective surgery in 2018 and 2019 were invited to enter the study. The Informed consent form was obtained from all patients. In the next step, patients who did not meet the criteria for admission to the study were eliminated. Then, using the table of random numbers, the patients were divided into two groups of treatments, including intervention and Random Allocation. In all patients, vitamin D levels were measured and recorded 15 days before surgery.

The two study groups included: 1- The first group of patients who received 2 tablets of fifty thousand units of vitamin D seven to ten days before the operation and 2- The second group of patients who did not undergo any intervention and notes in order to maintain blindness. They received the same size as the first group.

Finally, all patients were followed at intervals of one, three, seven, and thirty days after surgery, and then the rate of infection at the site of surgery and other variables that we assessed at the beginning of the study, in each Marked from these time intervals points (check) were re-measured and compared in each of the two groups.

All patients who underwent surgery at Shariati Hospital from 1397 to 1398, with all of the following indicators, were examined for study:

Inclusions criteria

1- Patients are candidates for thoracic and abdominal elective surgery.

2- Age over 10 years and less than 80 years.

Exclusion criteria

1- patient's unwillingness 2- Cancer or receiving chemotherapy, taking corticosteroids and immunosuppressive drugs 3- Having diabetes and other metabolic diseases 4- Laparoscopic or emergency operation.

Initially, in all patients undergoing surgery, all of the following were recorded before surgery and then re-examined at intervals of one, seven, and thirty days after surgery.

- Measurement of serum vitamin D levels.
- Measurement of blood factors including: albumin, hemoglobin, hemoglobin A1C, blood sugar and etc.

The information about each patient was collected in the design information collection form by the relevant

nurse who was blind to the surgery. Some of the information related to the patient's surgery was completed in the operating room by the surgeon, which indicated findings during surgery, accidents during surgery, and duration of surgery.

Our final outcome in this study was determined in both groups of patients by examining and measuring vitamin D levels and the incidence of infection at the surgical site at each time interval, which were eventually compared to obtain a result.

First group intervention: All patients in the intervention group received 100,000 units of vitamin D in two 50,000-unit tablets 7 days before surgery.

Second group intervention: These patients received notes to maintain the same level of blindness at the same time as the first placebo group, which had no therapeutic effect on the patient. The placebo used in terms of size, shape and taste was exactly the same as the vitamin D pill and was ordered from a pharmaceutical company that used the vitamin.

Data analysis methods

The relationship between vitamin D consumption and surgical site infection was assessed using statistical tests (t-test, Chi-Square, Mann Whitney U test, Fisher exact Test and the method of matching tables). Then We modified other statistical methods, including regression modeling and classification, to eliminate or mitigate the effects of disinfectants or other factors influencing the infection that may affect the results.

Results

In general, in this study, 200 persons with mean age of 47.78 years (standard deviation: 15.63 and suffering: 16-81 years) were examined in 2 intervention and control groups (100 persons in each group). According to the study, 57.5% (115 persons) were female patients and 42.5% (85) were men. The average age of men and women was 49.67±15.9 and 46.23±15.4 years, respectively. Also, the mean age of the patients in the intervention and control group was 50.20 and 45.9 years, respectively, which was statistically significant in the age group (P=0.029).

In total, 19 patients (9.5%) of the study patients underwent surgery at the site of follow-up during one month of follow-up. So that 14 persons (14% of the whole group) were in the control group and 5 persons (5% of the whole group) were in the intervention group. Based on the findings, it was shown that a statistically significant difference was observed between the two groups in terms of infection (P=0.030).

The mean levels of vitamin D in the subjects were 56.20±43.35 ng/dL (ranged 10-235), which in the intervention and control group were 69.77 and 42.64, respectively, which had a statistically significant difference (P<0.001).

Also, based on the results of this study, the mean hospitalization time in the intervention group was significantly lower than the control group, so that the average number of hospital days in the treatment and control group was 3.20±1.85 and 5.22±2.44 days, respectively. This difference was statistically significant (P<0.001). The two groups under study did not have significant differences in terms of other variables.

Based on the results of this study, a group of patients with higher vitamin D levels were less likely to develop surgical site infections (P=0.032). In general, based on the results of the analysis, in the present study, there was a statistically significant relationship between surgical site infection with low serum vitamin D level, increase in the number of hospital days, female gender, wound classification, ASA class of patients and vitamin D consumption before surgery (P<0.05).

Table 1. Comparison of qualitative variables studied according to the two studied groups

Variables		Study groups		*P*
		Intervention	Placebo	
Surgical Site Infection (SSI)	**No**	95	86	0.030 *
	Yes	5	14	
Sex	**Male**	37	48	0.116
	Female	63	52	
Vit. D intake befor OP.	**No**	87	83	0.422
	Yes	11	7	
ASA class	**I**	47	42	0.387
	II	38	47	
	III	14	10	
Smoking	**No**	81	74	0.942
	Yes	18	16	
Blood injection before OP.	**No**	94	90	0.194
	Yes	4	7	
Blood injection after OP.	**No**	88	77	0.972
	Yes	7	6	

* Significant

Table 2. Comparison of quantitative variables studied according to the two studied groups

Variables	Study groups	Mean	Std. Deviation	*P*
Age (yr.)	**Intervention**	50.20	15.28	0.029*
	Placebo	45.29	15.67	
Vitamin D level	**Intervention**	69.77	52.39	<0.001*
	Placebo	42.64	25.74	
ICU (day)	**Intervention**	2.37	1.377	0.127
	Placebo	4.51	6.63	
Hospitalization (day)	**Intervention**	3.20	1.85	<0.001*
	Placebo	5.22	2.42	
Blood lost (ml)	**Intervention**	265.18	253.23	0.228
	Placebo	226.67	128.95	
BMI (kg/m^2)	**Intervention**	26.69	5.52	0.314
	Placebo	28.60	17.37	

* Significant

Table 3. Investigating the relationship between the studied variables and surgical site infection (SSI)

Variables		Surgical site infection		*P*
		Positive	**Negative**	
Study Groups	**Intervention**	5	95	0.030 *
	Placebo	14	86	
Age (yr)		46.83	48.1	0.074
25-hydroxy vit. D (ng/dl)		24	57	0.032*
BMI		23	27	0.221
Albumin (g/dl)		3.68	3.88	0.271
HGB A1c (%)		5.97	5.76	0.079
HTN (no.)		4	42	0.082
Cr (mean)		0.855	0.933	0.364
Sex (no.)	**Male**	4	81	0.047*
	Female	15	100	
Smoking (no.)	**No**	1	33	0.201
	Yes	15	140	

*Significant

Table 4. Investigating the relationship between other variables studied with surgical site infection (SSI)

Variables	Level	Surgical site infection		*P*
		Positive	**Negative**	
ASA classification	1	4	85	0.008 *
	2	8	77	
	3	6	18	
Hospital LOS (D)	Mean± SD	15.42	4	< 0.001*
Blood lost (cc)	Mean± SD	255	195	0.235
Blood transfusion (before)	No	17	167	0.265
	Yes	2	8	
Blood transfusion (after)	No	152	14	0.921
	Yes	12	1	
Wound classification	Dirty	5	2	0.033*
	Clean/ contaminated	12	158	
	Contaminated	3	12	

*Significant

Discussion

Today, due to the importance of nosocomial infections, especially surgical infections due to complications, mortality, as well as the imposition of direct and indirect costs on the patient and the health care system, the issue of controlling and preventing these infections is very important. On the other hand, due to the prevalence of vitamin D deficiency in Iran and the known effects of vitamin D on wound healing in

the laboratory, as well as the existence of some studies on the relationship between vitamin D deficiency and further prevalence of nosocomial infections, including wound infections of some types. Specific surgery, as well as the absence of comprehensive studies in this field, this information was designed and implemented as an intervention with the aim of investigating the relationship between vitamin D pills before elective surgery and the rate of wound infection after surgery.

Surgical site infection (SSI) is one of the most important and costly complications of surgery and is known in quality improvement programs as a very important indicator for evaluating the performance of surgeons and hospitals. Therefore, examining the factors affecting these infections and finding new methods to improve this index is an important issue. Recent studies have shown interesting effects on vitamin D, such as antimicrobial effects, wound healing, immune regulation, cell growth, and effects on diabetic wounds, and have been shown to be effective in laboratory and animal models. In the present study, it was shown that taking vitamin D tablets in the amount of 50,000 units has a significant effect on reducing infection at the surgical site (P=0.030).

In general, based on the findings, the incidence of surgical site infection in the studied patients was 9.5% (19 cases: 14 in the control group and 5 in the intervention group). It was relatively higher than other studies, for example, in the United States, Italy (12), Turkey (13) and India (9), the rate of infection at the surgical site was 1.9, 2.6, 4.1, and so on. 5% reported. However, the study found that most of these studies were mainly retrospective and almost all were performed on a specific type of surgery, which may be due to differences in the results of the study. Because in this type of study, the probability of misuse of information and consequently distortion of results is high. However, studies in Brazil (14) on the incidence of infection at the site of general surgery have shown that the SSI rate is high, at about 11%, which is consistent with our study. Another reason for the differences in the results of different studies is the existence of different care systems in these countries, each of which has a different level of sensitivity in identifying patients. Also, in a study that Monshizadeh *et al*., Conducted in 2019 as a forward-looking group on 200 adult patients (over 18 years of age) who underwent surgery (emergency or elective) in the general surgery department, the incidence rate of Surgical infection was estimated to be 11%, which is consistent with the present study.

According to our research in reputable scientific databases, few studies have been conducted on the relationship between the incidence of surgical site infection and vitamin D deficiency in specific types of surgery alone. But so far, no clinical trials have been published on the effect of vitamin D on surgical site infections. The results of this study showed that vitamin D intake before surgery is associated with infection, and the findings showed that serum levels of vitamin D before surgery can affect the location of surgery. Quraishi *et al*., Also reported in a 2014 study that vitamin D deficiency before surgery increases the risk of nosocomial infections, including SSI, which is consistent with our study. However, the authors acknowledged that their study was only performed on patients who had undergone a specific type of surgery (R & Y Gastric Bypass) and that their findings could not be generalized to other surgeries (12).

Today, vitamin D deficiency, especially in specific geographical areas, is a major problem in health systems and its prevalence is reported to be between 20-80% (15). According to the results of this study, 88 (44%) of the 200 subjects had abnormal levels of vitamin D. The prevalence of vitamin D deficiency was consistent with reports published domestically. A 2014 study in Brazil found that 54 percent of pre-operative vitamin patients were abnormal. The findings of this study were consistent with the present study. Also, in our study, vitamin D deficiency was less common at older ages.

In our study, a group of patients with higher vitamin D levels before surgery were less likely to develop surgical site infections, according to Quraishi and colleagues' findings on patients undergoing R & Y Gastric Bypass surgery (12). Also, using the multivariate analysis experience, our study showed that oral administration of vitamin D before surgery is associated with a reduction in the length of hospitalization time. In the present study, classification of wound type (in a variable analysis), female gender, ASA class of patients, low serum levels of vitamin D and the number of hospitalization days were independent risk factors for surgical site infection. This finding was consistent with the findings of other studies, with Rafael Lima *et al*., 's study showing that preoperative hospitalization, surgical duration, labor class, and ASA classification were independent risk factors for surgical site infection. (16). ANVISA *et al*., (17) also showed in a study that increasing the length of hospital stay before and after surgery has the best chance of causing infection at the surgical site. The study by Monshizadeh *et al*., also showed that gender variables, hospital duration and ASA Classification play an independent risk factor in

surgical site infection (18).

The results of this study also showed that there was a relationship between the level of infection at the surgical site with age variables, the number of days hospitalized in the ICU, BMI, the amount of bleeding during surgery, receiving blood before and after surgery, and smoking. Statistically, it was not significant (P>0.05). Also, no significant relationship was observed between other laboratory factors and infection at the surgical site. The use of cigarettes in our study was not a risk factor for surgical wound infection (despite the increased incidence of surgical wound infections in smokers), the results were different in relation to smoking and surgical site infection, so Malone *et al*., Surgery for wound infection has not been reported (19), but other studies have identified tobacco as risk factors (20,21).

The results of this study showed that there is a significant relationship between surgical site infection with pre-operative vitamin D consumption and pre-operative vitamin D level, so that vitamin D deficiency can be considered as an independent risk factor for infections. He was hospitalized with an infection at the surgery site. It was also shown that there was a statistically significant association between infection at the site of surgery and gender, ASA class, wound classification, and number of hospitalization days after surgery. Therefore, performing preoperative tests as well as performing the required interventions can be very effective in improving this index and reducing surgical site infections.

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