EFFECT OF SERUM PTH, CALCIUM AND VITAMIN-DSUPPLEMENTATION ON FRACTURE HEALING

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ABSTRACT

Introduction: A bone fracture is a complete or incomplete discontinuity of bone caused by a direct or indirect force. Irrespective of the reason, type, severity, the fracture will badly affect the regular activities of an individual. Upon studies it has been found that the levels of serum calcium, vitamin-D and parathyroid hormone are related to better fracture healing. The present study is focused on effect of supplementation of calcium, PTH and vitamin-D on the duration of bone fracture healing in individuals with those who are not under any supplementation

Materials & Methods: Among the two groups, one group is supplemented with calcium, PTH and vitamin-D whereas another group patients have not received any supplementation. The results were averaged for each parameter subgroups separately for Diabetics & Non-diabetics. Statistical analysis was done using IBM SPSS.

Results: It is observed that the mean levels of vitamin-D are higher in the supplementation group. Similarly, the levels of calcium and PTH were also found to be higher in the supplementation group.

Discussion: In the present study, the correlation between the levels of serum calcium, PTH, vitamin D are highly significant. This signifies the probability of correlation of bone fracture healing with the levels of calcium, PTH and vitamin-D of the individuals. Studies have shown that vitamin D affects bone healing through action on inflammatory cells, cytokines, growth factors, osteoblasts, osteoclasts, and the mineralization process; however, this effect is considered insufficient to achieve complete repair. The effect of calcium with vitamin D supplementation on fracture healing might require higher doses of vitamin D alone if used. This dose–response concept is supported by studies indicating that low levels supplementation vitamin D has a similar effect when given in combination with calcium and PTH.

Keywords**:**Fracture, calcium, PTH, Vitamin D, healing.

INTRODUCTION

A bone fracture is a complete or incomplete discontinuity of bone caused by a direct or indirect force [1]. The dictionary definition of a 'fracture' is 'breakage of a bone, either complete or incomplete' [2]. Irrespective of the reason, type, severity, the fracture will badly affect the regular activities of an individual. Every individual wants to recover fast and lead a normal routine regular lifestyle as early as possible. For early recovery and better performance, medical management of all the types of fractures is a must. Individuals receiving better medical support will recover early and better.

Along with the medical support, if the individual also gets support of body healing process, the fracture can be healed earlier. Upon studies it has been found that the levels of serum calcium, vitamin-D and parathyroid hormone (PTH) are related to better fracture healing [3].Low dietary calcium intakes and inadequate vitamin D stores have long been implicated in the pathogenesis of age-related bone loss and osteoporosis [4]. In this scenario, lowered levels of calcium, parathyroid and vitamin-D are commonly observed in the present population. This leads to increased risk and severity of fracture and poor healing.

Calcium is an important mineral mainly in bones and acts as a reservoir for calcium homeostasis. Vitamin-D is crucial in regulating the levels of calcium by absorption from intestines and kidneys and bone remodeling [5,6]. Calcium and vitamin D deficiency results in bone resorption [7,8].Because of the significance of calcium and vitamin D in normal bone structure, the management of fractures and osteoporosisincludes their supplementationfor the people who are at high risk of osteoporosis, postmenopausal females along with regular dietary calciumand vitamin D intake [9].

PTH shows its effect on kidneys, intestine, and bone resulting the regulation of serumcalcium level. In kidneys, calcium and PTH receptorsoverlap; so, PTH levels have direct effect on calcium levels. PTH results in reabsorption of raised calcium from glomerularfiltrate. On bones, PTHeffect depends on the condition. The effect on bonein early effect include, release ofcalcium from bones into blood, and late effect, includes reabsorption and bone remodeling. Among the twotypes of bone cells, only osteoblasts are found to respond to PTHhormone. Osteoclastslack PTH receptor response [10]. PTHpromotes calcium absorption from the bone indirectlythrough the action of calcitriol[11].

The present study is focused on effect of supplementation of calcium, PTH and vitamin-D on the duration of bone fracture healing in individuals with those who are not under any supplementation. In our routine patient services, we have found some correlation between the PTH, calcium and vitamin-D. This made us to explore further the correlation of supplementation of the same with time taken for healing in the cases of fractures.

MATERIAL & METHODS

The present analysis study was carried out on the patients who took treatment for the different fractures at Maheshwara Medical College & Hospital. Subjects brought for initial management for different fractures were included in the study. A totalof about 235 people have given their initial consent for participating in the study. Out of these, about 214 were eligible as

per the inclusion criteria. Among these, 200patients wererandomly included in the present analysis after considering the inclusion and exclusion criteria.Immediate cases of fractures were included in the present study. Patients withrenal diseases, hepatobiliary diseases, other bone diseases and some drugs that may affect hormone levels were excluded; already under previous other medical treatment, under PTH, calcium, vitamin-D supplementation or taking any other hormones which may alter bone composition, with previous history of fracturesare excluded from the study.Out of total 200 patients, 100 patients were randomly selected in supplementation group, to whom PTH, calcium and vitamin D supplementation is given. Other 100 patients included control group for whom any type of such supplementation was not given. Care is taken for age and gender matching among the two groups.The fracture which not reachedthe standard of complete healing of fracture within 4months was defined as bone delayed healing.The Ethics Committee of the Maheshwara Medical College & Hospital, Sangareddy, Telangana has approved the study protocol. Writteninformed consent has been obtained from all the participants of the study.

Laboratory analysis was performed on the morning afterinjury in fasting state. Among typical routine laboratoryvalues, serum calcium, vitamin D and parathyroid hormone levels were assessed. Blood samples were collected into serum separator tubes(BD Vacutainer, Australia). Blood sampleswere left to clot for 30 min before being centrifuged at 1500g for 10 min at 4°C. Serum was obtained and calcium, PTH and vitamin D concentrations were measured by chemiluminescent immunoassay (Access 2; Beckman Coulter, CA).

The data was arranged in suitable tables for analysis under different headings. The results were averaged as(mean ± standard deviation) for each parameter subgroups separately for Supplementation& Non-supplementation groups. Statistical analysis was done using IBM SPSS Statistics 20 package. p-value of <0.05 is considered as statistically significant and p-value of <0.005 is considered as statistically highly significant. Conclusions were drawn based on outcome of this statistical analysis.

RESULTS

On statistical analysis of the levels of Serum calcium, Vitamin D and PTH in supplementation group and Non-supplementation group, the following results are observed.

Table 1: Paired samples statistics among supplementation and Non-supplementation groups.

		Mean	N	Std. Deviation	Std. Error Mean
Vitamin-Dng/mL	Non-supplementation group	14.02	50	3.94	0.55
	Supplementation group	30.72	50	10.00	1.41
Ca mg/mL	Non-supplementation group	6.62	50	1.82	0.25
	Supplementation group	8.86	50	1.05	0.14

PTH pg/mL	Non-supplementation group	23.02	50	12.46	1.76
	Supplementation group	27.34	50	9.30	1.31

Upon observation of the results, it is observed that the mean levels of vitamin-D are higher in the supplementation group. Similarly, the levels of calcium and PTH were also found to be higher in the supplementation group when compared to non-supplementation group as shown in table-1.

On analysis of the levels of serum calcium, PTH and vitamin-D, it is confirmed that the levels are higher in the supplementation group in which there was early healing of fractures noted. By this we can confirm that the supplementation of calcium, PTH and Vit-D will help in early healing of the bone fractures.

Table 2: Paired Differences among supplementation and Non-supplementation groups.

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Vitamin-Dng/mL	-16.70	11.01	1.55	-19.83	-13.56	-10.721	49	0.000
Ca mg/mL	-2.240	2.14	0.30	-2.84	-1.63	-7.390	49	0.000
PTH pg/mL	-4.320	15.01	2.12	-8.58	-0.05	-2.035	49	0.047

The mean values of Vitamin D levels were 14.02 and 30.72ng/mL respectively in non-supplementation and supplementation groups. Similarly, the mean calcium and PTH levels were found to be 6.62mg/mL; 23.02pg/mLin non-supplementation group and 8.86mg/mL; 27.34pg/mLin supplementation group.

DISCUSSION

In the present study, the correlation between the levels of serum calcium, PTH, vitamin D are highly significant. This signifies the probability of correlation of bone fracture healing with the levels of calcium, PTH and vitamin-D of the individuals.

In their study by Haines et al. which included study on 50 patients each for studying effect of supplementation. They found a very low non-union rate. Two cases each were found in both control andsupplementation groups. Even the results cannot be considered due to very less number of study participants[12].In another study by Gorter et al. also reported low non-union rates[13].This cohort study analysed the correlation between the differencesin fracture healing of those who were vitamin D deficienteven after receiving supplementation, with those who were found to have increased levels aftersupplementation.

Studies have shown that the fracture healing process in bones includes the effect of vitamin-D on inflammatory cells, growth factors,osteoclasts,osteoblasts, cytokines and mineralization[14,15,16]. It is also observed that incidence of certain diseases like diabetes, vitamin D has an effect on bonetissue resulting increased bonedemineralization due to disease itself [17]. Other studies also have signified the role of vitamin D in the clinical management of osteoporosis, bone regeneration and increased chondrogenesis at injury site [18].

Parathyroid hormoneis a 84amino acid hormone which regulatescalcium and phosphorus metabolism.Increased PTH levels are responsible for formation of adiponectinin the adipose tissue [19]. Intermittent low-dose PTH therapy results in increased bone healing bymore mRNA and protein levelsduring initial stages of fracturehealing [20]. Parathyroid hormone is used in management of osteoporosis and also to decrease the risk of fractures.PTH is related to fracturehealingand also of bone growthfactor. In a prospective study by Kastirr et al. it is observed that 95% of non-union patients when given PTH, resulted in better fracture healing [21]. In the present study, we observed that PTH levels in supplementation group were raised compared to other group without supplementation after fracture, indicating therole of PTH in fracture healing.

When calcium and vitamin D supplementations are given to fracture patients, its dosage was less when compared to only vitamin D. to get the same effect the only vitamin D dose has to be raised. This concept is supported by studies indicating that supplementation has a lowered effect or no effect on the risk of fracture [22-24], whereas in other studies, the levels of supplementation needs to be higher [22,25-28].

CONCLUSION

In the present study, it is found that there is significant importance to the diet taken.A certain quantity of vitamin D is present in foods such assalmon, eggs, milk, cheese, and above all in animal fats. Sunlightusually covers 80% of vitamin D needed [29].When a vitamin D supplementation is needed, it can be prescribedboth as ergocalciferol (vitamin D2) and cholecalciferol(vitamin D3).Thus, to optimize clinical efficacy, vitamin Dshould be complemented with calcium, PTH [30].

It would be useful, though to undertake further studiesto discover more about the mechanism and the effect ofvitamin D, calcium, PTH on the cells of the bone causing early healing. These type of correlation studies have to be further done extensively to understand role of certain minerals, hormones and Vitamins and its actions in large population with varied factors.

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