ORIGINAL ARTICLE

Effect of Calcium and Vitamin D Supplementation in Patients with Fracture Nonunions

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ABSTRACT

Objective: To study the effects of calcium and vitamin D supplementation in cases of fracture nonunion.
Study design: Non-randomized intervention study.
Place and duration of study: This study was carried out at Combined Military Hospital Gujranwala Cantonment, from October 2010 to October 2011.
Methodology: 14 patients were included. Serum calcium, vitamin D and parathormone (PTH) levels were determined in all of these patients. The patients were divided into 2 main groups. Group 1 was medical where only calcium and vitamin D supplementation was done. Group 2 was surgical which was again divided into two subgroups. In sub-group (A) surgery was supplemented with calcium and vitamin D administration, and second sub-group (B) underwent surgery with no supplementation. Tab Qalsan, 1 OD and tab Bone One 0.5ug was administered as calcium and vitamin D supplementation. Follow up of the cases was done on monthly basis. Calcium and vitamin D supplementation was continued till union of fractures.
Results: In this study males were 85.71%. Mean age was 37.71 years. The mean duration from injury to presentation with nonunion in our study was 11.4 months. Out of 14 patients, 5 cases were managed with calcium and vitamin D3 therapy only. 2 cases underwent operative intervention with calcium and vitamin D3 therapy. 7 cases underwent operative intervention without calcium and vitamin D3 administration. 2 patients had low serum calcium, 6 had low serum vitamin D and 1 had low serum parathyroid hormone level. 95% confidence interval for having a metabolic or endocrine abnormality for patients with nonunion was 26.8% to 73.2% by Adjusted Wald Method. All of the patients achieved bony union. The mean time for union was 6. 4 months.
Conclusion: Vitamin D deficiency was detected in 6 of our patients suffering with long bones nonunion. With oral calcium and vitamin D replenishment, union was achieved. This shows that metabolic supplements do have a role in union of fractures in addition to appropriate surgical intervention.

Key words: Fracture nonunion, bone, hormone, vitamin D

INTRODUCTION

Nonunions of fractures occur infrequently and may be multifactorial.[1] Approximately 5% to 10% of all patients will have some problems obtaining final union of their fractures. The most advanced form of difficulty is a fracture nonunion, where the normal biologic healing process ceases to the extent that solid bony union will not occur without further treatment.

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Some predisposing factors include fracture instability, poor vascularity, inadequate fracture reduction and poor bone-to-bone contact. In other cases, a patient may present with a well stabilized fracture that fails to unite.[2] The role of metabolic bone disease and endocrine abnormalities in nonunions is often overlooked.[3] Abnormalities of vitamin D, calcium, and parathyroid hormone may adversely affect fracture healing due to their significance in bone metabolism.[3,4] To the best of our knowledge, only one large consecutive series has attempted to document a relationship between metabolic and endocrine abnormalities and fracture nonunion.[2]

In our set-up we do not routinely prescribe calcium and vitamin D supplementation. The purpose of our study was to determine the effect of calcium and vitamin D supplementation on bony nonunion. What could be done further to enhance union? Metabolic and endocrine array included

detection of calcium, phosphorus, vitamin D3 and parathormone levels.

PATIENTS AND METHODS

20 cases of fracture nonunions were received at Combined Military Hospital Gujranwala from October 2010 to October 2011. All patients with infected, defect or pathological fracture nonunions were excluded. 14 cases met the inclusion criteria.

The inclusion criteria were:

1. Nonunion that occurred despite adequate initial reduction and stabilization
2. History of multiple low-energy fractures with at least one progressing to a nonunion
3. Undisplaced or minimally displaced fractures progressing to nonunion.

The diagnosis of nonunion was confirmed in all cases by the presence of one or more of the following:

1. Gross motion at the injury site on physical examination.
2. Motion at the injury site under fluoroscopic stress views
3. Bridging bone on 0 of 4 cortices of the anteroposterior and lateral radiographs, as described by Heckman et al.[5]

Hospital Ethics Committee approval was sought for the study. All patients were sent to pathologist for metabolic screening.

The distribution of nonunion types[6] was: oligotrophic, atrophic, and hypertrophic. The treating orthopaedic surgeon based on plain radiographs determined the nonunion type. Oligotrophic nonunions were identified as those with an apparently adequate blood supply but little or no callus formation. Atrophic nonunions were identified as those with an apparently inadequate blood supply and no callus formation. Hypertrophic nonunions were identified as those with abundant callus but a clear radiolucent line at the fracture site.

Evaluation for metabolic/endocrine abnormalities in the study group included serum calcium (Ca), Vitamin D3 (Vit D3) and parathormone (PTH) levels. All of the tests results were evaluated. Two main groups were identified. Group1A comprised of patients who had metabolic derangements but did not undergo operative intervention. They were managed with calcium and vitamin D3 supplementation only. Group 1B comprised of patients who had no metabolic derangements but were treated with calcium and vitamin D3 supplements. Group 2A comprised of patients who had metabolic derangements but underwent operative intervention with supplementation by calcium and vitamin D3. Group 2B comprised of patients who had metabolic derangements and underwent operative intervention without calcium and vitamin D3 supplements. Group 2C comprised of patients who did not have metabolic deficiency but underwent operative intervention for nonunion.

Tab Qalsan 1 OD and tab Bone one (0.5ug) 1 OD were administered as calcium and vitamin D supplementation. Criteria for surgical intervention was:

1. Mechanical failure of implants with nonunion.
2. Conservatively managed fractures with distracted nonunited fragments.
3. Nonunions subsequent to treated open fractures.

Follow up of the cases was done on monthly basis. The rate of union in different groups was calculated. Data was analysed using SPSS version15. Descriptive statistics were used to describe the data.

RESULTS

There were 2 females (14.28%) and 12 males (85.71%) in this study. Mean age was 37.71 years. Mean period from initial fracture to this presentation was 11.4 months. There were 5 (35.71%) atrophic, 5 (35.71%) oligotrophic and 4 (28.57) hypertrophic types of nonunion. Sites of nonunion were 1 (7.14%) scaphoid, 1 (7.14%) intertrochanteric femur, 2 (14.28%) shaft of fibula, 1 (7.14%) shaft of ulna, 2 (14.28%) distal third femur, 2 (14.28%) lateral malleolus, 2 (14.28%) tibial diaphysis, 1 (7.14%) shaft of humerus and 3 (21.42%) shaft of femur.

4 (28.57) cases belonged to group 1A (fracture shaft tibia and fibula, fracture shaft of femur, fracture lateral malleolus, fracture shaft of fibula), 1 case (7.14%) belonged to group 1B (fracture shaft of femur), 2 (14.28%) cases belonged to group 2A (fracture lateral malleolus, fracture distal femur), 1 (7.14%) case belonged to group 2B (fracture shaft of tibia), 6 (42.86%) cases belonged to group 2C (fracture scaphoid, fracture intertrochanteric femur, fracture shaft of ulna, distal third femur and shaft of humerus).

Table 1: Salient characteristics of 14 patients included in the study

Sr No	Age (yrs)	Sex	Duration at presentation (months)	Location of Nonunion & Type	Group	Metabolic abnormality &Normal range of values	Medical and surgical treatment given	Outcome of treatment
1	29	male	7	Fr shaft tibia and fibula (Right) (oligotrophic)	1A	- Vit D3 [55nmol/l], (deficiency <30nmol/l, insufficiency 30-75nmol/l, sufficiency >75 nmol/L), - Serum calcium ionized [1.13mmol/l] (1.16-1.32 mmol/l)	Conservative management. Tab Qalsan 1x OD and Tab Bone One 0.5ug 1xOD	Showed union in 6 months
2	59	male	12	Fracture shaft of femur (Right) (hypertrophic)	1A	- VitD3 [22nmol/l], (deficiency <30nmol/l, insufficiency 30-75nmol/l, sufficiency >75 nmol/L)	Closed intramedullary interlocking nail two yrs ago. Put on tab Qalsan 1xOD and tab Bone One (0.5 ug) 1xOD after one year	Showed union in one year
3	37	male	6	Fracture lateral malleolus (Left) (atrophic)	1A	PTH was low [0.45pmol/l] (0.8-6.0pmol/l)	Tab Qalsan 1xOD, Tab Bone One (0.5ug) 1xOD	Showed union in 3 months
4	32	male	30	Shaft of fibula (Left) (oligotrophic)	1A	Vit D3 <10nmol/l] (deficiency <30, insufficiency 30-75, sufficiency >75 nmol/L)	Tab Qalsan 1x tab OD, Tab Bone One 0.5 ug 1 x OD	Showed union at 1 year
5	34	male	12	Shaft of femur (Right) (atrophic)	1B	None	Closed intramedullary interlocking nail 02 yrs ago. Put on tab Qalsan 1xOD, tab Bone One (0.5ug) 1xOD for last one year	Union in one year
6	30	male	12	Lateral malleolus (Left) (atrophic)	2A	Vit D3 was deficient [12nmol/l], PTH was low [0.36pmol]	Tension band wiring + bone grafting + tab Qalsan 1 x OD and tab Bone One 0.5ug 1xOD.	Showed union in 2 months
7	19	female	14	Distal femur (Right) (hypertrophic)	2A	Vit D3 was insufficient [32 nmol/l]	ORIF + bone grafting + tab Qalsan 1xOD and tab Bone One 0.5ug 1xOD	Showed union in 2 months
8	19	male	6	Tibial diaphysis (Right) (atrophic)	2B	Vit D3 was insufficient [35 nmol/l] (deficiency <30, insufficiency 30-75, sufficiency >75 nmol/L),	Ex Fix converted to Closed Interlocking Nail	Showed union in 6 months

						Serum Ca [1.88mmol/l], (2.1-2.65mmol/l)		
9	28	male	6	Scaphoid (Right) (atrophic)	2C	None	Matti Russe technique	Union in 6 months
10	65	male	6	Intertrochanteric Fr Femur (operated CRIF-DHS) (oligotrophic)	2C	None	Revision DCS+ bone grafting	Union in 8 months
11	62	male	12	Shaft of ulna (Right) (hypertrophic)	2C	None	ORIF and bone grafting	Union in 4 months
12	35	male	9	Distal third femur (Right) (hypertrophic)	2C	None	DCS replaced with LCP distal femoral LCP + bone grafting	Union at 6 months
13	57	female	12	Humerus (Right) (oligotrophic)	2C	None	ORIF and bone grafting	Showed union in 4 months
14	22	male	12	Shaft of femur (Left) (oligotrophic)	2C	None	DCP was replaced with intramedullary interlocking nail.	Showed union in 3 months

6 (42.86%) patients had vitamin D3 derangement. 3 (21.42%) patients had vitamin D3 deficiency and 3 had insufficiency. Out of these 6, 2 patients had low serum calcium and 1 had low PTH serum level. 95% confidence interval for having a metabolic or endocrine abnormality for patients with nonunion was 26.8% to 73.2% by Adjusted Wald Method. The adjusted Wald interval (also called the modified Wald interval) provides the best coverage for the specified interval when samples are less than about 150. In other words, if you want a 95% confidence interval then this formula will produce an interval that will contain the observed proportion on average about 95 percent of the time. All of the patients achieved bony union. The mean time for union was 6.4 months. We found union happened in 8.25 months in group 1A, 12 months in group 1B, 2 months in group 2A, 6 months in group 2B, 5.16 months in group 2C. Quicker union rates observed in 1A and 2A showed that metabolic supplementation made union quicker. Laboratory tests for serum Ca, PO_4, vitamin D3 for group 1A, 2A and 2B were done at the end of 2 months, which revealed normal values. Calcium and vitamin D3 supplementation resulted in union in one case belonging to group 1B where there was no Calcium or vitamin D3 deficiency. This patient had nonunion of shaft of femur for one year after initial intramedullary interlocking nailing. (Table 1).

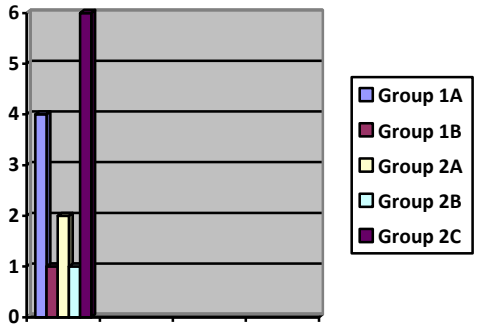

Figure 1: Patients' distribution in groups:

DISCUSSION

Our sample data indicates that 50% of our patients with nonunion had undiagnosed metabolic abnormalities. This findings did not vary by patient

age, gender, or nonunion type. Our results suggest that metabolic abnormalities play a role in the development or persistence of nonunion in some patients.

While our study does not prove a causal link between metabolic abnormalities and either the development or healing of nonunions, 4 patients of group 1A achieved bony union following medical treatment alone after the identification of a metabolic abnormality. There was one patient of group 1B who did not have metabolic derangement yet responded well to oral calcium and vitamin D supplementation. The response to fracture involves many metabolic and endocrine factors, including biochemical interactions of growth factors, bone morphogenetic proteins, vitamins, minerals, and hormones. Impairment of any of these factors could potentially affect fracture healing. Many endocrine and metabolic disorders that affect these factors have been shown to be associated with alterations in bony metabolism.[7-10]

Based on the results of our study, we suggest that all patients with nonunion who fall within our inclusion criteria preferably be referred to an endocrinologist for evaluation. According to our data, these patients are likely to have undiagnosed metabolic or endocrine abnormalities. The goal of the evaluation is to identify any metabolic or endocrine abnormalities and to have the endocrinologist institute medical treatment. Treatment of the metabolic or endocrine abnormalities may facilitate the biological component of bone healing during orthopaedic treatment of the nonunion.

We recommend further investigation to determine whether all patients with nonunion should receive an endocrine evaluation. The biological factors that contribute to development of a nonunion are currently not completely understood. Patients with clinically undetected metabolic or endocrine abnormalities may be at greater risk for persistent nonunion, just as patients with certain metabolic disorders are known to be at greater risk for fracture.[2,11-14]

It may be possible to develop simple clinical screening criteria for patients with fractures to identify those who are at risk for developing nonunion due to an undiagnosed metabolic or endocrine abnormality. If metabolic or endocrine abnormalities are shown to be a causative factor in the development of nonunion, identifying patients with such abnormalities and providing the appropriate medical treatment early in the fracture healing process may decrease the incidence of fracture nonunion. For example, given the high prevalence of inadequate vitamin D levels in the general population,[15] it is likely that many patients who sustain a fracture may also have a vitamin D deficiency that can contribute to the occurence of nonunion. Development of such screening criteria would require prospective studies of large samples of patients with a fracture who all receive an endocrinology evaluation.

Our study revealed that half of our patients with nonunions had metabolic and endocrine abnormalities. However our study design did not allow us to prove a causal link between nonunion and metabolic deficiency. Medical treatment alone was effective in 4 out of 7 metabolically deficient patients, 1 patient responded to oral calcium and vitamin D despite having no deficiency and achieved solid bony union.

CONCLUSION

Metabolic supplements do have a role in union of fractures in addition to appropriate surgical intervention. Large multicenter studies are needed to confirm the causal association of metabolic and endocrine abnormalities with the development of nonunion. Appropriate clinical screening criteria to identify patients with fractures who are at high risk for nonunion due to these abnormalities may also be developed through such studies. Till the time we find a causal link, bone mineral supplements like oral calcium and vitamin D may be administered to patients suffering with fractures as a routine.

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