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SERUM ALKALINE PHOSPHATASE: BIOMARKER FOR ASSESSMENT OF FRACTURE HEALING

Mukunth K[1], Santhosh Kumar Shanthi[2]*, Prabhakar Reddy E[3]

[1] Associate Professor, Department of Orthopaedics, Sri Lakshmi Narayana Institute of Medical Sciences, Affiliated to Bharath Institute of Higher Education and Research, Pondicherry-605 502, India.
[2]Associate Professor, Department of General Surgery, Sri Lakshmi Narayana Institute of Medical Sciences, Affiliated to Bharath Institute of Higher Education and Research, Pondicherry-605 502, India.
[3]Professor, Department of Biochemistry and Central laboratory Head, Sri Lakshmi Narayana Institute of Medical Sciences, Affiliated to Bharath Institute of Higher Education and Research, Pondicherry- 605 502, India.

ABSTRACT

Large increases in serum alkaline phosphatase (ALP) concentrations after fractures in elderly patients have been noted in specialist journals, but standard textbooks either make scant reference or comment that there is little or no rise. Measurements of biochemical parameters appear to be the only objective evidence of the changes occurring during bone regeneration. The aim of this study was to examine whether the assessment of Serum bone specific ALP as a biochemical parameter in the early posttraumatic phase may indicate the course of fracture healing. The level of serum alkaline phosphatase is often valuable in the diagnosis of metabolic bone disease but rises after any uncomplicated fracture, and since such a rise may limit the diagnostic usefulness of this measurement. We studied alkaline phosphatase concentrations in young and elderly patients who had been admitted to an orthopaedic ward because of a fracture and to be continued in our endeavour to find a bone turnover marker as a diagnostic or prognostic tool for monitoring bone healing.

Key words: Alkaline Phosphatase, Osteomalacia, Bone Specific Alkaline Phosphatase.

INTRODUCTION

Serum alkaline phosphatase (ALP) is a member of a family of zinc metalloprotein enzymes that function to split off a terminal phosphate group from an organic phosphate ester. This enzyme functions in an alkaline environment (optimum pH of 10). Active center of ALP enzymes includes a serine residue. Mg and Zn ions are required for minimal activity. Enzyme activity is localized in the brush border of the proximal convoluted tubule of the kidney, intestinal mucosal epithelial cells, hepatic sinusoidal membranes, vascular endothelial cells and osteoblasts of bone.

The normal value of ALP is 20 to 140 IU/L (international units per liter). Adults have lower levels of ALP than children because children's bones are still growing.During some growth spurts, levels can be as high as 500 IU/L [1].

Fracture healing is a proliferative physiological process to facilitate the repair of a fracture [2]. This is a continuous physiological process to achieve union. This process of fracture union is characterized by the production of a new organic matrix, known as osteoid and its subsequent mineralization, thus bridging the gap between two bony fragments by bridging callus. This fracture healing process should be serially quantifiable / measureable [3]. Till date, there is no clinically validated method to measure healing progression. So a valid method for bone union is desired to measure the progress of union

Thus, the values yielded by measurement should be on a continuous numerical scale [4].

Corresponding Author :- **Dr . Santhosh Kumar Shanthi** Email:- drpebyreddy@yahoo.com

However till now, clinicians watch for an end point of complete union without bothering for documenting the values signifying progress of healing [5]. Bone-formation markers are indicative of osteoblastic activity. Although type-III collagen, a non-osteoblastic protein, is the initial collagen laid down during the healing of fractures, it is replaced by type-I collagen when bone formation begins. More specific measures of osteoblastic activity include osteocalcin, the major non-collagenous protein of bone matrix, and the isoenzyme alkaline phosphatase (ALP) [6]. As ALP levels suggest the bone forming activity responsible for both bone matrix formation and its mineralization. This study was carried out to serial ALP levels with progression of fracture healing process which might predict the fracture healing outcome earlier and may allow to intervene earlier.

MATERIAL AND METHODS:

So far as possible we chose patients admitted consecutively who were expected to remain in hospital for at least four weeks. Serum alkaline phosphatase was measured in 45 patients (37 women, 8 men). A sample size of 45 patients 20-65 year, of isolated simple, fresh (< 7 days), traumatic, closed fracture of shaft of femur, treated close reduction and interlocking nail femur in young adults was studied. Isolated simple closed fracture of shaft of femur bone managed as close reduction and interlocking nail femur. Study was obtained Patient giving informed consent. Alcoholism, Pathological fracture, Metabolic bone diseases, Peripheral Neuropath, Inflammatory arthritis, Diabetes mellitus, Malignancy, Patients on medications including (steroids, calcium and fluorides), Chronic liver disease, Chronic renal failure Pregnant women were excluded. The routine investigations blood glucose level, serum alkaline phosphatase levels were done for all the patients. Follow up will be done on the day of admission, 1st day, 15th day, 1 month and 2 month counted from day of trauma and last sample was collected when serum alkaline phosphatase level returned to in its normal range.

The mean serum alkaline phosphatase concentration within one week of the fracture was 65 IU/1, rising to a peak of 119 IU/l in the fourth week. Thereafter concentrations of serum alkaline phosphatase declined slowly but had still not returned to the baseline by eight weeks. Increases in serum alkaline phosphatase concentrations varied considerably between individuals- from 0 to 535 above baseline. There were no differences in the percentage rise above the baseline with age or types of fracture or according to whether the patient had undergone surgery. Likewise there was no difference in the behavior of the serum concentrations between those who remobilized rapidly and those who had a slow course because of general illness or periods of traction.

RESULTS:

Table:1. Baseline characteristics of the study population

Sl. No	Age group	
1	20-35	21 (46.67%)
2	36-50	17 (37.78%)
3	51-65	07 (15.56%)
Gender		
4	Female	8 (17.78%)
5	Male	37 (82.22%)

Table:2. Serum Alkaline phosphatase (ALP) concentration after fracture

Week No	01 (7days)	02 (15days)	04(1month)	08(2months)
ALP	104.32±24.5	230.6±37.5	272.6±43.0	136.0±33.8

DISCUSSION:

In this study, adults of age group 20-65 years have included as the level of serum alkaline phosphatase varies with age. Majority of patients were males. Alkaline phosphatase is a marker of bone formation and the significantly raised levels of serum alkaline phosphatase at 07 days (1^{st} week),15^{th} (2^{nd} week), 1 Month (4^{th} week) and 2 months (8^{th} week) after fracture signify the increased osteoblastic activity occurring at the fracture site. There was no statistically significant difference in the levels of the marker with patient characteristics such as age, sex, and injury factors like the mode and severity of injury, level and pattern of the fracture and presence or absence of comminution in fracture.

The outcome of this study is that estimation of serum alkaline phosphatase correlates with the clinico-radiological signs of fracture healing in femur diaphyseal fracture. There is a significant rise in the level of the bone formation marker demonstrating an increased osteoblastic activity. Level of serum alkaline phosphatase suggesting its role in the mineralization of the callus and consolidation of the fracture. The bone turnover markers are suggested as a non-invasive aid for monitoring fracture healing. They may help in the monitoring of fracture healing, complementing the clinico-radiological evaluation [7]. This study has

further confirmed that a significant change in total serum alkaline phosphatase concentrations occurs after a fracture, so that on average there is a doubling of baseline values, but with considerable individual variation. These changes might be thought to represent osteoblastic activity after bone damage and repair, but the limited isoenzyme data available showed that the increase was not always due to the bone isoenzyme and in some cases was entirely due to the liver isoenzyme. These changes may represent postoperative liver damage due to anaesthetic agents or other factors. Detailed studies of postoperative liver function values have suggested that a rise in total alkaline phosphatase concentrations may occur in about a third of patients in the first few days after operation [8-10] Causes of high bone ALP include bone growth, healing fracture, acromegaly, osteogenic sarcoma, or bone metastases, leukemia, myelofi brosis, and rarely myeloma, so ALP is used as a tumor marker. Bone pain (especially in the spine, pelvis and legs) and muscle weakness appear fi rst. If blood calcium becomes very low there may be muscle spasm in the hands, feet and throat. As bone softens, weight-bearing may lead to bowing of the legs, compression of the vertebrae and fl attending of the pelvis. Weakened bones may break on slight injury.

Diagnosis of vitamin D-deficiency necessitates measurement of serum 25 hydroxy vitamin D concentration. Very low serum 25 hydroxy vitamin D levels are not simply a biochemical abnormality. It is associated with physiological, pathological, and clinical evidence of vitamin D deficiency. Serum 25 hydroxy vitamin D provides evidence of vitamin D status, and levels below 20–25 nmol/L indicate vitamin D deficiency [11]. Skeletal turn-over can be assessed easily and non-invasively by the measurement of turn-over markers. Thus, early knowledge of the individual progress of fracture could help to keep of delayed or non-union by enabling modification of the host biological response. ALP level at 3rd week was correlated with future outcome of these fractures. We may predict the future outcome of these fractures at as early as 3rd week. Our findings were related with ALP level variation during fracture healing were corresponding with that of other studies. In our study, changes in serum ALP level. Serum alkaline phosphatase significantly difference between osteoporotic groups compared to control group but their value within normal range. alkaline phosphatase also agree with study done by Rana [14] and Selvapandian et al.[15] India for all women while disagree with Ramesh et al.[16[who showed raised level in alkaline phosphatase. This may be due to AIP can be drain from osteoblast which is rich with AIP also it found in plasma membrane of the cell in the liver, intestine, and placenta, all of which is may contribute to the total amount of alkaline phosphatase.

Alkaline phosphatase levels were measured in forty five patients six to eight weeks after fracture. The majority were still raised, the most important factor determining the level being the prevailing maximum value. Mildly elevated levels of alkaline phosphatase persisted in several patients when reviewed three months or more after fracture. Comparable figures were not available for those with osteomalacia because vitamin D therapy had been instituted once the diagnosis had been established. Estimation of serum alkaline phosphatase appears to be a useful screening procedure for the detection of osteomalacia in the elderly patient presenting with a fracture of the femoral neck. The level of phosphatase activity remains unchanged in the first week after injury and appears unaffected by the type of fracture. Delay between injury and admission is a most important factor resulting in a high initial value. Since some of these elderly patients are confused or overtly demented, and may normally be relatively immobile, a femoral fracture may remain unsuspected for days or weeks, during which time the alkaline phosphatase level may become considerably raised. It is the initial level of alkaline phosphatase that appears to be of the greatest diagnostic significance [12]. The rise in normal subjects after a fracture is proportionately greater than in those with osteomalacia whose high initial values remain relatively unchanged after their injury. Maximum levels of alkaline phosphatase are therefore oflittle discriminatory value. Since this in turn appears to be the major determinant of the time taken for normal levels to be achieved, persistent abnormality in the six to twelve weeks after fracture is of little significance [13].

CONCLUSION:

The bone turnover markers are suggested as a non-invasive aid for monitoring fracture healing. They may help in the monitoring of fracture healing, complementing the clinico-radiological evaluation. From a practical point of view, the diagnostic value of changes in alkaline phosphatase concentrations in elucidating the cause of jaundice or indicating the presence of osteomalacia or other bone disease is greatly reduced. The present study suggests that as the level of alkaline phosphatase is unaffected by the presence of a fracture during the first week after injury, it can be used as a useful screening test for the presence of metabolic bone disease.

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Conflicts Of Interest

The authors declare no conflict of interest.

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