

Technetium-99m-Phytate Uptake in Bone Fractures

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Three traumatic skeletal fracture cases were investigated with technetium-99m- (^{99m}Tc) phytate, sulfur colloid, and methylene diphosphonate (MDP), to study the behavior of the radiopharmaceuticals at the fracture site. The radiopharmaceuticals were intravenously administered and imaging of the fracture site and its contralateral part was performed at 15 min and 1 hr postinjection for ^{99m}Tc -phytate and ^{99m}Tc -sulfur colloid and after 3 hr for ^{99m}Tc -MDP. It was observed that ^{99m}Tc -phytate shows significant uptake at the fracture site and continues to persist whereas ^{99m}Tc -sulfur colloid does not show any significant uptake. The ^{99m}Tc -phytate scans at the fracture site were similar to ^{99m}Tc -MDP scans. The possible mechanism of the unusual behavior of ^{99m}Tc -phytate is discussed.

The technetium-99m (^{99m}Tc) complexes of phosphate and phosphonates, such as methylene diphosphonate (MDP), pyrophosphate, EHDP etc., generally behave as bone-seeking agents and are used extensively for this purpose. However, an exception to this general behavior was reported in 1973 by Subramanian et al. (1). It was found that the ^{99m}Tc complex of inositol hexaphosphate (phytate) concentrates in the reticuloendothelial system. This unusual behavior of a phosphate complex was explained on the hypothesis that the complex forms an in vivo colloid by chelating with serum calcium, which is subsequently trapped by phagocytes in the reticuloendothelial system.

Technetium-99m-phytate is routinely used in our center for liver/spleen scintigraphic imaging. During such routine studies, we observed an unusual concentration of ^{99m}Tc -phytate at the site of biopsy-proven osteosarcoma (2). Since this initial observation, we have been considerably interested in the possible mechanism of ^{99m}Tc -phytate uptake in bone in disease conditions. Towards this end, we have subsequently carried out studies in other patients with primary bone tumor, such as Ewing sarcoma, and have also compared the behavior of ^{99m}Tc -phytates with ^{99m}Tc -sulfur colloid (SC) (3). Based on these studies, it was postulated that ^{99m}Tc -phytate uptake at the tumor site was probably due to new malignant bone formation associated with the tumor.

The present investigation in three cases of bone fracture due to trauma was performed to elucidate the mechanism of uptake of ^{99m}Tc -phytate in general. The basic aim was to determine whether or not the ^{99m}Tc -phytate uptake is specific to tumor-related bone disease. The results of our investigation and the probable mechanism of ^{99m}Tc -phytate uptake are reported in this paper.

MATERIALS AND METHODS

Three subjects with traumatic injuries, who were screened clinically and radiologically to rule out pathologic fracture, were selected. Table 1 summarizes the clinical findings for each of the three patients. These patients presented with pain, local swelling, marked local tenderness over bone and difficult mobility of the affected limb at the time of first examination. The patients were treated by applying a plaster-of-paris cast before referral for bone and liver scans. Scintigraphic studies were carried out at 8, 3, and 5 wk after sustaining fracture, respectively, in these subjects.

Approximately 10-15 mCi (370-555 MBq) of ^{99m}Tc -MDP were intravenously administered. Bone imaging was performed 3 hr postinjection by employing a large field of view gamma camera fitted with a low-energy general-purpose collimator and a 20% energy window setting. The gamma camera was coupled to a computer system.* Sufficient time was allowed between the investigations to avoid residual activity from the previous study.

Approximately 3-5 mCi (111-185 MBq) of ^{99m}Tc -phytate or ^{99m}Tc -SC was injected intravenously following MDP. The fracture site and its normal counterpart were scanned at 15-min and 1-hr intervals. Each frame was recorded for 10 min. Data were acquired in 128 \times 128 word matrix. Regions of interest (ROIs) were drawn over the fracture site and corresponding normal limb and the radiopharmaceutical uptake was quantified. A liver scan was performed at ~30 min postinjection.

RESULTS

Typical results of radiographic studies shown in Figure 1 revealed compound fracture of affected bone with no associated bone pathology. Bone scans were performed with ^{99m}Tc -

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TABLE 1. Clinical and Radiographic Data

Patient	Age/Sex	Time between fracture and scanning	Clinical		X-ray findings	
			History of trauma	Nature of trauma	Site of fracture	Associated bone pathology
1	25/M	8 wk	+	Road traffic accident	Upper 1/3 of tibia	Negative
2	7/M	5 wk	+	Road traffic accident	Lower 1/3 of humerus	Negative
3	27/M	7 wk	+	Road traffic accident	Lower end of tibia	Negative

MDP. These investigations indicated increased uptake of the radiopharmaceutical at the fracture site (Fig. 2). The rest of the bone scan was normal.

Liver scans were performed with ^{99m}Tc -phytate and ^{99m}Tc -SC. The liver scans were found to be normal in all three patients. However, the ^{99m}Tc -phytate scans differed from ^{99m}Tc -SC scans in that the radiopharmaceuticals concentrated at the fracture site. Scans taken at 15 min and 1 hr indicated that ^{99m}Tc -phytate uptake at the fracture site persisted and in fact increased when compared to the contralateral part. The ^{99m}Tc -SC did not show any significant uptake at the fracture site. The ^{99m}Tc -phytate scan results are shown in Figures 3-4 and the typical result of ^{99m}Tc -SC in Figure 5.

The ^{99m}Tc -phytate and ^{99m}Tc -SC uptake at the fracture site was quantitated by drawing the ROI around the affected site and its contralateral part. The counts thus obtained were compared and these results are shown in Table 2. Quantification was done at two different time periods, 15 min (early scans) and 60 min (delayed images). In the case of ^{99m}Tc -MDP, no such quantification was done, however, visual observation indicated increased uptake of the radiopharmaceutical at the affected site in each of the patients studied.

Comparison of the scan results for ^{99m}Tc -MDP and ^{99m}Tc -phytate (Figs. 2-3) indicated similarity in behavior of the two radiopharmaceuticals with respect to uptake at the fracture site.

DISCUSSION

Bone is comprised of organic matrix, reinforced by inorganic mineral crystals such as hydroxyapatite. In traumatic fracture, bone regenerates primarily by apposition (4). Osteoid is formed by osteoblasts, which is rapidly mineralized by calcium phosphate complexes. The increased uptake of



FIG. 1. AP and lateral radiographic views of right leg with knee joint show compound fracture of upper one-third of right tibia. No associated fracture in fibula.

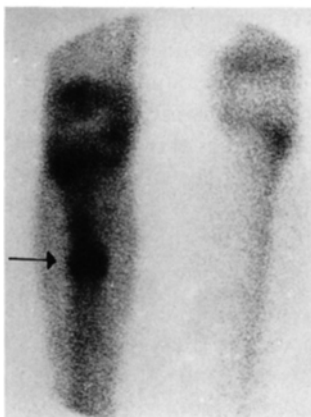


FIG. 2. Bone scan-spot image of fracture site. Note increased radiopharmaceutical uptake at fracture site.

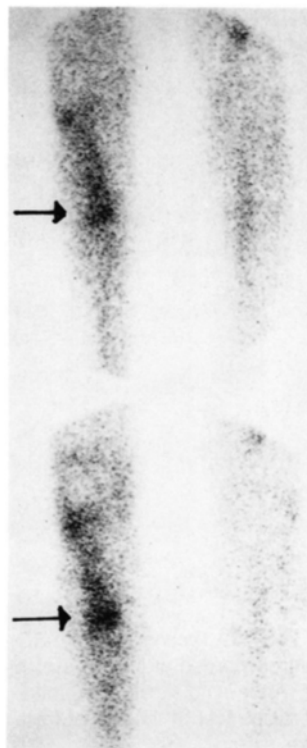


FIG. 3. Technetium-99m-phytate scan. Upper half recorded at 15 min and lower half at 1 hr, demonstrates augmented concentration of radiotracer and persistent uptake.

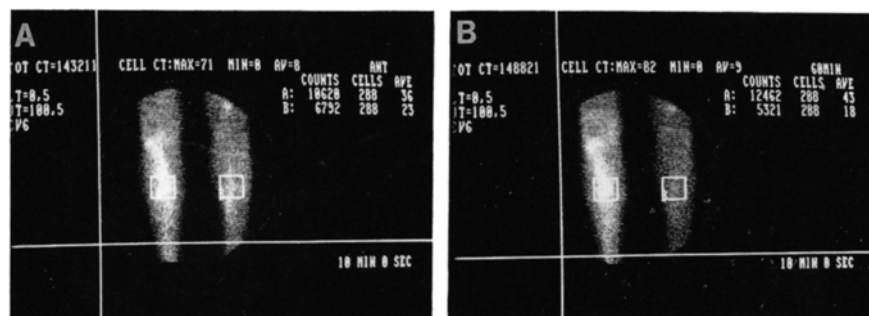


FIG. 4. ROI drawn over fracture site and its contralateral part at (A) 15 min and (B) 1 hr.

TABLE 2. Quantification of Radiopharmaceutical Uptake: Normal Contralateral Part Versus Fracture Site

Patient	MDP Local-ization	Phytate						SC					
		15 min			1 hr			15 min			1 hr		
		NL*	FS	R	NL	FS	R	NL	FS	R	NL	FS	R
1	Increased	6792	18628	1:2.7	5321	12462	1:2.3	2851	3446	1:1.2	1521	2314	1:1.5
2	Increased	2854	7701	1:2.6	2690	9137	1:3.3	1478	1542	1:1	320	551	1:1.5
3	Increased	5112	9618	1:1.8	4370	10816	1:2.4	2931	4519	1:1.5	1816	2816	1:1.6

* NL = normal limb; FS = fracture site; and R = ratio.

the radiotracer ^{99m}Tc -MDP at the fracture site is due to localized increased metabolic bone activity and blood flow relative to normal bone. Additionally, hyperemia is an important secondary factor, accounting for increased availability of the agent at the bone repair site.

The results of our investigation, in three patients with bone fractures due to trauma, with ^{99m}Tc -phytate and ^{99m}Tc -SC indicated that ^{99m}Tc -phytate is taken up at the fracture site

and that distribution of the radiopharmaceutical at the site of uptake is similar to that of the bone agent (Figs. 2-3).

The quantification studies shown in Table 2 indicate that the ^{99m}Tc -phytate uptake ratio of fracture site versus the normal contralateral part varies from 1.8 to 2.7 at 15 min to 2.3 to 3.3 in delayed images obtained at 1 hr. The phytate distribution pattern is similar to that of MDP.

The behavior of ^{99m}Tc -phytate is obviously different from that of ^{99m}Tc -SC, with respect to its uptake at the fracture site. The quantification results of ^{99m}Tc -SC indicate that there is no significant uptake of tracer at the site. The results clearly indicate that ^{99m}Tc -phytate uptake at the fracture site is not due to any generalized reticuloendothelial phenomena.

From the present results along with our previous observation of ^{99m}Tc -phytate behavior in osteosarcoma and Ewing Sarcoma (2, 3), it may be concluded that the mechanism of the phytate uptake in these cases is similar to any other phosphate or phosphonate complexes. The only difference is that skeletal uptake can be observed only when there is high activity associated with bone formation either as in the case of malignant new bone formation or healing of fracture. Thus, although phytate under normal conditions does not behave like a typical phosphate/phosphonate compound, it does exhibit its basic property of bone seeking in diseased conditions. This could directly be related to the kinetics of in vivo colloid formation. The kinetics of colloid formation can probably be described as fast when compared to the rate process of normal bone activity and as slow in relation to new bone formation associated with malignant tumor or fracture and, thus, is taken up at these sites.

NOTES

* PDP 11 computer, Digital Corp., Marlboro, MA.

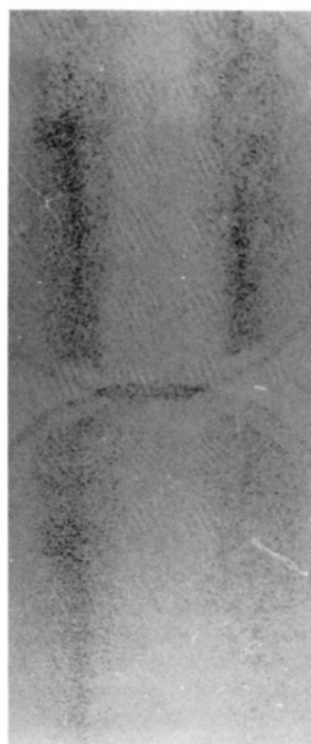


FIG. 5. Technetium-99m-SC study recorded at 15 min and 1 hr. There is no significant uptake of radiotracer at the site of fracture.

ACKNOWLEDGMENTS

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NOTE ADDED IN PROOF

Please note the following changes for the September 1990 Instrumentation article, "Assessment of Camera Uniformity Using a Dynamic Line Phantom" by Trevor Craddock and Ellinor Busemann-Sokole.

In the Materials and Methods section, the line source of activity is 0.1 cm, not 0.1 mm. Also in this section, the collimator used with camera 1 is a low-energy all-purpose collimator.

In Table 1, the CFOV (%) integral for the cobalt sheet source is 5.39 and not 5.93.

Lastly, in the second paragraph of the Discussion section, the contrast test pattern refers to a single camera and collimator (i.e., the low-energy all-purpose collimator and camera 1).