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EVALUATION OF FRACTURE HEALING IN MAN BY SERIAL ^{99m}Tc-Sn-PYROPHOSPHATE SCINTIMETRY

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Serial ^{99m}Tc-pyrophosphate (^{99m}TcPP) uptake measurements were performed, during the healing period, in 12 patients with fracture of the distal end of the radius without displacement. A peak value in uptake ratio was seen within 4 weeks in all patients. For clinical reasons the patients were divided into a normal healing and a slow healing group. ^{99m}TcPP uptake at 6 weeks after the fracture was significantly higher in the slow healing group. Quantitation of the healing process in forearm fractures is possible using ^{99m}TcPP and a gamma camera, and concentrating on small selected areas of interest.

Key words: forearm fracture; scintimetry; ^{99m}Tc-pyrophosphate; healing course

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The use of ^{99m}Tc-Sn-pyrophosphate (^{99m}TcPP) as a radio-pharmaceutical in clinical work is well established in the early diagnosis of skeletal metastases and primary bone tumours. Furthermore, a great deal of interest has been devoted to the application of other radioactive tracers to study osteonecrosis of the head of the femur in fractures, fractures of the tibial shaft displaying delayed union and non-union, infected endosprotheses and some metabolic bone diseases (Merrick 1975).

Bone-seeking tracers have been less intensively studied during normal healing processes, although this application has been suggested by several authors (Bauer & Wendeberg 1959, Wendeberg 1961, Bessler 1968, Bauer 1975, Puranen et al. 1975, Rosenthall et al. 1976).

The present study was undertaken to investigate the change in ^{99m}TcPP uptake in a fracture of the distal end of the radius during the healing period, and to correlate the clinical healing to ^{99m}TcPP scintimetry.

MATERIAL AND METHODS

Twelve patients, all women aged from 40 to 76 years (mean 56 years) were examined. All had fractures, without displacement, of the distal end of the radius. The patients were selected in such a way that the radiological appearance of the fractures was identical.

Scintigraphy was performed every second week over a period of 6 to 8 weeks after the trauma. A final scintigraphy was made 24 weeks after the accident in eight of the patients. In four patients the final scintigraphy was omitted, in one case because of refracture, in one because of operation on the wrist and the remaining two patients refused further follow-up.

In 10 patients admitted for bone scintigraphy because of diseases in the spine or lower extremities but without any injury or disease in the

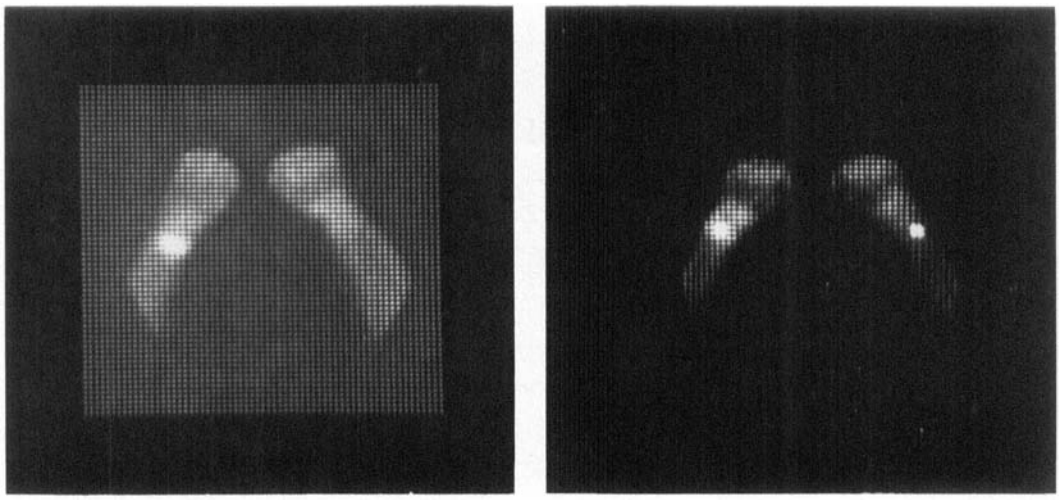

Figure 1. Scintigraphic appearance of forearms and hands. (A) digitalized picture in 64 × 64 points frame. (B) 2 × 2 points area of interest at the fracture site and a symmetrical area on the contralateral arm.

upper extremities, a single scintigraphy of the forearms was obtained as a control.

A total of 61 scintigraphic examinations were performed.

Six to 10 mCi ^{99m}TcPP (Solcoscint ®Diphosphate, Solco Nuclear Basle, Switzerland) was given intravenously. Three hours later scintigrams were obtained with a General Electric Maxicamera using a high-resolution, parallel-hole, low energy collimator. The systemic resolution was 10 mm. 250,000 counts were collected and the data stored on magnetic tape in a 64 × 64 points frame for later digital analysis (General Electric Med Stor®).

In order to obtain reproducible and symmetrical geometry, a PVC mould with excavations for the forearms was used. The dorsal plaster casts were left *in situ* and the forearms were examined from the volar surface.

In the digitalized picture of the forearms an area of interest was selected in the fracture region, being the area showing the maximum of collected counts. A symmetrical area of the same size was located in the image of the contralateral forearm (Figure 1). The size of the areas chosen (2 × 2 points in the frame) was the minimal area which was possible using the available equipment. The area corresponded to approximately 1.6 × 1.6 cm on the examined object. In the non-injured control patients equivalent areas in the distal end of the radius were examined.

The uptake of ^{99m}TcPP in the fracture was expressed as the ratio between the counts recorded in the two areas described. 3,500–15,000 counts were recorded at the fracture site and 500–2,000 in the contralateral arm. Thus the coefficient of variation of the ratios between the fracture site and the control arm was less than 4.5 per cent.

Healing of the fracture was evaluated by recording disappearance of local pain and achievement of free mobility. The clinical examination was carried out by a member of the staff of the orthopaedic department, who had no knowledge of the scintimetric results. Additionally the immobilization time in plaster was recorded.

Blood samples were collected to estimate the calcium and vitamin D status. 25-hydroxycholecalciferol was measured by a competitive protein binding assay according to Haddad & Chyu (1971).

Statistical evaluation was made using Wilcoxon rank sum tests for paired and unpaired data.

RESULTS

As illustrated in Figure 2, a variation in the ^{99m}TcPP uptake rate was seen after the fracture.

The accumulation of ^{99m}TcPP increased to reach a maximum within 4 weeks after the injury. This was followed by a decrease to the lowest values 24 weeks after the fracture.

A fracture of the distal end of the radius without displacement is normally united and free of local pain within 5 weeks. Based upon

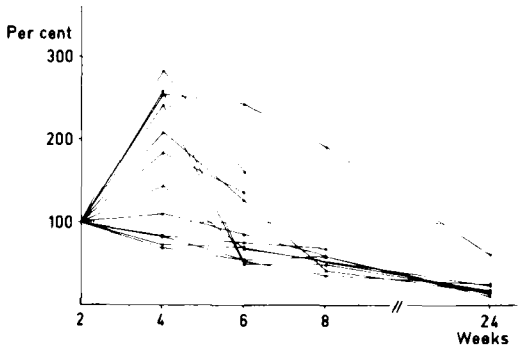

Figure 2. The percentage variation of ^{99m}TcPP uptake ratio related to the 2-week value.

this criterion the patients were separated into two groups (Table 1). Seven patients healed within 5 weeks and five patients had a healing time of more than 5 weeks. Furthermore, the latter group required a significantly longer period for full mobility of the wrist and fingers to be achieved ($P < 0.05$). The plaster casts were applied for a shorter period in the fast healing group, but the difference was not significant.

The results of scintimetry showed no difference between the two groups after 2 and 4 weeks, whereas the ^{99m}TcPP uptake 6 weeks after the fracture was significantly higher in the slow-healing group ($P < 0.05$). No difference was seen after 8 and 24 weeks (Table 2).

After 6 weeks all patients with normal healing had values below those found in the second week. This was, however, also found in one patient in the slow-healing group.

Normal values of serum calcium (2.12 ± 0.26) and (2.15 ± 0.20) and slightly elevated 25-hydroxycholecalciferol values (50.5 ± 14.8) and (40.3 ± 15.4) were seen in the normal and the slow-healing groups, respectively.

The patients without fractures had uptake ratios of 0.93 ± 0.05 (mean $\pm$ s.d.).

DISCUSSION

The present investigation was undertaken to study the scintigraphic course of healing of fractures of the distal end of the radius. This type of fracture was chosen because the healing usually proceeds without delayed or

Table 1. Clinical evaluation of healing in normal (A) and slow healing (B) patients

Group	Disappearance of local pain (range in weeks)	Fixation with plaster casts (range in weeks)	Free mobility (range in weeks)
A	4–5	4–5	6–7
B	6–10	5–7	8–11
		NS	$P < 0.05$

Table 2. Variation of uptake ratio in the normal (A) and slow healing group (B). (Mean $\pm$ s.d.)

Weeks	2	4	6	8	24
Group A $n = 7$	10.3 ± 3.9	12.2 ± 3.2	6.7 ± 3.7	4.8 ± 3.0	1.8 ± 0.7
Group B $n = 5$	8.6 ± 3.0	15.7 ± 3.9	11.5 ± 2.4	7.6 ± 3.1	2.5 ± 1.3
	NS	NS	$P < 0.05$	NS	NS

non-union. The availability of reproducible values from the contralateral arm also makes these fractures particularly suitable for this kind of study. Moreover, it might serve as a model for the healing process of other types of fractures where exact clinical and radiological evaluation is more difficult.

In the first radionuclide uptake study in fractures in man, Bauer & Wendeberg (1959) demonstrated with cation tracers ^{85}Sr and ^{45}Ca a maximal activity 6 weeks after a hip fracture. These patients were investigated under rather varying conditions.

Scintimetric evaluation of fracture healing has been carried out on tibial shaft fractures (Wendeberg 1961, Muheim 1973, Puranen et al. 1975). Generally the maximum uptake at the fracture site was seen 4–8 months after the injury. In delayed healing Bauer & Wendeberg (1959) found a high uptake ratio, whereas Puranen et al. (1975) observed low uptake ratios in delayed union. This discrepancy was noted by Muheim (1973) and may be related to different types of delayed union.

In the present study a different tracer was used. ^{99m}TcPP is preferentially bound by immature collagen, whereas the cation tracer ^{45}Ca is bound predominantly in the bone mineral (Kaye et al. 1975). This may explain the earlier peak activity seen in our studies. Furthermore, it is well-known that there are differences in the natural healing course of fractures of the forearm and tibial fractures.

The combination of good information density and safety of the radionuclide deposit at the lesion site, facilitated by the vascularity of the fracture, make ^{99m}TcPP a good tracer for describing the events of fracture in the healing period (Lentle et al. 1976).

As mentioned earlier maximal activity in small selected areas of interest was measured because they were exactly defined and reproducible when working with a digitalized computer system connected to a gamma camera. This is in accordance with the results reported by Gumerman et al. (1977) who were able to indicate the course of healing by sequential scanning with quantitative analysis of the fracture line in a rabbit model using ^{99m}Tc methylenedisphosphonate.

A relation between osteoporosis, osteomalacia, and occurrence of juxta articular fractures has been described (Aaron et al. 1974). Seventy per cent of women with such fractures are osteoporotic (Bollet et al. 1965). Furthermore, it has been demonstrated that 30 per cent of osteoporotic patients have histological but not biochemical signs of osteomalacia (Lund et al. 1977, Sørensen et al. 1977). Thus we examined Se-calcium and 25-OH-cholecalciferol to evaluate the vitamin D metabolism. This metabolite affords the best evaluation of vitamin D-status according to Avioli & Haddad (1977). The metabolic analyses were done to exclude differences in vitamin D metabolism in the groups described. Several authors (Harris et al. 1965, Rosenthall & Kaye 1975, Fogelman et al. 1977) have described alteration in radionuclide uptake in patients showing hypo- as well as hypervitaminosis D.

Our preliminary investigation indicates that it is possible to quantitate the healing process using ^{99m}TcPP and a gamma camera and concentrating on small areas of interest. By this method fractures of the distal end of the radius can be separated into normal and slow healing types. This technique can probably be applied to other fractures.

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