Scintigraphic Demonstration of the Adherence of Technetium-99m-Sucralfate to Oral Microlesions

TO THE EDITOR: Technetium-99m-Sucralfate has been used in the detection of gastric and duodenal ulcers because it adheres to the site of mucosal ulceration. It forms insoluble complexes with exposed proteins in an acid milieu (1). Unlabeled sucralfate is effective in preventing chemo- and radiotherapy-induced oral mucositis (2). We tried to demonstrate the adherence of sucralfate to oral lesions in a small nonselected group of patients. Thirteen patients were studied: four patients with chemo-radio-induced mucositis, four with non-neoplastic oral lesions, and five controls without gross mucosal abnormalities. Patients were invited to simply swish in the mouth a 2-ml suspension of Tc-sucralfate obtained from a carefully mixed commercial preparation. Activity was about 50 MBq for each patient. After swishing, patients spat out the sucralfate and rinsed their mouths with water several times. No radioactive sucralfate was swallowed. Static images at 15 min were acquired with a large field of view gamma camera with an electronic 3.5 zoom in the anterior and R-L lateral views. In the control patients, there was a slight, diffuse, persistence of activity in the mouth, without focal uptake (Fig. 1). In all cases with macroscopic lesions, a relatively larger uptake of labeled sucralfate was detected (Fig. 2). In two out of five control patients, diffuse activity of the hard palate associated with diffuse microlesions caused by dental prosthesis (Fig. 3) was found.

In conclusion, we think that sucralfate is a valuable agent against therapeutically induced oral mucositis. The scintigraphic demonstration of a more active sucralfate adherence to minimal lesions in control patients suggests that: (a) sucralfate adheres even to microscopic lesions and (b) a prophylactic effect could result from a prevention of the worsening of such lesions induced by therapy.

REFERENCES

Tracer Resorption and Apposition in a Rat Tibial Fracture Model

TO THE EDITOR: Recently, Shani et al. published their excellent results in the Journal on “Correlations Between Uptake of Technetium, Calcium, Phosphate, and Mineralization in Rat Tibial Repair” (1). One conclusion of this investigation states “The observation that the increased uptake of 99mTc occurs at a time when bone formation is predominant, and before any bone

<table>
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<tr>
<th>Component</th>
<th>Fraction</th>
<th>T½ bio in days</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.31</td>
<td>2.0</td>
</tr>
<tr>
<td>II</td>
<td>0.69</td>
<td>55.4</td>
</tr>
</tbody>
</table>

* Fraction resorbed = 1 - \((0.31e^{-0.347t} + 0.69e^{-0.0125t})\).
up takes (treatment/control) by approximately 15 days, after a maximum treatment/control uptake of approximately 1.75 after 6 days for \(^{99m}\text{Tc-MDP}\). By Day 6, this ratio, as calculated by the allometric growth equation, is equal to (1.06)(10\(^{0.345}\)) + (8.32E – 11)(10\(^{7.75}\)) = 1.97. This value agrees with that reported by Shani et al., which was 1.75.

Why our tibial rat fracture continued to exhibit increased \(^{99m}\text{Tc-MDP}\) uptake relative to normal at 30 days, while that of Shani et al. showed uniform uptake by Day 15 is presently unknown. It has been documented, however, that human fractures are positive on bone scans for an extended period of time after their induction and that this time period is a function of fracture type (4).

REFERENCES

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REPLY: We would like to express our appreciation in allowing us the opportunity to respond to Dr. Castronovo’s letter. It is indeed gratifying to note that our results are in agreement with the results of Drs. Castronovo’s and Strauss’ study. The differences in the sequence of events between the two studies was expected. The model of tibial bone fracture used by the authors is a complex sequence of events through blood clot formation, primary callus formation including cartilage formation, calcification and then reorganization of the callus through primary to mature bone. These events take 30 to 60 days before completion of the process. In our model, the process is far more rapid as there is no bone fracture. The healing process goes through the organization of the initial blood clot directly to primary bone formation. After this, the primary bone is completely resorbed and replaced by bone marrow. In fact, by the 14–21st day, no more bone formation occurs.

Thus, we believe that the difference referred to in Dr. Castronovo’s letter can be explained by the difference in the sequence of events, while both models confirm the similarity in the \(^{99m}\text{Tc-MDP}\) uptake during their respective periods of bone apposition.

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TABLE 2
Technetium-99m-MDP Apposition onto Fracture Site as a Function of Time

<table>
<thead>
<tr>
<th>Component</th>
<th>b</th>
<th>k</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>1.06</td>
<td>0.345</td>
</tr>
<tr>
<td>II</td>
<td>8.32E-11</td>
<td>7.75</td>
</tr>
</tbody>
</table>

* for, y = b(x^t)

The release of \(^{125}\text{I-phenylphosphonic acid}\) from normal bone, after tracer equilibrium, has a monoexponential biological halftime of 962 days (J).

Table 2 lists the biexponential constants associated with the \(^{99m}\text{Tc-MDP}\) time-dependent apposition pattern at the fracture site relative to normal bone. The rate of increase as a function of time follows the mathematical law of allometric growth; y = b(x^t), where b is the y intercept and k is an exponent of a power function (4).

By Day 10, the fraction of \(^{99m}\text{Tc-MDP}\) uptake relative to normal bone (FA) is:

\[
FA = (b(x^t)_1 + (b(x^t)_2)
\]

\[
FA = (1.06)((10)(0.345)) + (8.32E – 11)((10)(7.75))
\]

By 30 days, FA becomes:

\[
FA = (1.06)(((30)(0.345)) + 8.32 E – 11))((30)(7.75))
\]

FA = 3.43 + 23.32
FA = 26.75.

The ratio of apposition-to-resorption after 10 days equals 2.36/0.383 = 6.16, and after 30 days; 26.75/0.526 = 50.86. This biologic behavior undoubtedly plays a major role in bone healing.

As shown above, the apposition is significantly greater than resorption for the healing fracture in our rat model. This pattern continued to increase at the time the investigation was terminated at 30 days. The results of Shani et al. show a return to uniform

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