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Detecting Coronary Artery Disease Using SPECT Imaging: A Comparison of Thallium-201 and Teboroxime

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ABSTRACT **Thirty subjects underwent single photon emission computed tomography (SPECT) imaging with technetium-99m teboroxime (TEBO). Of these, 26 underwent thallium SPECT imaging and 25 underwent quantitative coronary arteriography (QCA). Twenty-one of the subjects underwent all three studies. SPECT images were reviewed by two independent observers blinded to the clinical data. Stenoses were considered significant if there was a ≥ 50% diameter narrowing as defined by QCA analysis of the coronary arteriograms. The overall sensitivity and specificity was 78% and 78%, respectively, for thallium-201. The overall sensitivity and specificity for teboroxime was 72% and 80%, respectively. The results obtained for these two tracers were not statistically different. Some of the false-positive results obtained from teboroxime imaging appear to have been due to the 10-min acquisition protocol and can be reduced with the use of new software programs using a continuous 3-min acquisition and dipyridamole. Teboroxime's rapid biologic half-life allows completion of SPECT imaging within 60–90 min, compared with the minimum of 4 h required for thallium SPECT imaging.**

Key words: Quantitative coronary arteriography (QCA), SPECT imaging, teboroxime, thallium-201

INTRODUCTION

The use of thallium imaging as a tracer of myocardial perfusion has been limited by a low photon energy of 80 KeV with resultant attenuation problems. Additionally, thallium's relatively long half-life of 73 h reduces the amount of thallium that can be given to overcome these artifact problems. Technetium-99m (Tc-99m) is essentially a monoenergetic (89%) radionuclide with a higher photon energy (140 KeV) and less compton scatter than thallium, making it ideally suited for single photon emission computed tomography (SPECT). Because Tc-99m has a physical half-life of 6 h and a biological half-life of 5.3 min, the patient can receive up to 20–30 mCi without receiving excessive amounts of the radioisotope.

The lipophilic character of Tc-99m teboroxime (TEBO) provides greater than 90% extraction by myocardial tissue over a wide range of coronary blood flow [1]. This is greater than uptake obtained by tracers that behave like microspheres [2,3] and do not appear to be dependent on the sodium–potassium ATPase pump. As previously demonstrated [4] the results of visual interpretation of coronary arteriograms can lead to erroneous conclusions about the results obtained with different nuclear tracers. To reduce these errors, this study was designed to look at the overall sensitivity, specificity, predictive values, and accuracy of thallium and teboroxime using quantitative coronary arteriography (QCA).

METHODS

Study population

Thirty subjects who were suspected of having coronary artery disease were enrolled in the study. These subjects received approval to enter the study from their primary care physicians and signed a consent form approved by the Institutional Review Board for the Protection of Human Subjects. Patients were excluded from the study if they had a history of cardiomyopathy, severe valvular disease, unstable angina, morbid obesity, pregnancy, or had a recent myocardial infarction that would preclude them from undergoing the exercise portion of the SPECT studies. Additionally, subjects were excluded if they had continuing angina, myocardial infarction, or underwent angioplasty or coronary artery bypass surgery between SPECT studies and coronary arteriography.

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Of the 30 patients, 40% were women and 60% were men, with an average age of 55 years. All 30 subjects underwent SPECT teboroxime imaging, 26 underwent SPECT thallium imaging, and 25 underwent coronary arteriography with QCA analysis of coronary arteriograms as previously described [4].

Coronary arteriography and quantitative coronary arteriography

All subjects underwent conventional coronary arteriography via a Judkins approach. The images were obtained using a Philips Poly Diagnost C/Lateral ARC system with magnification and pincushion correction as previously described by Brown.[5] The films were analyzed with a DEC VAX 11/780 mainframe computer. Hardcopy reports were generated by a Tektronics 4207 graphics computer. The most severe percent diameter reduction for each of the major coronary arteries (including branches) was reported as the percent diameter stenosis for each artery.

Exercise protocol

SPECT images were obtained after subjects exercised using the Bruce protocol. Subjects were exercised until symptom (angina, fatigue) limitation, or 2-mm depression occured in two continuous leads on their electrocardiograms. Thallium was given intravenously 1 min prior to cessation of the exercise period. Teboroxime was given at peak exercise and the subject immediately transferred to the SPECT table for imaging.

SPECT imaging

Each SPECT image was obtained using a General Electric 400 AC Starcam, using a 64 × 64 matrix, Hanning Filter (0.83 Hz cutoff), and a multipurpose collimator, with image reconstruction along short, horizontal, and vertical long axis. Thallium images were acquired after 3 mCi of thallium-201 were injected during the exercise period of the study. Each of the 32 images required 40 sec for acquisition. Subjects were returned 4 h later for redistribution images using the same protocol.

Teboroxime image acquisition began within 2 min of intravenous injection of 20 to 25 mCi of teboroxime. The same SPECT camera, matrix, filter, and collimator was used. Subjects returned 1 h later for a second injection of teboroxime, using the same dose used during the stress component of the study. Each teboroxime image was acquired over 15 sec.

SPECT images interpretation

Images were analyzed by two observers blinded to clinical and QCA data. Perfusion of regions were scored on a continuous scale from 0 to 5, where 0 equaled "normal" perfusion, 1 represented "probably normal" perfusion, 2 was "equivocal," and 3 to 5 defined "mild," "moderate," and "severe" defects. Eight regions were analyzed per image including anterior, anterolateral, posterolateral, posterior, inferior, posteroseptal, anteroseptal, and apex. Averaged values from two observers ranging from 0 to 2 were reported as not significant for perfusion abnormalities. Mean values from 3 to 5 were reported as remarkable for the presence of perfusion deficits. Segments were matched to the region of arterial distribution. The anterior and anteroseptal regions were matched to the left anterior descending artery. The anterolateral and posterolateral were matched with the circumflex artery. The inferoposterior region was matched to the right coronary artery. Assignment of the posterior and apical regions was determined by reviewing individual coronary arteriograms.

Order of testing

The order of QCA and SPECT imaging occurred randomly to prevent any biasing of entry into the study. Studies were completed without any intervening changes in the patients' condition or electrocardiogram.

Statistical methods

Chi-square analysis with correction for continuity was used to determine whether there were statistical differences between the two tracers as compared with results obtained by QCA analysis of the coronary arteriograms. Differences between thallium and teboroxime stress tests were compared by Student's t-test for paired data.

RESULTS

Exercise results

When results of maximum heart rate were achieved, and rate–pressure product (maximal systolic blood pressure × maximal heart rate), angina pectoris, and electrocardiographic changes were compared, there were no differences between results obtained during thallium and teboroxime components of the study. All subjects were exercised to fatigue or symptom limitation. No subject was arbitrarily discontinued at 85% of maximum predicted heart rate.

Interobserver variability

There were no statistical differences in the interpretation of SPECT thallium and teboroxime images. Perfusion scores differed by one or were in total agreement between 75% and 83% of the time.

Comparison of thallium and teboroxime

Table I shows the overall results obtained when all 30 subjects were studied using the previously described protocols. Significant coronary artery disease was present in all three arteries in 36% of those studied by thallium and in 33% of those studied by teboroxime. The sensitivity and specificity for thallium was 78% and 78%, respectively, with an accuracy of 78%. For teboroxime, the overall sensitivity and specificity was 72% and 80%, with an accuracy of 77%.

The best results, regardless of tracer, were obtained when there was a greater prevalence of disease in that region. For example, with thallium there was a 57% prevalence of disease in the left anterior descending (LAD) artery, with a sensitivity of 75%, specificity of 89%, and an accuracy of 81%. The same findings were present in the teboroxime images where there was significant disease in 52% of the LAD arterial distributions studies. Here the sensitivity was 69%, specificity 92%, and the accuracy was 80%. There

TABLE I. Detection of Overall Disease and the Ability to Discriminate Specific Regions of Coronary Blood Flow*

	Thallium-201					
	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Disease prevalence	Accuracy
All regions	78%	78%	67%	86%	36%	78%
LAD	75%	89%	90%	73%	57%	81%
LCx	67%	89%	50%	94%	14%	86%
RCA	88%	54%	54%	88%	38%	67%
	Teboroxime					
	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Disease prevalence	Accuracy
All regions	72%	80%	64%	85%	33%	77%
LAD	69%	92%	90%	73%	52%	80%
LCx	50%	81%	33%	89%	16%	76%
RCA	88%	71%	58%	92%	32%	76%

*LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery.

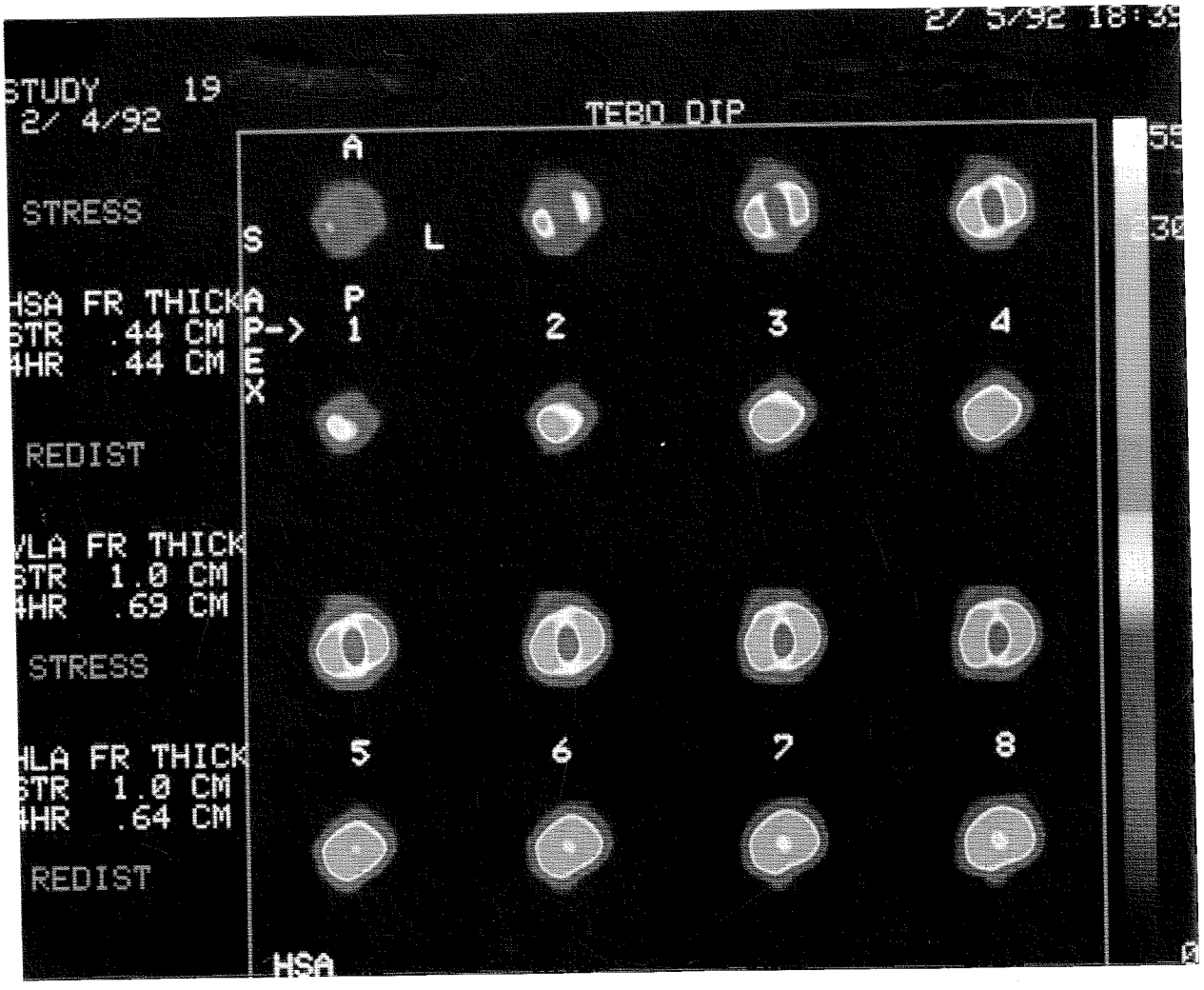

Fig. 1. Stress and rest dipyridamole teboroxime SPECT images. Image reconstruction in the short axis view reveals dipyridamole stress images in rows 1 and 3. Rest images are represented in rows 2 and 4. Slices begin at the apex (slice 1) and proceed toward the base (slice 8). The anterior wall is located at the top of each image, the inferior wall at the bottom, septum to the left, and lateral wall to the right. Note the decreased teboroxime activity in the anterior and inferior regions during dipyridamole stress, with normal perfusion during the rest study 1 h later.

were no statistical differences between results obtained with thallium and those obtained with teboroxime.

DISCUSSION

The use of technetium-99m teboroxime SPECT imaging has recently been investigated as a possible alternative to thallium-201 imaging. Teboroxime has several advantages over thallium, including a shorter half-life of 6 h, the monoenergetic photon peak of 140 KeV ideally suited for SPECT imaging, and the ready availability of technetium-99m from molybdenum–technetium generators. The results of this study using a 10-minute acquisition protocol demonstrated that results obtained from thallium and teboroxime are comparable with no statistical differences. Given the reduced amount of time necessary to obtain stress/rest images with teboroxime (60–90 min) as compared with thallium stress/redistribution (4 h) images, a considerable amount of time can be saved for the patient. Additionally, only 20 min of table time are required to image a patient with teboroxime as compared with 40 to 80 min for thallium.

Despite the higher photon energy available with Tc-99m, there continued to be a problem with false positives inferolaterally, as was previously seen with thallium. This rate of false positives inferiorly and laterally appear to be due to the original protocol, which acquired images over 10-min and began in the right anterior oblique (RAO) position and rotated to the left posterior oblique (LAO) position. Given teboroxime's biologic half-life of 5.3 min, only 25% of the activity was left by the time imaging was completed in the lateral regions of the myocardium. Additionally, if the left circumflex was not significantly diseased, washout resulted in low counts being present by the time the SPECT camera was laterally located. False-positive defects in the inferior wall appear to be due to liver uptake of the tracer interferring with result interpretation. Also, with the step and shoot approach, approximately 25% of the data were lost. These problems may have been minimized in this study given the relatively high prevalence of disease in the population. Two-thirds of the patients had significant disease in at least one coronary artery.

In an attempt to overcome these limitations, a new protocol was written using dipyridamole and teboroxime. The patient was administered 0.568 mg of dipyridamole per kilogram body weight over 4 min. At 6 min 25 mCi of teboroxime was administered, immediately followed by a 10 cm^3 flush of normal saline. Forty-five seconds later a 250 mg bolus of aminophylline was administered to reverse the effects of dipyridamole and prevent the rapid washout of teboroxime. Continuous image acquisition then began in LAO and rotated to the RAO position during a 3-min acquisition time. Imaging was completed with an Elscint Apex SP-4 γ camera with reconstruction in short axis, vertical, and horizontal long axis views after software removal of the liver was accomplished. The patient was reimaged 1 h later at rest with 30 mCi of teboroxime and a continuous 3-min acquisition. The patient experienced no adverse effects.

Fig. 1 demonstrates the results of this new protocol in a clinical study with a patient who had a 26% diameter narrowing of the left circumflex, 64% narrowing of the proximal left anterior descending, and 72% narrowing of the mid right coronary artery, as determined by quantitative coronary arteriography (QCA). There was no collateral circulation noted on the coronary arteriogram. The results of the QCA and the dipyridamole teboroxime study using this new protocol matched without giving false positive defects laterally.

CONCLUSION

Teboroxime SPECT imaging provides equivalent results to that obtained with conventional thallium SPECT imaging. These results can be obtained in one-quarter of the time (1 h) with considerably less time spent lying on the SPECT table. Given the current changes in the imaging protocol, the number of false positives should be considerably reduced, making teboroxime not only faster, but potentially more accurate. Additionally, given the rapid washout of teboroxime, rest images can probably be acquired in 30 min rather than 1 h after stress/dipyridamole images. The use of adenosine may reduce the washout of teboroxime and eliminate the need for aminophylline.

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