Acetazolamide Intervention for Technetium-99m HMPAO SPECT Brain Imaging

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This is the third article in a series of four on interventional nuclear medicine. Upon completion, the technologist will be able to (1) discuss the purpose of using acetazolamide with technetium-99m HMPAO brain imaging, (2) describe the imaging parameters, and (3) list the interpretation criteria.

Analysis of vascular perfusion reserve allows objective evaluation of the effect on cerebral blood flow of carotid artery disease. Using acetazolamide (ACZ) as a cerebral vasodilator, the change in distribution between control (rest) and ACZ-stimulated exametazime (HMPAO) images easily demonstrates areas of the brain supplied by vessels with reduced perfusion pressure and blood flow. Our initial experience with 60 patients, of whom 97% were symptomatic and 82% had a carotid stenosis of greater than 70%, found that 87% had abnormal HMPAO SPECT exams. Of these, 79% showed new or additional abnormalities after ACZ. The addition of a vasodilator markedly increased the sensitivity of these exams.

Acetazolamide is an enzyme inhibitor that works on carbonic anhydrase, affecting the reactions of carbonic acid dehydration and carbon dioxide hydration. Used in the control of glaucoma and treatment of epilepsy, ACZ is a nonmercurial diuretic. However, the intravenous administration of ACZ produces repeatable short-term elevations of cerebral blood flow (CBF) (*1*). The exact mechanism causing the increase is not understood, but has been demonstrated in both animal and human studies (*2–4*). The increases are dose-dependent, and a one-gram dose will cause a near doubling of flow in young normal subjects. Larger doses seem to have little additional effect. Recent studies on normal subjects utilizing xenon-133 (^{133}Xe) tomography found a 30% mean increase in blood flow, and we have shown a similar increase in retention of HMPAO after ACZ (*5*).

The use of acetazolamide is not without potential pharmacological problems. ACZ is a non-bacteriostatic sulfonamide and any allergy to the sulfa family of drugs would rule out its use. Likewise, if the patient has active, current transient ischemic attacks (TIA) symptoms at the time of the study, we do not use ACZ, although this is not an absolute contraindication.

Patients are carefully questioned by both the technologist and the nuclear physician about current symptoms and allergies. We encountered one patient who developed bronchospasm after ACZ. He was treated for an allergic reaction and experienced a rapid recovery. We later learned that the patient had an intolerance to sulfa not previously mentioned. A physician should be available during ACZ use.

Normally there are mild side effects. Common sensations include numbness or tingling around the mouth or fingers. Lightheadedness and blurred vision have been reported as well as a flushed feeling in the face or neck. These symptoms resolve in about 10 to 15 min. We caution all patients to expect some sensation, but only about half seem to experience any. ACZ has been used in a wide variety of patients including those with stroke and head injury. It is said to be contraindicated for patients with increased cerebral pressures (*6*).

MATERIALS AND METHODS

We use a two-day protocol for most studies, with the ACZ stimulation on Day 1 and the baseline study on Day 2 or later. Each time, the patient is taken to a quiet area for the injections. We make no specific attempt to limit sight or sound stimuli nor personnel movement within the area. One gram of ACZ in a 10-cc volume is intravenously injected over a 2-min interval; 30 mCi of technetium-99m (^{99m}Tc) HMPAO is given 25 min later (T = 25–30 min). We have found that it requires at least 15 min to properly formulate and do quality assurance testing on HMPAO. The technologist should have everything ready in advance in order to meet the time constraints of the protocol. ACZ has a peak action 20 to 30 min after injection and a continuing effect for about 30 additional min.

Once HMPAO has been injected, we wait at least 15 min before starting the imaging to allow for background clearance. We have found that the camera set-up time for the patient is usually at least another 15 min. There is no hurry at this point, as the background clearance improves with time. Except for the increased imaging time required due to radioactive

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decay, the acquisition could be delayed some hours after injection. If an acquisition is defective, repeats can be done immediately.

Since changes in ACZ studies are seldom focal, we find extremely high resolution SPECT equipment is not really necessary. Standard, late model SPECT cameras with short-scale contrast color displays, such as the "Rainbow" color table (Siemens Gammasonics, Schaumburg, IL) easily show these changes. Our systems have a nominal resolution of the brain of about 1.5 cm and are very satisfactory for routine use.

The patient is placed supine on the scan pallet, with knees elevated by a foam bolster to ease back strain. We then ask the patient to make himself or herself as comfortable as possible, but no attempt is made to position the head transverse planes perpendicular to the camera. Acquisition times range from 30 to 50 min, and we have found far fewer problems with motion if the patient is made as comfortable as possible. The head is immobilized with tape. Patients who are unable to lie quietly and motionless for whatever reason are excluded. The camera, a Siemens Orbiter 75, (Siemens Gammasonics, Schaumburg, IL) is adjusted so that the collimator makes minimal contact with the patient's nose in the anterior projection and clears the pallet/headholder in the posterior projection by ~1/4 inch. We check the lateral position to make sure the entire brain is within the field of view.

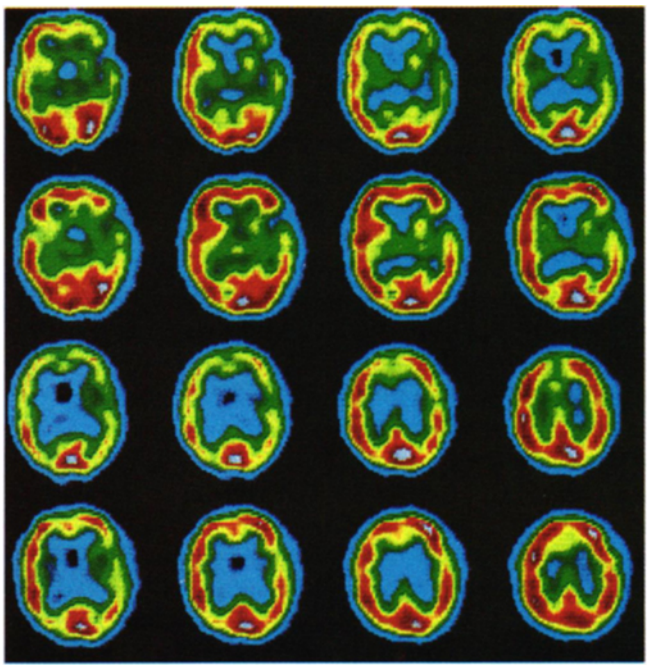

FIG. 1. The patient is a 70-yr-old male with known stroke, mild dementia, and tremor. Top and third rows are double-thickness sections acquired after ACZ was given. Second and fourth rows are the concordant sections of the control (no ACZ) study. The control exam has an area of hypoperfusion in the left parietal area and a second lesion high in the cortex on the right, corresponding to the known stroke. The ACZ study shows extensive loss of reactivity in both hemispheres extending into the frontal lobes with more extensive damage on the left. Diagnosis: diffuse cerebrovascular disease.

We acquire 100K counts in the anterior position; this time is then used as the imaging time per stop. Acquisition is a 360° rotation, 64 stop, 64 x 64 matrix, using a long-bore/high resolution tomographic collimator (TOMO, Nuclear Fields, Des Plaines, IL). Reconstruction is done using a Butterworth filter: Nyquist 0.5, order 10 with no prefiltering. Oblique sections for the transverse axis following the orbital-meatal line are created to make the scan compatible with radiographic computed axial tomography studies; sagittal and coronal sections are also made but seldom used.

We create double-thickness slices (approximately 12 mm), normalize each section to a common maximum pixel, then display them with a color palette. The upper intensity level of the images is set to 98% of maximum, and the lower level set between 28% and 31% for background subtraction. Concordant slices of ACZ SPECT and control SPECT are displayed in adjacent rows, one above the other, using software usually used for stress/redistribution thallium images (Fig. 1). This allows easy inspection and comparison of the sections.

Interpretation criteria used by our physicians are detailed in another publication (*7*). They are similar to those of myocardial perfusion imaging. Briefly, they are as follows.

Normal: Even symmetrical uptake without qualitative change between ACZ and control

Compromised Perfusion Reserve: Normal control images with asymmetry of distribution after ACZ.

Chronic Ischemia with Compromised Perfusion Reserve: Asymmetric control with further asymmetries after ACZ.

Infarction with Compromised Perfusion Reserve: Severe, focal, reduction of tracer uptake at control with additional areas of asymmetry after ACZ.

Infarction: Focal decrease as above without additional changes after ACZ.

In young subjects, collateral circulation to the brain is usually well developed and occlusion of one isolated artery may produce little effect. In older patients, the collateral supply is frequently compromised. Stenosis or occlusion leads to reduction in brain-blood perfusion pressure with compensation by local or regional vasodilation to maintain adequate blood flow. This produces increases in regional blood volume maintaining oxygenation, but when pressure falls below a critical value, brain dysfunction or infarction occurs (*1*). This sequence is probably accentuated when clots or emboli are added to the stenosis or obstruction.

When maximum compensation has occurred, no further vasodilation is produced when ACZ is given, although other normally perfused areas still react. Blood flow to normal regions increases, producing increased uptake of HMPAO and easily seen asymmetries. There is little or no change in flow to compromised areas. It seems likely that patients with these findings are in the most urgent need of corrective therapy. We found regional loss of reactivity very common in symptomatic patients with high grade stenosis (*7*) (Table 1). We also found that most patients show recovery of reactivity following successful carotid endarterectomy (CEA) (*8*, *9*). This may explain the improvement in these patients in a CEA trial conducted by the National Institutes of Health (*10*).

TABLE 1. Change in Findings After Diamox in 58 Patients with Documented Carotid Stenosis

% Carotid Stenosis by Angiography	No Change Between Control and ACZ Stress	New or Additional Findings After ACZ
Less Than 70%	4 (7%)*	5 (9%)†
Greater Than 70%	11 (19%)‡	38 (65%)§

* 3 of 4 had abnormal control exams.
† 2 of 5 had normal control exams.
‡ 5 of 11 had abnormal control exams.
§ 12 of 38 had normal control exams.

Although additional investigation to detail the further application of this technique to cerebral vascular and carotid disease is needed, several indications now seem probable or have been demonstrated for these studies. We and others have described the findings with ACZ imaging to confirm and localize the presence of TIA foci (*11,12*). This is quite useful to confirm the vascular cause of the symptoms and direct further evaluation.

It seems reasonable that those patients with carotid artery disease who have developed loss of reactivity clearly need relief of the stenosis, if our finding that this is very common and related to the symptoms in symptomatic patients is confirmed (*7*). The usual change in reactivity following CEA confirms the improvement in cerebral perfusion produced by this procedure; conversely, those without improvement also tend to have recurrent symptoms (*8,9*). This may be used to direct more invasive procedures and the presence of regional loss of reactivity will direct attention to cerebral blood supply.

The differential diagnosis of dementias may be facilitated by HMPAO SPECT imaging and we have preliminarily shown that Alzheimer's and Pick's diseases show little or no loss of reactivity after ACZ. Loss of reactivity is common in multi-infarct dementia (MID), which would be expected (*13*). We use this type of workup to increase sensitivity.

In summary, ACZ SPECT imaging is simple and safe, has few significant side effects, and markedly increases the sensitivity of these exams. It can be used to confirm disease, evaluate effects and direct timing of relief of known disease, and help in the differential diagnosis of several diseases.

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