CARBON DIOXIDE ANGIOGRAPHY
EXPERIENCE WITH AN AUTOMATIC INJECTOR

The University of Melbourne, Departments of Radiology and Nephrology, The Royal Melbourne Hospital, Melbourne, Australia

AIM
To determine the clinical usefulness and safety of carbon dioxide as an angiographic contrast medium.

INTRODUCTION
Conventional iodinated contrast media may cause acute renal failure and allergic reactions even when expensive non-ionic agents are used. In the setting of a busy Nephrology unit there is a need for extensive angiography for the detection and treatment of renal artery stenosis and occlusion. Other methods of assessment of the renal arteries such as colour doppler ultrasound, helical CT and magnetic resonance angiography are not always available or accurate because of patient factors such as obesity or because of workload or these modalities may not be relevant if interventional radiology is indicated at the same time. At the University of Melbourne we routinely perform angiography in all cases of suspected renal artery stenosis and in most patients with no other obvious cause for renal insufficiency. Stenoses which are identified are treated aggressively by angioplasty and arterial stenting. Leaving aside the risk of atheroembolism associated with catheter angiography, the major other risk of angiography is iodinated contrast media induced renal failure regardless of the type of contrast considered.

Carbon dioxide is rapidly absorbed into the blood and there is an efficient transport and clearance system which does not require a metabolic process. The only contra-indication to its use is severe chronic obstructive respiratory disease. As it is cleared in the lungs on the first pass there is no danger of cerebral toxicity provided it is injected below the diaphragm.

Carbon dioxide has been used in the past for angiography but because of problems in delivery the results have been less satisfactory and less predictable than with conventional iodinated contrast media. A hand injection technique we used initially was sometimes satisfactory.

This poster demonstrates our experience with an automatic carbon dioxide injector which has been designed to overcome these problems. The injector uses a disposable catheter system which comprises electrocardiograph leads, a blood pressure transducer, gas infusion tubing and a saline tubing set.

Figure 1. Hand injection CO2 Angiography.

Hand injection of 50 ml of gas (1 atmosphere) compressed to 25 ml in a large bore syringe and released in an explosive fashion. The patient is lying in a left anterior oblique position. Reason for angiography - chronic renal failure. The right renal artery is obscured by the superior mesenteric artery. There is no proximal stenosis in the left renal artery.

The problems with hand injection of carbon dioxide are:
1. Variable compression of the gas.
2. Explosive delivery of gas.
3. Risk of contamination with air.
4. No control of injection if the catheter tip is subintimal.
5. Overall unpredictability of injection (particularly with small volumes)

Figure 2. Disposable set used with carbon dioxide injector.

Figure 3. Carbon dioxide injector.
A microprocessor within the injector analyses the cardiac cycle and blood pressure wave and selects an injection point which is in diastole. The gas is infused at low pressure with an acceleration slope set to match the normal pulse wave of the patient's circulation. The incoming gas is filtered and the injector has a closed system which is automatically flushed with saline at the completion of the injection sequence and prevents air contamination. The operator sets the catheter size and length to allow calibration and then selects the appropriate flow rate and volume of gas to be delivered.
METHOD
Patients referred for angiography were given either contrast media when possible or only carbon dioxide if the renal function was reduced.
The serum creatinine was measured in patients in whom carbon dioxide was the only contrast medium used, prior to the angiogram, one week later and at their most recent visit to the hospital.
The overall diagnostic quality of each angiogram was assessed by two radiologists and graded using a 4-point scale as follows:
- 0. Inadequate study
- 1. Poor quality
- 2. Diagnostic
- 3. Equivalent to iodinated contrast

A total of 33 patient examinations were performed but it was possible to grade injections and film runs of separate areas and a total of 55 regions were available for assessment.
The anatomical sites were:
- Aorto-renal: 31
- Selective renal: 11
- Ilio-femoral: 13

In 25 regions the patients were also given iodinated contrast and it was possible to make a direct comparison of the results of iodinated non-ionic contrast (Ultravist) with the films obtained after carbon dioxide angiography.

Inadequate: Filling of the aorta is adequate but breathing has been inadequate. Most of the degradation of the image is due to misregistration of the image.

Figure 4. Standard radiographs for grading.

Poor: The aorta is well filled but the right renal artery is obscured and the left renal artery contains a bubble.

Diagnostic: This oblique view of the aorta shows the renal arteries and stenosis of the proximal main renal arteries is excluded. The catheter is a little low but was positioned without use of contrast.

Equivalent: Both renal arteries are well shown and there is no interference from the aorta and superior mesenteric arteries.
TECHNIQUE OF ANGIOGRAPHY

A standard 5 French multi-sidehole pigtail angiographic catheter was used for almost all the non-selective angiograms. Selective injections were made using a 5.5 French Cobra visceral catheter with 2 side-holes near the tip of the catheter.

The pigtail catheter was positioned using fluoroscopy only, to avoid the use of iodinated contrast which produced some variability in the quality of the resulting images as a result of catheter position.

Volumes delivered ranged from 4 ml to 25 ml for iodinated contrast (Ultravist 300) and from 20 ml to 70 ml for carbon dioxide.

Flow rates were:
- Aorto-renal: 15 ml per second (Ultravist)
- 140 ml per second (CO₂)
- Iliac / Femoral: 10 ml per second (Ultravist)
- 60 ml per second (CO₂)
- Single Femoral: 2 ml per second (Ultravist)
- 10 ml per second (CO₂)

The injector automatically terminated the injection if there was any alteration in parameters and the actual amount was sometimes less than set prior to the injection. The maximum limit of 1 litre built into the injector software was not reached in any patient.

Images were created with either a GE EP5000 or a GE DX3 Digital Subtraction Angiography (DSA) unit. Exposure rates were typically 3 per second for the iodinated contrast run and 5 per second for the carbon dioxide run.

Films were made from a Kodak model 1180 laser printer using the analog video port or from a GE multi-format video camera. Apart from normal post-processing the images are not modified.

Figure 5. Aortogram and bilateral selective renal angiogram
Carbon dioxide angiogram in a patient with hypertension and allergy to iodinated contrast media. A flush aortogram (centre panel) and bilateral selective angiograms were performed. The selective catheter was positioned by “touch” in each renal artery. The injection parameters were:
- Aorto-renal: 70 ml at 140 ml per second
- Selective renal: 20 ml at 10 ml per second
Carbon dioxide does not produce a nephrogram and normally the renal vein is not opacified. The right kidney is more in this patient. No renal artery stenosis was seen.
RESULTS.

1. Adverse effects
   - Carbon dioxide alone - 13 patients
     - No allergy-like reactions, no significant increase in serum creatinine.
   - Carbon dioxide and iodinated contrast - 20 patients
     - No allergy-like reactions, no significant increase in serum creatinine.

   One patient with a history of angioneurotic oedema after intravenous iodinated contrast had no reaction after carbon dioxide (Figure 5).

   Warmth: ubiquitous; slightly greater with carbon dioxide
   The film quality was poor in two cases after the carbon dioxide injections due to patient movement secondary to discomfort.

   Nausea: occurred in three patients after carbon dioxide and in one patient after Ultravist but no treatment was required in any case

   Other: in one patient who had a selective injection with the kidney elevated, there was an area of poor filling of the renal arteries which was not present on iodinated contrast injections prior to, and after the carbon dioxide injection. The patient had flank pain with the carbon dioxide injection but the pain passed rapidly.

2. Diagnostic Efficacy

   Although the iodinated contrast images provided a nephrogram, the carbon dioxide images were diagnostically satisfactory in all but 4 segments. Only in one patient was the carbon dioxide examination totally inadequate (Figure 4 (a)).

   The intrinsic density reduction produced by carbon dioxide is less than the density increase produced by Ultravist and for the same film image density the carbon dioxide angiograms contain more “noise” than the equivalent Ultravist angiogram. Careful observers will have noticed that the window levels are negative for carbon dioxide and positive for Ultravist.

   If the aorta was underfilled, the carbon dioxide angiogram tended to overestimate the degree of branch narrowing and irregularity of the aorta. This is because the gas displaces the blood and does not mix with the blood like iodinated contrast does.

Figure 6. Serum creatinine levels in patients who had carbon dioxide only as an angiographic contrast.
Normal range for the laboratory is 0.5 - 0.11 mOsmol/l. Most patients are in chronic renal failure but were no worse after carbon dioxide angiography.

Figure 7. Complication of selective carbon dioxide injection
Iodinated contrast media (Ultravist) angiogram after carbon dioxide injection. Note the incomplete filling of the arcuate arteries in the lateral aspect of the upper pole of the kidney presumably due to a gas lock or perhaps spasm.

Figure 8. Diagnostic quality of carbon dioxide angiography
Figure 9. Comparative angiography - Acute renal failure. The carbon dioxide angiogram (left panel) shows apparent occlusion of each renal artery. The Ultravist angiogram (right panel) shows that only the left renal artery is in fact patent but that it is very severely narrowed.

Figure 10. Comparative angiography - Renal stent assessment at 4 years. There is no significant restenosis on either side on the Ultravist angiogram (centre panel) despite a malpositioned stent on the right side. The carbon dioxide angiograms were performed in oblique projections (outer panels) and show clearly the effect of position as only one renal artery is filled in each film. The superior mesenteric artery is filled in each carbon dioxide angiogram. Bubbles have formed in the aorta after the injection into the left renal artery (left panel). The left injection was automatically terminated by the injector after 15 ml because the catheter tip was against the wall of the artery. The malpositioned stent is clearly half inside the aorta.

Figure 11. Comparative angiography - Left renal artery stenosis. This pair of images shows the marked difference in filling of branch vessels with each contrast medium. In the Ultravist angiogram (right panel) the interlobar arteries are well filled and the superior mesenteric artery is not. In the carbon dioxide angiogram (left panel) the coeliac and superior mesenteric arteries obscure the right renal artery. The stenosis in the proximal left renal artery looks worse on the carbon dioxide study.
Figure 12.
Comparative angiography - Right and left iliac artery occlusion.
Each image of this pair accurately reflects the disease showing occlusion of each external iliac artery and reconstitution of the femoral arteries below the inguinal ligament. The small branches are better filled on the Ultravist angiogram (right panel).

Figure 13.
Comparative angiography - Right and left renal artery stenosis.
The carbon dioxide angiogram (upper panels) showed a severe proximal stenosis of the right renal artery (left panel) and later images from the same injection (right panel) showed a wandering anastomotic mesenteric artery which indicated a stenosis of the superior mesenteric and coeliac arteries.

Subsequent angiography prior to angioplasty (lower panels) validated the carbon dioxide angiography findings. Palmaz stents were placed in each renal artery and a wallstent was placed across the superior mesenteric artery stenosis also.
Figure 14 Comparative angiography - Bubble formation
The Ultravist angiogram shows no stenosis in the right iliac artery (left panel). The carbon dioxide angiogram shows breakup of the gas column with production of an apparent stenosis (centre panel). A later image from the same run (right panel) shows better filling but still suggests some degree of narrowing. The degree of breakup is related to the rate of flow of the blood and the volume of gas delivered. This problem can be overcome by image averaging.

Figure 15.
Comparative angiography - Distal limb arteries
For carbon dioxide angiography of the lower limb the leg is elevated about 20 - 30 degrees to take advantage of the buoyancy of the gas and to avoid breakup of the gas column. In a severely ischaemic limb the elevation may become painful and as a result there is the potential for movement mis-registration. This set of 4 images shows comparison at the popliteal bifurcation and at the ankle in the same patient. The multiple tibial artery stenoses are shown quite well on the carbon dioxide angiogram (upper left panel) at the level of the upper calf. The films of the ankle are much better seen on the Ultravist angiogram (lower right panel) because the patient moved with the carbon dioxide injection before the dorsalis pedis artery was filled. The state of the plantar artery was also not well seen on the carbon dioxide angiogram.

The upper images show the increase in noise produced when the densities of the two techniques are matched. Note that the carbon dioxide window width (120) is set at one quarter that of the Ultravist (512).
Figure 16. Occult bleeding - utility of carbon dioxide. When carbon dioxide passes from an artery into a lower pressure site, either a vein or a viscus, the gas expands and becomes more obvious than iodinated contrast media which has a much higher viscosity. In this example the patient had left sided macroscopic haematuria defying further localisation. Urography, retrograde pyelography and CT scanning showed no abnormality. An angiogram showed only faint filling of a renal vein but the carbon dioxide injection (right panel) showed rapid filling of the renal vein from the malformation. This was successfully embolised with cure of the bleeding. This technique has been used for detection of haematuria and other gastrointestinal bleeding.

CONCLUSION.

1. Carbon dioxide is an effective contrast medium for DSA.
2. Patients who are allergic to conventional iodinated contrast media may have abdominal and lower limb angiography with carbon dioxide with a good expectation (about 90%) of an adequate angiogram.
3. For consistent results carbon dioxide angiography requires attention to detail and a dedicated injector.
4. A sensation of heat and nausea are more noticeable after carbon dioxide than after injections of low osmolar non-ionic iodinated contrast. The cause for this is presumed to be due to gas lock.
5. When used in the lower limbs the current technique results in more patient movement than low osmolar non-ionic iodinated contrast.
6. Carbon dioxide is useful in the investigation of bleeding especially low-rate bleeding.

At the University of Melbourne, Department of Radiology, carbon dioxide angiography is firmly established as a primary method of renal artery assessment, as a contrast agent for lower limb angiography in selected cases and it is also used for angiography to localise arterial bleeding. The safety of carbon dioxide in the heart and cerebral circulation has not yet been established.

PRESENTED AT THE ANNUAL MEETING OF THE CARDIOVASCULAR AND INTERVENTIONAL RADIOLOGICAL SOCIETY OF EUROPE CRETE, GREECE JUNE, 1994