CO_2 DSA Angiography

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Since the first cadaveric arteriogram in 1896 angiographic contrast media has improved tremendously. However, adverse reactions, including mortality secondary to "anaphylaxis" and renal failure still occur(1). Since 1971 we have used carbon dioxide (CO_2) as an arterial contrast agent at the University of Florida(2,3) in over 800 patients. We became interested in CO_2 as a contrast agent since it was routinely used intravenously at that time for the detection of pericardial effusion(4 5). It has been used intravenously in thousands of patients without reported complications(5). We initially used CO_2 by hand injection with standard cut film subtraction techniques(2). The CO_2 was difficult to reliably deliver, the images were frequently suboptimal, and the subtraction process was time consuming.

DSA IMAGING

In 1980 with the advent of digital subtraction angiography (DSA), imaging of this "low density" contrast agent became quite reliable. The newer 1024 matrix digital systems presently provide both contrast and resolution approaching film screen systems. Recently modifications of software to add a subset of images into a single, composite "stacked" images has decreased the injections rates and volumes from 50-100cc per injection to 5-10cc per injection. This has made interpretation of the arteriogram much easier when small amounts of CO_2 are delivered or when collateral flow "breaks up" the CO_2 column. During the last two years, we have also used CO_2 as a medium to displace blood for more clear angioscopic viewing in endovascular procedures(6,7).

GENERAL PRINCIPLES

Liquid contrast mixes with blood and, if delivered properly, will fill the entire vascular tree. To increase the density, and thus the quality of the arterial image, either the injection rate or the concentration of the iodinated contrast agent is increased. In contrast, CO_2 gas produces an arterial image by totally displacing blood from the vessel. The minimal difference in the density of the gas compared to the surrounding soft tissue is then distinguished using digital subtraction and electronic enhancement. If the blood has been totally displaced from the vessel being examined, addition of more CO_2 will not improve the image. The image can only be improved by electronic enhancement.

BUOYANCY

CO_2 gas is extremely buoyant, which can both impede and facilitate vascular filling. Arteries that are dependent (posterior in supine position) such as the lumbar arteries are not well filled with CO_2. On the other hand, anterior arteries (celiac, superior mesenteric (SMA) and inferior mesenteric (IMA) arteries) are always well filled even when inadequate amounts of CO_2 are delivered. It is therefore imperative to position the area of interest higher than the injection site. The analogy of injecting helium into a hollow tree can be used. If the tree is inverted, the distal branches would be very difficult to fill with helium. If this tree is lying on its side, the upper branches would fill and if the tree is in its normal upright position, all the branches would readily fill.

During lower extremity angiography the horizontal iliac and proximal superficial femoral arteries (SFA) fill quite well with CO_2 when the patient is supine. However, the more distal vessels that are lower than the injection site are more difficult to fill, especially in patients with poor arterial flow. The SFA slopes downward from its location anterior to the proximal femur to a position posterior to the distal femur. The injected CO_2 tends to float to the higher portion of the SFA when the patient is supine. Approximately 20 to 30 degrees of Trendelenburg improves filling of the more distal vessels. A tilting table provides the elevation and stability required for a good DSA image. Elevating the legs with wedges, etc. will also suffice, but when the legs are elevated without a tilting table, motion frequently occurs, degrading the image.

LOW VISCOSITY

The very low viscosity of CO_2 (1/400 of iodinated contrast) greatly facilitates filling of collaterals and stenotic vessels. In addition, this low viscosity expedites identification of arterial venous shunting within malignant tumors and arterial venous malformations(3). The low viscosity of CO_2 gas permits its delivery through very small catheters and through the narrow space between instruments such as guidewires, lasers, atherectomy devices or angioscopes and the inner wall of guiding catheters.

DOES CO_2 BLOCK CAPILLARIES?

Injection of CO_2 gas into the arterial system potentially could lead to ischemia due to capillary occlusion from trapped gas bubbles. However, CO_2 gas is extremely soluble in blood (20 times that of oxygen) so that gas bubbles should be quickly dissolved. In addition, when large volumes of CO_2 are injected into the aorta of dogs, the renal veins are always seen. This suggests that CO_2 either floats through capillaries or passes into the renal vein through precapillary shunts. CO_2 gas in the renal veins returns to the inferior vena cava and is eliminated very quickly by the pulmonary circulation. Because CO_2 gas does return to the right heart, it is important to limit the volume of CO_2 per injection to 200cc. In two animals, delivery of massive amounts of CO_2 directly from a CO_2 gas cylinder totally displaced blood in the right heart causing the animals' demise.

INJECTION TECHNIQUE

CO_2 is very difficult to deliver for angiography because it is compressible, invisible and heavier than air. Initially, for aortography and extremity angiography we filled a 50cc syringe with CO_2 using a standard oxygen regulator connected to a medical grade CO_2 cylinder. Using a three-way stop cock, air was purged from the syringe by filling and emptying it multiple times. The syringe was then connected to the angiographic catheter and the CO_2 was pushed rapidly into the catheter. The DSA imaging series was initiated prior to injecting the CO_2. We attempted to deliver the 50cc of CO_2 in 2-3 seconds, as would be done with standard iodinated contrast. Unfortunately, because of the compressibility of the gas, the plunger initially moves forward quite easily but little CO_2 is delivered. Movement of the plunger then becomes increasing difficult and the entire 50cc of gas is delivered in the last half-second of the injection ("explosive, inconsistent delivery".)

Delivery of CO_2 gas using a standard mechanical liquid injector is somewhat more reliable. The injector can be programmed to advance the plunger at a constant rate, such as the equivalent of 25cc of liquid per second for 4 seconds (total of 100cc). However, even using this system, CO_2 is not injected instantaneously, but is simply compressed compressed for 3.5 seconds and the entire 100cc is delivered during the last one-half second of injection. This results in a flow rate somewhere between 100-200cc per second, which creates an "explosive type" delivery. If the injector is programmed to deliver 10cc per second for a total of 50-80cc, again, the gas is initially compressed, but during the last several seconds is delivered at a lower rate of approximately 20-70cc per second.

We have developed several dedicated CO_2 injectors during the last six years. The most recent injector is gated to the electrocardiogram and delivers CO_2 so that blood is totally displaced during the duration of the injection. No more than 200cc per injection can be delivered and the injector includes many other fail-safe systems. Multiple 0.24 micron filters ensure sterility of the injected gas, and the injector is hermetically sealed to prevent air contamination. The injection rates and volumes of injection can be Programmed and indicators will show the rates and volumes of CO_2 gas actually delivered. A system to automatically flush the angiographic catheter with saline between injections will also be included. The injector is presently undergoing clinical trials.

DIAGNOSTIC ACCURACY

Imaging of the aorta and first- and second-order branches is excellent approximately 90% of the time using CO_2 angiography. Failure of CO_2 aortograms to provide diagnostic information is usually due to respiratory and bowel motion. In the pelvis and lower extremities, the success rate is higher. However, the vessels below the knee are definitely more difficult to fill, especially in patients with poor flow. If the extremity is not elevated and only a small amount of CO_2 is delivered, the CO_2 may become absorbed before it reaches the trifurcation. In contrast, if the leg is elevated, the CO_2 will readily flow to the trifurcation and even to the level of the digital arteries. Filling of distal vessels can also be improved by advancing the angiographic catheter doser to the area of interest. Using such techniques, at times collaterals and distal vessels will fill better with CO_2 than with liquid contrast. Even structures with little or no flow will readily fill because of the buoyancy of CO_2. For example, we have seen many tumors that appeared totally avascular using iodinated contrast but were seen to be very vascular using CO_2.

Interpretations of the images from CO_2 angiography are considerably more difficult than when iodinated contrast is used. For accurate interpretation, one must be assured that the CO_2 has totally displaced the blood from within the vessel. The "stacking" program, at least in the last 20 patients, has provided accurate images even with very small volumes of CO_2 (10cc per injection.)

COMPLICATIONS

The only documented complication directly related to CO_2 injection in our series has been severe diarrhea after CO_2 aortography in one patient. Two thousand cc's of CO_2 were injected into the abdominal aorta during this study and the inferior mesenteric artery circulation was exposed to very high volumes of CO_2 because it originated from an aneurysmal infrarenal aorta. The CO_2 was apparently trapped in the aneurysm and the multiple injections created a "vapor lock" in the IMA, resulting in ischemia. Although this is the only complication from CO_2 injection that has been observed in patients undergoing CO_2 angiography at the University of Florida, other potential toxic effects of CO_2 gas used as a contrast agent have been carefully investigated.

NEUROTOXICITY

We do not use CO_2 above the diaphragm since a preliminary study in rats suggest that it may be neurotoxic(10). We also do not inject CO_2 into the aorta when patients are in the prone position because the buoyancy of the gas may fill vessels that feed the spinal cord. Until the question of neurotoxicity of CO_2 gas is resolved, **CO_2 is definitely contraindicated** in any situation where the cerebral circulation could be exposed to the gas.

RENAL TOXICITY

Since CO_2 is eliminated by the lungs in a single pass, if the injection is distal to the renal arteries, there is no impact whatsoever on renal function. For aortography and selected renal injections in patient in renal failure we have noted no decrease in renal function; however, in the majority of the cases, the distal renal arteries will not fill well because of the buoyancy. The distal vessels will perfuse better with CO_2 in transplanted kidneys that are anteriorally located.

USE IN RESPIRATORY FAILURE

CO_2 should not be used in patients with severe respiratory compromise unless blood gases are obtained at frequent intervals during the procedure. We have used CO_2 angiography in several patients with respiratory failure without untoward effects. However, patients who are acidotic, with high PCO_2 values, may not be able to eliminate the excess carbon dioxide which accumulates during CO_2 angiography and thus, be at risk from this procedure.

DISCOMFORT

In over 90% of the patients minimal or no discomfort occurred during CO_2 injection. Only if large volumes are injected very rapidly does discomfort which approaches that of iodinated contrast occur. Injections of 5-10cc with the new stacking program usually produce no sensation whatsoever or motion.

CO_2 has many significant advantages for both angiography and angioscopy(3,7,11). With CO_2 used as a contrast agent, there is no chance whatsoever of allergy in any patient population, no renal toxicity, minimal discomfort, and it is inexpensive compared to nonionic contrast agents. In addition, the low viscosity of CO_2 permits delivery by very small catheters. The unlimited total volume of CO_2 may play a key role in long endovascular procedures where large volumes of saline and contrast are required. The disadvantage is its compressibility. Although C02 can be delivered by hand injection or with a standard liquid contrast injector, we would not recommend its general use until a dedicated delivery system is available, which would prevent any possibility of air contamination, explosive delivery or inadvertent injections of large volumes. Presently, C02 has not been FDA approved.

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