

## *Commentary on the Preceding Articles*

### **CO<sub>2</sub> Digital Subtraction Arteriography— Advantages and Current Solutions for Delivery and Imaging**

This discussion reviews the advantages and disadvantages of CO<sub>2</sub> digital subtraction arteriography (DSA), recent indications, and potential risks of CO<sub>2</sub> delivery.

Compared to low-cost, high osmolality, ionic, vascular contrast agents, low osmolality contrast agents have reduced the incidence of complications and pain, especially during peripheral angiography. Unfortunately, low osmolality agents, including non-ionic contrast agents are not free from allergic and nephrotoxic complications. Compared to ionic, high osmolality agents, they are very expensive currently, costing about \$1 per milliliter in the USA, which adds a considerable overall cost to contrast-enhanced imaging procedures. On the other hand, CO<sub>2</sub> is very inexpensive (\$.005 per milliliter). A cylinder of 3,000,000 ml of CO<sub>2</sub> costs approximately \$80. Most importantly, however, allergic reactions and renal failure are not associated with its administration. If time is allowed to elapse between injections, unlimited amounts of CO<sub>2</sub> can be delivered. This is also cost-effective in that both diagnostic and therapeutic interventional procedures can be performed in one sitting without the risk of contrast overload.

Additional advantages of CO<sub>2</sub> are its flow viscosity which permits use of catheters as small as 1.5 Fr and the ability to inject it through very small lumens between needle and guidewire or small catheter and guidewire. We and others have found that CO<sub>2</sub> occasionally provides information that cannot be obtained with iodinated contrast. Apparently, the low viscosity results in improved demonstration of collateral flow and minute amounts of bleeding. This is seen in gastrointestinal hemorrhage not diagnosed by conventional angiography but well demonstrated with CO<sub>2</sub>. Occasionally, vascular lesions with pronounced stasis (e.g., cavernous hemangiomas and tumors with large vascular lakes) appear avascular with iodinated contrast, but become very vascular with CO<sub>2</sub>. Arteriovenous shunting in malignant tumors may be better seen as well. CO<sub>2</sub> has also been

beneficial for guidance during transjugular intrahepatic portosystemic shunt procedures when CO<sub>2</sub> hepatic wedge venography frequently fills the portal vein. The two articles on CO<sub>2</sub> in vascular imaging in this journal present additional advantageous applications.

CO<sub>2</sub>, in itself, is extremely safe if it is delivered in a controlled, nonexplosive manner with small volumes per injection. Bendid [1] reported 1600 cases in which 200 ml of CO<sub>2</sub> were injected intravenously without significant complications. However, the patients were placed in the left lateral decubitus position, resulting in CO<sub>2</sub> being trapped in the capacious right atrium with the venous return flowing under the CO<sub>2</sub> into the right ventricle. If very large amounts of CO<sub>2</sub> are injected in a very short period of time, the right ventricle and pulmonary artery can be completely filled with CO<sub>2</sub>, resulting in a "vapor lock" type phenomenon and possible death. This was exemplified in our early experience on laboratory animals where high pressure inadvertent injection of excessive CO<sub>2</sub> volumes resulted in their deaths.

The two papers presented earlier in this journal give minimal details on delivery; however, they state that a closed system was used. This suggests that the cylinder was indeed connected to the patient. Because of our initial experience of inadvertently injecting excessive volumes in animals, until recently we have avoided using a closed system. In the early 1980s, we found that CO<sub>2</sub> was delivered more consistently with a standard angiographic injector. Since we did not use a closed system, the required multiple loading and purging was very time-consuming. Since the syringe was filled with compressible gas, the syringe's stopcock was open with the syringe pointed upward (CO<sub>2</sub> is heavier than air) to vent the excess CO<sub>2</sub> [2, 3]. If a mechanical injector is used, the venting step is extremely important. If the regulator which dispenses CO<sub>2</sub> malfunctions, excessive volumes can be loaded into the delivery syringe, and when the stopcock is opened, CO<sub>2</sub> can flood the vascular system. Since both CO<sub>2</sub> and air are invisible, the syringe can easily be contaminated by the room air and, if explosively delivered, could reflux into the cerebral circulation causing stroke and death.



*Caution:* Because of possible neurotoxicity and/or air contamination, CO should not be used in any application where the cerebral circulation could be exposed. (Arterial injections should not be made above the diaphragm.) Also, to prevent "vapor lock" in the right heart and possible buoyant flow into the left heart, via a patent foramen ovale, the *right side should be elevated* before any venous or arterial injections where arteriovenous shunting is expected.

The compressibility of CO<sub>2</sub> is also a factor in the delivery. When the plunger of either a mechanical or hand-held syringe is moved forward in a syringe containing CO<sub>2</sub> under moderate pressure, the volume would simply compress, then within a fraction of a second CO<sub>2</sub> would be delivered in an explosive, noncontrolled manner.

Because of these difficulties, we have developed several prototype delivery systems during the last 10 years. The most recent is a very sophisticated computer-controlled device with multiple pressure transducers and mass-flow meters gated by pressure and EKG [4]. More CO<sub>2</sub> is injected at a higher rate during systole and a lower rate during diastole, resulting in a more uniform filling, especially in larger arteries. The device is also equipped with multiple computer-controlled fail-safe systems. The CO<sub>2</sub> injector is connected to the patient with a closed system incorporating two one-way check valves. This prevents reflux of blood from the catheter into the CO<sub>2</sub> tubing and also permits automatic flushing of saline after the CO<sub>2</sub> is injected. The incorporated transducer provides continuous pressure monitoring. This system is currently available in most countries outside the United States; however, it is not likely to be approved by the FDA until 1997.

Recently, we have used the same principles of the dedicated injector for a hand-held closed delivery system which eliminates important problems: (1) CO<sub>2</sub> contamination with air; (2) uncontrolled explosive delivery; and (3) injection of excessive volumes.

The dedicated injector's computer will calculate the exact amount of CO<sub>2</sub> required to displace the saline from the catheter. After the saline is displaced from the catheter, CO<sub>2</sub> can be delivered in a nonexplosive manner. The hand-held system incorporates this principle by using a 3-ml syringe in tandem with the delivery syringe. The saline is removed from the angiographic catheter by rapid delivery of CO<sub>2</sub> via the 3-ml syringe. After the fluid has been removed from the catheter, only minimal CO<sub>2</sub> compression occurs as the delivery syringe barrel is advanced, permitting a more controlled delivery. The dedicated injector is equipped with one-way check valves which prevent reflux of blood into the catheter and permit automated flushing with saline. The hand-held system also includes mul-

tiple "check valves" which eliminate confusion of turning the stopcock in the incorrect direction during delivery. The one-way check valves also permit rapid loading and CO<sub>2</sub> delivery without manipulating any stopcocks.

The CO<sub>2</sub> is transferred from the CO<sub>2</sub> cylinder into a plastic bag which is filled only to atmospheric pressure. The flexible bag will collapse incrementally as the CO<sub>2</sub> is withdrawn. Since the bag is subjected to only one atmosphere, if the injection syringe is filled with 100 ml, only 100 ml will be delivered. There is no possibility of delivering an excessive amount of CO<sub>2</sub> and venting is not required.

Although the hand-held system is not EKG-gated and is not as consistent or easy to use as the dedicated injector, we feel that it will provide a safe delivery of CO<sub>2</sub>.

This system requires a disposable CO<sub>2</sub> source to fill the bag and a sub-micro filter to filter out any bacteria or particulate matter as the bag is being filled. Currently, there is an FDA-approved CO<sub>2</sub> injector available for double-contrast barium enemas, which operates on a similar principle. A bellows mechanism is filled from the tank under atmospheric pressure and the closed system can be directly connected to the hand-held delivery system.

Lastly, gasses are never as "dense" as iodinated contrast agents. However, the DSA equipment even in the early 1980s provided reliable imaging of CO<sub>2</sub>. The 1024 × 1024 × 10-bit DSA systems have considerably increased the contrast and resolution of the gas. Acquisition has been modified to enhance electronically the CO<sub>2</sub> contrast. The biggest advance has been the addition of the "stacking" program. This enables injections of very small volumes (10–20 ml) without the patient experiencing any sensations; thereby decreasing motion. In addition, CO<sub>2</sub> does not mix with blood and small bubbles of CO<sub>2</sub> will expand and contract as they pass through the arterial tree. With the "stacking" program and a relatively fast film rate, multiple images can be added together as the segment of CO<sub>2</sub> passes distally. This results in a composite, accurate image of the entire area of interest obtained rapidly with low, safe CO<sub>2</sub> volumes. However, if large volumes of CO<sub>2</sub> are injected in an explosive manner, the patient tends to move and the image is degraded. Tilting tables are now available to use CO<sub>2</sub>'s buoyancy to maximum advantage to fill the area of interest. For example, the feet are elevated for improved filling. Other methods to improve image quality include selective injection and vasodilator enhancement.

In summary, CO<sub>2</sub> is our contrast agent of choice in patients with severe allergies and renal failure. However, because it is safe and inexpensive, we are frequently using it for routine studies either exclusively

or in conjunction with ionic contrast. The delivery system and imaging equipment we use are fast and user-friendly, while providing safe diagnostic studies of excellent quality.

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