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CO₂ as a Venous Contrast Agent: Safety and Tolerance

Kyung J. Cho  
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INTRODUCTION

CO₂ has been used increasingly as a contrast agent in both the arterial and venous circulations, particularly in patients with hypersensitivity to iodinated contrast material and renal insufficiency. CO₂ can be used as a contrast agent for upper extremity venography, wedged hepatic venography, fine-needle transjugular intrahepatic portosystemic shunt (TIPS), and splenoportography (1–6). With the advent of the plastic bag system (7), the safety and ease of gas delivery has been improved, allowing multiple injections from the CO₂ bag.

GAS FLOW DYNAMICS

The unique physical properties of CO₂ affect the flow dynamics of the gas in venous circulation. The low viscosity of CO₂ allows its injection through a small catheter or needle as small as 27 gauge. When injected into a vein, CO₂ flows through the venous system and into the central veins rapidly, usually faster than contrast material. From the right atrium, the gas bubbles pass through the right ventricle into the pulmonary artery. In the supine position, the gas bubble is trapped in the pulmonary outflow tract (Fig. 1A). In the left lateral decubitus position, the bubble is trapped in the right atrium (Fig. 1B), allowing the blood to flow underneath the bubbles. In the Trendelenburg position and in the presence of elevated right heart pressure, the gas bubble may reflux into the hepatic vein from the right atrium (Fig. 2).

In general, the gas flow in small veins depends on the injection pressure. The injection pressure (explosive delivery) is the force used to push gas bubbles through the veins. In the larger veins, venous pressure and the flow of blood push the gas into the heart. The luminal gas filling depends on the size of the vessels injected. In small veins, the percent luminal gas filling should exceed 80%, whereas in the large veins, such as the vena cava, luminal gas filling is about 60% to 80% due to its buoyancy.
Although CO₂ was used as an intravenous contrast agent as early as the 1950s for the
diagnosis of pericardial effusion (8–10), little is known about the effects of bolus
central venous injections of the gas on the hemodynamic and ventilatory functions. We,
therefore, evaluated the effects of single intracaval injections of increasing amounts of
CO₂ on the hemodynamic and ventilatory parameters in order to determine the safety
and tolerance of the gas, and the adequacy of the routine monitors used during the use
of CO₂ as a venous contrast agent.

The cardiopulmonary effects of the intracaval administration of increasing
amounts of CO₂ (0.2–6.4 cc/kg body weight) were studied in 15 pigs (25–38 kg body
wt) placed in the supine, left, or right lateral decubitus position. One animal from the

**Figure 1** Right central venograms in the supine (A) and left lateral decubitus (B) positions follow-ing injections of CO₂ into a right arm vein. In the supine position, CO₂ flows promptly into the pulmonary artery (arrow). In the lateral decubitus position (right side up), CO₂ bubbles are trapped in the right atrium (arrow).

**EFFECTS OF CO₂ ON THE CARDIOPULMONARY FUNCTION**

Although CO₂ was used as an intravenous contrast agent as early as the 1950s for the
diagnosis of pericardial effusion (8–10), little is known about the effects of bolus
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**Figure 2** CO₂ injection into the right hepatic vein in a patient with pulmonary hypertension. CO₂ injected into the right HV, has refluxed into the middle and left HVs, and the IVC. **Abbreviations:** HV, hepatic vein; IVC, inferior vena cava.
left-side-up group died upon the intracaval injection of 6.4 cc CO₂/kg, apparently from a gas embolism. All of the other animals survived the intracaval injections of CO₂ in doses increasing to 6.4 cc/kg body weight. All of the animals showed no significant changes in their vital signs when administered 0.2–1.6 cc CO₂/kg. The systemic and pulmonary arterial pressure responses to incremental increases of CO₂ volumes in swine placed in the supine position is shown in Figure 3. A significant drop in the systemic blood pressure started to occur at the dose of 3.2 cc CO₂/kg, regardless of the body positions (Fig. 4). Pulmonary arterial pressure increased with the injection CO₂ at a dose of 0.4–3.2 cc/kg (Fig. 5). Despite the significant fall in the blood pressure after the injection of CO₂, SaO₂ remained above 90% (Fig. 6).

In summary, CO₂ given in diagnostic quantities is safe and causes no significant cardiopulmonary effects. Because CO₂ increases pulmonary arterial pressure, the gas should be used cautiously in patients with pulmonary hypertension. Blood pressure monitoring and capnography provide the earliest signs of a potentially life-threatening venous gas embolism. The body position has no influence on the severity of cardiopulmonary responses to CO₂. However, in the event of an accidental injection of an excessive amount of CO₂, placing the patient in the right-side-up position will help trap the gas bubbles in the right atrium, allowing continued blood flow underneath the gas bubbles.

**Figure 3** Polygraph tracings of the systemic (SBP, upper record) and pulmonary (MPAP, lower record) arterial pressures following intracaval injections of CO₂ at 1.6 cc/kg (A), 3.2 cc/kg (B), and 6.4 cc/kg (C) in swine placed in the supine position during CO₂ injection. At 1.6 cc/kg, SBP decreased 6% and MPAP increased 25%. At 3.2 cc/kg, SBP decreased 24% and MPAP increased 32%. At 6.4 cc/kg, SBP decreased 74% but pulmonary arterial pressure changed slightly. Arrow = Time of CO₂ injection.
Carbon dioxide has been generally used as an alternative venous contrast agent in patients with renal failure or a history of contrast allergies. At our institution, CO₂ is the contrast agent of choice for a variety of venous studies, including subclavian venography, wedged hepatic venography, percutaneous splenoportography, and inferior vena cavaography prior to filter placement in patients with renal failure or contrast allergy and fine-needle TIPS. CO₂ is a useful contrast agent during venous interventions including catheter-directed thrombolysis, hepatic vein stent placement, inferior vena caval stent placement, and visualization of collateral veins.

Since CO₂ is visible fluoroscopically, it can be used to opacify target veins for percutaneous acces, such as the basilic vein for PICC placement and the subclavian vein for Hickman placement.

There are no absolute contraindications to the use of CO₂ in venous circulation. The only possible contraindication to CO₂ injection is a history of intracardiac shunts.

Figure 4  Average per cent changes in systemic blood pressure following intracaval injections of ascending doses of CO₂ in swine placed in the supine (A), left lateral decubitus (B), and right lateral decubitus (C) positions. At the doses of 3.2cc/kg, systemic blood pressure started to fall significantly, regardless of the body position. The hemodynamic response to the intracaval injections of large amounts of CO₂ was greater when the animals were placed in the right lateral decubitus position.

**CLINICAL APPLICATIONS**

Carbon dioxide has been generally used as an alternative venous contrast agent in patients with renal failure or a history of contrast allergies. At our institution, CO₂ is the contrast agent of choice for a variety of venous studies, including subclavian venography, wedged hepatic venography, percutaneous splenoportography, and inferior vena cavaography prior to filter placement in patients with renal failure or contrast allergy and fine-needle TIPS. CO₂ is a useful contrast agent during venous interventions including catheter-directed thrombolysis, hepatic vein stent placement, inferior vena caval stent placement, and visualization of collateral veins.

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Figure 5  Average percent changes in pulmonary arterial pressure with ascending doses of CO$_2$ (0.2–6.4 cc/kg) in swine in the supine position. Pulmonary arterial pressure started to rise in 10–15 seconds following injection of 0.2 cc/kg CO$_2$. The degree of the rise in pulmonary arterial pressure increases with ascending doses of CO$_2$ up to 3.2 cc/kg.

Figure 6  Average changes in SaO$_2$ following intracaval injection of increasing doses of CO$_2$ in a supine pig. There were minimal changes in SaO$_2$ despite significant fall in the systemic blood pressure and ET-CO$_2$. 
Because CO\textsubscript{2} can increase pulmonary arterial pressure by 30\% to 40\%, the gas should be used cautiously in patients with severe pulmonary hypertension. We have not encountered a single incidence of a clinically significant paradoxical gas embolism in hundreds of patients who had undergone venous CO\textsubscript{2} injection studies. It is generally known that a patent foramen ovale is present in 10\% to 15\% of the population. This suggests that the CO\textsubscript{2} from the intravenous injection does cross the patent foramen ovale into the left atrium, or that small amounts of CO\textsubscript{2} entering the left heart cause no clinically significant systemic gas embolism. The known clinical signs for gas embolism of the coronary artery are bradycardia, hypotension, and an abnormal electrocardiogram (ECG).

**SAFETY**

The bolus administration of CO\textsubscript{2} into either the peripheral vein or the central vein in quantities of 30–50 cc, required for diagnostic imaging, causes no change in vital signs. Any significant change in vital signs after the intravenous injection of CO\textsubscript{2} should raise suspicion of a possible air contamination or paradoxical embolism. CO\textsubscript{2} injection should be stopped and vital signs should be re-evaluated. Then fluoroscopy should be performed over the lung and mediastinum in search for a retained gas bubble. If the gas bubble is visible in the pulmonary artery over 30 seconds after the injection, air contamination has occurred.

There is no simple method for distinguishing CO\textsubscript{2} from air. We have used either the digital subtraction technique or fluoroscopy to detect air contamination during CO\textsubscript{2} venous studies (Fig. 7). Our experimental study has shown that 45cc of CO\textsubscript{2} trapped in the right atrium dissolves completely in 70 sec (45–90 sec). If CO\textsubscript{2} is injected in the supine position, the gas bubble trapped in the main pulmonary artery should disappear within 15–20 seconds. If air contamination has occurred, the bubble will remain visible one minute after the injection.

There is no dedicated CO\textsubscript{2} injector in the U.S. Currently the hand-held syringe and the plastic bag system are used for CO\textsubscript{2} delivery. The hand-held syringe is a simple method for CO\textsubscript{2} delivery. This is inconvenient when multiple injections are required. When filling the syringe with CO\textsubscript{2}, it should be filled and emptied three times before filling for injecting into the catheter. Once the syringe has been filled with CO\textsubscript{2}, the tip of the syringe should be closed using a one-way stopcock. When the syringe is open to the ambient air, CO\textsubscript{2} in the syringe is rapidly replaced by air through gas diffusion because of the difference in the partial pressure of CO\textsubscript{2} between the syringe and the air. A gas chromatographic study has shown that 43\% of the CO\textsubscript{2} in a 20-mL syringe will be replaced by air in 30 minutes. Although CO\textsubscript{2} is heavier than air, we found that the speed of air contamination is not affected by the syringe position.

The Plastic Bag system (AngioFlush 111 Fluid Management System, AngioDynamics, Queensbury, New York, U.S.A.) is quite useful when multiple CO\textsubscript{2} injections are needed. We routinely use this system for our venous CO\textsubscript{2} studies. It is comprised of the fluid collection bag and fluid management system. The check valves of the system have eliminated the need for the use of a stopcock and all connections are air tight. The residual air in the bag is removed by filling and emptying it three times. Once the bag has been filled with CO\textsubscript{2}, it is connected to the side arm port of the fluid management system. A 60 mL luer-lock syringe is connected to the injection port of the system. Once all connections have been made, the stopcock between the bag and the CO\textsubscript{2} fluid management system is closed before aspirating the syringe to check for an air leak.
When CO₂ is used as a venous contrast agent, air contamination precautions should be taken, regardless of the type of delivery system used. Since early detection of air contamination can prevent serious or even fatal accidents, we check blood pressure one minute after CO₂ injection and check the pulmonary artery for a persistent gas bubble fluoroscopically. Any significant fall in blood pressure after CO₂ injection may be due to air contamination, and the gas delivery system should be checked for an air leak. Capnography provides both the hemodynamic and ventilatory information in a real time manner. We found it to be an effective monitor for CO₂ venous studies. Heavy sedation should be avoided before CO₂ delivery because the hemodynamic and ventilatory responses to the sedation may mimic an air embolism. For upper extremity venography or inferior vena cavaography we generally perform the procedure without conscious sedation.

When the patient develops significant hemodynamic and ventilatory abnormalities following the injection of gas, he/she should be placed in the lateral decubitus and in the Trendelenburg position to trap the gas in the right ventricle and atrium so that the blood continues to flow underneath the gas bubbles. Oxygen should be administered by mask. If possible, catheter aspiration may be performed.

CONCLUSION

Carbon dioxide is a safe and useful venous contrast agent. There should be no significant changes in vital signs following the intravenous injection of CO₂ in quantities used.
for diagnostic CO₂ imaging. The gas should be used whenever possible, even in patients
with or without normal renal function. Because of the low viscosity, the gas can be
injected using a small catheter or needle, and it visualizes the central veins well. The
current CO₂ delivery system must be used correctly to prevent air contamination.
Excessive doses of sedatives and narcotics should be avoided because it can result in
respiratory depression and hypotension. These side effects can mimic the side effects of
the inadvertent administration of large amounts of CO₂ and air contamination. All
patients who receive CO₂ should be awake and alert. When repeated doses of CO₂ are
administered, sufficient time must be allowed for the gas to be absorbed completely. In
the event of accidental injection of large amounts of CO₂ or an inadvertent injection of
air, the maximal derangement in the cardiopulmonary functions will occur within one
minute after the injection. CO₂ should be used with caution in patients with severe
pulmonary hypertension since CO₂ causes a transient rise in the pulmonary arterial
pressure.

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