Cerebral angiography with gaseous carbon dioxide CO_2

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SUMMARY.—Large quantities of gaseous carbon dioxide CO_2 were rapidly injected into the ascending aorta or common carotid artery of 14 dogs. Good filling of the arteries and intracranial veins was documented by cineangiography or digital subtraction angiography. No adverse effects occurred as a result of this procedure: the electroencephalogram showed no changes throughout the experiments and the dogs were neurologically normal for up to 6 months of follow-up. Further investigation of carbon dioxide as an arterial and cerebrovascular contrast agent is justified based on these results.

KEY WORDS.—CO_2 injection · Cerebral angiography · Cerebral vessels.

CO_2 gas appears to be a safe venous and peripheral arterial contrast agent with no adverse reactions reported to date.[1-10] The development of digital subtraction angiography (DSA) with its greatly improved contrast sensitivity has made possible the use of intravascular CO_2 imaging with encouraging results.[9 10] The possible effects of gaseous CO_2 in the cerebral, spinal and coronary arteries of humans is unclear. In a recent study by Coffey *et al.*[11] there were profound neurological defects and pathological changes of infarction after the injection of CO_2 into the carotid arteries of rats. This study presents the results of CO_2 aortography and selective carotid angiography in dogs under conditions more closely simulating routine clinical practice in humans.

Materials and methods

Fourteen mongrel dogs of both sexes weighing between 13 and 16 kg were anaesthetised with intravenous 6% phenobarbitol. A 6-French sheath was inserted into a femoral artery by cutdown and used for the introduction of arteriographic catheters.

The electroencephalogram (EEG) was monitored continuously throughout the experiment (in 9 dogs) using a Grass 6-channel recorder with subcutaneous needle electrodes. The ECG was also monitored continuously. The opposite femoral artery was used for direct constant blood pressure measurements using a Sanborn transducer. Arterial PO_2 and PCO_2 were checked periodically before, during, and after the procedure.

Nine dogs had injections into the ascending aorta only, 3 into the right common carotid artery and 2 into both arteries. Each dog received from 4 to 9 injections of CO_2 through 5-French catheters introduced via the sheath under fluoroscopic control.

Small quantities of iodinated contrast material were used to confirm the catheter position. Each injection consisted of 3-5 cm^3/kg pure CO_2 gas injected by hand as a compressed bolus from a 60 cc syringe. Prior to injection, the syringe and connecting tubing were flushed a number of times with CO_2 to remove air from the system. Details of the site and number of injections, total dose of CO_2 and length of follow-up for each dog are given in Table I. During injection and filming, the dog's head was elevated by approximately 30° to facilitate preferential filling of cranial vessels by the gas. One dog received an injection of 30 cm^3 of room air into the ascending aorta.

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Table 1.—Data on cerebrovascular angiography using CO_2 in 14 dogs.

	Site of CO_2 injection		No. of injections	Total amount of CO_2 (cm^3)	EEG control	Clinical manifestation after CO_2 injections			Follo
	Ao Arch	Rt CCA				Hemipar.	Hemipl.	Stroke	
1.	+	—	8	270	+	—	—	—	2 w
2.	+	—	7	210	+	—	—	—	4 w
3.	+	—	9	270	+	—	—	—	6 m
4.	+	—	6	240	+	—	—	—	3 m
5.	+	—	7	250	+	—	—	—	5 m
6.	+	—	7	210	+	—	—	—	7 w
7.	+	—	9	300	+	—	—	—	3 w
8.	+	—	8	250	—	—	—	—	4 w
9.	+	—	5	200	—	—	—	—	2 m
10.	+	+	7	180	+	—	—	—	4 hr
11.	+	+	7	210	—	—	—	—	3 m
12.	—	+	7	260	+	—	—	—	8 w
13.	—	+	7	240	—	—	—	—	36 hr
14.	—	+	4	120	—	—	—	—	36 hr

*Dead after intraarterial air injection.

In 8 dogs who had injections into the aortic arch, filling of the great vessels with CO_2 was documented by cineangiography. In the remaining 6 dogs including 5 who had selective injections into the right common carotid artery, DSA filming was carried out at 3 frames per second using a Diasonics DF 100 unit.

Two dogs were sacrificed 36 hours after CO_2 angiography for macroscopic evaluation of the brain (No. 13 and 14).

Results

None of the 14 dogs demonstrated change in EEG, ECG, and arterial blood gases during or after the injection of CO_2 gas (Fig. 1). The dog who had air injected into the aortic arch died approximately 20 seconds later (No. 10). The 13 dogs who were followed after the procedures were neurologically intact with no evidence of brain damage on examination or by observation of their behavior.

DSA demonstrated excellent visualisation of large and medium-sized arteries (Figs. 2, 3). CO_2 appeared in the cerebral veins as soon as one second after injection with good visualisation of venous anatomy (Fig. 4).

The macroscopic evaluation of the brains of sacrificed dogs did not reveal any pathologic changes (Fig. 5).

Discussion

CO_2 gas can be used as an intravascular contrast agent because of its high solubility which is about 20 times that of oxygen and results in rapid dissolution of the gas bubbles.[12 13] Its safety in the venous system has been borne out by numerous experiments as well as by clinical experience.[4-7 9] In most of these studies, CO_2 was injected into systemic veins.

CO_2 in medium-sized or small vessels is difficult if not impossible to detect with standard radiological techniques. The vastly im

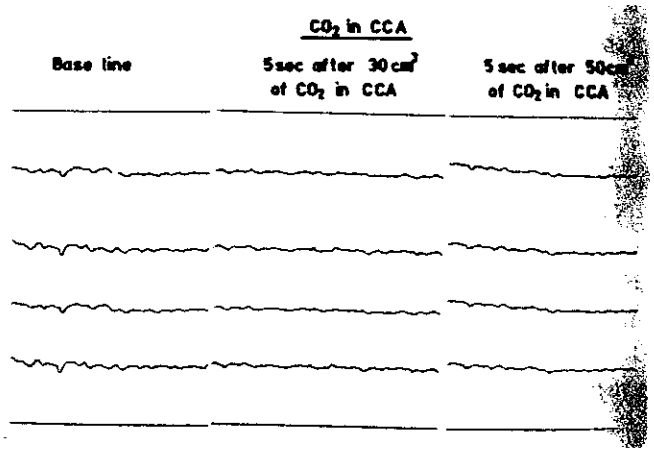

Fig. 1.—Composite EEG tracing demonstrating no change immediately after the injection of 30 and 50 cm^3 of CO_2.

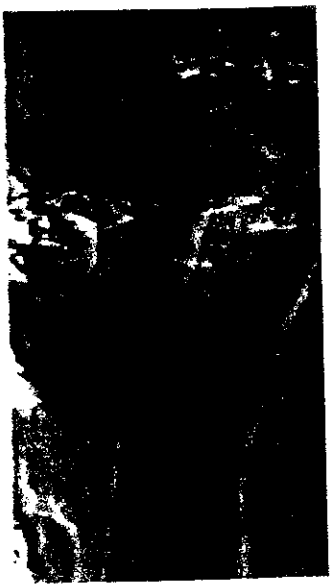

Fig. 2.—DSA of the aortic arch after the rapid injection of 50 cm^3 of CO_2. **Fig. 3.**—Lateral cerebral DSA after the injection of 30 cm^3 of CO_2 into the RCCA. Early arterial phase showing detail of large and medium sized vessels. **Fig. 4.**—Venous filling of large and medium sized veins 1 sec after intraarterial rapid injection of 30 cc of CO_2.

proved contrast sensitivity of DSA has made possible CO_2 angiography of diagnostic quality and reawakened interest in its use and safety in the systemic circulation.[9-11] The intraarterial effects of CO_2 were studied in 1940 by Moore and Braselton [14] who injected up to 3 cc per pound weight into the pulmonary veins of cats in the horizontal position without any morbidity. They observed CO_2 filling the coronary arteries and vanishing in 15 to 20 seconds. Oppenheimer *et al.*, who injected CO_2 into the carotid arteries of an unspecified number of dogs, reported no ill effects.[13]

Plich *et al.*[8] injected 3-5 cm^3/kg of CO_2 into the right-sided cardiac chambers of 147 children, often in the left anterior oblique position. In 57 cases of arterial septal defect, 44 of ventricular septal defect, 11 of aortic coarctation, and 1 of corrected transposition with the aorta arising from the right ventricle, CO_2 reached the systemic circulation in quantities sufficient to allow cineangiographic diagnosis. Since the head was not elevated in any of these patients, it is possible that none of the CO_2 reached the cerebral circulation.

Intraarterial injection of CO_2 in humans was reported by Bartley *et al.* in 1970 as cited by Miller [10] as a means of treating severe lower extremity ischemia. In 1982 Hawkins [9] reported 20 cases of CO_2 angiography with injections into the abdominal aorta and extremities. Each injection consisted of 15-75 cm^3 of gas injected at 12-25 cm^3/second for an average total of 110 cc per patient. They had no complications. Circulation time was similar to that of iodinated contrast, and in three renal tumors there was good parenchymal staining and venous filling. A subsequent report by Miller *et al.*[1] described CO_2-DSA of the abdominal aorta or more distal arteries in nine patients with no complications.

The volume of iodinated contrast material that

Fig. 5.—Macroscopic pathology of brain after intracarotid CO_2 angiography.

can be used in a study is limited by osmolality and renal and tissue toxicity. These limitations are not known to apply to CO_2. In addition, CO_2 is not known to be associated with any hypersensitivity reactions and its low viscosity allows the use of small catheters. The absence of significant discomfort decreases the likelihood of patient motion during filming. It also has the advantage of negligible cost. However, despite these advantages, there has been considerable reluctance to using CO_2 for cerebral angiography in humans because of fears of its possible neurological damage.[11]

In this study, all 14 dogs had filling of the carotid arteries with multiple injections as documented by DSA or cineangiography. The absence of any neurological deficit in these dogs, either acutely or during follow-up of up to six months shows that CO_2 can be used for carotid angiography with a large margin of safety. In fact, 2 dogs (No. 12 and 13; Table I) each had 7 injections selectively into the right common carotid artery, totaling well over 200 cm^3 per dog.

The report by Coffey *et al.*[11] describes immediate and dramatic neurological deficits, blood brain barrier disruption, and multifocal ischemia infarction after intracarotid injection of CO_2 in rats. We have difficulty explaining the discrepancy between their results in rats and ours in dogs.

In the light of our data and in view of the potential benefits of CO_2 gas angiography, its safety in the cerebral circulation requires a careful re-evaluation.

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