Comparison of Air, Oxygen and Carbon Dioxide Embolization *

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WITH the advent of open heart surgery, the problems of gas embolization has assumed increased importance. Bubble oxygenators have been accused of delivering small oxygen emboli to the patient. In all open cardiac operations, there exists an opportunity for trapping of air within the heart. Air emboli have produced ventricular fibrillation, cerebral dysfunction, and sometimes death. Various methods have been used in attempts to eliminate or reduce the frequency of air embolization; however, none has been entirely satisfactory. Because it was our impression that carbon dioxide was relatively well tolerated, it has been our practice during open cardiotomy to cover the field of operation with this gas. Others have reported the use of carbon dioxide gas for the same purpose.[1,2] It has been our clinical impression that the patient was afforded some protection by the use of this simple procedure. When using this technic, we have, on occasion, observed gaseous emboli in the coronary arteries which have not produced obstruction but which have quickly traversed the artery and disappeared. Although the clinical results seem to indicate that carbon dioxide was better tolerated than air, it seemed desirable to study the effect of air, oxygen, and carbon dioxide emboli in a controlled experiment.

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Method

White mice and mongrel dogs were used. A mouse was placed under a glass beaker with the tail exposed. A number 23 gauge needle was then introduced into the tail vein and the appropriate gas was delivered into the vein through a graduated syringe. The duration of the injection was about five seconds and was terminated with the onset of convulsions. The animal was then observed.

The dogs were anesthetized with the intravenous administration of thiopental sodium. An endotracheal tube was placed in the trachea and the lungs were rhythmically inflated with oxygen by a mechanical respirator. A left thoracotomy was performed through the fifth intercostal space. The pericardium was opened and a number 20 gauge needle was inserted into the left ventricle through a purse-string suture. Gas was then introduced into the left ventricle as rapidly as possible. A previously determined amount of gas, related to the animal's weight, was delivered. Just before the injection was carried out, the descending aorta, which had been dissected free just below the origin of the left subclavian artery, was occluded with a Pott's coarctation clamp. This was left in place for only a very short period of time, usually about 30 seconds. It was removed as soon as the coronary arteries were seen to fill with gas. This maneuver was performed to force the gaseous emboli into the carotid arteries and insure that the animal would always suffer the maximum cerebral insult. After the gas

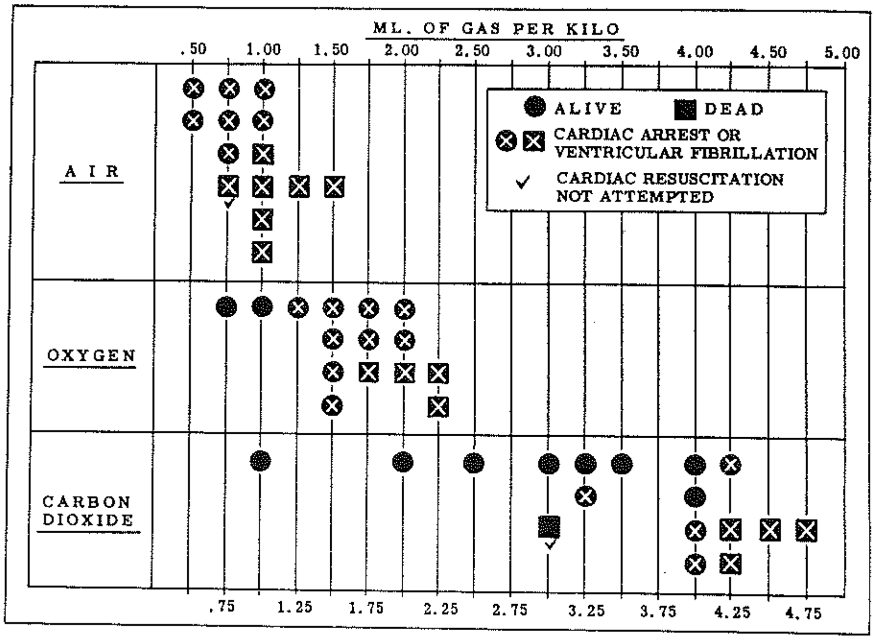

Fig. 1. Graph comparing injections of air, oxygen, and carbon dioxide into the left ventricle of dogs.

was introduced into the left ventricle, the needle was withdrawn and the animal was observed. By introducing the gas in this manner, none was seen to leak through the needle hole in the left ventricle. If cardiac arrest occurred, the heart was massaged, and if ventricular fibrillation resulted, it was given one or more electrical shocks. If the animal survived the initial insult, it was observed during the succeeding hours or days. Since aseptic operative technic was not used, some developed infections in the postoperative period and died from this cause.

Experimental Results

Gas was injected into the left ventricle in 46 dogs (Fig. 1). Air was administered to 14. Two were given an amount of air equal to .5 ml. per Kg. of body weight and both survived. Four were given .75 ml. per Kg. of body weight. Three survived and one died on the operating table from ventricular fibrillation due to coronary embolization. This experiment was carried out early in the course of the study and cardiac massage was not attempted. Six were given 1.0 ml. per Kg. and all developed either cardiac arrest or ventricular fibrillation. Four died at the time of operation even though cardiac resuscitation was attempted and two were long-term survivors. One was given 1.25 ml. per Kg. and another 1.5 ml. per Kg. of air. Both developed ventricular fibrillation and neither survived.

Fifteen dogs were given an injection of oxygen. One was given .75 ml. per Kg., one 1 ml. per Kg., and one 1.25 ml. per Kg., and all three survived. Four were given 1.5 ml. per Kg. All four developed either ventricular fibrillation or cardiac standstill. It was possible, however, to force the gas through the coronary circulation with cardiac massage and all four were long-term survivers. Three received 1.75 ml. per Kg. Two survived and one died. Three were given 2 ml. per Kg. with two eventual survivors and one death. Two were given 2.25 ml. per Kg. and both developed ventricular fibrillation and eventually succumbed.

TABLE 1. *Comparison of Amounts of Carbon Dioxide and Air Necessary to Produce Convulsions in Mice*

Type of Gas	Number of Mice	Average Weight in Grams	Average Amount of Gas Necessary to Produce Convulsions in Milliliters	Number of Survivors	Per Cent of Mice Surviving
Carbon dioxide	45	28.1	0.96	17	37.7
Air	28	31.8	0.18	3	10.7

Carbon dioxide gas was administered to 17 dogs. Three were given 1, 2, and 2.5 ml. per Kg. of oxygen respectively. All survived. Two were given 3 ml. per Kg. One survived and one developed cardiac irregularity and died. Cardiac shock and massage was not done in this animal. Two were given 3.25 ml. per Kg. and both survived. One received 3.5 ml. per Kg. Cardiac irregularity did not occur and it survived. Four were given 4 ml. per Kg. In two, ventricular fibrillation did occur and electric shock and cardiac massage was necessary, while in two, cardiac irregularity did not occur. All four were survivors. Three were given 4.25 ml. per Kg. Two developed ventricular fibrillation and died. One developed cardiac dilatation and weak contractions but was resuscitated and survived. One was given 4.5 ml. per Kg. and one 4.75 ml. per Kg.: both developed ventricular fibrillation and neither survived.

During this experiment, the heart and coronary arteries were closely observed. Air and oxygen characteristically produced emboli which were stable and produced arterial obstruction. Once the air embolus ceased to move, it remained permanently in that position. Other air emboli would follow the first, and long immobile columns of air would form in the coronary arteries. On the other hand, the carbon dioxide emboli behaved in an entirely different manner. Typically the bubbles of carbon dioxide gas would rapidly traverse the extent of the artery and disappear. As larger amounts were given, the emboli were sometimes seen to pause at a bifurcation point and then rapidly to proceed. When a toxic amount was given, a long column of gas would become immobile, block the artery and behave essentially as an air embolus.

Two groups of mice were studied. In the first, a total of 73 were used (Table 1). Their weight ranged from 23 to 43 grams. Carbon dioxide was injected into 45 and air was introduced into 28 mice. An average of .18 ml. of air per mouse was necessary to produce convulsions. Twenty-five of the animals injected with air died and three survived. In those in which carbon dioxide was injected, an average of .96 ml. per mouse was necessary to produce convulsions. Seventeen survived and 28 died. When air is compared with carbon dioxide as to the amount needed to produce con-

TABLE 2. *Comparison of Air and Carbon Dioxide Emboli in Mice Which Had Previously Survived Convulsions Produced by Carbon Dioxide*

Type of Gas	Number of Mice	Average Weight in Grams	Average Amount of Gas Necessary to Produce Convulsions in Milliliters	Number of Survivors	Per Cent of Mice Surviving
Carbon dioxide	12	30.2	1.05	12	100
Air	12	32.3	0.24	1	8.3

vulsions, 5.3 times more carbon dioxide was needed than air. Comparison of the surviving mice reveals that in these groups 6.2 times more carbon dioxide than air was necessary to produce convulsions.

The second group of mice studied consisted of 12 which received carbon dioxide in the first study and survived (Table 2). Their weight, initially, varied from 25.5 to 33.0 grams and averaged 30.2 grams. A mean of 1.05 ml. per mouse of carbon dioxide gas was necessary to produce convulsions in this group. They were observed for a week and the experiment was then repeated using air. During the observation period, all with one exception had gained 1 to 5 grams in weight; and at the time of the second experiment, their average weight was 32.3 grams. A mean of .24 ml. of air per mouse was necessary to produce convulsions. In this group of 12 mice, 4.6 times more carbon dioxide was necessary to produce convulsions than air.

Discussion

These controlled observations agree well with our clinical impression and with previous experimental studies of these gases. The general belief that small amounts of air are very poorly tolerated when introduced into the left side of the circulation is confirmed. Geoghegan and Lam [3] rapidly introduced air into the left ventricle and found that 1.5 ml. per Kg. was uniformily lethal. They believed the high mortality resulted from coronary artery obstruction. In another group of animals, a similar amount of air was given but when ventricular fibrillation began, the left ventricle was aspirated of contained gas and cardiac massage was carried out. Seventeen of 20 dogs managed in this way were resuscitated. Our results were essentially the same. When small amounts of air were introduced into the left ventricle, ventricular fibrillation practically always occurred, and, in our experiments, this was encountered with amounts of air as small as .5 ml. per Kg.

We also found that electric shock and cardiac massage would increase the number of survivors. With cardiac massage most dogs could tolerate .75 ml. per Kg. but only about one-third could tolerate 1 ml. per Kg. The slightly decreased tolerance of our animals as compared with those of Geoghegan and Lam is probably due to the fact that most of the air we introduced was forced either into the coronary or carotid arteries. Furthermore, before they began cardiac resuscitation, the air remaining in the left ventricle was aspirated.

Oxygen was tolerated about two times as well as air when introduced into the left ventricle. This increased tolerance to oxygen as compared with that of air agrees with the results of Fries and associates [4] who injected air and oxygen slowly into the carotid artery. Harkins and Harmon [5] compared air and oxygen embolization when the gases were introduced into the right side of the circulation and found that oxygen emboli were only slightly less toxic than air and concluded that there was no marked difference.

The carbon dioxide injections, both in dogs and mice, showed that carbon dioxide is much better tolerated than either air or oxygen. In our dogs, carbon dioxide was tolerated 5.3 times as well as air, and in the mice, from 4.6 to 6.2 times as well. It is interesting that, although two different species of experimental animals were used and although the route of administration in one was into the left circulation and in the other into the right, the ratio of tolerance of carbon dioxide as compared with air was practically the same. Moore and Braselton [6] injected air and carbon dioxide into the pulmonary veins of dogs and found a much greater tolerance to carbon dioxide. Oppenheimer and associates [7] found carbon dioxide embolization to be well tolerated and suggested this gas for use in intracardiac diagnostic radiology. Other investigators have found carbon dioxide to be absorbed better than air in the tissues, and technics for the use of this gas in retroperitoneal pneumography have been devised.[8]

When compared with air, carbon dioxide is about 34 times as soluble in water at 30° C.[9] It is only slightly less soluble in serum at 38°.[10] This probably explains why the carbon dioxide embolus is so unstable. When a stable embolus is produced, the bubble is probably no longer composed of pure carbon dioxide gas. It has been found that bubbles of carbon dioxide rapidly equilibrate with the blood gases and analysis performed within a few seconds on undissolved emboli have revealed large amounts of other gases.[7, 11] Thus, it is likely that when carbon dioxide bubbles persist for over a few seconds that they equilibrate with the dissolved gases in the blood and rapidly become much less soluble.

This study gives support to the simple clinical procedure of bathing the field of operation in an atmosphere of carbon dioxide gas. Since it is 1.53 times as dense as air, it should largely displace air in the operative field. If during open cardiotomy gas is retained in one or both of the heart chambers, the greater concentration of carbon dioxide in the gas bubbles should permit their more rapid absorption into the blood stream and should lower the incidence of serious complications.

Summary

Comparison of air, oxygen, and carbon dioxide embolization shows oxygen to be tolerated about two times and carbon dioxide five times as well as air.

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