Measurement of spinal cord blood flow by an inhalation method and intraarterial injection of hydrogen gas

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Purpose: **This study was performed to determine spinal cord blood flow using the H_2 clearance method.**
Methods: **In 12 dogs we measured blood flow determined by hydrogen clearance techniques (BF) in both gray and white matter by spinal cord puncture, and compared the results with BF measured by a catheter inserted intrathecally to avoid spinal cord injury. We studied direct intraarterial and intravenous injection of hydrogen in addition to the inhalation method because hydrogen is an explosive gas.**
Results: **BF measured intrathecally with catheters adherent to either the ventral or the dorsal funiculus did not differ significantly from that of the gray matter. BF measured with a catheter inserted into the epidural space was about one fourth of the BF measured intrathecally. Values measured by the intraarterial injection method did not differ significantly from those obtained by the inhalation method.**
Conclusions: **BF measured with a catheter inserted intrathecally reflects blood flow in the gray matter of the spinal cord. Using intraarterial injection of H_2, BF was safely and accurately measured while avoiding the risk of explosion. (J Vasc Surg 1997;26:623-8.)**

The cause of paraplegia after aortic surgery is considered to be spinal cord ischemia. Presently, somatosensory evoked potentials and evoked spinal cord potentials have been used as indicators of spinal cord ischemia. However, false-positive and false-negative results have been reported[1,2] using these measures, and there is a delay between the occurrence of ischemia and a change in waveforms. Therefore, development of a more precise, reliable, and rapid method of monitoring spinal cord ischemia is desirable. To estimate spinal cord ischemia by the H_2 clearance method, we measured spinal cord blood flow in gray and white matters and compared these values with blood flow measured by a catheter that was inserted intrathecally to avoid spinal cord injury.

The principle of the H_2 clearance method has been outlined previously.[3] As hydrogen gas accumulated in the tissue is washed out, the declining values are recorded as a clearance curve. The curve is replotted against time on semilogarithmic paper. The tissue blood flow is calculated using the formula[4] $K = 69.3/(T/2)$. $T/2$ is half of the time in minutes for desaturation of hydrogen. Tissue blood flow is derived as an absolute value in ml/min/100 g independently of its weight.

The inhalation method is simple and usually is used as the standard hydrogen clearance technique, but because of the risk of explosion with hydrogen inhalation, we tested direct intraarterial and intravenous injection of hydrogen in addition to the inhalation method. To confirm the accuracy of a less injurious alternative to spinal cord puncture, we compared the blood flow measured with a catheter that was inserted intrathecally alongside the spinal cord with blood flow measured using spinal cord puncture. We tested two hypotheses: first, that intrathecal catheters would be as reliable as intraparenchymal electrodes in determining spinal cord blood flow by hydrogen clearance techniques; and second, that intraarterial and/or intravenous administration of hydrogen substituted for inhaled hydrogen would prove effective and have a lower risk of explosion.

MATERIALS AND METHODS

Twelve dogs (mean, 9.8 ± 0.2 kg) were sedated with ketamine hydrochloride, intubated, and mechanically ventilated using halothane, oxygen, and

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0741-5214/97/$5.00 + 0 **24/1/84161**

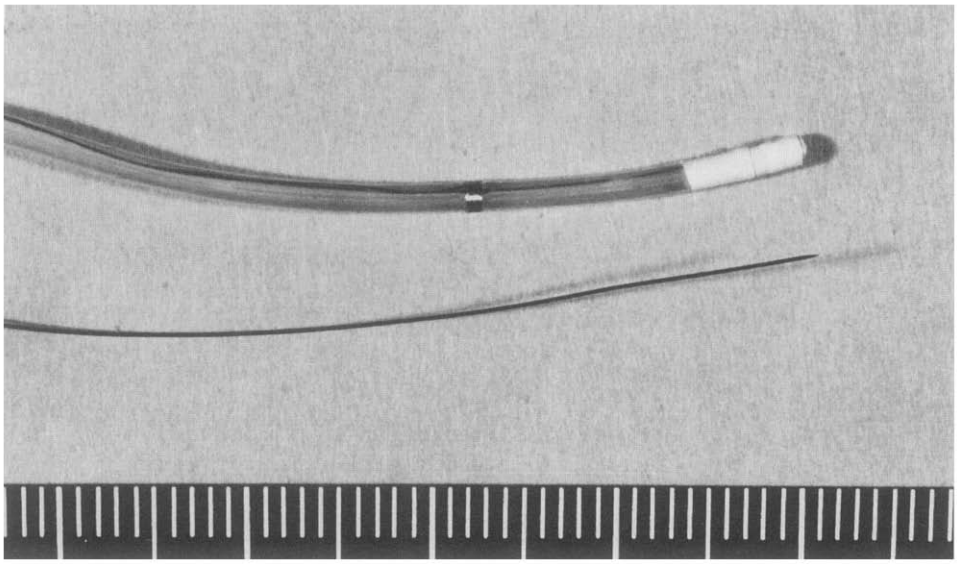

Fig. 1. Upper electrode is 2 mm in diameter. Tip of catheter is globular to avoid spinal cord injury, and platinum electrode for measuring H_2 clearance is placed 3 mm from tip. Lower electrode is 200 μm in diameter. Tip of catheter is sharp to minimize tissue injury by spinal cord puncture. Platinum electrode for measuring H_2 clearance is placed in tip.

nitrous oxide. The electrocardiogram was monitored continuously. The animals were turned on their right side. A catheter was placed through the femoral artery for distal aortic pressure monitoring.

Dorsal or ventral laminectomy was performed from Th12 to L1 to expose the dura mater. A platinum and stainless steel electrode 2 mm in diameter (Inter Medical Co., Nagoya, Japan) was inserted with a catheter into the epidural space. Then the dura mater was opened, and the catheter was inserted intrathecally toward the head until adherent to either the dorsal or ventral funiculus. A similar electrode 200 μm in diameter was inserted into the gray or white matter by puncture under direct vision. Thoracotomy was performed, and a catheter was positioned in the descending aorta for proximal aortic pressure monitoring. An oblique abdominal incision was made, and the aortic bifurcation was exposed using an extraperitoneal approach.

The tip of the 2 mm catheter was globular to avoid spinal cord injury; platinum electrodes for measuring H_2 clearance were placed 3 mm from the tip. The tip of the 200 μm catheter was sharp to minimize tissue injury during spinal cord puncture (Fig. 1).

Blood flow determined by hydrogen clearance techniques (BF), pH, and temperature were recorded before aortic cross-clamping. BF was measured both by the inhalation method and by the direct hydrogen bolus injection method. In the inhalation method, pure hydrogen gas was directly administered at 2 to 4 L/min for 5 to 20 breaths by puncture of the endotracheal tube with a 22-gauge needle. BF was monitored and recorded before, during, and after cross-clamping. Fig. 2 shows an example of BF recording before cross-clamping. The procedure required some 5 to 6 minutes to perform. The descending aorta was cross-clamped both immediately beyond the left subclavian artery and above the aortic bifurcation. Occlusion at the aortic bifurcation was performed by manual compression to reduce injury. This maneuver could be accomplished easily with the fingers given the small size and pliability of the canine aorta. To minimize spinal cord injury by aortic cross-clamping, aortic occlusion was maintained for only 2 minutes each time, which represented the minimum time required to ensure that the concentration of hydrogen remained below measurable limits. The procedure (BF recording before, during, and after clamping) was performed three times on each dog. We sought to avoid irreversible ischemic change of the spinal cord from prolonged aortic cross-clamping, intending to ensure that after removing aortic occlusion BF would recover to the level before clamping.

In direct hydrogen bolus injection, the intravenous injection method (n = 2) was performed first. A bolus of saline solution (80 ml) saturated with hy-

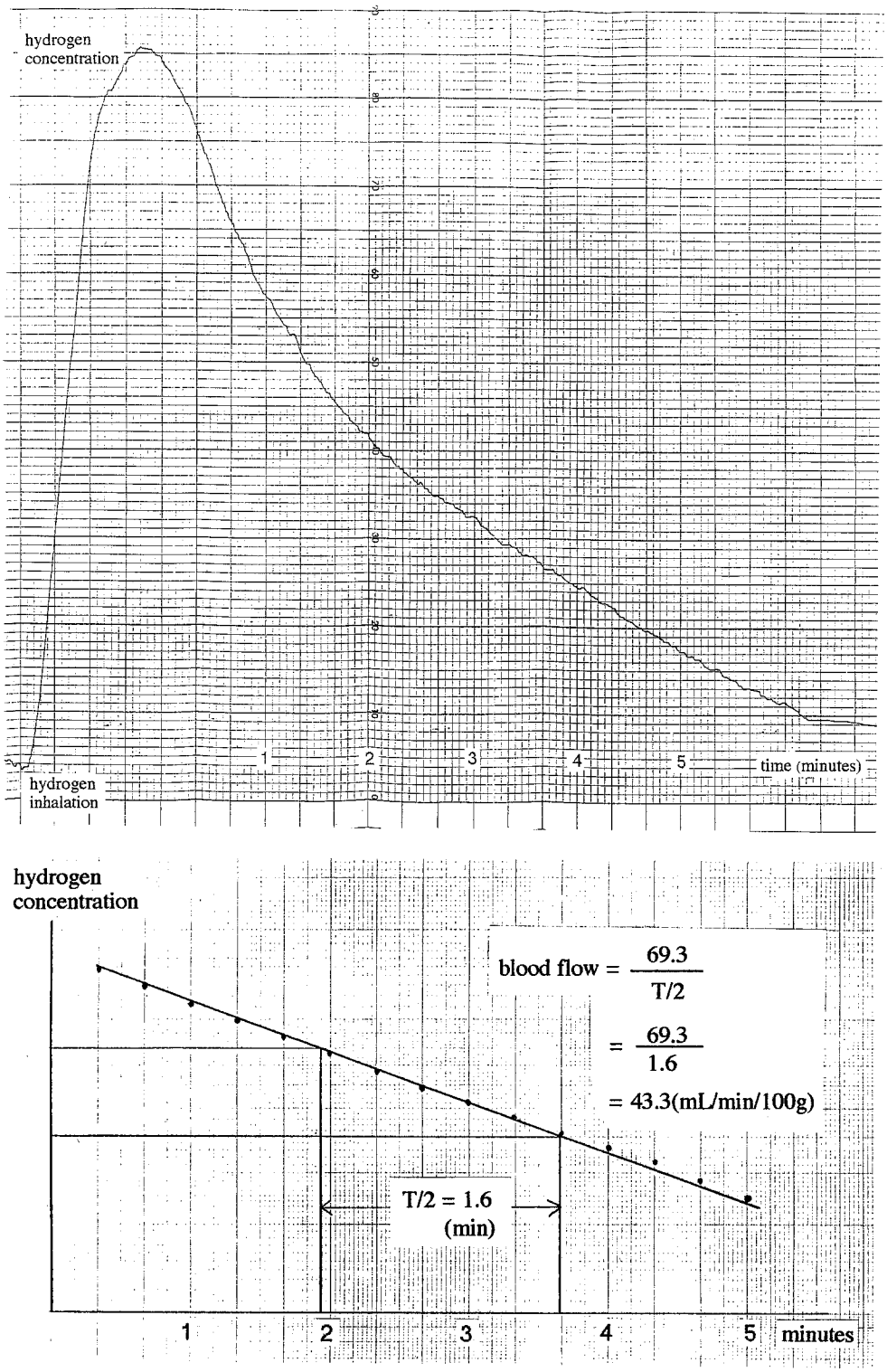

Fig. 2. *Upper figure* shows example of BF recording before cross-clamping. BF is calculated from *lower figure. T/2* is the half time in minutes for desaturation of hydrogen. The relationship of clearance to passage of time can be seen.

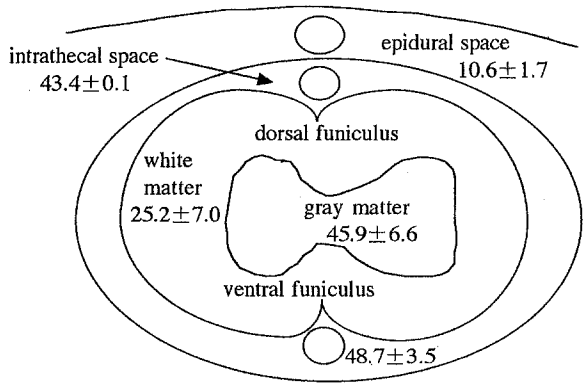

Fig. 3. Spinal cord cross-section and BF of each region by inhalation method (ml/min/100 g).

drogen at normal temperature was created after removing all air from one 500 ml package of saline solution, adding pure hydrogen gas, and then shaking. This mixture was injected into the femoral vein several times. The methods for aortic cross-clamping and measurement of BF were the same as those in the inhalation method. In the intraarterial injection method (n = 6), 50 ml of saline solution saturated with hydrogen by the same method was injected into the ascending aorta on each occasion. After completion of the experiment, the animals were killed with an intravenous bolus of KCl. Then the portion of spinal cord adherent to the 2 mm catheter and the portion punctured by the 200 μm catheter were removed and placed in formalin for future microscopic study. The animals received humane care in compliance with the *Guide for the Care and Use of Laboratory Animals* published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985). Significance of the data was determined by the paired *t* test. Values were expressed as mean ± SD.

RESULTS

Fig. 3 shows a cross-section of the spinal cord and BF of each region by the inhalation method. BF measured using an intrathecal catheter adherent to either the ventral or dorsal funiculus did not significantly differ from that of the gray matter ($p > 0.05$). BF measured by the catheter inserted into the epidural space was approximately one-fourth the BF measured by the intrathecal catheter.

On intravenous injection, a clearance curve could not be obtained because the concentration of hydrogen remained below measurable limits.

By the intraarterial injection method, measured values did not differ significantly from those obtained by the inhalation method ($p > 0.05$). In both the inhalation method and the intraarterial injection method, during clamping of the descending aorta BF measured by the catheters inserted intrathecally and in the gray matter remained below measurable limits. After declamping the aorta, BF values both intrathecally and in the gray matter recovered to the level before clamping (Fig. 4).

The spinal cord specimens did not show any injury that resulted from catheter placement, such as bleeding or necrosis (Fig. 5).

DISCUSSION

Hydrogen, the most diffusible of all gases, is easily absorbed from the lung. The saturation volume of hydrogen per liter of water is 21 ml under standard conditions. Hydrogen is easily removed from the circulation via the lung. The hydrogen clearance method is well established, and many studies have used it to determine blood flow for various organs since Aukland et al.[4] reviewed this method of blood flow measurement in 1964. Spinal cord blood flow has been measured using clearances, autoradiography, and other techniques. In the literature,[5] gray matter blood flow has been reported to be in the range of 40.6 to 63 ml/min/100 g, and white matter blood flow has been reported in the range of 10.3 to 21.7 ml/min/100 g. In our study, using the inhalation method, the gray matter blood flow was 45.9 ± 6.6 ml/min/100 g, and the white matter blood flow was 25.2 ± 7.0 ml/min/100 g.

Many investigators have concluded that BF reflects the values for the small volume of tissue immediately surrounding the electrode. It has been proposed that the volume of tissue that BF reflects depends on the electrode diameter[6] and that BF reflects several cubic millimeters of tissue blood flow.[3] BF measured by a catheter inserted intrathecally, adherent to either the ventral or dorsal funiculus, did not differ significantly from BF of gray matter. It may be argued that BF measured by intrathecal catheter reflected the blood flow in a marginal volume of white matter. However, because measurements showed the same changes as BF of gray matter during ischemic manipulation of the spinal cord, we conclude that BF measured by intrathecal catheter reflects the blood flow in the gray matter.

Because catheters are placed into the epidural space to monitor evoked spinal cord potentials, an attempt was made to measure BF using a catheter inserted into the epidural space. As BF measured by the epidural catheter was approximately one-fourth

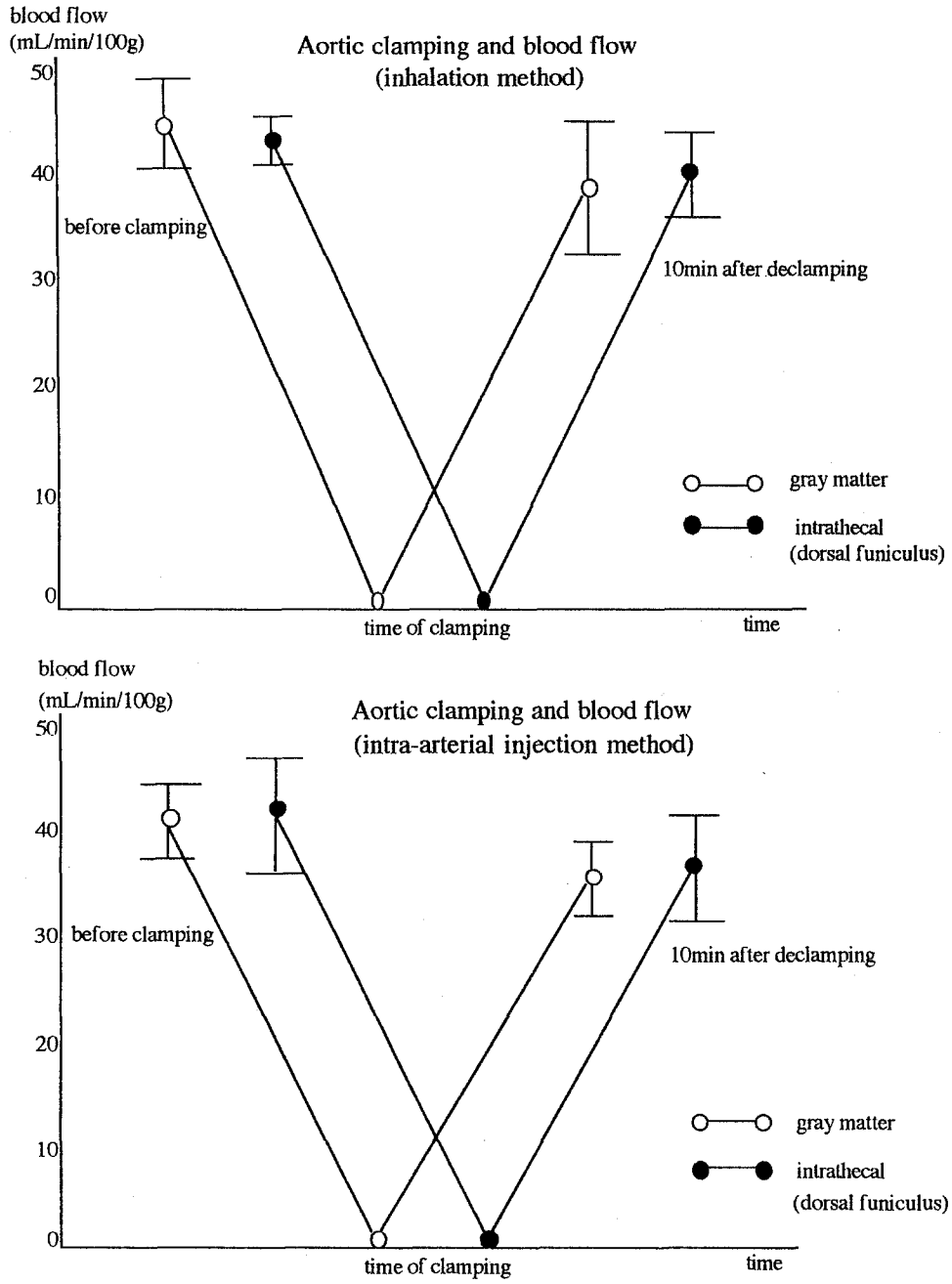

Fig. 4. Aortic clamping and blood flow (inhalation method and intraarterial injection method).

the BF measured by the intrathecal catheter, it did not reflect intraparenchymal blood flow and was judged unsuitable for monitoring spinal cord ischemia.

We compared the hydrogen inhalation method, which is simple and widely used but which is associated with a risk of explosion, with the intraarterial hydrogen injection method, and we confirmed that there was no significant difference between the two methods.

Hydrogen has been injected into the carotid artery to calculate blood flow in the cerebral hemisphere of monkeys[7,8] and human beings[9] and has been injected into the aortic ostia to identify spinal radicular arteries.[10] Theoretically, the difference between the inhalation method and the intraarterial

Fig. 5. Spinal cord specimen does not show injury caused by catheter, such as bleeding or necrosis.

injection method is only the administration route of the hydrogen: in the inhalation method, hydrogen gas is absorbed from lung, passes through the arteries, and enters the tissues; in the intraarterial injection method, hydrogen is injected directly into the artery and then enters the tissues. Once hydrogen reaches the tissues, the principle of measuring blood flow by the hydrogen clearance technique is much the same by both methods. With the intraarterial injection method, BF can be safely measured.

Our two hypotheses were supported by our results, except that intravenous administration of hydrogen did not produce detectable levels and therefore cannot be used for BF measurement.

The present study should be expanded to trials in aortic surgery to compare BF during aortic cross-clamping with BF before clamping to assess need for reattaching segmental arteries. If BF during clamping does not differ significantly from BF obtained before clamping, reattachment of segmental arteries may be unnecessary. Also, comparing BF after clamping with BF obtained before clamping may be useful in judging success of reattachment of segmental arteries.

CONCLUSION

Spinal cord blood flow measured in dogs showed that BF measured by an intrathecal catheter did not significantly differ from that of the gray matter of the spinal cord. By the intraarterial injection method, BF was safely measured and gave values not significantly different from those measured by the inhalation method. Therefore, measurement of BF with a catheter inserted intrathecally by the intraarterial injection method should be applicable to detection of spinal cord ischemia in aortic surgery.

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Submitted Mar. 18, 1997; accepted June 18, 1997.