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The Use of Hyperventilation in Contrast-Enhanced MR of Brain Tumors

Igor N. Pronin, Andrei I. Holodny, Valery N. Kornienko, Alexei V. Petraikin, A. V. Golovanov, and Huey-Jen Lee

Summary: Angiographic studies have demonstrated improved visibility of glial tumors after hyperventilation. The present study was undertaken to determine whether hyperventilation would change the MR enhancement characteristics of various glial tumors. Eighteen patients were studied twice: once with standard contrast-enhanced MR imaging and again with standard imaging plus hyperventilation. After hyperventilation, six low-grade astrocytomas showed no change and three showed a small decrease in relative enhancement (<10%). The ependymomas showed a 10% to 13% increase in the degree of enhancement, but no change in the area of enhancement. All the anaplastic astrocytomas showed an increase in the degree of enhancement (mean, 38%). Three of the anaplastic astrocytomas showed new foci of enhancement that were not seen on the nonhyperventilation study. Hyperventilation appears to be an inexpensive and safe method for increasing the conspicuity of abnormal areas of the blood-brain barrier.

Index terms: Brain neoplasms, magnetic resonance; Magnetic resonance, technique

Angiographic studies have demonstrated improved visualization of primary brain tumors in patients undergoing hyperventilation (1–4). This improvement is thought to be due to the difference between the way normal and tumoral vessels respond to hypocapnia (low P_{CO_2}) induced by hyperventilation. The response of normal intracranial arteries to hypocapnia is vasoconstriction and resultant increased resistance (2, 5–7). This response is seen angiographically as narrowing of intracerebral arteries. Tumoral vessels do not respond in this manner to hypocapnia; rather, they remain dilated (1). Consequently, tumoral vessels accumulate more contrast material during angiography. Glial tumors of different histologic grades respond differently to hyperventilation. The more benign tumors show almost no change in their angiographic characteristics. Malignant tumors, on the other hand, show a distinct tumoral blush and an increase in speed of circulation. Contrast enhancement with gadopentetate dimeglumine in magnetic resonance (MR) imaging is related to blood flow in the area of interest. This study was undertaken to determine whether the changes in the cerebral perfusion pattern induced by hyperventilation result in changes in the enhancement characteristics of gliomas of different grades.

Technique

Eighteen patients, nine men and nine women ranging in age from 21 to 49 years (mean, 35 years), were studied prospectively. All MR imaging studies with hyperventilation were performed in the presence of an anesthesiologist. All the patients gave informed consent.

Studies were performed on a 1.0-T superconducting magnet. T1-weighted images were acquired using a spin-echo sequence of 600/15 (repetition time/echo time). T2-weighted images were acquired using a spin-echo sequence of 3000/80. The matrix size was 256 × 256, the section thickness was 5 mm with an intersection gap of 0.2 mm. Contrast material (Magnevist, Schering AG, Germany) was injected at a dose of 0.1 mmol/kg at a rate of 10 mL/min. Following contrast injection, the T1-weighted sequence was repeated, using the same parameters.

The MR imaging study with hyperventilation was performed 48 to 72 hours after the initial MR study. Scanning parameters for both studies were identical. Because of potential difficulties with using ferromagnetic equipment for controlled ventilation, spontaneous hyperventilation was used. Hyperventilation was instituted for 2 minutes before injection of the contrast agent. The rate of respiration was 30 to 40 breaths per minute, which constituted

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From the Departments of Radiology (I.N.P., V.N.K., A.V.P.) and Neurosurgery (A.V.G.), the Burdenko Institute of Neurosurgery, Moscow, Russia; the Department of Radiology, UMDNJ-New Jersey Medical School, Newark (A.I.H., H-J.L.); and the Section of Experimental Radiology, the National Hospital, University of Oslo (Norway) (A.I.H.).

Address reprint requests to Andrei I. Holodny, MD, Department of Radiology, UMDNJ-New Jersey Medical School, University Hospital C-320, 150 Bergen St, Newark, NJ 07103.

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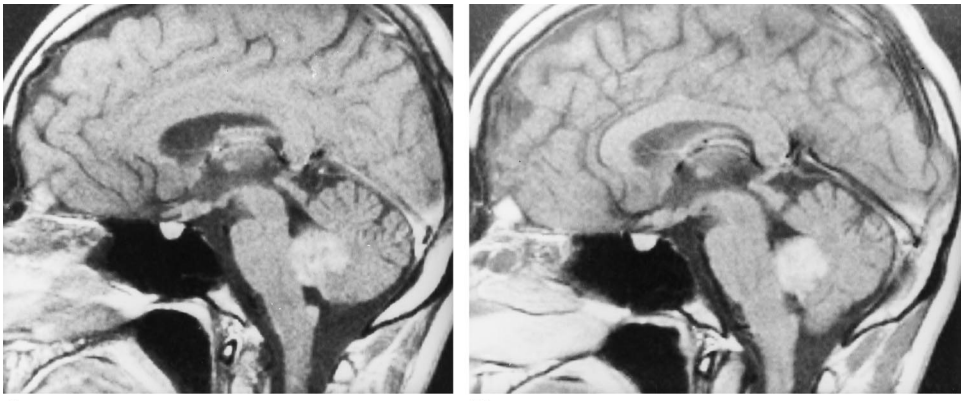

Fig 1. Sagittal contrast-enhanced T1-weighted (600/15) MR images without (*A*) and after (*B*) hyperventilation in a patient with an ependymoma of the fourth ventricle. *A* shows enhancement of the lesion, but *B* shows more intense enhancement. The volume of enhancement remains unchanged.

150% to 200% of the normal ventilation volume per minute.

The two studies were first compared subjectively by two neuroradiologists who were blinded to the presence or absence of hyperventilation. The following parameters were evaluated: presence and degree of enhancement, apparent area of enhancement, and definition of the border of enhancement.

Objective measurements were obtained of the relative degree of enhancement, using the following equation:

$$dC = \frac{St - Swm}{Swm} \times 100\%$$

where dC = degree of contrast enhancement, Swm = signal intensity of normal white matter, and St = signal intensity from the tumor.

Quantitative data for the degree of enhancement were obtained from regions of interest of the tumor as a whole, as well as from specific areas of the tumor in the event that the tumor exhibited inhomogeneous signal or enhancement characteristics.

All the patients in this study were untreated. All the tumors were histologically verified, and included nine low-grade astrocytomas, six anaplastic astrocytomas, and three low-grade ependymomas.

For the low-grade astrocytomas, routine MR images showed no significant contrast enhancement. On the post-hyperventilation images, no change was observed in the relative degree of enhancement in six of nine patients. In three studies, there was a slight decrease in the degree of enhancement of the tumors with respect to images obtained without hyperventilation (<10%, *P* not significant).

In the three ependymomas, the posthyperventilation MR study showed a quantitative increase (10% to 13%) in relative degree of enhancement as compared with the routine MR examination. The internal architecture of the tumors, as well as their borders, were seen better after hyperventilation. There was no change in the size of the area of enhancement after hyperventilation (Fig 1).

The six anaplastic astrocytomas were hypointense on the noncontrast T1-weighted images and hyperintense on the T2-weighted images. Contrast-enhanced MR images without hyperventilation showed varying degrees and patterns of tumoral enhancement. The areas of enhancement were smaller than the areas of abnormal signal intensity present on the T1- and T2-weighted images. On the post-hyperventilation MR images, these tumors exhibited an increase in the degree of enhancement measured objectively (mean = 38%, $P < .05$). In addition, three of these tumors showed an increase in the area of enhancement. These new areas of enhancement were distributed asymmetrically around the original enhancement seen on the nonhyperventilation studies. In one tumor, new areas of enhancement that were not in direct continuity with the previously seen areas of enhancement were noted (Fig 2). In one anaplastic astrocytoma, enhancement of the walls of cysts was appreciated on the posthyperventilation images but not on the nonhyperventilation images, suggesting that these cysts were tumoral—a finding that was confirmed pathologically.

None of the patients experienced any ill effects from hyperventilation. Clinically apparent seizures were not noted. One patient reported a sensation of "crawling ants" on the arm contralateral to the tumor.

Discussion

Our data show an increase in degree and volume of enhancement, as well as new areas of enhancement, on contrast-enhanced MR images of anaplastic astrocytomas following hyperventilation. Such changes were, however, not identified in low-grade astrocytomas. In patients with ependymomas, hyperventilation resulted in consistently higher enhancement of the tumor with better visualization of the borders.

In high-grade gliomas, vasoconstriction of normal arteries shunts blood to nonconstricted tumoral vessels. Angiographically, a prominent tumoral blush is seen (1, 4, 5, 8). We postulate that blood, and consequently contrast, is shunted to areas of abnormal blood-brain bar-

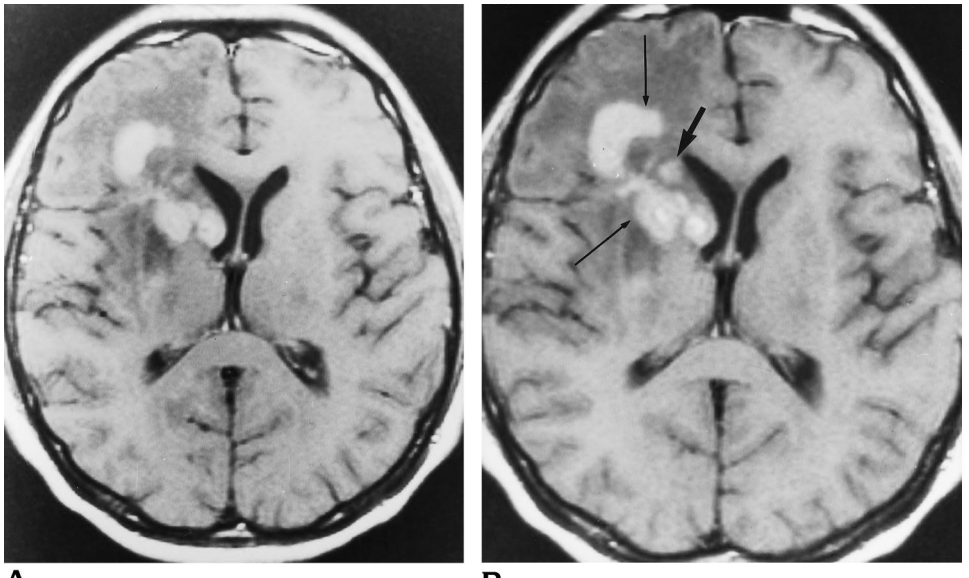

Fig 2. Axial contrast-enhanced T1-weighted (600/15) MR images without (*A*) and after (*B*) hyperventilation in a patient with an anaplastic astrocytoma. *A* shows enhancement, but *B* shows an increase in volume of enhancement with new areas of enhancement (*arrows*).

rier in patients with anaplastic gliomas undergoing MR imaging with hyperventilation. The effect of hyperventilation is more than what one would expect if one simply increased the dose of contrast material. An increase in dose would also increase the amount of contrast available to areas of normal brain with normal vessels. After hyperventilation, there is shunting of blood (and consequently contrast material) away from these normal areas and toward areas containing abnormal blood vessels. This leads to more contrast being available to tumor and less to normal brain. Therefore, not only is the absolute degree of enhancement of the tumors increased but the conspicuity of tumors with respect to normal tissue is increased also.

Three of the anaplastic astrocytomas showed new areas of enhancement. Shunting of blood away from normal brain and toward tumor may serve to dilate vessels in areas of tumor that did not enhance under normal conditions. This may lead to a greater availability of contrast to traverse the perhaps only slightly abnormal blood-brain barrier. Such a hemodynamic situation may lead to enhancement of areas of the tumor that otherwise did not enhance on standard MR images. This concept is supported by the angiographic literature, in which it has been noted that tumoral vessels undergo paradoxical vasodilatation following hyperventilation (5).

The differences in enhancement characteristics of high- versus low-grade tumors on MR images obtained after hyperventilation may also aid in differentiating the types of histologies. In all the high-grade tumors there was a greater degree of enhancement on the hyperventilation image. In 67% of the low-grade tumors there was no significant change, and in 33% there was only a slight decrease in enhancement.

The question of safety of hyperventilation must be addressed, since mass lesions in the brain may act as sources of seizure activity. Hyperventilation is known to induce seizures in certain patients with epilepsy (9). Therefore, the investigators took the safety precautions outlined above. During the study, none of the 18 patients experienced any seizure activity. One patient experienced a rather vague complaint of feeling "crawling ants" on his arm.

A review of the literature failed to uncover any cases in which hyperventilation induced a seizure in patients without spontaneous epileptic activity. In researching the work of a number of authors (1–4, 6–8, 10), in which 239 patients were studied angiographically following spontaneous or mechanical hyperventilation, we found no reports of seizures or any other complications. Kornienko (5) studied 112 patients angiographically after hyperventilation, 100 of whom had no history of seizures. In this group, there were no reported complications associated with hyperventilation and subsequent angiography. Twelve of these patients had documented electroencephalographic abnormalities and a history of clinically apparent seizures. Following spontaneous hyperventilation for 3 minutes, all the patients showed changes in their electroen-

cephalographic pattern and two of them had clinical seizures. Therefore, it can probably be said that hyperventilation is a safe procedure for patients without spontaneous epileptic activity, since no complications were reported in this group of 339 patients. However, hyperventilation should probably be avoided in patients with spontaneous seizure activity.

In conclusion, in our small sample of patients, hyperventilation was an inexpensive and safe method for increasing the conspicuity of an abnormal blood-brain barrier. In anaplastic astrocytomas, hyperventilation increased the degree and volume of enhancement and defined new areas of enhancement that were not appreciated on images obtained without hyperventilation.

References

1. Grange RA, Hawkins TD, Samuel JR. Influence of carbon dioxide tension on the angiographic appearance of intracranial tumors. *Acta Radiol Diagn* 1969;9:292–299
2. Huber P, Handa J. Effect of contrast material, hyperventilation, hypertonic glucose and papaverine on the diameter of cerebral arteries. *Invest Radiol* 1967;2:17–32
3. Huber P. Functional test in angiography of cerebrovascular disease. *Neuroradiology* 1970;1:122–131
4. Huber P. Functional tests in angiography of brain tumors. *Neuroradiology* 1970;1:132–141
5. Kornienko VN. *Functionalnaya Cerebralnaya Angiographia*. Leningrad, Russia: Meditsina; 1981:50–73
6. Bradac GB, Simon RS, Heidieck CH. Angiographically verified transient alteration of the intracranial arteries and veins in dependence on different CO_2 tensions. *Neuroradiology* 1976;10:257–262
7. Dallas SH, Moxon CP. Controlled ventilation for cerebral angiography. *Br J Anaesth* 1969;41:597–602
8. Huber P. Demonstration of impaired autoregulation in tumors and cerebral infarction by angiography. *Acta Radiol Diagn* 1972;13:115–123
9. Laidlaw J, Richens A, Oxley J. *A Textbook of Epilepsy*. 3rd ed. Edinburgh, New York, NY: Churchill Livingstone; 1988:163, 319
10. Edmonds-Seal J, du Boulay G, Bostick T. The effect of intermittent positive pressure ventilation upon cerebral angiography with special reference to the quality of the films: a preliminary communication. *Br J Radiol* 1967;40:957–958