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Regulation of Intracranial Pressure in the Rat with Chronic Moderate Hypercapnia

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Study objectives: **In this animal study we investigated whether CO_2-induced intracranial hypertension was sustained in chronic hypercapnia.**
Design: **We kept five rats in a 10% CO_2-air mixture ($PaCO_2$ 73.4 ± 6.2 Torr, mean ± 1SD) for 22 weeks, and then measured the rats' intracranial pressure while breathing the 10% CO_2-air mixture or the room air.**
Results: **The intracranial pressures recorded during chronic hypercapnia in systole and diastole were 7.0 ± 1.9 and 5.4 ± 1.6 mm Hg, respectively. When the rats were acutely exposed to the room air ($PaCO_2$, 51.9 ± 10.2 Torr), the intracranial pressures in systole and diastole were 6.1 ± 1.4 and 5.0 ± 0.8 mm Hg, respectively, were not significantly different from those during hypercapnia ($P > 0.05$, paired t-test).**
Conclusions: **The intracranial pressure in rats with chronic moderate hypercapnia was not significantly different from normocapnic rats, and this change was associated with a blunting of intracranial pressure autoregulation.**

Key Words: Cerebral blood flow, Chronic respiratory failure, Acclimatization, Intracranial pressure, Hypercapnia

INTRODUCTION

Intracranial pressure is increased by acute hypercapnia in human subjects [1] and experimental animals [2]. Recent advances in ventilatory support techniques, such as permissive hypercapnia [3], have facilitated the study of hypercapnia-induced intracranial pressure elevation. A previous report [4] has suggested that elevated intracranial pressure is sustained in patients with chronic hypercapnia. However, this speculation has not been proved. In this study rats were chronically exposed to moderate hypercapnia for 22 weeks and their ability to regulate intracranial pressure monitored by reducing the inhaled CO_2 concentration.

MATERIALS AND METHODS

Five Wistar rats were placed in a normoxic hypercapnic (O_2 19%, CO_2 10%, N_2 71%) environment for 22 weeks. This study was approved by the Institutional Animal Care and Use Committee of Tokai University School of Medicine. After 19 weeks of prolonged CO_2 exposure, a heparinized catheter (PE50) was implanted in the caudal artery during halothane anesthesia. Two hours after recovery from anesthesia, arterial blood gases were analyzed while the rats were awake and breathing normoxic hypercapnic gas, after which the arterial catheter was removed. After completion of the prolonged period CO_2 exposure, the rats were anesthetized with intraperitoneal pentobarbital (0.5 mg/g) and a catheter (PE50) was implanted in the right femoral artery. The rats were then placed in a stereotaxic frame in the prone position and a small incision was made in the head posteriorly. An intracranial catheter (PE50) was inserted through this incision and implanted in the cisterna magna. All the surgical procedures

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were performed during continuous exposure to high-flow 10% CO_2-air mixture with a face mask.

The rats were evaluated while in the normoxic hypercapnic environment for 1 hour, followed by the room air for 1 hour. Arterial blood pressure and intracranial pressure were measured continuously. Arterial blood gases were analyzed while breathing either normoxic hypercapnic gas or room air. The intracranial pressure while breathing the room air was measured in four of five rats. All the data were expressed as mean ± 1 SD. Statistical significance was assessed by the paired t-test and a $P < 0.05$ was considered significant.

RESULTS

Arterial blood gases, in an awake condition, measured at 19 weeks of prolonged 10% CO_2 exposure, were pH 7.31 ± 0.05, PCO_2 73.4 ± 5.4 Torr and PO_2 125.2 ± 4.8 Torr. During anesthesia, arterial blood gases measured after 22 weeks of breathing the CO_2-air mixture were pH 7.26 ± 0.40, PCO_2 85.8 ± 11.7 Torr, and PO_2 123.4 ± 19.5 Torr, while after breathing the room air they were pH 7.42 ± 0.06, PCO_2 51.9 ± 10.2 Torr, and PO_2 103.8 ± 15.7 Torr. The arterial pH increased significantly and the $PaCO_2$ decreased significantly with the change from 10% CO_2 to the room air.

The systolic and diastolic arterial pressures while breathing the 10% CO_2-air mixture were 139.2 ± 30.8 and 85.8 ± 18.7 mm Hg, and while breathing the room air were 123.6 ± 34.8 and 72.0 ± 18.9 mm Hg. These differences were not significant. The intracranial pressure fluctuated in parallel with the changes in systolic and diastolic arterial pressures. The intracranial pressure while breathing the 10% CO_2-air mixture was 7.0 ± 1.9 and 5.4 ± 1.6 mm Hg in systole and diastole, and while breathing the room air 6.1 ± 1.4 and 5.0 ± 0.8 mm Hg. The differences between these readings were not statistically significant (Figure 1).

DISCUSSION

It has been reported that acute hypercapnia caused rapid doubling or trebling of intracranial pressure up to 60 cm H_2O, whether in human subjects [1, 3, 5] or experimental animals [2]. The increase in

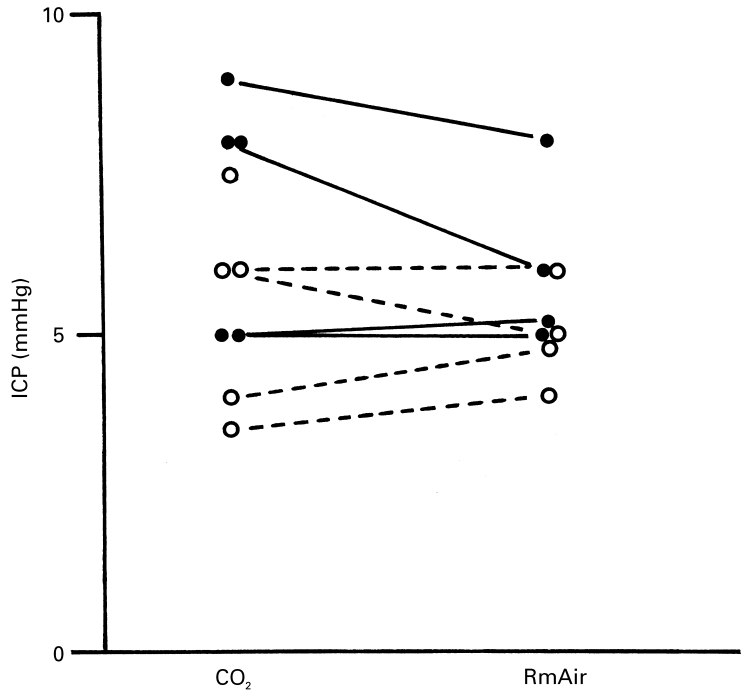

Fig. 1 Intracranial pressure (ICP) recorded while breathing 10% CO_2-air mixture (CO_2) or room air (RmAir). Open circles: intracranial pressure during diastole; Closed circles: intracranial pressure during systole.

intracranial pressure during acute hypercapnia is attributed to an increase in cerebral blood flow [6]. Whether the elevated intracranial pressure of acute hypercapnia is sustained during chronic hypercapnia has not yet been shown. We found that the intracranial pressure in chronic hypercapnic rats was in the normal range [9] and was not significantly different from normocapnic rats. This finding suggests that the intracranial pressure in rats may normalize during the course of chronic moderate hypercapnia. An exposure period of 19 weeks may be sufficient for ventilatory acclimatization to CO_2 in human subjects [7] and in dogs [8]. The slight elevation of $PaCO_2$, during measurement of intracranial pressure, was probably due to the general anesthesia and hypoventilation. However, since CO_2 accumulation generally increases intracranial pressure, the elevated $PaCO_2$ does not negate our conclusion.

We assessed the autoregulation of intracranial pressure by reducing the inhaled CO_2 concentration in chronic hypercapnic rats. We did not apply CO_2 levels higher than 10% because hypercapnia is known to be dangerous while respiratory acidosis [10]. Instead, we reduced the CO_2 concentration in an attempt to reduce cerebral blood volume [11] and thereby reduce intracranial pressure [12]. The intracranial pressure did not decline significantly when the $PaCO_2$ of the rat was reduced by breathing the room air. Therefore, normalization of intracranial pressure after chronic moderate hypercapnia was associated with a blunting intracranial pressure regulation to $PaCO_2$.

In conclusion, the intracranial pressure in chronic moderate hypercapnic rats did not significantly differ from normocapnic rats. This normalization of intracranial pressure may be caused by blunting intracranial pressure regulation to $PaCO_2$.

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REFERENCES

1) Levy B, Bollaert PE, Nace L, Larcan A. Intracranial hypertension and adult respiratory distress syndrome: usefulness of tracheal gas insufflation. J Trauma **39**: 799, 1995.
2) Clark RM, Capra NF, Halsey JH Jr. Method for measuring brain tissue pressure. J Neurosurg **43**: 1, 1974.
3) Feihl F and Perret C. Permissive hypercapnia. Am J Resp Crit Care Med **150**: 1722, 1994.
4) Newton DA, Bone I, Bonsor G. Chronic hypercapnia and radiological changes in the pituitary fossa. Thorax **33**: 684, 1978.
5) Miller A, Bader RA, Bader ME. The neurologic syndrome due to marked hypercapnia, with papilledema. Am J Med **33**: 309, 1962.
6) Sokoloff L. The action of drugs on the cerebral circulation. Pharmacol Rev **11**: 1, 1959.
7) Schaeffer KE, Hastings BJ, Carey CR, Nichols G. Respiratory acclimatization to carbon dioxide. J Appl Physiol **18**: 1071, 1963.
8) Jennings DB, Chen CC. Ventilation in conscious dogs during acute and chronic hypercapnia. J Appl Physiol **41**: 839, 1976
9) Nawashiro H, Shima K, Chigasaki H. Immediate cerebrovascular responses to closed head injury in the rat. J Neurotrauma **12**: 189, 1995.
10) Bone RC. Acute respiratory failure. In: Burton GG, Hodgkin JE, Ward J eds. Respiratory care (3rd ed). Lipincott NY, 1991,p. 845.
11) Fortune JB, Feustel PJ, deLuna C, Graca L, Hasselbarth J, Kupinski AM. Cerebral blood flow and blood volume in response to O_2 and CO_2 changes in normal humans. J Trauma **39**: 463, 1995.
12) Schettini A, McKay L, Mahig J, ModellJ JH. The response of brain surface pressure to hypercapnic hypoxia and hyperventilation. Anesthesiology **36**: 4, 1972.