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A New System to Supply Carbon Dioxide Safely to Glaucoma Patients

Yoshiaki Niwa,* Alon Harris,† Larry Kagemann,† Tetsuya Yamamoto,* Masayuki Matsubara,* Daisuke Takahashi* and Yoshiaki Kitazawa*

**Department of Ophthalmology, Gifu University School of Medicine, Gifu, Japan; †Departments of Ophthalmology, and Physiology and Biophysics, Indiana University School of Medicine, Indianapolis, IN, USA*

Purpose: To develop a new system for safely supplying carbon dioxide (CO_2) to open-angle glaucoma patients.

Methods: The orbital hemodynamics of 7 glaucoma patients were determined by color Doppler imaging under baseline conditions and during CO_2 supplementation sufficient to increase the end-tidal CO_2 partial pressure by 10%. Systemic conditions, including oxygen saturation and blood pressure, were monitored throughout the CO_2 inhalation.

Results: Our results demonstrate that this new system enables us to supply CO_2 in a safe, controlled manner to glaucoma patients.

Conclusions: This new system will be useful for investigating the effects of vasodilation by CO_2 on orbital blood flow. **Jpn J Ophthalmol 1999;43:16–19** © 1999 Japanese Ophthalmological Society

Key Words: Carbon dioxide, glaucoma, color Doppler imaging.

Introduction

The pathogenesis of glaucomatous optic neuropathy remains unknown. Although increased intraocular pressure is an evident risk factor, glaucomatous optic nerve damage can develop even with only a minimal increase in the intraocular pressure, suggesting that factors other than intraocular pressure may be involved in the development of glaucoma.[1] Recently, interest has increased in a possible vascular etiology for the glaucomatous changes. In glaucoma patients, evidence supporting a vascular mechanism can be found in the occurrence of optic disc hemorrhage, fluorescein angiographic findings, pulsatile ocular blood flow measurements, digital blood flow measurements, the associations with migraine or immune-related diseases, and nocturnal blood pressure drops in ambulatory blood pressure monitoring.[2–8]

Assuming a vascular pathogenesis for glaucomatous optic neuropathy, several researchers have advocated the improvement of optic nerve head circulation in addition to the reduction of intraocular pressure as treatment for open-angle glaucoma.[9–12] To effect vasodilation in the optic nerve head, breathing carbon dioxide (CO_2) has been tried.[6,13] It has been shown that CO_2 affects each part of the central nervous system differently.[6,13]

We have developed a new system of supplying CO_2 safely to glaucoma patients in order to investigate the effect of vasodilation by CO_2 on orbital blood flow. We report on this new system.

Materials and Methods

Outline of New System to Supply CO_2

The system to supply CO_2 and to monitor the patient is shown in Figures 1 and 2. The patient is kept supine and his pulse rate (PR) and blood pressure (BP) are monitored with an automatic apparatus (Omron HEM-705 CP, Matsuzaka). The nostrils are closed with a nose piece, and a low resistance mouthpiece with a T-style valve is applied (Figure 3). The

Received: December 9, 1997

Address correspondence and reprint requests to: Yoshiaki NIWA, MD, Department of Ophthalmology, Gifu University School of Medicine, 40 Tsukasa-machi, Gifu-shi 500, Japan

Published by Elsevier Science Inc.

0021-5155/99/$–see front matter
PII S0021-5155(98)00056-2

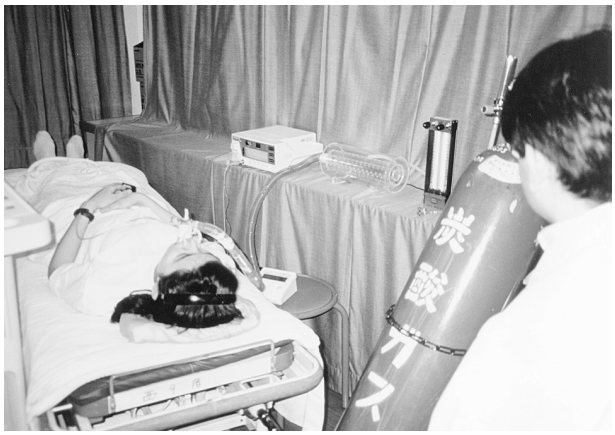

Figure 1. Our system of CO_2 supplementation.

end-tidal pressure of CO_2 (PCO_2 expressed as a percentage), and the respiratory rate are monitored by a combined rapid-response gas analyzer and pulse oximeter (Poette Plus®, Criticare Systems, Waukesha, WI, USA) that samples gas from the mouthpiece. In addition, the device monitors oxygen saturation (SpO_2%) and PR. A physician other than the color Doppler imaging (CDI) examiner manages the patient's systemic condition during the testing.

PCO_2 is manually increased by approximately 10% by adding 100% CO_2 to the inspired air. The oxygen saturation level is maintained throughout the CO_2 inhalation. Before CO_2 inhalation, patients are instructed to gesture when an examiner questions them to confirm safety.

Evaluation of Safety of System

Of the 7 patients, 5 had normal-tension glaucoma and 2 had primary open-angle glaucoma. None had any cardiovascular or respiratory disease. The patient ages ranged from 32–80 years, averaging 60.9 ± 16.4 years. Three were men and 4 were women (Table 1).

Each patient had been resting for 10 minutes when his PR and BP were first measured. End-tidal CO_2% was recorded on each breath for 3 minutes. Then the baseline CDI measurements of the ophthalmic artery (OA) and the central retinal artery (CRA) were taken. Once the baseline conditions had been established, CO_2 was supplied slowly to increase the end-tidal CO_2% by 10% under careful monitoring by the physician. After CO_2 had been supplied for 10 minutes, the PR and BP were measured again and end-tidal CO_2% was recorded on each breath for 3 minutes. Then CDI was performed on the OA and the CRA under the increased PCO_2 condition. When all measurements were completed, the CO_2 supply was terminated and the end-tidal CO_2% was monitored until it returned to the baseline value.

Statistical analysis was done using Wilcoxon's signed rank sum test to compare CDI parameters at the baseline and during the CO_2 supply.

The study protocol was approved by the Ethical Review Committee of Gifu University, and informed written consent was obtained from each patient.

Results

Carbon dioxide inhalation did not change the patient's SpO_2%, which remained between 98 and 99%. The fluctuation of the end-tidal CO_2% was approximately 5%, and end-tidal CO_2% returned to the baseline level approximately 30 seconds after the CO_2 supply was terminated. Carbon dioxide inhalation did not change PR and BP significantly. No patient complained of discomfort or shortness of breath during the CO_2 inhalation.

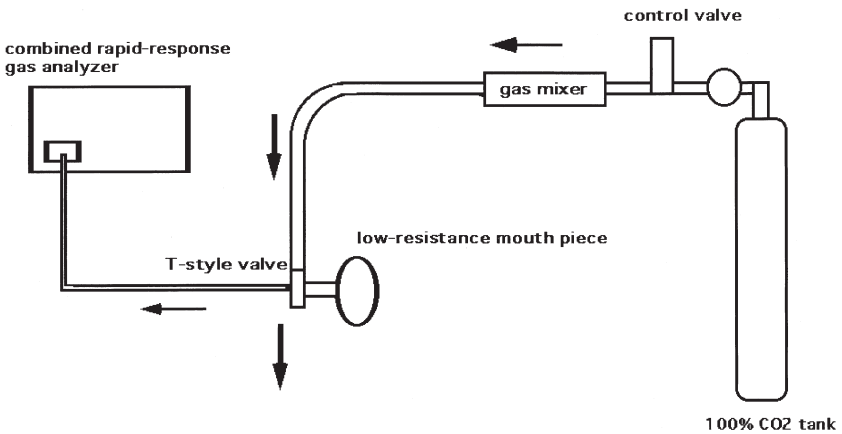

Figure 2. Scheme of system.

Jpn J Ophthalmol
Vol 43: 16–19, 1999

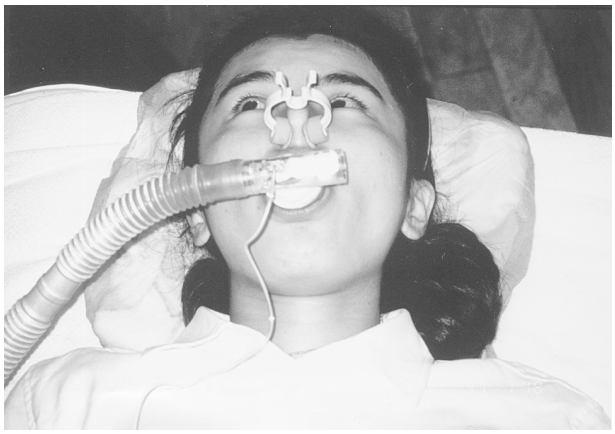

Figure 3. Patient with nose piece and mouthpiece.

Discussion

We have developed a new system of supplying CO_2 to glaucoma patients to investigate the vasodilatory effect of this gas on orbital blood flow. The system enables us to supply CO_2 safely because it provides close monitoring of the end-tidal CO_2% and delivers sufficient oxygen. Although the number of cases in this preliminary report was small, all patients tolerated the intervention well.

Physicians who support the theory of a vascular etiology in glaucoma prescribe vasoactive agents, such as calcium channel blockers, these agents are reported to have a favorable effect on the glaucomatous visual field.[11] Recently, CO_2 inhalation has been suggested as a new glaucoma treatment, to vasodilate the vessels in the optic nerve head.[6,14] Our system facilities this treatment, as we were successful in keeping the PCO_2 level within a narrow, safe range by supplying the minimum volume of CO_2 necessary and by closely monitoring the end-tidal CO_2%. In a previous study,[15] the effects of a predetermined concentration of CO_2 were investigated. Maintaining CO_2 at a fixed level can create problems because the same concentration of CO_2 can alter PCO_2 levels differently in different individuals. We successfully increased and maintained the CO_2 level approximately 10% higher than the determined baseline end-tidal CO_2%, so that we could study the effect of breathing CO_2 under a uniformly increased PCO_2 condition.

In vitro studies in the 1930s confirmed that CO_2 produces cerebral vasodilation.[16] In 1948, Kety and Schmidt[17] demonstrated by the nitrous oxide method that CO_2 inhalation increased cerebral blood flow. Now it is known that increased arterial PCO_2 causes the change in cerebral blood flow. Carbon dioxide does not directly affect the cerebral vessels, but accelerates the cerebral blood flow by lowering the extracellular fluid pH of the brain.[18] Patterson et al.[19] investigated the cerebral blood flow of normal volunteers and reported that inhalation of 2.5% CO_2 did not increase cerebral blood flow, but that 3.5% CO_2 inhalation increased it by approximately 10%. They speculated that PCO_2 had a threshold above which CO_2 increased cerebral blood flow.

In conclusion, the new system enables us to supply CO_2 to glaucoma patients in a safe and controlled manner. A prospective study is ongoing in an attempt to determine the response of orbital blood vessels to CO_2 inhalation in normal tension glaucoma patients and the results will be reported shortly.

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Table 1. Background of Subjects

Case No.	Sex	Age (years)	Systemic Disease	Treatment
1	Male	67	—	None
2	Female	34	—	1% carteolol hydrochoride, b.i.d. (OU)
3	Female	62	—	Brovincamine fumarate, 20 mg, t.i.d.
4	Male	46	—	Nilvadipine, 2 mg, b.i.d.
5	Female	67	—	None
6	Female	85	DM	Nilvadipine, 2 mg, b.i.d.
7	Male	65	DM	0.5% betaxolol hydrochoride, b.i.d. (OU)

DM: diabetes mellitus; OU: Oculus uterque (both eyes).

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