Taylor & Francis
Taylor & Francis Group

RENAL FAILURE

Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: informahealthcare.com/journals/irnf20

Impairment of Ventilatory Response to Metabolic Acidosis in Insulin-Dependent Diabetic Patients with Advanced Nephropathy

Naoki Ikegaya, Katsuhiko Yonemura, Takayuki Suzuki, Hiroko Kato-Ohishi, Tomohiko Tamhato & Akira Hishida

To cite this article: Naoki Ikegaya, Katsuhiko Yonemura, Takayuki Suzuki, Hiroko Kato-Ohishi, Tomohiko Tamhato & Akira Hishida (1999) Impairment of Ventilatory Response to Metabolic Acidosis in Insulin-Dependent Diabetic Patients with Advanced Nephropathy, Renal Failure, 21:5, 495-498, DOI: 10.3109/08860229909045189

To link to this article: https://doi.org/10.3109/08860229909045189

Renal Failure, 21(5), 495–498 (1999)

CLINICAL STUDY

Impairment of Ventilatory Response to Metabolic Acidosis in Insulin-Dependent Diabetic Patients with Advanced Nephropathy

Naoki Ikegaya,[1] Katsuhiko Yonemura,[1] Takayuki Suzuki,[1] Hiroko Kato-Ohishi,[2] Tomohiko Taminato,[2] and Akira Hishida,[1]

[1]*First Department of Medicine*
Hamamatsu University School of Medicine
Hamamatsu, Japan
[2]*Second Department of Medicine*
Hamamatsu University School of Medicine
Hamamatsu, Japan

ABSTRACT

Sudden cardiopulmonary arrest due to a defective respiratory reflex is observed in diabetic patients. Impaired ventilatory response in diabetic patients to acute hypoxia or hypercapnia induced by the inhalation of an artificial gas has been reported. Little is known regarding the respiratory compensatory ability for mild to moderate metabolic acidosis due to renal failure in insulin-dependent diabetic subjects. Arterial blood pH, HCO_3^-, $PaCO_2$ and PaO_2 were measured in 13 insulin-dependent diabetic subjects with advanced nephropathy and in 33 non-diabetic subjects with end-stage renal failure. The diabetic group consisted of six predialysis patients and seven on regular hemodialysis (HD) and the non-diabetic group, ten predialysis patients and 23 on HD. Differences between measured partial arterial pressure of carbon dioxide ($PaCO_2$) and predicted

Address correspondence to: Naoki Ikegaya MD, First Department of Medicine, Hamamatsu University School of Medicine, Hamamatsu, 3600 Handa-cho, Hamamatsu, 431-3192, Japan. Tel: 81-53-435-2261; Fax: 81-53-434-9447; E-mail: naoki001@hama-med.ac.jp.

$PaCO_2$ determined from HCO_3^- were examined. $PaCO_2$ was significantly higher in the diabetic than in non-diabetic group (40.0 ± 7.4 versus 31.1 ± 5.1 mmHg, $p < 0.05$ in predialysis, 42.0 ± 6.4 versus 36.0 ± 2.6 mmHg, $p < 0.05$ in HD), though plasma pH was essentially the same for either. Differences in measured $PaCO_2$ and predicted $PaCO_2$ were significantly larger in the diabetic group than in non-diabetic group. Ventilatory respose to uremic acidosis may thus be considered impaired in subjects with advanced diabetic nephropathy.

Key Words: Insulin-dependent diabetes mellitus; Metabolic acidosis; Ventilatory response; Predialysis.

INTRODUCTION

Sudden cardiopulmonary arrest due to a defective respiratory reflex has been observed in diabetic autonomic neuropathy (1). Previous studies demonstrate that ventilatory response to transient hypercapnia or hypoxia to result from the inhalation of high CO_2 or low O_2 gas is impaired in patients with diabetes mellitus (2–4). Wanke et al. suggest this situation to possibly arise from abnormality of the medullary chemoreceptor (4). Fulop reports ventilatory response to severe metabolic acidosis in diabetic ketoacidosis not to be impaired in diabetic patients (5). Acidemia in the patients studied by Fulop was too severe to permit evaluation of ventilatory response to metabolic acidosis. The present study was thus conducted to evaluate respiratory response to mild to moderate chronic uremic acidosis in diabetic patients.

METHODS

Thirteen insulin-dependent diabetic subjects (seven men and six women) (diabetic group) and thirty-three patients with renal failure due to non-diabetic diseases (chronic glomerulonephritis or nephrosclerosis) (24 men and nine women) (non-diabetic group) participated in this study, with informed consent in all cases. The diabetic group was comprised of six predialysis subjects and seven on regular hemodialysis (HD) with mean ages of 34.5 ± 5.9 and 35.9 ± 6.1 years, respectively. The non-diabetic group contained ten predialysis subjects and 23 on HD with mean ages of 49.3 ± 13.2 and 43.6 ± 4.2 years, respectively. The non-diabetic predialysis patients were older than the diabetic predialysis patients. No subject showed any indication of either any pulmonary disease or ketosis. Arterial blood samples were obtained in the supine position subsequent to at least a 30-min rest at around 10 a.m. and analyzed using a Ciba Corning 860 auto blood gas analyzer (Tokyo, Japan). From the HD patients, blood was obtained just before HD. The predicted fall in $PaCO_2$ in response to decrease in plasma HCO_3^- during chronic metabolic acidosis was computed by multiplying observed fall in plasma HCO_3^- by 1.2 (6). Predicted $PaCO_2$ was found by subtracting predicted fall in $PaCO_2$ from normal $PaCO_2$ (40 mm Hg). Delta $PaCO_2$ was expressed as the difference between measured and predicted $PaCO_2$. Alveolar-arterial oxygen tension difference ($AaDO_2$) was determined based on PaO_2 and $PaCO_2$ for subclinical parenchymal pulmonary disease.

The results are given as means ± SD. Statistical analysis was performed using the Student's t-test. p less than 0.05 was considered significant.

Table 1

Clinical Characteristics of Patients and Results for Arterial Blood Gas Analysis

	Predialysis Diabetic ($n = 6$)	Predialysis Non-diabetic ($n = 10$)	Hemodialysis Diabetic ($n = 7$)	Hemodialysis Non-diabetic ($n = 23$)
Male/Female	3/3	6/4	4/3	18/5
Age (year)	34.5 ± 5.9 [a]	49.3 ± 13.2	35.9 ± 6.1	43.6 ± 4.2
Serum creatinine (mg/dL)	9.1 ± 2.9	10.1 ± 2.7	9.1 ± 2.4	14.2 ± 2.7
pH	7.31 ± 0.06	7.32 ± 0.06	7.32 ± 0.04	7.35 ± 0.04
$PaCO_2$ (mmHg)	40.0 ± 7.4 [a, b]	31.1 ± 5.1	42.0 ± 6.4 [a, b]	36.0 ± 2.6
HCO_3 (mmol/L)	20.5 ± 5.6	15.3 ± 2.8	21.2 ± 2.9	20.2 ± 2.5
Predicted $PaCO_2$ (mmHg)	35.2 ± 5.9	29.9 ± 3.4	36.5 ± 3.3	35.4 ± 2.9
Delta $PaCO_2$ (mmHg)	4.7 ± 3.1 [a]	0.1 ± 3.4	5.6 ± 3.4 [a]	0.7 ± 1.8
$PaCO_2$ (mmHg)	77.5 ± 21.3 [a]	98.2 ± 9.0	97.1 ± 10.2	98.5 ± 12.4
AaDO2	29.1 ± 13.7 [a]	9.1 ± 6.0	14.6 ± 7.4	12.8 ± 10.0

IID; hemodialysis. *P* value; compared to non-diabetic group, [a] $p < 0.05$; compared to non-diabetic group. [b] $p < 0.05$, compared to predicted $PaCO_2$.

RESULTS

Arterial blood gas analysis data for each group are shown in Table 1. The degree of acidemia was essentially the same for the diabetic and non-diabetic groups of predialysis subjects and those on HD. In the predialysis subjects, plasma HCO_3 was significantly higher in the diabetic than in the non-diabetic group. Measured $PaCO_2$ was significantly higher in the diabetic than non-diabetic group. In the non-diabetic group, measured $PaCO_2$ was basically the predicted value. Measured $PaCO_2$ in the diabetic group was significantly higher than predicted. Partial arterial pressure of oxygen (PaO_2) in the diabetic group was significantly lower than in the non-diabetic group of predialysis patients. $AaDO_2$ in the diabetic group significantly increased beyond that in non-diabetic patients.

In subjects on HD, measured $PaCO_2$ in the diabetic group significantly exceeded that in the non-diabetic group, despite similar arterial pH in either. Differences in measured and predicted $PaCO_2$ were significant in the diabetic, but were not in the non-diabetic patients on HD. PaO_2 in the diabetic and non-diabetic groups on HD was basically the same. $AaDO_2$ did not significantly differ in diabetic and non-diabetic patients.

DISCUSSION

Respiratory compensation for simple chronic metabolic acidosis is quite predictable and differences in measured and predicted $PaCO_2$ are equal to the fall in plasma HCO_3^-

multiplied by 1.2 (6). Measured $PaCO_2$ in insulin-dependent diabetic subjects with advanced nephropathy was significantly higher than predicted $PaCO_2$, suggesting respiratory acidosis to accompany metabolic acidosis. But this is not due to renal failure or hemodialysis, since measured $PaCO_2$ was basically the same as that predicted in non-diabetic renal failure patients. The higher $PaCO_2$ in diabetic than non-diabetic subjects was not due to differences in arterial pH since arterial pH was the same in the two groups.

Consistent with the present data, diminished response to acute hypoxia or acute hypercapnia has been noted in diabetic patients (2–4). But, Fulop suggests ventilatory response to severe metabolic acidosis to be well maintained in diabetic patients (5). The reasons for differences in that and the present studies are not clear, but differences in arterial pH should perhaps be considered. This parameter in most of the patients of Fulop's was below 7.2 and above 7.2 in this study. The causes of acidosis were also different. Fulop directed attention to diabetic ketoacidosis whereas chronic metabolic acidosis due to renal failure was the focal point here.

Chronic respiratory acidosis in diabetic patients may result from defective respiratory center in the central nervous system, considering that Wanke et al. believe the response of medullary chemoreceptors to acute hypoxia or acute hypercapnia to be impaired in diabetic patients (4). Abnormal pulmonary function has been noted in nearly 60% of a cross section of a diabetic population (7). Reduced lung volume caused by diminished pulmonary elastic recoil (8,9) and/or impaired respiratory muscle performance (10) was reported in diabetic patients. These abnormalities may possibly contribute to impaired ventilatory response in diabetic patients. $PaCO_2$ was even less in diabetic predialysis patients whose $AaDO_2$ exceeded that of non-diabetic patients. Thus, in predialysis diabetic patients, parenchymal lung injury may be present, which would lead to impaired ventilatory response. However, $AaDO_2$ for diabetic and nondiabetic dialysis patients was virtually the same in this study and thus the present results suggest that impaired response would not arise solely from lung dysfunction.

Respiratory acidosis is shown by the present study to accompany metabolic acidosis in insulin-dependent diabetes mellitus with advanced nephropathy. The causes for the impaired ventilatory response should be elucidated.

REFERENCES

1. Page CBM, Watkins PJ: Cardiorespiratory arrest and diabetic autonomic neuropathy. *Lancet* 1:14–16, 1978.
2. Montserrat JM, Cochrane GM, Wolf C, Picado C, Roca J, Agusti Vidal A: Ventilatory control in diabetes mellitus. *Eur J Respir Dis* 67:112–117, 1985.
3. Williams JG, Morris AI, Hayter RC, Ogilvie CM: Respiratory responses of diabetics to hypoxia. hypercapnia. and exercise. *Thorax* 39:529–534, 1984.
4. Wanke T, Abrahamian H, Lahrmann H, Formanek D, Merkle M, Auinger M, Zwick H, Irsigler K: No effect of naloxane on ventilatory responses to progressive hypercapnia in IDDM patients. *Diabetes* 42:282–287, 1993.
5. Fulop M: The ventilatory response in severe metabolic acidosis. *Clin Sci and Med* 50:367–373, 1976.
6. Harrington JT, Cohen JJ: Metabolic acidosis. In: Cohen JJ and Kassirer JP. *Acid-Base*. Boston, Little Brown & Co. 1982, pp 128.
7. Sandler M, Bunn AE, Stewart RI: Cross-section study of pulmonary function in patients with insulin-dependent diabetes mellitus. *Am Rev Respir Dis* 135:223–229, 1987.
8. Sandlar M, Bunn AE, Stewart RI: Pulmonary function in young insulin-dependent diabetic subjects. *Chest* 90:670–675, 1986.
9. Innocenti F, Fabbri A, Anichini R, Tuci S, Pettina G, Vannucci F, DeGiorgio LA, Seghieri G: Indications of reduced pulmonary function in type 1 (insulin-dependent) diabetes mellitus. *Diabetes Res Cm Pract* 25:161–168, 1994.
10. Wanke T, Formanek D, Auinger M, Popp W, Zwick H, Irsigler K: Inspiratory muscle performance and pulmonary function changes in insulin-dependent diabetes mellitus. *Am Rev Respir Dis* 143:97–100, 1991.