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Preoperative hypoxemia in conscious patients after subarachnoid hemorrhage

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Abstract: We retrospectively examined partial arterial pressure of oxygen (Pao_2) afer subarachnoid hemorrhage (SAH), adjusted for patient-related risk factors for hypoxemia in 51 adult patients with no disturbance of consciousness undergoing surgery for clipping of intracranial aneurysms. A control group of 174 patients undergoing other operations were used for comparison. Arterial blood gas analysis was performed while patients were spontaneously breathing room air in the supine position before induction of anesthesia. The Pao_2 in the SAH patients was significantly lower ($p < 0.0001$) than that in the control group after adjustment for age, obesity, and smoking status. In three patients in the SAH group, Pao_2 was less than 60 mmHg. Close monitoring of arterial oxygenation with pulse oximetry is desirable, and supplemental oxygen should be considered during transfer from the patients' room to the operating suite, even for conscious patients of SAH without cardiopulmonary disease.

Key words: Hypoxemia—Subarachnoid hemorrhage—Pulse oximetry—Oxygen

Introduction

Impaired pulmonary gas exchange has frequently been noted in patients with intracranial diseases or conditions such as head trauma [1–3], intracranial hemorrhage [4], subarachnoid hemorrhage [5] (SAH), and increased intracranial pressure [6]. Several mechanisms have been proposed, including pulmonary arteriovenous shunting, ventilation-perfusion imbalance [7], and, in some severely ill patients, pulmonary edema [8]. Aspiration of the gastric contents may further aggravate respiratory dysfunction in unconscious patients. No previous reports have analyzed the combined effects of patient-related risk factors for hypoxemia when evaluating the effect of intracranial disorders on partial arterial pressure of oxygen (Pao_2).

After SAH, the most frequently encountered central nervous disorder requiring surgery in our hospital, patients undergoing surgery for clipping of intracranial aneurysms receive close observation, and have detailed records of vital signs, respiratory function, and levels of consciousness from the time of admission to the hospital. Detailed records minimize recall bias [9] that may confound retrospective studies. We performed this retrospective study to investigate the relationship between SAH and preoperative Pao_2, taking into account patient-related risk factors such as advanced age [10, 11], obesity [12, 13], and a history of smoking [14, 15].

Materials and methods

After approval of the protocol by the Human Investigations Committee, the necessary data were collected from medical records.

Candidates for the study group were patients aged 18 years or older undergoing definitive surgical treatment for SAH in Aomori Rosai Hospital in the period between January, 1989 and May, 1993. The patients included in the SAH group were Hunt's classification [16] grade 1 (alert, asymptomatic, or minimal headache and slight nuchal rigidity) or grade 2 (alert, moderate to severe headache, nuchal rigidity, and no neurological deficit other than cranial nerve palsy). Exclusion criteria included moderate or severe cardiac or pulmonary disease, which was judged by past medical records, electrocardiogram and chest X-rays, and absent arterial blood gas analysis on room air before induction of anesthesia. The patients were further stratified into three subgroups according to the interval from SAH to operation: (1) those operated within 3 days after SAH, (2) those operated between the 4th and 14th day after

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SAH, and (3) those operated at the 15th day or later after SAH.

The control group included all surgical patients aged 18 years or older, other than those who had suffered SAH in Aomori Rosai Hospital from January, 1992 to May, 1993. The same exclusion criteria were applied to the control group.

Arterial blood gas analysis was performed at the discretion of the anesthesiologist while patients were spontaneously breathing room air before induction of ansesthesia in the supine position. Body mass index (BMI) was calculated according to the following formula: body weight (kg)/height (m^2). BMI less than or equal to 25 was classified as normal. BMI over 25 and less than or equal to 30 as moderate obesity, and BMI over 30 as severe obesity. Smokers were classified at the time of occurrence of the SAH, or at the time of preanesthetic evaluation in the control group as light smokers (those smoking 20 or fewer cigarettes per day), heavy smokers (those smoking 21 or more cigarettes per day), and nonsmokers.

Statistical analysis was carried out using a computer statistical package, SYSTAT5.2 (SYSTAT, Evanston, IL, USA). One-way analysis of variance (ANOVA) was used to compare mean age, Pao_2, partial arterial pressure of carbon dioxide ($Paco_2$), base excess, and pH among the three SAH subgroups. Subgroups that differed significantly were further analyzed using the Bonferroni correction for multiple comparisons. Student's unpaired two-sided *t*-test was used to analyze continuous data in the SAH and control groups. The chi-square test was used to analyze discrete data. Analysis of covariance was used to describe the relationship between SAH and Pao_2, in comparison with the control group, while accounting for potentially confounding variables. A value of $p < 0.05$ was considered statistically significant.

Results

During the study interval, 87 SAH patients underwent surgery. Of these, 61 patients were classified as Hunt's grade 1 or grade 2. Among those 61, 9 patients were excluded from the study because arterial blood gas analysis was not performed, and 1 patient was excluded due to a history of congestive heart failure. Of the 51 remaining patients in the SAH group, 15 patients underwent surgery in ≤3 days, 9 in 4–14 days, and 27 in ≥15 days.

There were no significant differences among the SAH subgroups with respect to mean age, gender, ASA physical status, smoking, or obesity. Arterial blood gas analyses in the three SAH subgroups are presented in Table 1. Mean Pao_2 in the three subgroups was below 80 mmHg without significant differences among the subgroups. No differences in $Paco_2$ and base excess among the subgroups were observed. Although there was a statistically significant difference in pH between the patients undergoing surgery ≤3 days after SAH and those undergoing surgery ≥15 days after SAH, both values were within the normal range. Therefore, we considered the three subgroups to be similar for purposes of the following analysis.

The control group consisted of 174 surgical patients: 84 gastroenterologic, 46 orthopedic, 21 obstetric, 7 otolaryngologic, 6 urologic, 4 neurologic, 3 plastic, 2 vascular, and 1 ophthalmologic. Characteristics of the patents in the SAH and the control group are presented in Table 2. The patients in the SAH group were younger, taller, and less obese. Preoperatively, 20 patients (39.2%) in the SAH group and 156 patients (89.7%) in the control group received benzodiazepines. No other sedatives were given in either group. The Pao_2 was significantly lower in the SAH group than in the control group, 76.9 ± 1.2 mmHg and 81.9 ± 0.7 mmHg,

Table 1. Operative timing and arterial blood gas analysis while spontaneously breathing room air in the supine position

	Time of surgery after SAH			
	≤3 days	4–14 days	≥15 days	*P* value
No. of patients	15	9	27	
pH	7.413 ± 0.008*	7.443 ± 0.010	7.438 ± 0.006*	0.025
Pao_2 (mmHg)	76.2 ± 2.2	73.1 ± 2.9	78.6 ± 1.7	NS
$Paco_2$ (mmHg)	39.6 ± 1.2	36.6 ± 1.5	38.4 ± 0.9	NS
Base excess	0.9 ± 0.6	1.9 ± 0.8	2.3 ± 0.4	NS

All values are mean ± SEM.
SAH, subarachnoid hemorrhage; NS, difference not significant; Pao_2, partial arterial pressure of oxygen; $Paco_2$, partial arterial pressure of carbon dioxide.
* $P < 0.05$ surgery ≤3 days vs ≥15 days using Bonferroni's correction.

Table 2. Patient characteristics

	SAH	Control	*P* value
No. of patients	51	174	
Age (years)	52.5 ± 1.4	62.6 ± 1.1	0.0001
Sex (female/male)	28/23	98/76	NS
Height (cm)	158.6 ± 1.0	154.4 ± 0.7	0.001
Weight (kg)	57.9 ± 1.3	59.0 ± 1.0	NS
Obesity			0.023
BMI ≤ 25	76.5%	58.4%	
25 < BMI ≤ 30	23.5%	28.3%	
BMI > 30	0%	13.3%	
ASA physical status			NS
1	2.0%	1.2%	
2	88.2%	87.3%	
3	9.8%	11.5%	
4	0%	0%	
Smoking (cigarettes)			NS
none	58.0%	59.9%	
≤20 per day	26.0%	28.7%	
≥21 per day	16.0%	11.3%	

All values are mean ± SEM.
SAH, subarachnoid hemorrhage; BMI, body mass index; NS, difference not significant.

Table 3. Arterial blood gas analysis spontaneously breathing room air in the supine position

	SAH	Control	*P* value
pH	7.431 ± 0.004	7.408 ± 0.002	0.0001
Pao_2 (mmHg)	76.9 ± 1.2	81.9 ± 0.7	0.001
$Paco_2$ (mmHg)	38.5 ± 0.6	38.6 ± 0.3	NS
Base excess	1.8 ± 0.3	0.4 ± 0.2	0.0001

All values are mean ± SEM
SAH, subarachnoid hemorrhage; NS, difference not significant.

respectively (Table 3). pH and base excess were slightly but significantly higher in the SAH group although they were both within the normal range.

Analysis of covariance was performed to evaluate the influence of potential confounding variables and possible interactions. A significance-based testing algorithm [17] was used in the model-fitting process. Since the variables of age, smoking, and obesity were considered risk factors for the decrease in Pao_2, they were included in the model and turned out to be significant (all $p < 0.0001$). There were no significant interactions among those variables, or between those variables and patient status. Of other variables, gender, ASA physical status, height, weight, pH, $Paco_2$, and base excess were not significant. The ANOVA table and the estimates of effects on Pao_2 in the final model are presented in Table 4. The coefficient of multiple determination of the model is 0.303. The Pao_2 in the SAH group was significantly lower ($p < 0.0001$) than that in the control group after adjusting for age, smoking, and obesity.

Discussion

Respiratory problems of varying severity are common in patients with intracranial disorders, with or without primary pulmonary disease. Life-threatening cerebral pathology is associated with central neurogenic pulmonary edema [8]. With acute intracranial hypertension, apnea or hypoventilation may lead to death [18]. Surprisingly, a high percentage of patients of SAH with no disturbance of consciousness were hypoxemic preoperatively. Previous reports have not considered the

Table 4. Analysis of variance table and estimates of effects on partial arterial pressure of oxygen (Pao_2)

Variable	Estimates of effects on Pao_2	SS	DF	F-ratio
Constant	86.66			
Patient status		2020.93	1	32.13
SAH	−4.00			
Control	+4.00			
Age (year)	−0.22	1581.42	1	25.14
Smoking		2672.59	2	21.24
None	+4.62			
≤20 per day	+1.76			
≥21 per day	−6.38			
Obesity		2133.75	2	16.96
BMI ≤ 25	+5.09			
25 < BMI ≤ 30	−0.63			
BMI > 25	−4.46			
Residual		13209.99	210	

All variables in the table are significant in the model at the $p < 0.0001$ level.
SS, sum of squares; DF, degrees of freedom; SAH, subarachnoid hemorrhage; BMI, body mass index.

combined effects of patient-related risk factors when evaluating hypoxemia in this population.

Of the factors associated with impaired arterial oxygenation, age has been most extensively studied. Nunn [19] found a significant negative correlation between age and postoperative Pao_2, Several regression equations relating Pao_2 and age have been published using volunteers and patients free of cardiopulmonary disease [10]. Obesity is associated with an increased incidence of postoperative pulmonary complications [13, 20] due to decreased functional residual capacity, increased airway closure, and mismatching of ventilation to perfusion. As for smoking, Strieder et al. [14] reported that in young asymptomatic cigarette smokers, hypoxemia was accentuated by changing from the erect to the supine position. Increased nonspecific bronchial reactivity and a greater prevalence of cough and sputum production in cigarette smokers [21] could contribute to decreased Pao_2. We examined the relationship between SAH and Pao_2, taking into account these known risk factors.

Although the best operative timing of surgical treatment for SAH remains controversial, the effectiveness of early operation has become widely recognized [22, 23]. In our study, 29% (15 of 51 patients) underwent surgery within 3 days after SAH. Only one neurosurgeon decided the timing of surgery during the study period. In 1992, 69.2% (9 of 13 patients) underwent surgery within 3 days, and 30.8% (4 of 13 patients) underwent surgery ≥15 days after SAH. In contrast, in 1989 no patients underwent surgery in ≤3 days and 78.6% (11 of 14 patients) underwent surgery ≥15 days after SAH. With longer interval from SAH to operation, factors that affect the measurement of arterial blood gases could be increased, and the analysis would be more complicated. We first examined the characteristics of the patients in three SAH subgroups based on operative timing to determine whether these three subgroups could be regarded statistically as one group. Because there were no differences among the subgroups in several key variables, we concluded that combining the groups was appropriate.

The patients in the control group are a subgroup of surgical patients that is biased toward a higher risk for hypoxemia. They are older and more obese than the average of all surgical patients. Since the Pao_2 in the SAH group showed a lower value than that in this biased control group, the difference would be much larger if all surgical patients were used as a reference. The control group, consisting of patients undergoing surgery for nine diffferent sets of procedures, helps minimize selection bias [9] related to operative site.

Analysis of covariance revealed that Pao_2 in the SAH group was significantly lower than that in the control group provided age, smoking and obesity categories were held constant. Although only 30.3% of the variability in Pao_2 is explained by using the variables in the model, our primary objective in establishing this model was not prediction but adjustment for confounding variables. The mean Pao_2 in the SAH group was 76.9 mmHg, at which level we could not detect hypoxemia clinically. We consider, however, that these patients have potential pulmonary problems. We speculate that much greater decreases in Pao_2 would be found in patients with severely disturbed consciousness, and in those who have preexisting cardiopulmonary disease. The lowest Pao_2 of 53.6 mmHg was found in a nonobese patient aged 51 years who was a heavy smoker. Two other cases in the SAH group also showed values of Pao_2 less than 60 mmHg. No supplemental oxygen was provided for these patients in the ward and during the transfer from the ward to the operating room. We suggest that close monitoring of arterial oxygenation using a pulse oximeter may be desirable even for conscious SAH patients, and that supplemental oxygen should be considered during transfer from the patients' room to the operating suite.

The mechanism of hypoxemia in the patients with SAH might be complex. Typical neurogenic pulmonary edema (NPE) occurs shortly after severe SAH [8]. However, Fisher and Abol-Nasr [24] reported a case of NPE, which developed 4 days after SAH, and recurred when the patient was neurologically improving. This case report implies the prolonged residual effect of SAH on the centrally mediated sympathetic activity, and then on the pulmonary hemodynamics. Nishiwak et al. [25] noted the possibility of overlooking a high percentage of delayed NPE due to absent clinical manifestations. Our results also indicate the potential for such pulmonary problems.

There are several limitations of this retrospective study. Since the original medical records were written by a variety of doctors and nurses, information recording was not consistent. Although chest X-rays were checked before anesthesia, we cannot exclude the possibility of including unrecognized aspiration pneumonia in the SAH group because a transient decrease in the level of consciousness is often associated with the presentation of SAH. The patients in the SAH group had variable intervals during which smoking was interrupted. This might have caused us to underestimate the difference in Pao_2 between the SAH and control groups because interruption of smoking would at least lead to improved arterial oxygenation.

In summary, we examined the relationship between SAH and preoperative hypoxemia, taking into account patient-related risk factors for poor arterial oxygenation. The Pao_2 in the conscious SAH patients was significantly lower than that in control patients. It would be logical to assume, but we have not shown, that a

much greater decrease in Pao_2 would be found in patients with severe disturbance of consciousness and in those with preexisting pulmonary disease. We conclude that monitoring of oxygenation with pulse oximetry may be desirable, and that supplemental oxygen should be considered during the transfer from the patients' room to the operating suite.

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