Changes in Level of Consciousness and Association with Hyperglycemia as Tool for Predicting and Preventing Re-bleeding after Spontaneous Subarachnoid Hemorrhage

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Abbreviations:
CT = computerized tomography
GCS = Glasgow Coma Scale
SAH = subarachnoid hemorrhage

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Abstract

Introduction: It is crucial to predict and prevent re-bleeding from ruptured intracranial aneurysms in patients with subarachnoid hemorrhage (SAH). During the prehospital period and on arrival to the hospital, blood glucose and serum potassium levels, as well as changes in levels of consciousness were assessed in patients in the acute stage of spontaneous subarachnoid hemorrhage. These assessments were analyzed as possible risk factors for re-bleeding and as potential contributors to the prevention of re-bleeding, both in prehospital care and after hospital admission.

Methods: Upon the arrival of 202 patients with spontaneous subarachnoid hemorrhage, the following indications were examined retrospectively: (1) presence/absence of re-bleeding; (2) time interval between the onset of SAH and re-bleeding; (3) level of consciousness using the Glasgow Coma Scale (GCS) score before and on arrival; (4) amount and distribution of subarachnoid blood using Fisher's Computerized Tomography Classification; (5) blood pressure; (6) blood glucose concentration; and (7) serum potassium concentration. The patients were hospitalized in the Yokohama City University Critical Care and Emergency Center (Yokohama, Japan) between January 1991 and December 2000. The re-bleeding rate was analyzed using the *chi*-square (χ^2 test, and the averages and standard deviations of hematological data were compared using the Mann-Whitney *U*-test. The level of statistical significance was set at p <0.05.

Results: The overall re-bleeding rate was 20.8%. Among 119 patients with a GCS score of 3–7 before arrival, 42 (35.3%) had re-bleeding, but none of the 83 patients with a GCS score of 8–15 before arrival had re-bleeding. Of 105 patients with a GCS score of 13–15 on arrival, 14 (51.8%) of 27 patients whose consciousness level was a GCS score of 3–7 before arrival experienced re-bleeding. The re-bleeding rate of this group was high. Moreover, this re-bleeding group had a significantly higher blood glucose concentration than did the patients whose GCS score was 13–15 both before and on arrival. Between the patients with or without re-bleeding, there was no significant difference in the blood pressure on arrival or in distribution according to Fisher's Computerized Tomography Classification

Conclusion: Since the re-bleeding rate is high in patients who have hyperglycemia and a history of a level of consciousness as low as a GCS score of 3–7, a detailed assessment of level of consciousness and blood glucose tests performed on arrival provide important information that will contribute to predicting and preventing re-bleeding. This may be extended to the prehospital phase, because blood glucose tests are simple and safe when performed by paramedics.

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Introduction

Prevention of re-bleeding from ruptured intracranial aneurysms in patients with subarachnoid hemorrhage (SAH) is crucial. To date, much has been published about the risk factors for re-bleeding from ruptured intracranial aneurysms such as their size, shape, location, blood pressure, neurological grade on arrival at hospital, and amount of subarachnoid blood.[1–3] Changes in the consciousness level of patients with SAH also might predict the risk for re-bleeding.[4] However, information concerning changes in the level of consciousness not always are available because the assessment of consciousness level before arrival may not be reliable in some patients with disturbance of consciousness. On the other hand, various studies have demonstrated that the presence of hyperglycemia and hypokalaemia in the acute stage of some patients with SAH are predictors of outcome.[5,7,8,10–17] This study analyzed blood glucose and plasma potassium concentrations, and changes in the level of consciousness as possible risk factors for re-bleeding. Their potential contributions of these factors to the prevention of re-bleeding, both in prehospital and after hospital care settings also were examined.

Methods

A total of 281 patients with spontaneous SAH diagnosed by computerized tomography (CT) were hospitalized in the Yokohama City University Critical Care and Emergency Center (Yokohama, Japan) from January 1991 to December 2000. Among them, 74 patients (26.2%) were in cardiopulmonary arrest upon arrival, and five patients had undergone hemodialysis. These 79 patients were excluded from the study. An angiography detected an aneurysm in 172 (85.2%) of the remaining 202 patients. In the other 28 patients (1%), angiography was not performed because of the patients' poor clinical condition, and in two patients the angiogram revealed no abnormal findings that could have caused a SAH, such as an aneurysm or arteriovenous malformation.

The following factors were assessed: (1) the presence or absence of re-bleeding; (2) blood pressure on arrival; (3) time interval between the onset of SAH and re-bleeding; (4) the situation at the time of re-bleeding; (5) changes in consciousness level using the Glasgow Coma Scale (GCS) score; (6) amount and distribution of subarachnoid blood using Fisher's CT classification on arrival; and (7) blood glucose (mg/dL) and serum potassium (mEq/L) concentrations on arrival at the hospital.[18] In this study, re-bleeding was presumed when patients exhibited clinical signs of SAH, such as sudden headache or definite deterioration of the level of consciousness associated with rapid changes in vital signs. In most of these patients, the increase in subarachnoid blood on the CT was confirmed by comparison with a previously recorded CT. To determine the GCS score before arrival, anamnesis, including information about the prehospital condition of the patients, was obtained from patients, bystanders (such as family members), or ambulance crew. The worst GCS score recorded was adopted as the GCS score before arrival at the hospital if there were changes in the level of consciousness during the prehospital period. Blood samples were obtained on arrival, within 24 hours after arrival, and before the operation or re-bleeding. The rates of re-bleeding were analyzed using the chi-square (χ^2) test. The averages and standard deviations of blood pressure and hematological data were compared using the Mann Whitney *U*-test. The level of statistical significance was set at p <0.05. These data were analyzed using commercially available software (StatView 5.0 J; Abacus Concepts, Berkeley, California).

Results

The baseline characteristics of the 202 patients with SAH are listed in Table 1. Re-bleeding occurred in 42 (20.8%) patients. In 39 of these 42 patients (92.9%), the increase in volume of subarachnoid blood was confirmed by CT. The three remaining patients were determined to have re-bleeding after admission because of a sudden, definite deterioration of the level of consciousness. The re-bleeding occurred within 24 hours in 39 out of the 42 patients (92.9%) with re-bleeding. There was no statistically significant difference in the blood pressure on arrival or in the distribution by Fisher's CT Classification (Tables 2 and 3) between the patients with or without re-bleeding.

As shown in Table 4, no patient among the 83 patients with GCS score of 8–15 before arrival experienced re-bleeding. However, 42 of 119 patients (35.3%) with a GCS score of 3–7 before arrival had a statistically significant higher rate (χ^2 = 35.33, p <0.001) of re-bleeding. Of the 48 patients whose level of consciousness improved from the range of GCS scores of 3–7 before arrival to GCS scores of 8–15 on arrival, 23 (47.9%) had re-bleeding and their re-bleeding rate also was significantly higher (χ^2 = 44.394678, p <0.001). Similarly, 14 (51.8%) of the 27 patients whose level of consciousness improved from a GCS score of 3–7 before arrival to a GCS score of 13–15 on arrival had a statistically significant higher rate of re-bleeding (χ^2 = 42.287352, p <0.001).

The number of patients with or without re-bleeding distributed by their GCS scores before arrival and on arrival; the mean ±standard deviation (SD) of the blood glucose level (mg/dL) and the serum potassium level (mEq/L) on arrival are listed in Table 5. For the 105 patients with GCS score of 13–15 on arrival, there was a tendency toward lower serum potassium levels and higher blood glucose levels in these patients who experienced re-bleeding compared with those who did not re-bleed. The blood glucose level of the 14 patients with re-bleeding, whose GCS score was 3–7, before arrival, and who recovered to 13–15 by arrival was significantly higher than was that of the patients who did not experience re-bleeding and whose GCS score was 8–15 both before and on arrival (p <0.001). The mean value for serum potassium levels of the former was significantly lower than was that of the latter group (p <0.005). Similarly, the mean values for the blood glucose level of the 14 patients with re-bleeding was statistically significantly higher than was that of the 13 patients who did not have re-bleeding and whose GCS score was 3–7 before arrival and 13–15 on arrival (p <0.05).

A second blood sample was taken in 48 patients within 24 hours after admission, before surgery, or upon recognition of re-bleeding. The mean values for the interval times

Mean age (years)	58.0 ±13.0
Men:Women	76:126
Mean blood glucose level (mg/dL)	189 ±63.4
Mean serum potassium level (mEq/L)	3.51 ±0.52
Mean systolic blood pressure (mmHg)	167.8 ±37.0
Re-bleeding (n = 42)	91.4 ±20.1
After admission	
<6 hours	25
6–24 hours	14
25–48 hours	1
49 hours–7 days	2

Table 1—Baseline characteristics of 202 patients with acute, spontaneous subarachnoid hemorrhage (mean = average of values; ±standard deviation)

	Re-bleeding	
	Present (n = 42)	**Absent (n = 160)**
Systolic blood pressure (mmHg)	170.4 ±41.1	167.3 ±36.0
Diastolic blood pressure (mmHg)	91.9 ±23.6	91.9 ±18.7

Table 2—Relationship between the averages of blood pressure on arrival and re-bleeding (values are the mean ±standard deviation)

between the two blood tests was 650 minutes in the 11 patients with re-bleeding, and 740 minutes in the 37 patients without re-bleeding. The mean ±SD blood glucose levels and serum potassium are listed in Table 6. The blood glucose level of the patients with re-bleeding was significantly higher, not only on arrival, but also after admission (p <0.005).

Discussion

It is important to prevent re-bleeding in patients with ruptured intracranial aneurysms.[19,20] In this study, patients whose level of consciousness had once been low, as indicated by a GCS score 3–7 were at a high risk for re-bleeding, despite their positive level of consciousness on arrival. In addition, blood glucose levels were higher and serum potassium levels were lower in the patients at a high risk of re-bleeding.

Fisher's group	Re-bleeding	
	Present	**Absent**
1	0	3
2	1	31
3	15	54
4	26	72

Table 3—Distribution of 202 patients with subarachnoid hemorrhage according to Fisher's Computerized Tomography Cassification and re-bleeding

Many authors have reported on the risk factors for re-bleeding from ruptured intracranial aneurysms.[1–4,21–26] Concerning the time interval from the onset, Kassel *et al* and Jane *et al* reported that the higher rates of re-bleeding occurred within the first 24 hours of the initial hemorrhage.[21,22] On the other hand, Røsenorn *et al* demonstrated that the maximum rate for re-bleeding was observed from Day 4 to Day 9.[23] Aoyagi *et al* noted that the re-bleeding rate was highest in those patients who underwent angiography within three hours after the onset of their symptoms.[24] Amagasa *et al* reported that patients seldom had re-bleeding when the first angiography was performed six or more hours after the onset.[25] In the current series, the rate of re-bleeding was highest within the first 24 hours after the onset of the symptoms. Although angiography was avoided within six hours of the onset of the symptoms, nine patients had re-bleeding during or just after the performance of angiography.

Concerning levels of consciousness, Ito *et al* and Røsenorn *et al* pointed out that the re-bleeding rate of the patients with a poor clinical grade was high.[23,26] In the current series, the re-bleeding rate of the patients with a low level of consciousness also was higher compared with those with a higher level of consciousness. However, the level of consciousness of the patients with SAH may change with time after onset. Therefore, the changes in the level of consciousness between, before, and on arrival to the hospital were examined. In addition, the rate of re-bleeding of the patients with GCS scores 3–7 before arrival to the hospital was higher than for those patients with GCS scores 8–15 on arrival at the hospital. There is a high risk for re-bleeding for those patient groups that are considered to be a low risk for re-bleeding if their level of consciousness is assessed using the GCS scores on arrival. Therefore,

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Glasgow Coma Scale Score		Re-bleed	
Before arrival	On arrival	Present	Absent
3-7	3-7	19[a]	52
3-7	8-12	9[b]	12
3-7	13-15	14[b]	13
8-12	3-7	0	0
8-12	8-12	0	5
8-12	13-15	0	3
13-15	3-7	0	0
13-15	8-12	0	0
13-15	13-15	0	75

Table 4—Relationship between re-bleeding and the changes in the level of consciousness
[a]$\chi^2 = 44.394678, p < 0.001$
[b]$\chi^2 = 44.394678, p < 0.001, \chi^2 = 42.287352, p < 0.001$

a detailed anamnesis and information about the level of consciousness before arrival are important to predict and prevent re-bleeding from a SAH, especially if the level of consciousness was recovered and remained good on arrival.

Various degrees of hyperglycemia and hypokalaemia commonly are observed in patients with an acute SAH. Le Roux *et al* noted that the blood glucose concentrations on admission to the hospital were higher in patients with a poor clinical grade.[6] Berek *et al* and Longstreth *et al* reported that the initial blood glucose concentrations seemed to be an accurate predictor of the outcome.[5,7] Lanzino *et al* reported that the blood glucose concentrations on admission could be used as a simple and objective prognostic predictor after SAH.[8] Alberti *et al* demonstrated that the degree of hyperglycemia correlated with the clinical severity and radiological extent of the extravascular blood in patients with an acute SAH.[9] As for hypokalaemia, Lanzion *et al* reported that hypokalaemia of varied degree often was observed in association with electrocardiographic changes after an actute SAH.[16] Andreoli *et al* also reported hypokalaemia, a rise in the level of circulating catecholamines, and hypercortisolism in 36 (51%) of 70 patients with SAH.[17] Hyperglycemia and hypokalaemia were observed in patients with SAH in the current study. Moreover, there was a tendency towards a higher blood glucose and lower serum potassium concentration in patients with re-bleeding. Furthermore, since the degree of hyperglycemia of the patients with re-bleeding was higher than without re-bleeding, hyperglycemia on arrival and a low level of consciousness before arrival to the hospital could indicate a high risk for re-bleeding.

Hyperglycemia present in patients with ischemic and hemorrhagic strokes is regarded as a "stress hyperglycemia". Alberti *et al* indicated that a disturbance of hypothalamic regulation is the cause of metabolic derangement that results in hyperglycemia in patients with an acute SAH.[8] Lanzino *et al* reported that blood glucose concentration on admission to the hospital was an indirect marker of sympathetic activation.[9] James reported hypokalaemia, and elevated level of catecholamines in patients with SAH.[27] Lim *et al* explained that hyperglycemia and hypokalaemia were due to activation of the sympathetic nervous system and ß-receptor stimulation.[28] Satoh defined the value obtained by dividing the blood glucose level by the serum potassium level as the *stress index*, and reported that the stress index correlated well with changes in the serum level of catecholamines in patients with an acute SAH.[29] In the present study, the stress index of the patients with re-bleeding also was higher compared to those without re-bleeding. Among the 48 patients who had blood tests done both on arrival and after admission, the blood glucose concentration of the patients with re-bleeding was higher both on arrival and after admission than for those that did not develop re-bleeding. Thus, the degree of activation of the sympathetic nervous system due to the first attack may be stronger and last longer in those patients with re-bleeding than in those without re-bleeding.

As stated, it is important to prevent re-bleeding in patients with ruptured intracranial aneurysms before treatment. This is important not only after arrival, but also before arrival. A SAH can be suspected through sudden onset headache, various degrees of disturbance of consciousness, nausea, vomiting, etc. Although the definite diagnosis of SAH requires a CT, and the measurement of blood glucose, commonly done by patients with diabetes mellitus, now is safe and simple. Furthermore, by using local surface anesthesia, the pinprick from the blood glucose test can be less painful. Therefore, the blood glucose test could be less stressful for patients with suspected SAH if it would be done in prehospital stage. Thus, paramedics might do more to predict and prevent re-bleeding during the prehospital stage if they do a blood glucose test and perform a detailed level of consciousness assessment when a SAH is suspected.

Conclusion

There is a high rate for re-bleeding group within the group of patients with a satisfactory level of consciousness on

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Glasgow Coma Scale Score		Re-bleed		Blood glucose (mg/dL)	Serum potassium (mEq/L)
Before arrival	On arrival	Present	Absent		
3-7	13-15	14	0	200 ±44.9	3.24 ±0.38
3-7	13-15	0	13	167 ±35.5[a]	3.29 ±0.34
8-12	13-15	0	3	171 ±29.6	3.78 ±1.04
13-15	13-15	0	75	151 ±37.1[b]	3.65 ±0.48[c]

Table 5—Re-bleeding, changes in the level of consciousness, blood glucose level, and serum potassium level of 105 patients with Glasgow Coma Scale score of 13 through 15 on admission. Blood glucose level and serum potassium level are shown as the mean ±standard deviation.
a <0.05
b <0.001
c <0.005 vs. present

	Re-bleeding present (n = 11)			Re-bleeding absent (n = 37)		
	On arrival	After admission	Changing rate	On arrival	After admission	Changing rate
Blood glucose level (mg/dL)	228 ±59.9	236 ±66.7*	12.70%	171 ±63.5	168 ±51.8	11.00%
Serum potassium level (mEq/L)	3.22 ±0.50	3.56 ±0.33	5.60%	3.49 ±0.39	3.84 ±0.36	3.00%

Table 6—Changes in the blood glucose level and serum potassium level of the 48 patients who had blood tests done both on arrival and within 24 hours after admission (Data are the mean value ±standard deviation)
*p <0.005

arrival at the hospital, usually considered to have a comparatively low re-bleeding rate. Emergency physicians, neurosurgeons, and paramedics should pay special attention to the patients whose level of consciousness has been defined as a GCS score 3–7 at the time of the first bleed as their risk for re-bleeding risk is high. A detailed assessment of consciousness, and the blood glucose concentration on arrival provide important and useful information to predict and prevent re-bleeding, which may be extended into the prehospital period.

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References

1. Yasui T, Kishi H, Komiyama M, *et al*: Re-bleeding of ruptured intracranial aneurysm in the acute stage. *No Shinkei Geka* 1994;22:1119–1122.
2. Fujii Y, Takeuchi S, Sasaki O, *et al*: Ultra-early re-bleeding in spontaneous subarachnoid hemorrhage. *J Neurosurg* 1996;84:35–42.
3. Inagawa T, Kamiyama K, Ogasawara H, Yano T: Re-bleeding of ruptured intracranial aneurysms in the acute stage. *Surg Neurol* 1987;28:93–99.
4. Kitsuta Y, Suzuki N, Yoshida T, *et al*: The risk factor if re-bleeding from ruptured cerebral aneurysms from the view point of interval change of consciousness level. *Surg Cereb Stroke* 2000;28:454–457.
5. Longstreth WT Jr., Nelson LM, Koepsell TD, *et al*: Clinical course of spontaneous subarachnoid hemorrhage. *Neurology* 1993;42:712–718.
6. Le Roux PD, Elliott JP, Newell DW, *et al*: Predicting outcome in poor-grade patients with subarachnoid hemorrhage: A retrospective review of 159 aggressively managed cases. *J Neurosurg* 1996;85:39–49.
7. Berek K, Kiechl S, Pfausler B, *et al*: Prognostic indices in subarachnoid haemorrhage. *Lancet* 1992;339:68. (Letter).
8. Alberti O, Becker R, Benes L, *et al*: Initial hyperglycemia as an indicator of severity of the ictus in poor-grade patients with spontaneous subarachnoid hemorrhage. *Clin Neurol Neurosurg* 2000;102:78–83.
9. Lanzino G, Kassell NF, Germanson T, *et al*: Plasma glucose levels and outcome after aneurismal subarachnoid hemorrhage. *J Neurosurg* 1993;79:885–891.
10. Ikeda Y, Nakazawa S: A study on changes of plasma catecholamines concentrations and clinical prognosis in patients with ruptured intracranial aneurysms. *No Shinkei Geka* 1984;12:571–578.
11. Dilraj A, Botha JH, Rambiritch V, *et al*: Levels of catecholamine in plasma and cerebrospinal fluid in aneurismal subarachnoid hemorrhage. *Neurosurgery* 1992;31:42–51.
12. Neil-Dwyer G, Cruikshank J, Stott A, *et al*: The urinary catecholamine and plasma cortisol levels in patients with subarachnoid haemorrhage. *J Neurol Sci* 1974;22:375–382.
13. Feibel JH, Hardy PM, Campbell RG, *et al*: Prognostic value of the stress response following stroke. *JAMA* 1997;238:1374–1376.
14. Benedict CR, Loach AB: Sympathetic nervous system activity in patients with subarachnoid hemorrhage. *Stroke* 1978;9:237–244.
15. Kanemoto Y, Kamata K, Sasaoka Y, *et al*: The mechanism of cardiorespiratory arrest due to subarachnoid hemorrhage. *No Shinkei Geka* 1995;23:575–579.
16. Lanzino G, Kongable GL, Kassell NF: Electrocardiographic abnormalities after nontraumatic subarachnoid hemorrhage. *J Neurosurg Anesthesiol* 1994;6:156–162.
17. Andreoli A, Di Pasquale G, Pinelli G, *et al*: Subarachnoid hemorrhage: Frequency and severity of cardiac arrythmias a survey of 70 cases studied in the acute phase. *Stroke* 1987;18:558–564.
18. Fisher CM, Kistler JP, Davis JM: Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. *Neurosurgery* 1980;6:1–9.
19. Findlay JM: Current management of aneurismal subarachnoid hemorrhage guidelines from the Canadian Neurosurgical Society. *Can J Neurol Sci* 1997;24,2:161–170.
20. Yonekawa Y, Marugg R, Imhof HJ, Ogata N: Current treatment concepts in patients in the acute stage of subarachnoid hemorrhage due to rupture of an intracranial aneurysm. *Schwieiz Rundsch Med Prax* 1995;84:667–674.
21. Kassel NF, Torner JC: Aneurysmal re-bleeding: A preliminary report from the cooperative aneurysm study. *Neurosurgery* 1983;13:479–481.
22. Jane JA, Kassel NF, Torner JC, *et al*: The natural history of aneurysms and arteiovenous malformation. *J Neurosurg* 1985;62:321–323.
23. Røsenorn J, Eskesen V, Schmidt K, *et al*: Clinical features and outcome in 1,076 patients with ruptured intracranial saccular aneurysms: A prospective consecutive study. *Br J Neurosurg* 1987;1:33–46.
24. Aoyagi N, Hayakawa I: Re-rupture of intracranial aneurysms during angiogarphy. *Acta Neurochir (Wien)* 1989;98:141–147.
25. Amagasa M, Yoshimoto T, Mizoi K, *et al*: Early cerebral angiography after aneurysm rupture—Analysis of 197 cases. *J Neurosurg* 1986;64:537–542.
26. Ito S, Kwak R, Emori I, *et al*: Risk factors of cerebral aneurysm re-rupture during angiography. *No Shinkei Geka* 1985;13:399–407.
27. James IM: Electrolyte changes in patients with subarachnoid haemorrhage. *Clin Sci* 1972;42:179–187.
28. Lim M, Linton RAF, Band DM, Chir B: Continuous intravascular monitoring of epinephrine-induced changes in plasma potassium. *Anesthesiology* 1982;57:272–278.
29. Satoh A: Clinicopathological features and treatment of severely ill patients with a subarachnoid hemorrhage. *Jpn J Neurosurg* 1998;7:24–31.