Evaluation of changes in circulating blood volume during acute and very acute stages of subarachnoid hemorrhage: implications for the management of hypovolemia

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Object. Circulating blood volume (cBV) is reported to decrease in patients who suffer a subarachnoid hemorrhage (SAH), but little is known about the correlation between changes in cBV, and patient clinical condition and time course after SAH, especially during the very acute stage. To determine appropriate management of patients with SAH, the authors measured cBV by using pulse spectrophotometry immediately after patient admission. They also evaluated whether the timing of surgery influenced changes in cBV.

Methods. Circulating blood volume was measured in a total of 73 patients who were divided into the following three groups: Group A (very acute SAH) consisted of 14 SAH cases, Group B (acute SAH) included 34 SAH cases, and Group C (controls) included 25 other neurosurgical cases. All patients in Group A underwent aneurysm clipping within 6 hours after onset of SAH, whereas all patients in Group B underwent aneurysm clipping within 72 hours after onset. Hypovolemic therapy was not performed in patients with SAH.

Before surgery, cBV was significantly lower in patients in Group B than in those in Group C, but there was no significant difference in this parameter when comparing Groups A and C. Although there was a transient drop in cBV in Group B patients for at least 3 days after surgery, there was no significant change in cBV in Group A patients during the study period. None of the Group A patients suffered from symptomatic vasospasm; however, four Group B patients did experience symptomatic vasospasm.

Conclusions. The authors assert that normovolemic fluid management is appropriate for patients who undergo surgery during the very acute stage of SAH, whereas a relatively hypervolemic therapy is necessary for 3 to 5 days after operation to prevent early hypovolemia in patients who undergo surgery during the acute stage of SAH.

KEY WORDS • circulating blood volume • early surgery • fluid management • hypovolemia • subarachnoid hemorrhage • symptomatic vasospasm

Clinical Material and Methods

Patient Population
The study was approved by the Ethics Committee of the Hospital Profession, and informed consent was obtained from each patient. A total of 73 neurosurgical patients, including 48 with SAH and 25 with other neurological disorders, were enrolled in this study and divided into the following three groups.

Group A consisted of 14 consecutive patients, including 11 women and three men whose ages ranged from 41 to 80 years (mean age 62.7 years), who were studied during the very acute period of SAH. Preoperative Hunt and Hess grades were I in two cases, II in five, III in three, and IV in four. Preoperative cBV was measured at an average of 5.5 hours (range 2.5–6 hours) after onset of SAH. All patients underwent surgery immediately after admission and within 6 hours after onset of SAH. Postoperatively, cBV was measured on the 3rd, 7th, and 14th days.

Group B consisted of 34 consecutive patients, including 25 women and nine men whose ages ranged from 35 to 87 years (mean age 57.1 years), who were studied during the

UTCOMES in patients with aneurysmal SAH have improved over the past two decades due to advances in microneurosurgery and neurointensive care as well as an emphasis on early aneurysm surgery to prevent rebleeding. Nonetheless, cerebral ischemia related to vasospasm remains an important cause of morbidity and mortality. Hypovolemia and fluid restriction have been implicated as risk factors for delayed cerebral ischemia related to vasospasm. The importance of monitoring cBV in critically ill patients during the perioperative period is widely recognized, however, no report is available concerning changes in cBV beginning immediately after onset of SAH. Indocyanine-green pulse spectrophotometry has recently been developed to facilitate minimally invasive, simple, and repeated measurement of cBV by progressively estimating the arterial blood hemoglobin/ICG ratio. The purpose of this study was to investigate the changes in cBV in various clinical situations and to determine appropriate fluid management in patients with SAH.

Abbreviations used in this paper: cBV = circulating blood volume; ICG = indocyanine green; SAH = subarachnoid hemorrhage.
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apple period of SAH. Preoperative Hunt and Hess grades were I in five cases, II in 15, III in eight, and IV in six. Preoperative cBV was measured at an average of 56 hours after onset of SAH, and all patients underwent surgery within 72 hours after onset. Postoperatively, cBV was measured on the 1st, 3rd, and 7th days.

Group C consisted of 25 patients with non-SAH-related neurosurgical issues, including eight with unruptured aneurysms, eight intracerebral hemorrhages, four meningiomas, two pituitary adenomas, two cervical spondylloses, and one cerebral infarction. Circulating blood volume was measured before surgery, immediately after, and on the 3rd and 7th days after surgery.

Data Collection

In Group A patients, 20 mg of ICG was injected just after admission to the hospital, following sedation with diazepam and pentazocine. In patients in Groups B and C, cBV was measured just before surgery. Normovolemic fluid management was determined for all Group B patients by assessing in–out fluid balance before the operation. In all cases, cBV was measured using a dye densitogram analyzing system (DDG-2001; Nihon Kohden, Inc., Tokyo, Japan). In both Groups A and B, normovolemic fluid management was determined by assessing in–out fluid balance, renal function test results, and electrolyte examination results after the surgery.

Statistical Analysis

All parameters were expressed as the means ± standard deviations. The unpaired t-test was used to compare groups. The parameters of SAH, non-SAH, and patient distribution by sex were analyzed using the chi-square test for independence. Probability values less than 0.05 were considered significant.

Results

The clinical course of patients was not affected by the injection of ICG just after hospital admission, with no rerupture of the aneurysm or changes in vital signs.

Preoperative cBV

Circulating blood volume was significantly lower in Group B patients than in Group C volunteers (62.8 ± 12.3 ml/kg compared with 73.3 ± 11.2 ml/kg, p < 0.05), particularly in women (women 56.7 ± 10.1 ml/kg compared with men 70.3 ± 13.8 ml/kg, p < 0.01) before surgery. The cBV was significantly higher in Group A patients than in those in Group B (76.9 ± 17.1 ml/kg compared with 62.8 ± 12.3 ml/kg, p < 0.01; Fig. 1). There was no significant difference in this parameter when comparing Groups A and C.

Postoperative cBV

There was no significant change in cBV during the study period in Group A patients (Fig. 2). In Group B patients, particularly in women, cBV values on the 1st, 3rd, and 7th days postoperatively were 62.1 ± 14.1 ml/kg, 73.4 ± 16.3 ml/kg, and 76.6 ± 18.5 ml/kg, respectively (Fig. 3). Circulating blood volume values on the 3rd and 7th days after operation were significantly higher than preoperative values (p < 0.01). There was no significant difference in sex, age, or preoperative Hunt and Hess grade when comparing Groups A and B. None of the Group A patients suffered from symptomatic vasospasm, whereas four patients in Group B did.

Discussion

Standard methods for measuring cBV have included the indicator dilution method with a radioisotope or Evans blue dye. Using these methods, it is difficult to measure a continuous or repeated cBV at the bedside of patients with SAH. Recently, however, repeated cBV measurement using non-radioisotope tracer became possible with the induction of ICG. Indocyanine green rapidly binds to plasma proteins and travels throughout the circulatory system; the liver then quickly and exclusively eliminates it. Several investigators have reported methods of cBV measurement with the aid of ICG and assert that it has good accuracy compared with other standard methods. Continuous measurement of cBV with ICG tracer has also become possible after adopting
sympathetic activity. Moreover, a marked increase in intracranial pressure has been proposed as a primary cause of decreased cBV, especially during the acute stage of SAH. An extensive literature search revealed that cBV measured using this method and the 131I-labeled human serum albumin method, with an estimated error of less than 10%,6,11 Its accuracy has also been analyzed using the dye dilution cuvette method. High reproducibility indicated by a low intra-subject coefficient of variation of 3.94 ± 2.03% has also been reported in the literature. Therefore, precise management of cBV can be facilitated by ICG pulse spectrophotometry. Clinically, it enables neurosurgeons to measured cBV continuously and repeatedly at the bedside of patients with SAH.

In the present study, preoperative cBV in Group B patients (acute SAH) was significantly lower than that in Group C (controls), but cBV in Group A patients (very acute SAH) was not lower than that in Group C volunteers. Because there was no significant difference between these two patient populations, except in preoperative measurement time (56 hours in the acute SAH group compared with 4.8 hours in the very acute SAH group), it appeared that cBV decreased over time, at least preoperatively.

Maroon and Nelson17 have suggested that the cause of decreased cBV in patients who have suffered SAH is related to bed rest, supine diuresis, negative nitrogen balance, decreased erythropoiesis, and iatrogenic blood loss. The combination of these processes almost certainly contributes to the development of hypovolemia after a certain period following the onset of SAH. An extensive literature search reveals studies in which changes in sympathetic nervous system activity may account for another mechanism of reduction in cBV, especially during the acute stage of SAH. It has been reported that catecholamine concentration is increased in patients with SAH.18 It has also been reported that cBV is decreased under conditions of increased sympathetic activity. Moreover, a marked increase in intracranial pressure has been proposed as a primary cause of abnormal changes in sympathetic activity. These findings suggest that the catecholamine storm after the onset of SAH reduces systemic vascular compliance. On the other hand, reduction in cBV during extracorporeal circulation in cardiovac surgery is thought to result from fluid shift to the interstitial space.1 The amount of fluid shift between intravascular and extravascular compartments depends on the increase in infiltration pressure. Capillary pressure is sensitive to changes in postcapillary resistance; the increase in venous pressure produced by an increase in sympathetic activity, as reflected by a rise in venous tone, may result in a loss of fluid to the extravascular space. Thus, Hirasawa and colleagues6 investigated changes in cBV and hormone levels following craniotomy and noted that cytokine release and systemic inflammatory response during surgery promote an acute-phase endocrine, metabolic, and systemic response, including an alteration of capillary permeability that may also promote fluid shift. Regarding another mechanism of hypovolemia in the acute stage of SAH, it has been reported that sodium-dependent diuresis is induced by the increased production of natriuretic peptide in the subacute stage of SAH, resulting in reduced cBV.12,21,25 Data from recent studies have demonstrated that this phenomenon is frequently associated with hypovolemia, which is caused by salt-wasting syndrome and not the inappropriate secretion of antidiuretic hormone. Some authors have reported that atrial natriuretic and digoxin-like peptides may cause hyponatremia,21 whereas others have suggested that brain natriuretic peptide may play an important role in hypovolemia and hyponatremia in patients with acute SAH. But little is known about the natriuretic peptides in the very acute stage of SAH, and further investigation, including hormone studies in the acute and very acute stages of SAH, are required to determine the mechanism of cBV depletion during this period.

Maintenance of an adequate intravascular volume is important in the management of patients with aneurysmal SAH, especially because they are threatened by the risk of vasospasm, which can lead to cerebral ischemia. Cerebral blood flow may be further impaired in patients with blood volume depletion. The importance of an adequate intravascular volume has been corroborated by reports in which authors describe improvements in signs attributed to cerebral ischemia and effectiveness of volume expansion.15 Aneurysm clipping during the very acute stage of SAH allows for prompt administration of adequate fluid from the time that anesthesia was induced; however, the same fluid management is difficult in patients who have undergone acute surgery because of a risk of aneurysm rerupture before operation. Comparing the changes in cBV in Groups A and B, we suggest that aneurysm clipping during the very acute stage of SAH may avoid cBV depletion by the prompt administration of fluid beginning during the period of anesthesia. This may explain why there was no significant change in cBV during the study period in Group A. We also suggest that relatively hypovolemic fluid therapy for 3 to 5 days after surgery may be essential for patients who have undergone surgery during the acute stage of SAH, whereas normovolemic fluid management is available for patients who have undergone surgery during the very acute stage of SAH due to a continuously stable cBV after operation.

Conclusions
Before surgery, cBV was significantly lower in the acute SAH group than in the control group. There was no signifi-
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icant difference in this parameter when comparing patients in the very acute group and those in the control group. Although there was a transient drop in cBV in the acute SAH group for at least 3 days after surgery, there was no significant change in cBV during the entire study period in the very acute SAH group. We suggest that normovolemic fluid management is appropriate for patients who undergo surgery during the very acute stage of SAH due to a continuously stable cBV after operation, whereas a relatively hypervolemic therapy administered for 3 to 5 days after surgery is necessary to prevent early hypovolemia for patients undergoing operation during the acute stage of SAH.

References

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