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Brief Report

Continuous Antihypertensive Therapy Throughout the Initial 24 Hours of Intracerebral Hemorrhage

The Stroke Acute Management With Urgent Risk-Factor Assessment and Improvement–Intracerebral Hemorrhage Study

Junpei Kobayashi, MD; Masatoshi Koga, MD; Eijirou Tanaka, MD; Yasushi Okada, MD; Kazumi Kimura, MD; Hiroshi Yamagami, MD; Satoshi Okuda, MD; Yasuhiro Hasegawa, MD; Yoshiaki Shiokawa, MD; Eisuke Furui, MD; Jyoji Nakagawara, MD; Kazuomi Kario, MD; Takuya Okata, MD; Shoji Arihiro, MD; Shoichiro Sato, MD; Kazuyuki Nagatsuka, MD; Kazuo Minematsu, MD; Kazunori Toyoda, MD; for the SAMURAI Study Investigators

Background and Purpose—A short duration (<24 hours) of antihypertensive therapy (AHT) after acute intracerebral hemorrhage (ICH) may be sufficient because active bleeding generally ceases within several hours. We aimed to determine the association between sequential systolic blood pressure (SBP) levels during AHT and outcomes in ICH patients.

Methods—In 211 hyperacute ICH patients who underwent AHT based on predefined protocol, the mean of hourly SBP (mSBP) measurements was calculated over 1 to 8 hours (first mSBP), 9 to 16 hours (second mSBP), and 17 to 24 hours (third mSBP) after the initiation of AHT. Outcomes included neurological deterioration (72-hour Glasgow Coma Scale decrease ≥2 or National Instititutes of Health Stroke Scale increase ≥4), hematoma expansion (>33%), and unfavorable outcome (3-month modified Rankin Scale score 4–6).

Results—The median first, second, and third mSBPs were 132, 131, and 137 mm Hg, respectively. A higher first mSBP (odds ratio [OR], 2.41; 95% confidence interval [CI], 1.34–4.69 per 10 mm Hg) or second mSBP (OR, 2.08; 95% CI, 1.20–3.80) was independently associated with neurological deterioration, and a higher second mSBP (OR, 1.40; 95% CI, 1.02–2.00) or third mSBP (OR, 1.45; 95% CI, 1.05–2.05) was associated with unfavorable outcome. None of the mSBPs was associated with hematoma expansion.

Conclusions—The continuation of AHT throughout the initial 24 hours after ICH may improve outcomes.

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Key Words: antihypertensives ■ cerebral hemorrhage ■ patient outcome assessment ■ stroke, acute

Blood pressure (BP) is often elevated after the onset of intracerebral hemorrhage (ICH). Elevated BP is associated with hematoma expansion,[1] neurological deterioration,[2] and unfavorable outcome.[3,4] The recent results of the Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial 2 (INTERACT2) demonstrated that BP lowering may be beneficial for patients with hyperacute ICH.[5] Although several trials, including the INTERACT2 and Antihypertensive Treatment of Acute Cerebral Hemorrhage II, required strict BP lowering during the initial ≥24 hours,[5,6] the appropriate duration of antihypertensive therapy (AHT) in acute ICH is not clear. Hematoma expansion generally occurs within the initial several hours.[7] Therefore, we hypothesized that AHT duration <24 hours may be sufficient to prevent hematoma expansion and improve clinical outcomes. We aimed to determine if the hourly systolic BP (SBP) levels during 1 to 8, 9 to 16, and 17 to 24 hours after the initiation of AHT are associated with different outcomes.

Methods

This study was a subanalysis of the Stroke Acute Management with Urgent Risk Factor Assessment and Improvement (SAMURAI)-ICH

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study, which was a prospective, multicenter, observational study. Details of SAMURAI-ICH were described previously.[8,9] The predefined standardized protocol of AHT was used to lower and maintain SBP from 120 to 160 mm Hg during the initial 24 hours. BP was measured hourly for 24 hours, as well as at 48 and 72 hours. The hourly SBP measurements were averaged over 1 to 8 hours, 9 to 16 hours, and 17 to 24 hours after the initiation of AHT, and these values are referred to as the first, second, and third mean SBPs (mSBPs), respectively.

Outcomes included hematoma expansion (>33% in volume from baseline to 24 hours), neurological deterioration (a decrease ≥2 in Glasgow Coma Scale score or an increase ≥4 in National Instititutes of Health Stroke Scale score from baseline to 72 hours), and unfavorable outcome (modified Rankin Scale score 4–6 at 3 months). Multivariate logistic regression analysis was performed to determine the associations between the 3 different outcomes and each hourly SBP during the first 24 hours, SBPs at 48 and 72 hours, and first, second, and third mSBPs. The regression model was adjusted for known predictors of outcomes and interaction terms between the covariates of interest. Details of study methods are available in the online-only Data Supplement.

Results

We enrolled 211 patients (81 women; median age, 65 [interquartile range, 58–74] years) in the SAMURAI-ICH study.[8] The first, second, and third mSBPs [expressed as median (interquartile range)] were 132 (126–138), 131 (125–140), and 137 (130–144) mm Hg, respectively. Baseline characteristics are listed in Table I in the online-only Data Supplement. Briefly, hematoma expansion was observed in 36 patients (17%), neurological deterioration in 17 (8%), and unfavorable outcome in 87 (41%).

SBP course >24 hours was higher in those with neurological deterioration than in those without it (*P* trend=0.041), and there were no significant differences in SBP course over the entire 24 hours between those with and without hematoma expansion (*P* trend=0.568) and between those with and without unfavorable outcome (*P* trend=0.150; see Figure). However, SBP in the last 12 hours of AHT was lower in those without unfavorable outcome (*P* trend=0.027). The association between hourly SBP and outcomes demonstrated that neurological deterioration was significantly related to high SBP at 4, 8, 13, 15, and 17 hours, and unfavorable outcome was significantly related to high SBP at 4, 15, 19, and 22 hours (Figure I in the online-only Data Supplement). SBP levels at 48 and 72 hours were not significantly related to any outcome (data not shown).

The results of multivariable logistic regression analyses based on the 3 mSBP levels are presented in the online-only Data Supplement. There were no significant interaction terms between covariates from logistic regression models predicting outcomes. The first mSBP (odds ratio [OR], 2.41; 95% confidence interval [CI], 1.34–4.69 per 10 mm Hg) and the second mSBP (OR, 2.08; 95% CI, 1.20–3.80) were independently associated with neurological deterioration. Furthermore, the second mSBP (OR, 1.40; 95% CI, 1.02–2.00) and the third mSBP (OR, 1.45; 95% CI, 1.05–2.05) were independently associated with unfavorable outcome, although none of the mSBPs was associated with hematoma expansion.

Discussion

The first major finding of this study was that mSBPs during the first 16 hours of AHT were independently associated with neurological deterioration. The second major finding was that mSBPs during the last 16 hours of ATH were independently associated with unfavorable outcome. An additional important finding was that mSBP in the first, second, or third 8-hour period was not associated with hematoma expansion.

AHT has been performed during the initial ≥24 hours in recent successful trials, including INTERACT2.[5] However, it may be practical to shorten the time period of AHT for strict BP control. Hematoma expansion is an important predictor of mortality and poor functional outcome after ICH[1] and has been shown by pathological studies to occur within the initial several hours.[10] A previous study at our institute based on CT showed that hematoma expansion was identified in 36% <3 hours of ICH onset, in 15% to 16% between 3 and 12 hours, in 6% between 12 and 24 hours, and in none after ≥24 hours.[7] Thus, we hypothesized that SBP levels of the early hours (0–3), but not of the later hours (12–24), may affect chronic outcomes when AHT was given for the first 24 hours. Because the present results did not support this hypothesis, BP levels should be controlled throughout the first 24 hours after ICH onset.

Our results on the association between SBP and outcomes were unexpected with a lack of connection to hematoma expansion. INTERACT2 also demonstrated that intensive BP lowering did not reduce the rate of hematoma expansion or neurological deterioration, but tended to improve functional outcome.[5] Perihematomal edema formation may be a potential mechanism to connect high BP levels during the later hours with poor outcomes.[11] Another potential explanation for our results might be that 11% of our study patients were taking antithrombotic medications, and active bleeding in these patients might be prolonged. Therefore, a longer duration of AHT might be warranted.

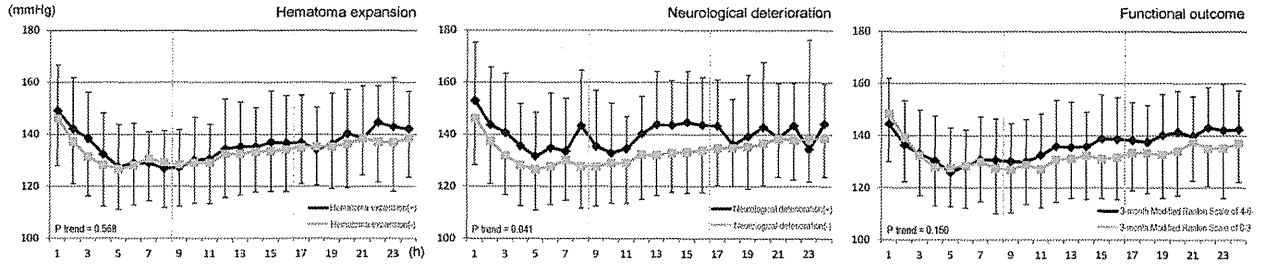

Figure. Time course of systolic blood pressure (SBP) during the initial 24 hours of antihypertensive therapy. Hourly means and 95% confidence intervals of SBP are shown.

In conclusion, the continuation of AHT during ≥24 hours after ICH onset may improve clinical outcomes in patients with hyperacute ICH.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Continuous antihypertensive therapy throughout the initial 24 hours of intracerebral hemorrhage: the SAMURAI-ICH Study

Supplemental detailed explanation of Methods

The Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI)-ICH study was a prospective, multicenter, observational study in 10 Japanese stroke centers to determine if BP lowering therapy for acute hypertension in patients with ICH was safe and feasible. We enrolled spontaneous supratentrial ICH patients, who were treated within 3 hours of onset between July 2009 and June 2011. The following inclusion criteria were employed: age ≥20 years; total Glasgow Coma Scale (GCS) score ≥5; initial SBP >180 mm Hg on two repeat measurements at least 5 minutes apart; computed tomography (CT) within 2.5 hours of onset that demonstrated a supratentorial intraparenchymal hematoma with a volume <60 mL measured manually; and absence of extensive intraventricular hemorrhage associated with intraparenchymal hemorrhage. Written informed consent was obtained from each patient, their legally authorized representative or their next of kin. The study was approved by each institutional ethics and hospital management committee. We excluded patients who met the following criteria: uncertain time of symptom onset; previously known cerebral neoplasms, arteriovenous malformation, or aneurysms; intracerebral hematoma considered to be related to trauma; ICH located in infratentorial regions such as the pons or cerebellum; isolated intraventricular hemorrhage; extensive intraventricular hemorrhage associated with intraparenchymal hemorrhage; candidates for immediate surgical intervention for ICH; current pregnancy, parturition within previous 30 days or active lactation; any history of bleeding diathesis or coagulopathy; use of warfarin with prothrombin time international normalized ratio 1.7 or more; a platelet count less than 50 000/ml; or inappropriate candidate judged by attending neurologist or neurosurgeon.

The predefined standardized protocol of AHT was used to lower and maintain the SBP level below 160 mmHg but above 120 mmHg. Intravenous nicardipine was titrated with an initial dose of 5 mg/h starting within 3 hours of symptom onset and continuing for 24 hours. BP and pulse rate were measured every 15 minutes during the initial 2 hours and every 60 minutes for the next 22 hours, as well as at 48 and 72 hours. Bolus infusion of 1mg nicardipine was allowed prior to the titrating infusion. Titrating of intravenous nicardipine was started within 3 h of symptom onset and continued for 24 h to achieve and maintain the target SBP level below 160mmHg and above 120mmHg. Intravenous nicardipine was initiated at a rate of 5 mg/h. If SBP was not reduced to 160mmHg or less after 15 min, the infusion dose was increased by another 2.5 mg/h. The 2.5 mg/h increments continued every 15 min until the maximum dose of 15 mg/h was reached. If SBP was more than 160mmHg despite infusion of the maximum nicardipine dose for 30 min, other antihypertensive

drugs including intravenous nitroglycerin and diltiazem were used additionally or alone. Once the target SBP was reached, the infusion rate was adjusted by 1–2.5 mg/h to maintain SBP in the target range. If SBP fell below 120mmHg, nicardipine was reduced until the rate of infusion was 0 mg/h, and was not restarted unless SBP rose above 160mmHg. BP management after the first 24 h was at the primary neurologist's discretion. To test our hypothesis, the hourly SBP measurements were averaged over 1 to 8 hours, 9 to 16 hours and 17 to 24 hours after the initiation of AHT, and these values are referred to as the 1^{st}, 2^{nd} and 3^{rd} mean SBPs, respectively.

The patients' clinical characteristics, including sex, age, cardiovascular risk factors, and comorbidities were recorded. Routine blood biochemistry examinations were performed on admission. Neurological manifestations were assessed using the GCS score and the National Institutes of Health Stroke Scale (NIHSS) score on admission and 72 hours after admission. Functional outcome was evaluated using the modified Rankin Scale (mRS) score. Hematoma volume was evaluated with non-contrast CT on admission and 24 (±6) hours after the initiation of AHT. The ABC/2 (length×width×height/2) method was used to determine hematoma volume.

Outcomes included hematoma expansion (>33% increase in volume from baseline to 24 hours), neurological deterioration (a decrease in GCS score of ≥2 or an increase in NIHSS score of ≥4 from baseline to 72 hours), and unfavorable outcome (mRS score of 4-6 at 3 months). Patients who received surgical intervention for ICH within the initial 72 hours were considered to have neurological deterioration, regardless of their GCS or NIHSS scores. Those who received surgical intervention for ICH during hospitalization were considered to have unfavorable outcome, regardless of their mRS score.

Supplementary Tables

Supplementary Table I. Baseline characteristics

Total, n	211
Women, n (%)	81 (38.4)
Age, y	65.6±12.0
Body height, cm	160.4±9.9
Body weight, kg	61.6±14.9
Body mass index, kg/m^2	23.7±4.2
Risk factors, n (%)	
Hypertension	176 (83.4)
Diabetes mellitus	29 (13.7)
Dyslipidemia	87 (41.2)
Alcohol intake	57 (27.0)
Co-morbidity	
Liver cirrhosis	10 (4.7)
Renal failure on hemodialysis	23 (10.9)
History of stroke/TIA	26 (12.3)
Ischemic stroke or TIA	19 (9.0)
Hemorrhagic stroke	10 (4.7)
Prior medication, n (%)	
Antiplatelet	22 (10.4)
Anticoagulant	2 (0.9)
Systolic blood pressure, mmHg	201.8±15.7
Diastolic blood pressure, mmHg	107.9±15.0
Pulse rate, per minute	81.8±16.1
Hematoma volume, ml, median (IQR)	10.2 (5.6-19.2)
Hematoma location, n (%)	
Putamen	112 (53.1)
Thalamus	75 (35.5)
Subcortex	12 (5.7)
Mixed	10 (4.7)
Caudate nucleus	1 (0.5)
Internal capsule	1 (0.5)
Admission NIHSS score, median (IQR)	13 (8-17)

TIA, transient ischemic attack; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale.

Data are mean±standard deviation unless otherwise stated.

This table is cited from Reference No 1.

Supplementary Table II. Results of multivariate regression to predict outcomes for a 10-mmHg increment in each mSBP.

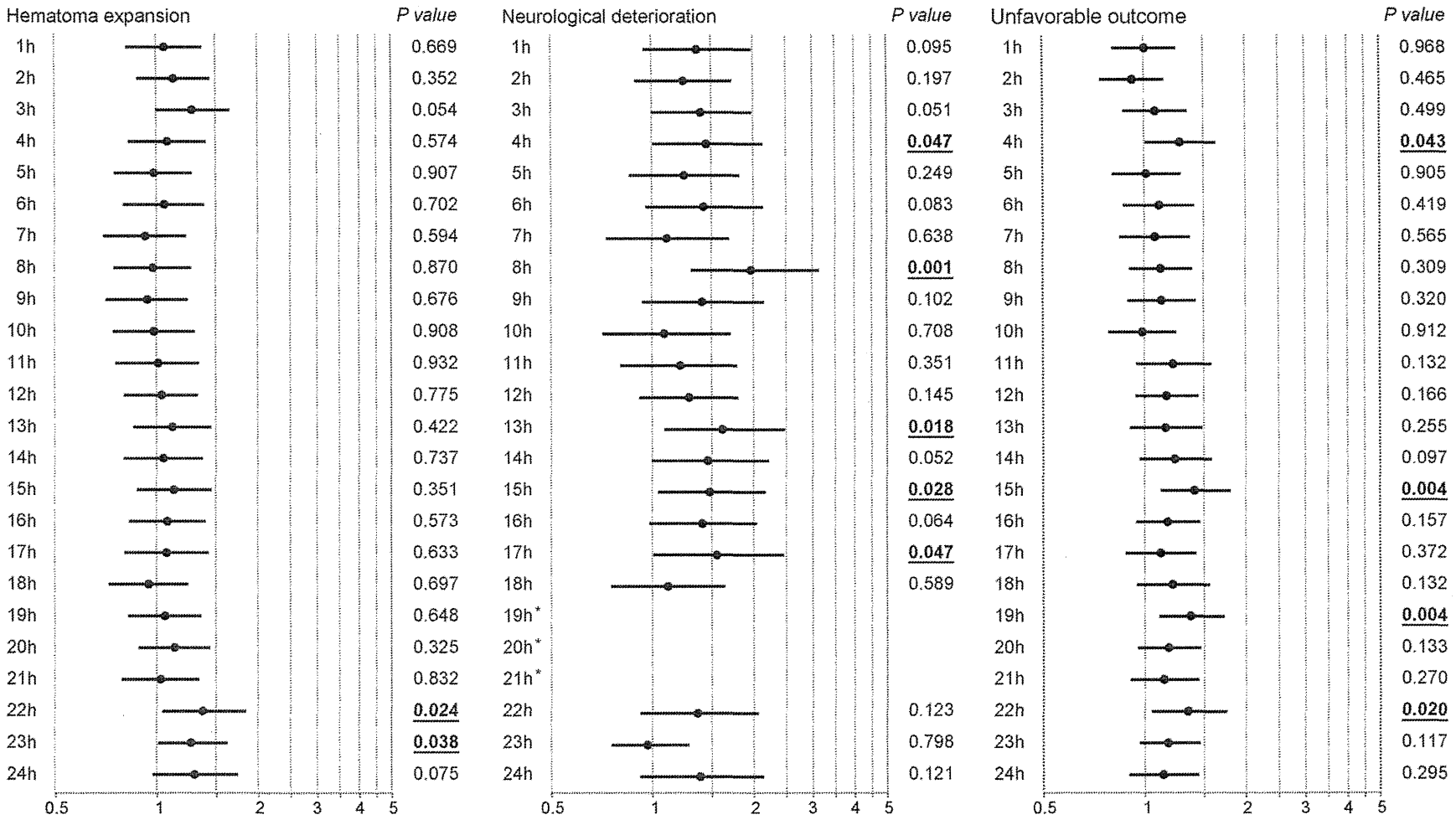
	1st mSBP		2nd mSBP		3rd mSBP	
	Estimated OR (95% CI)					
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Hematoma expansion	1.29 (0.92-1.82)	1.20 (0.79-1.83)	1.22 (0.88-1.70)	1.17 (0.81-1.71)	1.23 (0.88-1.73)	1.29 (0.89-1.89)
Neurological deterioration	2.01 (1.26-3.31)	2.41 (1.34-4.69)	2.22 (1.34-3.87)	2.08 (1.20-3.80)	1.29 (0.79-2.09)	1.38 (0.82-2.34)
Unfavorable outcome	1.01 (0.78-1.32)	1.19 (0.83-1.71)	1.67 (1.27-2.25)	1.41 (1.02-2.00)	1.67 (1.27-2.25)	1.45 (1.05-2.05)

OR indicates odds ratio; CI, confidence interval; mSBP, mean systolic blood pressure.

Adjusted for sex, age, prior antithrombotic medication, initial systolic blood pressure, initial pulse rate, initial National Institutes of Health Stroke Scale score, onset to treatment time, initial hematoma volume and baseline serum glucose level.

Supplementary Figure

Supplementary Figure I



SBP indicates systolic blood pressure; ICH, intracerebral hemorrhage.

The odds ratio per 10 mmHg with 95% confidence interval were adjusted for sex, age, prior antithrombotic medication, initial SBP, initial pulse rate, initial

National Institutes of Health Stroke Scale score, onset to treatment time, initial hematoma volume, and baseline serum glucose level. Bold and underline values indicate $P<0.05$.

*Multivariate analyses to determine the association between neurological deterioration and hourly SBP at 19, 20 and 21 hours could not be reliably performed due to missing SBP data at these time points in one patient with neurological deterioration who had antithrombotic medication prior to ICH. The remaining 16 patients with neurological deterioration did not take antithrombotic medication prior to ICH.

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Systolic blood pressure lowering ≤160mmHg and achieved systolic blood pressure in hyperacute intracerebral hemorrhage: the SAMURAI-ICH study

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Objective:

To determine the effects of systolic BP (SBP) lowering ≤160 mmHg using intravenous nicardipine and the association of achieved SBP with clinical outcomes in patients with for hyperacute intracerebral hemorrhage (ICH).

Methods:

This is a prospective, multicenter, observational study. Hyperacute (<3 h from onset) ICH patients with initial SBP >180 mm Hg, GCS ≥5, and hematoma volume <60 ml were initially treated with intravenous nicardipine to maintain SBP between 120 and 160 mmHg with 24-h frequent BP monitoring. The endpoints were neurological deterioration within 72 h [GCS decrement ≥ 2 or NIHSS increment ≥ 4; estimated 90% confidence interval (CI) on the basis of previous studies: 15.2-25.9%], serious adverse effects (SAE) to stopping intravenous nicardipine within 24 h (1.8-8.9%), hematoma expansion >33% at 24 h (17.1-28.3%), mRS ≥4 (54.5-67.9%) and death at 3 months (6.0-13.5%).

Results:

We enrolled 211 patients (81 women, 65.6±12.0 years old). At baseline, BP was 201.8±15.7/107.9±15.0 mmHg. Median hematoma volume was 10.2 ml (interquartile range 5.6-19.2), and NIHSS score was 13 (8-17). Neurological deterioration was identified in 17 patients (8.1%), SAE in two (0.9%), hematoma expansion in 36 (17.1%), mRS 4 or more in 87 (41.2%), and death in four (1.9%). All the results were equal to or below the estimated lower 90% CI. On multivariate regression analyses, mean achieved SBP was independently associated with neurological deterioration (odds ratio, 4.45;

95% confidence interval, 2.03-9.74 per 10 mm Hg increment), hematoma expansion (1.86; 1.09-3.16), and unfavorable outcome (2.03; 1.24-3.33) after adjusting for known predictive factors.

Conclusions:

SBP lowering to ≤160 mmHg using nicardipine appears to be well tolerated and feasible for hyperacute ICH. High achieved SBP after standardized antihypertensive therapy was independently associated with poor clinical outcomes. The final results were cited in J Hypertens (2012;30:2357-2364) and Stroke (2013;44:1846-1851).

CORRELATION BETWEEN ANTI-THROMBOTIC DRUGS AND HEMATOMA EXPANSION IN ACUTE INTRACEREBRAL HEMORRHAGE UNDER STRICT BLOOD PRESSURE-LOWERING MANAGEMENT: SAMURAI-ICH STUDY

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Background Few reports have documented the effect of pretreatment of anti-thrombotic agents on hematoma expansion in patients with intracerebral hemorrhage (ICH) under strict blood pressure-lowering management in the acute phase. **Methods** Patients (n=211) with hematoma in the supra-tentorial region were enrolled. Continuous intravenous administration of the anti-hypertensive drug nicardipine was commenced within 3 h of ICH onset at 10 hospitals in Japan, and systolic blood pressure was controlled between 120 and 160 mmHg. The correlation between pretreatment of anti-thrombotic agents and hematoma expansion (growth volume and rate 24 h after admission) was analyzed. **Results** Subjects (n=211; 81 females, mean age, 65.6±12.0 years) had a median NIHSS score on admission of 13. Twenty-four patients were taking anti-thrombotic agents on admission, 14 aspirin alone, 1 aspirin+dipyridamole, 2 aspirin+cilostazol, 1 aspirin+clopidogrel, 2 ticlopidine alone, 2 cilostazol alone, and 2 warfarin. When divided into 3 groups according to hematoma volume on admission (≤ 3.0 ml, 3.1-11.9 ml, > 11.9 ml), a significant difference (p=0.008) was observed between patients with and without pretreatment of anti-thrombotic agents (mean growth volume 24 h after admission: not taking anti-thrombotic agents, 4.73 ml: taking anti-thrombotic agents, 12.15 ml) only in the 3rd tertile group (volume > 11.9 ml). By three months after discharge, four deaths unrelated to anti-thrombotic agents had occurred. **Conclusions** Pretreatment of anti-thrombotic agents is likely significantly related to hematoma expansion in ICH patients with higher hematoma volume (> 11.9 ml) on admission under strict blood pressure management in the acute phase.

Key words anti-thrombotic drugs; intracerebral hemorrhage; hematoma expansion; strict blood pressure-lowering management; acute phase; SAMURAI-ICH Study

Intravenous nicardipine dosage for blood pressure lowering in acute intracerebral hemorrhage: the SAMURAI-ICH study

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Abstract

Purpose: Intravenous nicardipine is commonly used to reduce elevated blood pressure (BP) in acute intracerebral hemorrhage (ICH). We determined factors associated with nicardipine dose and the association of the dose with clinical outcomes in hyperacute ICH.

Methods: Hyperacute (<3 h from onset) ICH patients with initial systolic BP (SBP) >180 mmHg were registered in a multicenter observational study (the SAMURAI-ICH study). All patients initially received 5mg/h of intravenous nicardipine to lower BP. The dose was adjusted to maintain SBP between 120 and 160 mmHg based on BPs measured every 15 min during the initial 2 h and every 60 min in the following 22 h. Maximum hourly and total doses during the initial 24 h were calculated. Associations of the doses with neurological deterioration (a decrease of ≥2 in GCS or an increase of ≥4 in NIHSS score at 72 h after treatment initiation), hematoma expansion (>33% from baseline to 24 h), and unfavorable outcome (modified Rankin Scale score 4–6 at 3 months) were assessed.

Results: Of 211 patients in the registry, 206 patients (81 women, 65.8±11.8 years old) whose nicardipine data were available throughout 24-h observation were studied. Initial BP was 201.9±15.9/107.9±15.1 mmHg. Median time to reach target SBP range was 30 min (IQR 15-45). Maximum and total doses were 9.1±4.2mg/h and 123.7±100.2mg/day, respectively. Multivariate analyses revealed that male sex [standardized regression coefficient (β)=0.20, p=0.0030 for maximum dose; β=0.25, p=0.0002 for total dose], age (β= -0.28, p=0.0002; β= -0.25, p=0.0005) and initial SBP (β=0.19, p=0.0018; β=0.18, p=0.0021) were independently associated with both maximum and total doses. Body weight (β=0.20, p=0.0084) was independently associated with total dose. After multivariate adjustment, maximum dose (per 1mg/h; OR 1.25, 95% CI 1.09-1.45; p=0.0022) was independently and total dose (per 10mg/day; OR 1.06, 95% CI 0.998-1.132; p=0.0555) tended to be associated with neurological deterioration. Nicardipine dose was not associated with hematoma expansion and unfavorable outcome.

Conclusions: Nicardipine dosage is roughly predictable with sex, age, body weight and initial SBP in acute ICH. Maximum hourly nicardipine dose was associated with neurological deterioration.

Key words: stroke, acute; intracerebral hemorrhage; blood pressure; hypertension; nicardipine dose; calcium channel blocker

Clinical significance of antihypertensive therapy throughout the initial 24 hours in hyperacute intracerebral hemorrhage: The SAMURAI-ICH Study

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BACKGROUND and PURPOSE: Blood pressure (BP) lowering may be beneficial for patients with hyperacute intracerebral hemorrhage (ICH). Although several trials including INTERACT 2 and ATACH II have a design of the strict BP lowering during the initial 24 hours, shorter duration may be enough since active bleeding may not last 24 hours. We aimed to examine the associations between sequential systolic BP (SBP) levels during antihypertensive treatment (AHT) and clinical outcomes in acute ICH patients.
METHODS: Hyperacute (<3 hours from onset) ICH patients with initial SBP >180 mmHg were registered in a prospective, multicenter, observational study, the SAMURAI-ICH study (Koga J Hypertens 2012;30:2357). All patients received intravenous AHT, based on a predefined standardized protocol to lower and maintain SBP between 120 and 160 mmHg using intravenous nicardipine. BPs were measured hourly in the initial 24 hours. The mean of 8 SBP levels during 1 to 8, 9 to 16, and 17 to 24 hours after the initiation of AHT were calculated, and referred to as the 1st, 2nd and 3rd mSBPs, respectively. The associations between mSBPs and neurological deterioration (a decrease of ≥2 in GCS or an increase of ≥4 in NIHSS score), hematoma expansion (>33% in volume), and unfavorable outcome (modified Rankin Scale score 4–6 at 3 months) were assessed.
RESULTS: 211 patients (81 women, median age 65 [IQR, 58–74] years, median initial NIHSS score 13 [8–17]) were included. The baseline hematoma volume was 10.2 (5.6-19.2) mL. Neurological deterioration was observed in 17 patients (8%), hematoma expansion in 36 (17%), and unfavorable outcome in 87 (41%). The 1st, 2nd, and 3rd mSBPs were 132 (126-138), 131 (125-140), and 137 (130-144) mmHg, respectively. The 1st (OR 2.41, 95%CI 1.34–4.69 per 10-mmHg) and 2nd mSBPs (2.08; 1.20-3.80) were independently associated with neurological deterioration (17 patients) and the 2nd (1.40; 1.02–2.00) and 3rd mSBPs (1.45; 1.05–2.05) were associated with unfavorable outcome (87 patients), although no mSBPs were associated with hematoma expansion (36 patients).CONCLUSIONS: The continuation of AHT throughout the initial 24 hours may ameliorate clinical outcomes.

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超急性期脳出血における降圧療法開始からの経過時間毎の血圧と転帰の関係
— Stroke Acute Management with Urgent Risk-factor Assessment and Improvement (SAMURAI)- Intracerebral Hemorrhage 研究 —

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[目的] 超急性期脳出血への積極的降圧療法の有効性が示唆されている。血腫増大が懸念される発症直後の数時間のみで十分かもしれないが，どの時点まで継続すべきか不明である。本研究の目的は，降圧開始後 24 時間までの経過時間毎の収縮期血圧 (SBP) と転帰の関係を明らかにすることである。
[方法] 対象は，SAMURAI-ICH 研究 (Koga M, et al: J Hypertens 2012) に登録された 20 歳以上の天幕上脳出血，入院時 SBP≧180 mmHg，発症 3 時間以内にニカルジピン持続静注による降圧治療を開始可能であった症例である。治療開始後 24 時間は，目標 SBP120-160 mmHg に設定し，1 時間毎に血圧を測定した。評価項目は，早期神経学的悪化 (72 時間後 NIHSS-入院時 NIHSS≧4, 72 時間後 GCS-入院時 GCS≧2, 又は 72 時間以内の外科手術)，血腫拡大 (入院時，24 時間後 CT の比較上，33%以上の血腫量増加)，転帰不良 (発症 3 か月後 mRS 4-6)とした。治療開始後 1-8 時間, 9-16 時間, 17-24 時間の平均 SBP (1st mSBP, 2nd mSBP, 3rd mSBP) に加え，既知の転帰関連因子を用いて多変量解析を行った。
[結果] 症例は 211 例 (女性 81 例，年齢 65 歳 (58-74)，入院時 NIHSS 13 (8-17)，入院時血腫量 10.2mL (5.6-19.2), 初回 SBP 200 mmHg (189-213) であった。1st mSBP, 2nd mSBP, 3rd mSBP は，各々133±11 mmHg，132±12 mmHg，137±11 mmHg であった。多変量解析の結果，早期神経学的悪化と 1st mSBP (OR /10mmHg 2.42; 95%CI 1.34-4.69)，2nd mSBP (OR /10mmHg 2.08; 95%CI 1.20-3.80) が正の相関を示した。血腫拡大と各々の平均 SBP との間に，有意な関連はなかった。転帰不良と 2nd SBP (OR /10mmHg 1.41; 95%CI

1.02-2.00), 3rd mSBP (OR /10mmHg 1.45; 95%CI 1.05-2.05) が正の相関を示した。
[結論] 超急性期脳出血で SBP120-160 mmHg を目標に降圧を行うと，治療開始から 16 時間までの SBP 高値が早期神経学的悪化と，9-24 時間までの SBP 高値が転帰不良と独立して関連した。
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