Clinical Outcomes of Intracerebral Hemorrhage in Hemodialysis Patients

Noriaki Sakamoto[1,3], Eiichi Ishikawa[3], Kazuyasu Aoki[1,2], Yoji Uemae[1], Yoji Komatsu[1,3], Akira Matsumura[3]

Key words
- Chronic renal failure
- Hemodialysis
- Hypertension
- Intracerebral hemorrhage

Abbreviations and Acronyms
CI: Cerebral infarction
CRF: Chronic renal failure
CT: Computed tomography
GCS: Glasgow coma scale
HD: Hemodialysis
ICH: Intracerebral hemorrhage
IVH: Intraventricular hemorrhage
MB: Microbleed
MRI: Magnetic resonance imaging

From the [1]Department of Neurosurgery, Hitachi General Hospital, Ibaraki; [2]Department of Neurosurgery, Nerima Hikarigaoka Hospital, Tokyo; and [3]Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan

To whom correspondence should be addressed: Eiichi Ishikawa, M.D., Ph.D. [E-mail: e-ishikawa@md.tsukuba.ac.jp]

Citation: World Neurosurg. (2014) 81, 3/4:538-542.
http://dx.doi.org/10.1016/j.wneu.2013.10.033

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

BACKGROUND: **Chronic renal failure (CRF) is associated with a high incidence of stroke. In particular, the mortality rate for intracerebral hemorrhage (ICH) patients with hemodialysis (HD) due to advanced stage CRF is high, and the annual number of such cases is increasing. Therefore, we retrospectively investigated 5 years of clinical data from patients with ICH in our institution to reveal differences in the clinical courses of HD and non-HD patients and to identify risk factors for poor outcomes in ICH patients with HD.**

METHODS: **Three hundred sixty-six consecutive patients with nontraumatic spontaneous ICH, 91% of whom did not receive HD (non-HD group) and 9% of whom received HD for the treatment of CRF (HD group), were enrolled. Clinical data, including the presence of intraventricular hemorrhage (IVH), microbleeds, modified Rankin scale scores, previous medical disease history, the presence of HD, and the days on which ICH occurred, were evaluated.**

RESULTS: **In a comparison of HD patients and non-HD patients, the HD patients had higher rates of hematomas in the basal ganglia, IVH, use of antihypertensive drugs, antidiabetic drugs, and antiplatelet/anticoagulants. The mortality rate was higher in the HD group (44%) than in the non-HD group (21%). In the HD group, the risk factors associated with mortality were hematoma volume, the presence of IVH, and lack of antihypertensive drug use. Eighty-five percent of the ICH occurred on intermittent HD days or before the HD procedure on an HD day.**

CONCLUSIONS: **Mortality in ICH patients with HD was associated with lack of antihypertensive drug use. Therefore, strict control of blood pressure is needed in HD patients to prevent ICH, especially on intermittent HD days or before the HD procedure.**

INTRODUCTION

Chronic renal failure (CRF) is a worldwide public health problem that is associated with a high risk of occurrence of cardiovascular events (9, 19). Hemodialysis (HD) is performed in more than 90% of patients in advanced stages of CRF. The number of patients undergoing HD in Japan has increased from 1624.1 per million at the end of 2000 to 2279.5 per million in 2009. The total number of patients undergoing HD exceeded 281,996 in 2009; the highest rate since 1983 (17). The trend is similar in other countries, the total number of patients undergoing HD in the United States increasing from 281,355 in 2000 to 415,013 in 2010 (United States Renal Data System) (4, 26). Several studies have indicated that the incidence of ischemic and hemorrhagic events in the intracranial region (strokes) in patients with CRF is high (1, 7, 8, 10, 12, 14-16, 18, 21-23, 27). A single-center study in Japan showed that the frequency of intracerebral hemorrhage (ICH; 52% of 151 patients) in HD patients was higher than that of cerebral infarction (CI; 41%) between 1980 and 1996, whereas the rate of ICH (29%) between 1997 and 2002 was lower than that of CI (68%) (23). Intensive control of hypertension, diabetes, and hyperlipidemia may have reduced the incidence of ICH. However, the clinical status of HD patients with ICH remains severe—ICH being a common cause of death in patients with HD. The incidence of death due to ICH is two- to threefold higher than that due to CI (8, 10, 12, 15).

In the present study, we retrospectively investigated 5 years worth of clinical data from patients with ICH treated with or without HD at our institution. We reveal the differences in the clinical courses of HD and non-HD patients and identify the risk factors for poor outcomes in patients with ICH undergoing HD.

PATIENTS AND METHODS

We conducted a single-center retrospective study based on a review of medical records. The records of 366 consecutive patients with nontraumatic spontaneous ICH, who were admitted to the neurosurgical department of Hitachi General Hospital between January 2007 and December 2011, were examined. Patients with ICH due to secondary causes, such as ruptured aneurysm, primary ischemic stroke, arteriovenous malformation, or tumor, were excluded from this study. In all patients, a computed tomography (CT) scan was performed on admission. Magnetic resonance imaging (MRI) was performed on admission or after surgery for all patients with ICH except for deceased patients whose condition had been rapidly deteriorating.

The following clinical information, including baseline characteristics, was

collected: age, gender, location/side of the hematoma, volume of the hematoma, presence of intraventricular hemorrhage (IVH), microbleeds (MBs) as seen on MRI scans, modified Rankin scale scores at admission/discharge, type of surgical operation, use of antihypertensive or antidiabetic drugs and antiplatelets/anticoagulants, primary renal disease, current history of HD, and the day of the week on which the ICH occurred in relation to HD. The hematoma volume in each case was determined by one of the authors (N.S.) from CT scans obtained at the onset as follows: the maximum transverse diameter × the maximal anteroposterior diameter × the maximal superoinferior diameter × 1/2. Presence of IVH was also assessed using CT scans. Hematoma volume in the lateral ventricle was not included in the calculation of volume of hematoma in the present study.

The values are expressed as means ± standard deviation. Differences in patient data were evaluated using univariate logistic analysis as well as χ^2 test, Fisher's test, or Student's t-test. P values less than 0.05 were considered to indicate statistical significance. All calculations were performed using JMP 5 software (SAS Corp., Cary, North Carolina, USA). Multivariate logistic analysis was performed for data in which P values were less than 0.1 on univariate logistic analyses. Differences were considered statistically significant if the P value was <0.05 in this analysis as well. In the logistic analyses, continuous variables were dichotomized in terms of their mean or median values.

Table 1. Characteristics of Patients with ICH ($n = 366$)

	HD ($n = 32$)		Non-HD ($n = 334$)		Logistic Analysis (P Value, Exp) Univariate		Multivariate	
Background								
Median age (years)	64 (28–84)		69 (8–95)		(>0.1, Student's t-test)			
Age (≤65 years)	16	50%	134	40%	0.2801	(1.493)	—	—
Gender (female)	16	50%	135	40%	0.2952	(1.474)	—	—
Use of AHD (yes)	23	72%	108	32%	0.0001	5.348	0.0009	4.934
Use of ADD (yes)	13	41%	66	20%	0.0080	2.778	0.1880	(1.846)
Use of AP/AC (yes)	13	41%	58	17%	0.0023	3.256	0.0068	3.299
One drug/two drugs	9/4		45/13					
After ICH								
Location (BG)	27	84%	192	57%	0.0055	3.994	0.0087	4.130
BG (putamen, thalamus)/lobar (subcortical)/others (cerebellum, brainstem)	27/3/2		192/70/72					
Laterality (Left sided)	18	58%	166	56%	0.4800	(1.300)	—	—
Presence of IVH	17	53%	114	34%	0.0357	2.187	0.7968	(1.127)
Operation (yes)	10	31%	70	21%	0.2128	(1.654)	—	—
Surgical hematoma evacuation/hematoma drain placement in the lateral ventricle	8/2		45/25					
Patient outcome								
Outcome (mRS) (VI)	14	44%	71	21%	0.0054	2.881	0.3150	(1.741)
(V+VI)	22	69%	122	37%	0.0008	3.823	0.0093	4.338
I/II/III/IV/V/VI	2/5/0/3/8/14		51/92/22/47/51/71					

ADD, antidiabetic drugs; AHD, antihypertensive drugs; AP/AC, antiplatelets or anticoagulants; BG, basal ganglia; HD, hemodialysis; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; mRS, modified Rankin scale.

RESULTS

Comparisons Between HD and Non-HD Patients

Table 1 shows the clinical characteristics of the patients in the study. A total of 366 patients were admitted to our hospital with a diagnosis of ICH during the study period. They were divided into two groups: 32 patients (9%) with CRF who received HD (HD group) and 334 patients who did not receive HD treatment (non-HD group). All the patients with CRF in this study were on HD. Surgical hematoma evacuation was performed in 25% of the HD patients and in 13.5% of the non-HD patients, whereas a hematoma drain was inserted into the lateral ventricle of 6% and 7.5% of HD and non-HD patients, respectively. There were no differences in patient age, gender, laterality of hematoma, and surgical procedure between the two groups. The HD group had higher rates of hematomas in the basal ganglia (84% in the HD group vs. 57% in the non-HD group; $P < 0.05$), IVH (53% vs. 34%; $P < 0.05$), use of antihypertensive drugs (72% vs. 32%; $P < 0.01$), use of antidiabetic drugs (41% vs. 20%; $P < 0.01$), and use of antiplatelets/anticoagulants (41% vs. 17%; $P < 0.01$). The mortality rate (modified Rankin scale score VI) was higher in the HD group (44%) than in the non-HD group (21%). There were no significant differences in the existence of cerebral MBs between the two groups, as seen on MRI ($P > 0.1$, Fisher's direct test). As seen in Table 1, univariate logistic analysis showed that hematoma location, presence of IVH, use of antihypertensive drugs, use of antidiabetic drugs, use of antiplatelets/anticoagulants, patient mortality, and the number of patients with modified Rankin scale score ≥5 were significantly different between the HD and non-HD groups. Similar results were also shown using the χ^2 test or Fisher's test (data not shown). Multivariate logistic analysis showed that hematoma location, use of antihypertensive drugs, use of antiplatelets/anticoagulants, and number of patients with modified Rankin scale score ≥5 were different between the two groups (Table 1).