## **ARTICLE IN PRESS**

### Association between Delirium and Prehospitalization Medication in Poststroke Patients

Ryuichiro Hosoya,\* † Yohei Sato, MD, PhD,‡ Emika Ishida,§ Haruna Shibamoto, | Seiichi Hino,\* Hiroaki Yokote, MD, PhD,¶ and Tomoyuki Kamata, MD, PhD#

Purpose: Medication is an important risk factor for delirium; however, the association between delirium and prehospitalization medication is unclear. We investigated the association between prestroke medication and poststroke delirium. Materials and Methods: All patients hospitalized in the stroke care unit from September 2011 to September 2012 were selected, and their delirium symptoms, patient information, and pre- and poststroke medications were analyzed. Delirium was defined as a score of 4 or higher on the Intensive Care Delirium Screening Checklist. Factors that were related to delirium were extracted using univariate analysis, and the independent risk factors were determined using multivariate analysis. Results: Of the 269 patients analyzed, 97 (36%) experienced delirium. Univariate analysis revealed significant differences between the delirium and nondelirium groups in age, dementia, previous cerebrovascular disease, craniotomy, all insertion-tube types, and 6 categories of prestroke medication. Prestroke polypharmacy was associated with poststroke delirium (P = .002). Multivariate analysis showed that taking antianxiety agents or sleep aids was an independent risk factor for delirium (odds ratio: 3.17, 95% confidence interval: 1.16-8.82). Conclusions: The present study suggests that prestroke medication affects the onset of poststroke delirium. These findings can contribute to the prediction and prevention of this condition. Key Words: Derilium—stroke—medication—polypharmacy—sleeping pill.

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From the \*Department of Pharmacy, Japanese Red Cross Musashino Hospital, Musashino, Tokyo, Japan; †Department of Clinical Pharmaceutics, Meiji Pharmaceutical University, Kiyose, Tokyo, Japan; ‡Department of Neurosurgery; §Department of Nurse, Japanese Red Cross Musashino Hospital, Musashino, Tokyo, Japan; ‡Department of Nursing, Faculty of Nursing, Mejiro University Medical Staff Training Center, Wako, Saitama, Japan; ‡Department of Neurology, Nitobe Memorial Nakano General Hospital, Nakano, Tokyo, Japan; and #Department of Neurology, Japanese Red Cross Musashino Hospital, Musashino, Tokyo, Japan.

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Author contributions: Conception/Design: Ryuichiro Hosoya, Yohei Sato, Emika Ishida, Haruna Shibamoto, Seiichi Hino, Hiroaki Yokote, and Tomoyuki Kamata. Provision of study material or patients: Ryuichiro Hosoya, Emika Ishida, Haruna Shibamoto, and Seiichi Hino. Collection and/or assembly of data: Ryuichiro Hosoya. Data analysis and interpretation: Ryuichiro Hosoya and Yohei Sato. Manuscript writing: Ryuichiro Hosoya. Final approval of manuscript: Yohei Sato.

Address correspondence to Yohei Sato, Department of Neurosurgery, Japanese Red Cross Musashino Hospital, 1-26-1 Kyonan-cho, Musashino, Tokyo 180-8610, Japan. E-mail: satonsrg@musashino.jrc.or.jp.

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#### Introduction

Control of the onset of delirium in acute care units is important in the treatment of disease. In particular, delirium following stroke is not only a mental disorder but also a hindrance to rehabilitation, and therefore to treatment of the stroke. The reported incident rate of poststroke delirium is 10%-27%,<sup>1,2</sup> and the cause is believed to be multifactorial. This condition is easy to overlook, because there are few guidelines regarding the prevention or treatment of delirium in stroke care units.<sup>3</sup> Carin-Levy et al reported that the risk factors for poststroke delirium were old age, severe disease, visual disorders, and anticholinergic medication.<sup>4</sup> In fact, medication usage is an important risk factor for delirium overall, and is related to 12-39% of all delirium cases.<sup>5</sup>

Delirium is classified into 3 types: hyperactive, hypoactive, and mixed.6 Hyperactive delirium is caused by the functional decline of γ-aminobutyric acid; hence, anticholinergic medication can induce hyperactive delirium via dopamine hyperfunction and decreased acetylcholine.<sup>7</sup> It is also known that the hyperactive type is frequently induced by the withdrawal of drugs, such as benzodiazepine receptor-operated medication, or of alcohol.8 In a review by Alagiakrishnan et al, drug classification was shown to be related to delirium, and polypharmacy (combinations of 5 or more drugs) in particular was a risk factor; indeed, it has been shown to be associated with delirium, independently of the effects of the specific drugs in the combination.<sup>5</sup> In elderly patients with altered pharmacokinetics and pharmacodynamics, polypharmacy is a high risk factor for delirium. Other studies have also found that it is a risk factor for delirium, falls, and mortality.9-11

To date, there have been many studies on the association between delirium and medication; however, the association between delirium and prehospitalization medication usage has not been addressed. Most inpatients have been prescribed medication before hospitalization, which may affect the patient's condition and symptoms after hospitalization. In addition, it is difficult for many stroke patients to take medicines. This in itself may induce delirium, further affecting the stroke treatment.

It is thus important to clarify the association between prehospitalization medication and posthospitalization delirium in patients with stroke, from the viewpoint of the control and prevention of delirium. Therefore, we investigated the association between prestroke medication and poststroke delirium in patients treated in a stroke care unit.

#### Materials and Methods

Database

All patients hospitalized in the stroke care unit at our hospital from September 2011 to September 2012 were

selected for this study. Patient identification numbers were extracted and registered using linkable anonymization. This study was approved by Clinical Study and Ethics Committee in Musashino Red Cross Hospital (Application number: 26036).

#### Patients with Delirium

We defined patients with a score of 4 or more on the Intensive Care Delirium Screening Checklist (ICDSC) as having delirium.<sup>12</sup> Information regarding patients with delirium and the time of delirium onset were extracted, and all patients were classified into 2 groups: delirium and nondelirium.

The ICDSC is used frequently as a screening tool for the diagnosis of delirium, as is the Confusion Assessment Method for the ICU. Gusmao-Flores et al reported that the pooled sensitivity of the ICDSC was 74% (95% confidence interval [CI]: 65.3%-81.5%), and the pooled specificity was 81.9% (95% CI: 76.7%-86.4%), whereas the same metrics for the Confusion Assessment Method for the ICU were 80.0% (95% CI: 77.1%-82.6%) and 95.9% (95% CI: 94.8%-96.8%), respectively. It was also reported that the sensitivity of the Japanese version of the ICDSC is higher when the cutoff value is set as 3 points. He used the cutoff value as 4 points that was the most common methods. It

#### Medication-Related Delirium

We investigated the medication taken before hospitalization, using the electric medical chart system. Information regarding medication was extracted from pharmacist and nurse reports. We classified the medication according to efficacy.

#### Exclusion Criteria

Patients younger than 20 years old were excluded from this study, because delirium in nonadult patients is different from that in adults; hence, the same delirium screening tool cannot be used. We also excluded patients with an unclear medication history.

#### Patient Information

Patient clinicodemographic information (gender and age), medical background (main disease, history of present illness, past medical history, and history of surgery), region of brain affected by stroke, and present treatments were investigated. Furthermore, information about insertion tubes (intubation tube, gastric tube, peripheral vein catheter, central vein catheter, ureter tube, ventricular drain, and spinal drain) and poststroke symptoms (paralysis, neglect, aphasia, and somnolence) were extracted.

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