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Division of Neurology

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General Summary

Our clinical research in 2014 was performed in the following areas: 1) neurodegenerative disease, 2) cerebrovascular disease, and 3) autoimmune disease.

Research Activities

Clinical researches

Neurodegenerative disease

1. Randomized, double-blind, placebo-controlled trial of vitamin D supplement to prevent deterioration in Parkinson's disease

Parkinson's disease (PD) is a debilitating movement disorder, and its incidence is growing because of the aging of societies worldwide. In our previous study, higher levels of 25-hydroxyvitamin D and the vitamin D receptor *FokI* CC genotype were associated with milder PD. We evaluated whether vitamin D3 supplementation inhibits PD progression subgrouped by vitamin D receptor genotypes without triggering hypercalcemia. A total of 114 patients with PD were randomly assigned to receive vitamin D3 supplements (n = 56; 1200 IU/day) or placebo (n = 58) for 12 months in a double-blind setting. In conclusion, vitamin D3 supplementation may prevent worsening of symptoms in patients with *FokI* TT or CT genotypes without triggering hypercalcemia.

2. Electroencephalogram in PD

In patients with PD, slow waves are typically demonstrated with electroencephalography (EEG), but considerably fast waves also appear with them. On the hypothesis that released cortex affected by the restraint from basal ganglia to the cerebral cortex generates the surplus activity as fast waves on the EEG. We measured PD with EEG to examine the local existence of fast waves and their correlation with slow waves.

3. Evaluation of autonomic symptoms in de novo PD (with self-assessment questionnaires)

We collected the Survey of Autonomic Symptoms and the Japanese Sialorrhea Clinical Scale for Parkinson's Disease and evaluated the Unified Parkinson's Disease Rating Scale, orthostatic hypotension, and [¹²³I]meta-iodobenzylguanidine (MIBG) myocardial scintigraphy in patients with de novo PD. The existence of orthostatic hypotension was not correlated with the complaints of lightheadedness. Before being treated, patients with PD had cold feet and constipation. The complaints of leaking of urine were correlated with orthostatic hypotension in patients with de novo PD.

4. The usefulness of dopamine transporter single-photon emission computed tomography for reassessment of parkinsonian disorders

Dopamine transporter (DAT) single-photon emission computed tomography (SPECT) has been available since 2014 in Japan. It is the method used to detect presynaptic dopamine neuronal dysfunction, which is a hallmark of neurodegenerative parkinsonian disorders. We verified the usefulness of DAT SPECT for reassessing parkinsonian disorders that were diagnosed with conventional neuroimaging methods. We believe DAT SPECT is useful for excluding drug-induced parkinsonism or vascular parkinsonism from neurodegenerative parkinsonian disorders.

5. The quantitative motion analysis using portable gait rhythmogram after cerebrospinal fluid drainage in idiopathic normal pressure hydrocephalus

We aimed to reveal the quantitative gait differences between idiopathic normal pressure hydrocephalus, PD, and normal controls using portable gait rhythmogram (PGR). The PGR revealed narrower and more monotonous step lengths in patients with idiopathic normal pressure hydrocephalus than in patients with PD or healthy control subjects. In addition, PGR detected gait improvements following cerebrospinal fluid (CSF) drainage in patients with a CSF drainage response. Thus, PGR can easily be used to analyze long durational gait in daily life and can usefully provide additional quantitative data on former measurements of CSF drainage.

6. Clinical characteristics of supine hypertension in de novo PD

Older age, akinetic-rigid motor subtype, and preexistent hypertension are independent risk factors for supine hypertension. Supine hypertension may be associated with peripheral sympathetic nervous denervation that is milder than that associated with orthostatic hypotension. As for global cognitive decline, supine hypertension is a far riskier comorbidity of early-stage PD than is orthostatic hypotension.

7. Blood pressure fluctuation and clinical features in de novo PD

In patients with PD, daily fluctuation of blood pressure has been previously reported. Our aim was to investigate the relationship between blood pressure fluctuation and clinical characteristics in de novo PD. We found a correlation between the nocturnal reduction of systolic blood pressure and cardiac MIBG uptake. These results may help reveal features of the autonomic symptoms of PD.

8. Dysphagia and vocal cord palsy in multiple system atrophy

In cases of advanced multiple system atrophy, symptoms that are not rare include dysphagia and vocal cord palsy. Vocal cord palsy is a life-threatening risk at the time of percutaneous endoscopic gastrostomy (PEG). We estimated dysphagia and vocal cord palsy with laryngoscope in cases of multiple system atrophy. In many cases vocal cord palsy was presented at the time of PEG. In such cases, PEG was performed safely with noninvasive positive pressure ventilation therapy.

9. The relevance of hyposmia and MIBG scintigraphy in multiple system atrophy

Findings of denervative olfactory failure in MIBG myocardial scintigraphy are useful for discriminating PD and multiple system atrophy (MSA). We examined the relationship between olfactory failure and MIBG myocardial scintigraphy in patients with MSA at our hospital.

Of patients with MSA, 17% showed findings of denervation on MIBG myocardial scin-

tigraphy and 11% showed olfactory failure. However, no patients showed both findings. Olfactory dysfunction and MIBG myocardial scintigraphy were not related in patients with MSA.

Cerebrovascular disease

1. Sonothrombolysis for hyperacute stroke with low-frequency and fluctuating-frequency transducer

A new 500 ± 200 -kHz transducer promoted higher penetration through the skull without any distractive effects, such as extra enhancement of sonographic power. This transducer enhanced thrombolytic effects in comparison with the power of a standard 500-kHz transducer.

2. Evaluation of right-to-left shunt with a novel probe attached to the cervix

The purpose of this study was to compare the diagnostic accuracy of a novel pasteable soft ultrasound probe (PSUP) with that of transesophageal echocardiography (TEE) for right-to-left shunt. Subjects were patients with ischemic stroke and transient ischemic attack who underwent TEE. First, we performed TEE with a standard protocol for detecting a right-to-left shunt. Then, monitoring with a PSUP was performed at a common carotid artery with a similar preparation and procedure to those of TEE. For the diagnosis of TEE, the PSUP had a sensitivity of 83%, a specificity of 93%, and accuracy of 91%. The PSUP may be useful for patients with an insufficient temporal bone window.

3. Clinical characteristics of vertebrobasilar dolicoectasia in patients with cerebral infarction

Vertebrobasilar dolicoectasia (VBD) is a rare condition characterized by significant expansion and elongation of the vertebrobasilar arteries. However, the association of VBD with cerebral infarction has not yet been studied. Our aim was to investigate the clinical characteristics of VBD in patients with cerebral infarction. We enrolled 103 patients; of these patients, 9 (6%) had VBD. Distinct characteristics of VBD in patients with cerebral infarction were a stroke in the posterior circulation and the absence of cardiac embolism. These characteristics may play an important role in the mechanism of VBD in patients with cerebral infarction.

4. The relationship between small-vessel disease and intracranial vessel resistance

The neurological deterioration associated with the enlargement of a lesion is often seen in patients with small-vessel disease. The aim of this study was to clarify the relationship between the size of lesions in small-vessel disease and the evaluated factors by the transcranial Doppler.

5. Clinical characteristics of recurrence of cardiogenic cerebral embolisms in the acute phase

When treatment with oral anticoagulants should be started for secondary prevention in patients with acute ischemic stroke is unclear. Our aim was to investigate the clinical characteristics of cerebral embolic stroke and its recurrence in the acute phase. Of the 72 patients examined only 40% had received oral anticoagulants before admission. Recurrence in the acute phase was observed in 13% of all patients, and symptomatic recurrence was observed in 10%.

6. Grade of cortical vessel signs on susceptibility-weighted imaging predicts outcomes in

acute stroke patients

Cortical vessel signs (CVSs) on susceptibility-weighted magnetic resonance imaging (SWI) are frequently observed in patients with an acute ischemic stroke. However, the clinical implications of this sign have not yet been clearly defined. We assumed the hypothesis that the grade of CVSs on SWI predicts outcomes in patients with acute stroke. As with grade of CVSs, the proportional rate of unfavorable patients gradually increased ($P < 0.01$). The grade of CVSs on SWI can predict outcomes in patients with acute stroke.

Autoimmune disease

1. Single photon emission computed tomography findings after vaccination against human papillomavirus in Japan

We demonstrated relative hypoperfusion areas in 3-dimensional stereotactic surface projections with single event effect (SEE) analysis were most prominent in the cingulate gyrus in patients after human papillomavirus (HPV) vaccinations. Our study strongly suggested that various clinical symptoms in patients with HPV vaccination associated with neuroimmunopathic syndrome were caused by central nervous system impairment after HPV vaccination.

Publications

Mitsumura H, Sakuta K, Bono K, Yamazaki M, Sengoku R, Kono Y, Kamiyama T, Suzuki M, Furuhashi H, Iguchi Y. Stiffness parameter beta of cardioembolism measured by carotid ultrasound was lower than other stroke subtypes. *J Stroke Cerebrovasc Dis.* 2014; **23**: 1391–5.

Mitsumura H, Miyagawa S, Komatsu T, Sakamoto Y, Kono Y, Furuhashi H, Iguchi Y. Transcranial color flow imaging can evaluate the severity of periventricular hyperintensity. *J Stroke Cerebrovasc Dis.* 2015; **24**: 112–6.