37th Mihara Award Memorial Lecture

Advanced multifaceted approach to improve clinical outcome of acute stroke patients

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Acute stroke therapy has undergone a major change by introduction of intravenous rt-PA therapy and mechanical thrombectomy, but only 10% of the patients can receive these treatments in our country. Therefore, many patients without revascularization therapy suffered from neurological deficits subsequently. As cerebral infarction occupies 70% of stroke in population ageing, it is an urgent issue to improve the prognosis of acute stroke patients.

The purpose of this study is to improve prognosis of patients with acute ischemic stroke by performing multifaceted interventional treatments. In this project, we will perform the 4 multilateral interventions as below;

<u>1. A nationwide project to promote endovascular therapy for acute stroke(RESCUE-Japan Project)</u>

We performed a nationwide surveillance and obtained responses from 96.6% of specialist's belonging facilities. We created a map showing the number of treatments and specialists per population in all prefectures. Also, we made maps in each secondary medical zone. Now, we are investigating the reasons of their differences between the prefectures, focusing on the patient transportation system and so on. We are planning to collect the similar data of 2017, to know annual changes for further promotion.

2. Development of a new computer application to predict stroke subtypes at prehospital

In acute cerebral large vessel occlusion, the affected vessels should be recanalized as soon as possible for better patient s outcome. However, ambulance services are supposed to transfer the patient to the closest hospital. In this study, 1,200 patients with acute stroke patients were retrospectively analyzed and a new computer application to predict stroke subtypes was developed. Based on the prospective validation study with 1,000 patients suspected with acute stroke, the system are modified for better prediction. With this new IT device, we are aiming to establish appropriate patient transferring system.

3. A clinical trial to elucidate the efficacy and safety of PCSK-9 inhibitor for acute stroke patients

Lipid lowering therapy for acute stroke patients has been regarded important for better clinical outcome, but the effect of statins, HMG-CoA reductase inhibitors, is not sufficient in some occasions. The pro-protein convertase subtilisin-kexin type 9 (PCSK9) inhibitor is known to lower LDL-cholesterol concentrations strongly and reduce the risk of cardiovascular events in patients with atherosclerotic cardiovascular disease. However, its effect for acute ischemic stroke has not been established. The aim of this study is to elucidate its safety and efficacy in acute stroke patients.

<u>4. Basic and clinical studies of intravenous administration of ischemia-induced</u> <u>multipotent stem cells (iSCs) for acute stroke patients</u>

We have previously demonstrated that brain pericytes near cerebral vessels acquired multipotency following cerebral ischemia. Recently, we demonstrated that the cells, ischemia-induced multipotent stem cells (iSCs), are present within the post-stroke human brain. This cell can differentiate into vascular cells and also neural cells, so it can be a good candidate as donor cell for neural regeneration therapy. We have been working on its characterization and also its effects on functional recovery in animal models. Final goal of this study is to know its impact on functional recovery of acute stroke patients.