

Research Center for Medical Sciences

Division of Clinical Pharmacology and Therapeutics

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General Summary

The Division of Clinical Pharmacology and Therapeutics was established in July 1995. The aim of the division is to investigate drug treatment, mainly in the area of internal medicine, whereas other departments of clinical pharmacology in Japan focus on registration trials, particularly phase I trials. Because a clinical laboratory where we had performed many human pharmacological studies became unavailable in 2003, we shifted our research from human studies to multicenter clinical trials and pharmacoepidemiological studies.

Research Activities

Statins (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors) have been widely used to treat hyperlipidemia. However, they also have adverse effects on muscle, the liver, kidneys, and other organs. To investigate the incidence of these adverse effects and anti-hyperlipidemic effects, we performed a study according to a case-cohort design in which detailed data were collected from all cases and from a subcohort representing 5% of all subjects. A full-scale study has been completed with a large sample size of 7,000 patients from 68 institutions. A paper describing this study has been published.

The above-mentioned statin study took a long time to complete. We organized a research group comprising academic and industrial organizations (Japanese Society for Pharmacoepidemiology, Japanese Society of Clinical Pharmacology and Therapeutics, Japan Association for Medical Informatics, Japan Society of Clinical Trials and Research, Federation of Pharmaceutical Manufacturer's Associations of Japan, Pharmaceutical Research and Manufacturers of America, and European Federation of Pharmaceutical Industries and Associations Japan) to make postmarketing studies more efficient by utilizing the Standardized Structured Medical-record Information eXchange (SS-MIX). The SS-MIX system was started in 2006 as a project supported by the Ministry of Health, Labour and Welfare for promoting the exchange of standardized medical information. The SS-MIX system will increase the efficiency of pharmacoepidemiological studies by identifying "new users" who started the drug after some period of nonuse. The "new user" design is often essential for unbiased results.

To raise the literacy of clinical trials among researchers we held "Clinical Trial Seminar" 4 times this year. The themes were as follows: "Superiority trial and non-inferiority trial" (October 2015), "Equivalence trial" (November 2015), "Evolution of IRB and clinical trials" (January 2016), and "Clinical trial insurance for compensation to research subjects to meet the demand of Ethical guidelines for medical and health care research involving human subjects" (February 2016).

An administrative office for registration trials was established in the hospital in February 1999, and the system for registration trials in the hospital has been reformed to meet the demands of the new good clinical practice guidelines. Ten clinical research coordinators (CRCs) now facilitate clinical trials of which 2 CRCs have mainly been involved in monitoring. The CRCs have started to help with both registration trials and investigator-initiated trials. The CRCs have been introduced into all registration trials since 2004; the quality and speed of these trials were much improved.

As the introduction of CRCs into investigator-initiated trials increased, we invited CRCs from site management organizations to supplement CRCs involved in registration trials.

Publications

Kawamori R (Juntendo Univ Grad Sch Med), Kaku K (Kawasaki Med Sch), Hanafusa T (Osaka Med Coll), Ioriya K (Sumitomo Dainippon Pharma Co., Ltd.), Kageyama S, Hotta N (Chubu-Rosai Hosp). Clinical study of repaglinide

efficacy and safety in type 2 diabetes mellitus patients with blood glucose levels inadequately controlled by sitagliptin. *J Diabetes Investig.* 2016; **7**: 253-9.