Department of Infection Control

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General Summary

We performed both basic and clinical research in the following areas: bacterial infection and chemotherapy, opportunistic infection in patients with human immunodeficiency virus/acquired immunodeficiency syndrome, parasitic/vector borne diseases, and outbreak and infection control.

Research Activities

Clinical studies on patients with bacteremia due to methicillin-resistant Staphylococcus aureus

We investigated the clinical features and treatment of 32 patients with bacteremia due to methicillin-resistant *S. aureus* (MRSA). Catheter-related bloodstream infection accounted for 59.4% of source of infection. Since 2013, the number of MRSA bacteremia cases has decreased and the infection control team (ICT) intervention rate for MRSA bacteremia has increased. Therapeutic Drug Monitoring (TDM) was performed in all cases who vancomycin and teicoplanin was used for treatment. Some cases were changed to daptomycin or linezolid after prolonged use of initial treatment. ICT needs to actively intervene even after the start of treatment in addition to selecting anti-MRSA agents.

Interaction between integrase strand transfer inhibitors and calcium-free phosphate-binding agents in HIV patients on hemodialysis

The aim of this study was to determine the interaction between integrase strand transfer inhibitors (INSTIs) and calcium-free phosphate-binding agents. Blood samples were collected from two HIV patients with chronic kidney disease on hemodialysis. Patient 1 was administered dolutegravir and bixalomer, and Patient 2 was raltegravir and lanthanum carbonate. There was no significant reduction of the blood concentrations of dolutegravir or raltegravir. However, the time to maximum concentration of raltegravir was delayed in Patient 2. Therefore, further investigation will be needed to clarify the reason for this delay and the interaction between concomitantly administered INSTIs and calcium-free phosphate-binding agents.

Revisiting a method for diagnosing toxoplasmosis: Development of the Toxoplasma Killing Observation test

Toxoplasma gondii, the most successful protozoan infects approximately 1/3 of people worldwide. In most cases, Toxoplasmosis is self-limited disease with mild symptoms, even asymptomatic, except immunocompromised patient and pregnant women. Immuno-

compromised patients, such as AIDS, post organ transplant patients and steroid users are at the risk of Toxoplasma encephalitis, pneumonitis and retinitis. Documents show that most of these cases were caused by relapses and flares from the bradizoite; a slowly duplicating form of Toxoplasma, which dormant in host tissues. On the other hand, primary infection during pregnancy is a risk of congenital Toxoplasmosis, which causes intrauterine growth retardation, hydrocephaly, mental growth retardation, retinitis, and even fetal death.

Many types of serodiagnostic methods are widely used for the detection of Toxoplasmosis over the world. But in Japanese clinical site, Toxoplasma immunoglobulin G and M is the only serodiagnosis method that makes diagnosis complicated in some cases. In relapsed patients IgM is usually negative, and positive IgG could not discriminate the present infection from the past infection. Diagnosis of congenital toxoplasmosis with IgG and IgM are another issue. Some documents report that IgM remains over the threshold for more than two years, and the positive predictive value of IgM was only 45.98%. This kinetics of IgM has a risk of leading misdiagnosis.

Sabin and Feldman reported dye test in 1948. Dye test evaluates the aggregate ability of tachyzoite-cidal immunoglobulin titer with the serum of the subject. The classic serodiagnosis still owns high sensitivity and specificity as a referential diagnosis. Issue of the dye test is its complicated evaluation method that evaluator must count stained tachyzoites under visual recognition. We tackled this issue with a green fluorescent protein expressed tachyzoite, which is the alternative marker for evaluating deactivation of the tachyzoite. The new improved dye test, Toxoplasma killing observation (TOKIO) test has advantage of its objectivity and retention for evaluation, and equivalent outcome as classical dye test.

Seroepidemiology and risk assessment of Toxoplasma gondii infection in HIV/AIDS patients

In HIV-infected patients, AIDS develops with decreased CD4 positive lymphocytes. Toxoplasma encephalitis is one of the AIDS indicator diseases that its risk increases when CD4 positive lymphocyte becomes 100/μl or less. Majority of cases are caused by reactivation of bradizoites in brain, which forms latent infection. However, there is no adequate assessment of toxoplasma seroprevalences and its risk factors among Japanese HIV-infected patients. We collected serums from 400 HIV-infected patients who visited our hospital outpatient clinic and conducted serological evaluation of *T.gondii* specific-antibody levels. As a result, 33 cases (8.3%) of patients were T.gondii IgG antibody positive, and confirmed positive by Sabin-Feldman Dye test. The obtained prevalence of seropositivity was equivalent to the previous survey that was conducted in pregnant women in Japan; there was no correlation with HIV infection. Also, a strong correlation with a history of cat rearing was found, rather than having a habit of consuming rare meat from the questionnaire survey to the participants.

Disinfection effect of Chlorhexidine gluconate and Olanexidine gluconate on clinically isolated S.aures *strains*

We investigated the disinfecting effect of chlorhexidine gluconate (CHG) and olanexidine

gluconate (OLN) on clinically isolated Staphylococcus aureus strains. OLN had higher disinfecting effect on clinically isolated *S. aureus* strain than CHG.

Publications

Nakaharai K, Sakamoto Y[1], Yaita K[2], Yoshimura Y[1], Igarashi S[3], Tachikawa N[1] ([1]Yokohama Municipal Citizen's Hospital, [2]Kurume University, [3]Yokohama Brain and Spine Center). Drug-induced liver injury associated with high-dose ceftriaxone: a retrospective cohort study adjusted for the propensity score. *Eur J Clin Pharmacol.* 2016; **72:** 1003-11.

Matsumoto K[1], Kurihara Y[1], Kuroda Y[1], Hori S, Kizu J[1] ([1]Keio University). Pharmacokinetics and brain penetration of carbapenems in mice. *J Infect Chemother.* 2016; **22:** 346-9.