Department of Infection Control

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General Summary

Several clinical studies and 1 basic research study were performed in our department. Our retrospective clinical studies demonstrated several issues in patients with infectious diseases, catheter-related bloodstream infection, and antibiotic therapy. We will provide feedback to improve the outcome of cases of infectious diseases and to develop prospective clinical studies and basic research. On the other hand, we investigated biofilm formation using clinically isolated staphylococci. We will continue these clinical and basic research studies to obtain new evidence and to develop more effective treatments for infectious diseases.

Research Activities

Analysis of catheter-related bloodstream infections

Sixty-four cases (16%) of catheter-related bloodstream infections were identified among 384 cases of bloodstream infection at The Jikei University Hospital. Staphylococci, including methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci, were isolated from 31 of 50 patients with central venous catheters. On the other hand, Gram-negative bacilli, such as *Enterobacter* spp. and *Serratia* spp., were isolated from 8 patients with peripheral venous catheters. Effective strategies must be developed to prevent catheter-related bloodstream infections.

Clinical characteristics and risk factors for mortality in patients with bacteremia caused by Pseudomonas aeruginosa

In our hospital, we performed retrospective analyses to determine risk factors for mortality among patients with bacteremia caused by *Pseudomanas aeruginosa* (*P. aeruginosa*). A total of 134 patients with *P. aeruginosa* bacteremia were identified from April 2003 through March 2010. The 30-day mortality rate among all patients with *P. aeruginosa* bacteremia was 20.9%. The most common underlying disease was leukemia (20.9%), and the most common primary site of infection was the urinary tract (24.6%). Seventy-one patients (65.7%) were treated with an appropriate initial antimicrobial regimen for *P. aeruginosa* bacteremia. However, the 30-day mortality rate in these patients was similar to that in patients not given appropriate antibiotics. This study revealed that risk factors for 30-day mortality were thrombocytopenia and polymicrobial *P. aeruginosa* bacteremia (p<0.01). patients were men aged 22 to 42 years. The most common clinical features were fever and sore throat, followed by splenomegaly and skin eruption. The CD4-positive lymphocyte count was 100 to $635/\mu$ L, and the HIV RNA level was 1.9×10^5 to 9.6×10^6 copy/ mL. Acquired immunodeficiency syndrome developed in 2 patients; 1 patient had esophageal candidiasis, and another had pneumocystis pneumonia. Because clinical features were not specific and because antibodies against HIV were not detected in patients with acute HIV infection, we recommend that the polymerase chain reaction be used to diagnose acute HIV infection.

Biofilm formation of clinical isolated staphylococcus species

We analyzed the capacity of biofilm formation and the biofilm component *in vitro*, using the staphylococci isolated from patients at The Jikei University Hospital. Biofilm formation was observed in 29.2% (7 of 24 strains) of strains of methicillin-sensitive S. aureus (MSSA), 29.2% (7 of 24 strains) of strains of MRSA, and 25.0% (7 of 28 strains) of strains of Staphylococcus epidermedrs (S. epidermidis). Of the 7 biofilmforming staphylococci strains, 2 strains were induced by NaCl, and 5 strains were induced by glucose. Only 1 biofilm formed by MRSA was destroyed by a polysaccharide-degradative enzyme (dispersin B), but 4 biofilms formed by S. epidermidis were susceptible to dispersin B. On the other hand, a protein-degradative enzyme (proteinase K) destroyed 4 biofilms formed by MSSA and 4 formed by MRSA but only 2 biofilms of S. epidermidis. Seven of the 10 biofilms susceptible to proteinase K were destroyed by a DNAdegradative enzyme (DNase I). The frequency of biofilm formation did not differ markedly among the clinically isolated strains of MSSA, MRSA, and S. epidermidis. The biofilms of S. epidermidis were dependent on polysaccharides; on the other hand, the biofilms of S. aureus were dependent on proteins. These findings suggest that a large amount of extracellular DNA is contained in proteinaceous biofilms.

Comparison of susceptibility of P. aeruginosa to carbapenems

To compare the susceptibility of clinically isolated *P. aeruginosa* to 5 carbapenem antibiotics (imipenem, panipenem, biapenem, meropenem, and doripenem), minimum inhibitory concentrations (MICs) were determined with a broth microdilution method. A total of 566 clinical isolates of *P. aeruginosa* were collected at The Jikei University Hospital from January through December in 2009. The MICs of doripenem were lower than those of other carbapenems. In addition, doripenem might have antimicrobial activity against imipenem-resistant *P. aeruginosa*, because the MIC of doripenem needed to inhibit growth by 50% was 4 µg/mL among strains of imipenem-resistant *P. aeruginosa*.

Comparison of treatment with vancomycin, teicoplanin, or linezolid in patients with MRSA pneumonia in the intensive care unit

The aim of this retrospective study was to compare the results of treatment with vancomycin, teicoplanin, or linezolid in patients with MRSA pneumonia in intensive care units (ICUs) at The Jikei University Hospital. In ICUs, pneumonia due to MRSA was diagnosed in 29 patients. The pneumonia was treated with vancomycin in 22 patients, teicoplanin in 3 patients, and linezolid in 4 patients. Three of the 4 patients treated with linezolid showed rapid improvement. Our results suggest that linezolid should be the antibiotic of first choice for treating MRSA pneumonia in the ICU.

Publications

Hori S, Irimajiri S (Kasawaki Mun Hosp), Koido N (Kasawaki RA&IM Cli), Sunakawa K (Kitasato Inst Life Sci). Safety profile of pediatric tosufloxacin (in Japansese). Nihon Kagaku Ryoho Gakkai Zasshi 2010; **58 S-2**: 78-88.

Yoshikawa K, Okada H, Hasegawa T, Sakurai I, Kawaguchi Y, Onodera S. Clinical features and treatments of patients with urosepsis: comparison of community-aquired and hospital-aquired infections (in Japanese). Tokyo Jikeikai Ika Daigaku Zasshi 2010; **125**: 121-7.

Sato F, Iwase T, Tajima A, Shinji H, Mizunoe Y. Biofilm formation of clinical isolated Staphylococcus species (in Japanese). BACTERIAL ADHEREN & BIOFILM 2010; 23: 23-8.

Kizu J, Iwata S, Kusachi S, Sato J, Sato Y, Sandoh M, Takeda H, Tateda K, Hori S. Do doctors know of and use PK-PD-based antimicrobial agent dosage? (in Japanese) *Nihon Kagaku Ryoho Gakkai Zasshi* 2010; **58:** 460-5.

Kizu J, Hori S. Review of the literature on interaction of second-genration antihistamines with other drugs (in Japanese). *Iyakuhin Sogo Sayo Kenkyu* 2010; **34:** 23-31.

Kizu J, Maezawa K, Terashima T, Fukuda H, Akita H, Hori H. Examination of the prescription of antihistamines: based on a questionnaire survey involving practicing physicians (in Japanese). Arerugi Meneki 2010; 17: 2066-76.

Arakawa S, Kawai S, Hori S, Watanabe S, Totsuka K. A clinical phase III study of pazufloxacin in patients with sepsis (in Japanese). Nihon Kagaku Ryoho Gakkai Zasshi 2010; **58:** 650-63.

Kohno S, Aoki N, Kawai S, Niki Y, Watanabe A, Hori S, Watanabe S, Totsuka K. A clinical phase III study of pazufloxacin in patients with bacterial pneumonia. *Nihon Kagaku Ryoho Gakkai Zasshi* 2010; **58:** 664-80.

Reviews and Books

Hori S. Anti-fungal drugs, PK-PD (in Japanese). *Rinsho to Biseibutsu* 2011; **38:** 105-9.

Horino T. Prognostic factors and the role of interleukin-1 in bacteremia caused by Pseudomonas aeruginosa (in Japanese). *Nihon Kagaku Ryoho Gakkai Zasshi* 2010; **58**: 547-54.

Kato T. Non-AIDS defining malignancy (in Japanese). Nihon AIDS Gakkaishi 2010; **12:** 137-43.

Kato T. Fever with malignancy (in Japanese). Chiryo 2010; 92: 1954-7.

Hori S. Safety and drug interaction (in Japanese). In: Kono S, editor. How to use carbapenems. Osaka: Iyaku Janarusha; 2010. p. 54-65.