

Infectious complications in patients with severe acute pancreatitis

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Infectious complications associated with severe acute pancreatitis were investigated. Inclusion criteria were based on the Ministry of Health, Labour and Welfare severity classification ; there were 32 stage2 (ST2) patients, 25 at stage3 (ST3) and 7 at stage4 (ST4). Prophylactic antimicrobial agents such as continuous regional arterial infusion were administered against infectious disease for all patients. The incidence of all infectious complications, including pancreatic and extra-pancreatic infections was 43.8% , and were significantly lower in ST2 than ST3 and 4. In the late phase (14 days after admission), infections were significantly higher in ST4 than ST2, with the difference between ST2 and ST3/4 being especially remarkable in the late phase for extra-pancreatic infections. The rate of infectious disease in patients with necrotizing pancreatitis was significantly higher than in edematous pancreatitis, and all deaths were in the necrotizing pancreatitis group. Pancreatic infectious complications were seen in 1 patient on admission, 3 patients in the early phase and 4 patient in the late phase, and there were several bacterial infections. Many of the extra-pancreatic infections involved pneumonia and infection via the catheter and bacteremia. There were many resistant bacteria such as methicillin resistant *staphylococcus aureus* or *Pseudomonas aeruginosa* in the causative bacteria. Therefore, monitoring culture, shortening the duration of mechanical ventilation and early catheter removal should be required.

Clinical characteristics of *Stenotrophomonas maltophilia* infection and colonization in our intensive care unit

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Stenotrophomonas maltophilia (*S. maltophilia*) is non-fermentative, aerobic gram-negative bacillus which is frequently isolated from wet sites. The organism can be isolated from nebulizer and ventilator circuits in the hospital setting. *S. maltophilia* is considered as an opportunistic agent of ventilator-associated pneumonia. We examined the isolation of *S. maltophilia* in our ICU during past three years. *S. maltophilia* was most frequently isolated the specimens obtained from the respiratory tract. Other infectious microorganisms were often isolated together with *S. maltophilia*. The patients in whom *S. maltophilia* was isolated had longer duration of ICU stay and high mortality. Sulfamethoxazole-Trimethoprim, latamoxef, pazufloxacin, and minocycline were quite susceptible antimicrobial agents in vitro. Broad-spectrum antibiotics including carbapenems must be administered carefully because the use of these antimicrobials becomes the risk factor of *S. maltophilia* infection.

Continuous postoperative blood glucose monitoring and control using a closed-loop system (artificial pancreas, STG-22) in patients undergoing hepatic resection

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In a randomized trial of tight blood glucose control (4.5 ~ 6.1 mmol/L ; 80 ~ 110 mg/dL) compared with standard control (< 11.2 mmol/L ; < 200 mg/dl) in surgical intensive care unit patients, it was demonstrated that strict postoperative blood glucose control not only significantly reduced mortality but also reduced morbidity. Moreover, among the postoperative complications of major surgery remains especially problematic with its significant risk of a fatal outcome and prolongation of hospital stay. It is thus of clinical importance to keep the blood glucose levels as

normal as possible for the reduction of postoperative complication. Surgical stress is a major causative factor for hyperglycemia and also dysregulation in liver metabolism and immune system, resulting in impaired recovery of postoperative patients. Hypoglycemia is a counter-problem during intensive insulin therapy in patients with a high risk surgery, because there is no reliable technique to avoid hypoglycemia during intensive insulin therapy. In this postoperative hyperglycemic state, the STG-22 safely and quickly achieved glycemic control, indicating its clinical value in the postoperative management of pancreatectomized patients.

Causative organism and antibacterial therapy for SSI

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Isolates from surgical site infections (SSIs) have conventionally been calculated collectively regardless of the clinical course of the infection. Bacteriological investigation is also not often performed for mild SSI, so only the isolates from comparatively severe cases have been calculated. Consequently, drugs have been selected for treatment whose resistance has been highly modified and which have a broad antibacterial spectrum from the initial stage such as carbapenems, which is one reason for the increase in resistant bacteria. To show which therapeutic antibiotics are appropriate for each period, consistent with the clinical course of SSI. The incidence of resistant strains was rare among isolated strains from surgical site infections in the early stage. There were no strains resistant to second generation and fourth generation cephalosporins. The number of strains resistant to cephalosporins increased as the clinical course progressed, and carbapenem-resistant strains also emerged. SSI isolated strains and drug sensitivity changed according to the clinical course, so therapeutic antibiotics ideally should be selected after taking into account the clinical course of an infection.

Current measures to use antimicrobial drugs appropriately

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Control and prevention of bacterial infection is important for providing safe and high-quality surgical treatment. Because of the increasing threat of antimicrobial resistance attributed to the overuse and long-term administration, there is a greater responsibility within the medical community to use antibiotics properly. Optimal use of antibiotics consists of correct indication, drug selection, dose, times per day, and duration. In empiric therapy, antimicrobial drugs should be selected according to the antibiogram of each institution and the results of Gram's stain method if possible as well as clinical findings and laboratory data. Proper antimicrobial treatment is based on making full use of Pharmacokinetics/Pharmacodynamics (PK/PD) and therapeutic drug monitoring (TDM). To restrict the drug selection and the dose of antimicrobials by cycling therapy, mixing therapy, notification policy to ICT, or permission policy by ICT may be effective in preventing development of antimicrobial resistance.

Optimal use of anti-microbial agents by utilization of PK/PD

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Pharmacokinetics (PK)/Pharmacodynamics (PD) is at the heart of any selection of the dosage of antibiotics. It is useful to optimize safety and efficacy of anti-infective. Most of physicians believe utilization of PK/PD is required

special technique and special equipments. For high level analysis, these might be required. But we can start to utilize PK/PD immediately without any equipment. What is PK/PD ? What is core issue in PK or PD ? How to use the concept of PK/PD ? This article will introduce the point to consider on utilization of PK/PD at bedside.

Importance of an appropriate protocol of antibiotic use in maintaining antibiotic heterogeneity and preventing the emergence of antibiotic-resistant bacteria

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Widespread or long-term use of a broad-spectrum antibiotic leads to the development of bacteria resistant to that drug. Achieving antibiotic heterogeneity is a key to control antibiotic pressure, a step that may facilitate the prevention or minimization of antibiotic resistance. The aim of protocols of antibiotic use is to maintain appropriate antibiotic heterogeneity. Antibiotic cycling therapy is one such strategic protocol that helps in maintaining antibiotic heterogeneity and preventing the emergence of resistant bacteria. Although this therapy is effective against bacteria, especially gram-negative rods, its efficacy depends on the choice and rotation pattern of the antibiotics. Dual antibiotic rotation is superior to single antibiotic rotation with regard to preventing the emergence of antibiotic-resistant bacteria, because the latter is associated with a risk of increasing antibiotic pressure. Antibiotic cycling therapy is an effective strategy for preventing gram-negative-rod infection such as MDRP but not for MRSA infection. Exercising precautionary measures against acquiring MRSA infection would be an efficacious strategy for preventing this infection.

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Therapeutic drug monitoring (TDM) is defined as the measurement of the serum drug concentration and modify the dose regimens to optimize drug therapy of individual patients. Pharmacokinetics of drugs in the human body principally can be determined by two parameters ; volume of distribution (Vd) and clearance (CL). Population pharmacokinetics analysis has contributed to the development of the TDM for antimicrobials, especially in glycopeptides or aminoglycosides. Although TDM for antimicrobials has large clinical values, total pharmaceutical services related to antibiotic use in the antimicrobial stewardship will improve clinical outcomes furthermore. Multidisciplinary approach are needed to accomplish the infection control of today, well trained pharmacists with a specialty are required.

Clinical utility of a new PCR-based assay for rapid pathogen detection in patients with sepsis

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It is generally recognized that sepsis caused by bacteremia and/or fungemia is one of the major causes of mortality and morbidity in hospitals, and mortality from sepsis in Japan has been increasing in recent years. Blood culture remains the gold standard for diagnosing sepsis. Clinicians often select an empirical antibiotic therapy, since it takes from 2 days to 7 days to identify bacterial/fungal pathogens from blood culture. However, such treatment regimens are frequently suboptimal or inappropriate for the infecting pathogens. Accordingly, a more rapid diagnosis of bacteremia and fungemia is needed. A real-time PCR-based assay for rapid detection of bacterial and fungal DNA directly from whole blood in 4.5 h is currently developed. Although further evaluation is warranted, this assay holds promise for more rapid pathogen identification in clinical sepsis.

Proper use of the anti-MRSA drugs
— Proper use of the anti-MSRA drugs for post-operative infections
in the emergency and critical care medicine —

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Postoperative Infections are the quite big problem not only in the surgery but also in the emergency and critical care medicine. The patients of the emergency and critical care medicine are likely to catch infectious diseases and have various risks. Therefore, if they contract postoperative infection, they get the higher risk of their life than the patients in other medical fields. Especially, the infection with MRSA (Methicillin Resistant *Staphylococcus aureus*) is difficult to recover once a patient gets infected, and it has a great risk of spread as an inner hospital infection. It is important to have correct diagnosis in the early period and the proper use of anti-MRSA drugs. We must use the anti-MSRA drugs, considering the location of infections and sensitivity to the drugs. It should not be administered except to the case that certainly infected with MRSA.

Appropriate antibiotic therapy for MRSA infection after gastrointestinal surgery

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As there has not been an effective prophylaxis for methicillin-resistant *S.aureus* (MRSA) infection after gastrointestinal surgery, the incidence of this infection has not been reduced yet. The critical risk factor for MRSA infection is an invasive operation such as esophagectomy with much blood loss and longer operation time. The infection sites were frequently observed in sputum and intraperitoneal abscesses. In patients with MRSA infection, operation with much blood loss, longer operation time, plural morbidity, and mechanical ventilation were more frequent than those in patients with MRSA colonization. When a treatment for MRSA infection is performed, it is important to decide usage by therapeutic drug monitoring (TDM). Although glycopeptide or aminoglycoside had been used for the treatment of MRSA infection, oxazolidinone, which has another action mechanism, has been developed for the treatment of MRSA infection. Therefore, it is important to select optimal antibiotics considering each pharmaceutical characteristic for every case. Furthermore, it is essential for ICT to wrestle MRSA infection in order to prevent outbreak.

Current strategies against infections caused by multidrug-resistant gram negative bacteria

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Severe infections due to nosocomially encountered gram-negative bacteria, such as extended-spectrum beta-lactamase producing bacteria and multidrug-resistant *Pseudomonas* are current serious problems. While carbapenems are considered to be the preferred agents for treatment of infections caused by extended-spectrum beta-lactamase producing bacteria, carbapenemases have been recently reported. Colistin, an old antibiotic also known as polymyxin E, has attracted more interest because of significant activity against multidrug-resistant *Pseudomonas*. 'Break-point Checkerboard Plate' has been suggested to be useful to screen appropriate antibiotic combinations against highly resistant *Pseudomonas* spp.

Guideline for management of deep seated mycosis in surgical patients

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Early treatment of fungaemia improves the prognosis in surgical patients, however, early diagnosis of deep mycoses is difficult. Therefore, the "Guideline for management of deep-seated mycoses" was developed for early treatment of fungaemia, based on a combined assessment of the blood level of β -D-glucan and the degree of colonization by *Candida*, a revised version of which was published in 2007. In this report, we comment on the effects of treatment of deep mycoses in surgical patients in practice mainly based on the revised guideline. In both high-risk patients and antimicrobial-agent-unresponsive pyrexia patients, possible fungal infection is considered when ① the serum β -D-glucan test is positive or ② *Candida* colonization positive on monitoring culture, and empiric administration of antifungal agents must be initiated (first-choice agents, FFLCZ or MCFG). Mycotic endophthalmitis and pyrexia after CV catheter extraction may be extremely highly severe forms of ? clinical candidiasis. These cases are considered to have probable fungal infection. Fungal infection in these cases can be proven when the fungus is detected on abscess fluid culture or blood culture, and administration of antifungal agents should be initiated (first-choice agents, FFLCZ or MCFG) in both cases. When the first-choice agents fail, administration of VRCZ, L-AMB, ITCZ, or a short-term combination of FFLCZ and AMPH-B may be used as second-choice agents. For cases with hemodynamic instability, the second-choice agents must be used from the beginning. FFLCZ, ITCZ and VRCZ require administration in loading doses on the basis of the PK/PD theory. The therapeutic effect is judged after treatment for 5-7 days. In cases with suspected fungal infection, the drugs should be administered until resolution of the clinical symptoms or improvement of the clinical data. In cases with a definitive diagnosis, treatment should be continued for two weeks after the fungi disappear from the blood ?

Infection control in the operating room for anal surgery in HIV positive patients

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The positive rate of the human immunodeficiency virus (HIV) has increased in patients who receive anal surgery. Infection control and management against HIV infection would be necessary in the operating room of general hospital. We introduced antigen/antibody combination assay to detect the infection as early as possible. Infection control manual has been revised and anti-HIV agents have been prepared to prevent infection in medical workers in case of accidents. In the operating room, infection control procedures have been employed to prevent surgical incidents. Between August 06 and July 07, we performed anal surgery in seven patients with HIV without any complications. These included two cases of hemorrhoid, three cases of anal fistula, and two others. There has been no infection accident nor transmission of HIV in medical workers. Progress in anti-HIV drugs has kept the physical condition in HIV patients as good as those without HIV. As the results, there has been increasing in the number of HIV patients with indication of surgical treatments. We have employed preventive measures against HIV infection in the operating room.