

A Study of Plasma HIV RNA Viral Load Response to the Treatment with Low Dose Stavudine (D4T) in Lamivudine (3TC) and Efavirenz Containing Highly Active Antiretroviral Regimen (HAART) in Antiretroviral Naive HIV Patients

Apatcha Pungjitprapai, M.D.,
Mattana Hanvanich, M.D.

Abstract

Background: To determine the antiviral efficacy of reduced-dose stavudine in lamivudine and efavirenz-containing HAART regimen in antiretroviral naïve HIV patients.

Methods: An open-label, single arm study was conducted. Baseline clinical assessment and blood tests were done in 34 antiretroviral naïve HIV patients, at King Chulalongkorn Memorial Hospital, Bangkok, Thailand, who were received treatment with reduced stavudine [20 mg twice daily (BW < 50 kg) or 30 mg twice daily (BW > 50 kg)] in lamivudine (150 mg twice daily) and efavirenz (600 mg once daily)-containing HAART regimen. The patients were followed up at 2, 4, 8, 16, and 24 weeks. CD4 cell count and plasma HIV RNA viral load assays were done at 2 weeks before initiation of the regimen, and then at 4 and 24 weeks after the treatment. Primary end point of the study was the efficacy of the trial regimens at 24 weeks with plasma HIV RNA viral load less than 50 copies/ml.

Results: Thirty-four patients were enrolled. There were 21 males and 13 females, with a mean age of 35.8 years (range 22-51). The mean baseline CD4 cell count and mean plasma HIV RNA viral load were 85.9 cells/mm³ (range 11-198) and 540,388 copies/ml (range 40,300-2,620,000), respectively. At 24 weeks, 94.1 percent of patients (32/34) had achieved plasma HIV RNA viral load below 50 copies/ml. Two patients who had a very high plasma HIV RNA viral load initially had achieved a plasma HIV RNA viral load below 50 copies/ml at 48 weeks of the treatment. The mean CD4 cell count at 24 weeks of the treatment was 265.7 cells/mm³ (range 63-584). The mean increase in CD4 cell count from baseline was 179.8 cells/mm³ (range 52-386).

Conclusion: The study demonstrates that reduced-dose stavudine in lamivudine and efavirenz-containing HAART regimen is effective in suppressing of plasma HIV RNA viral load at 24 weeks of treatment in antiretroviral-naïve HIV patients. Further studies are needed to assess long-term virologic and clinical outcomes.

Diagnosis of Dengue Infection in Adults by Reverse-transcription Polymerase Chain Reaction (RT-PCR) from Saliva and/or Buccal Mucosal Cells

Jakrapun Pupaibool, M.D.*,
Sunisa Krajiw, M.D.*,
Kesinee Arunyingmongkol, M.D.*,
Ananda Nisalak, M.D.***,
Chitsanu Pancharoen, M.D.**,
Usa Thisyakorn, M.D.**,
Wanla Kulwichit, M.D.*

Abstract

Objective: diagnosis of dengue infection by ELISA method using saliva and RT-PCR method using urine were previously performed with the specificity of 100 percent and high sensitivity, comparable to the detection of dengue virus using serum specimens. But no previous study was performed to detect dengue viral genomes by RT-PCR method using oral specimens as the clinical specimens. We sought to perform the first study to determine the sensitivity, specificity, positive predictive value, and negative predictive value of RT-PCR method using saliva and/or buccal mucosal cells for diagnosis of dengue infection in adults, comparing with standard ELISA method from serum specimens.

Methods: Hospitalized adults with acute fever and suspected dengue infection were enrolled at King Chulaongkorn Memorial Hospital, Bangkok, Thailand. Saliva and buccal mucosal cells were collected from each patient for diagnosis of dengue infection by RT-PCR method. A dengue diagnosis was made by the standard method (ELISA method) using serum

specimens. Patients with negative ELISA served as the control cases.

Results: Sixty-six patients (36 males and 30 females) were enrolled in our study. Forty-two patients were dengue cases, and 24 cases served as the control cases. The sensitivity using saliva and buccal mucosal cells were 42.86 and 35.71 percent, respectively. The specificity of each type of oral specimens was 95.83 percent. Positive predictive values were 94.74 and 93.75 percent, and negative predictive value were 48.94 and 46.00 percent, respectively. Using both types of oral specimens gave the specificity of 91.67 percent, but increased the sensitivity to 54.76 percent. The sensitivity tended to increase when specimens were collected before the days of defervescence.

Conclusions: RT/PCR using saliva and buccal mucosal cells can be utilized as the diagnostic tools for dengue infection, particularly when the specimens are collected early in the course of illness. But future studies with more patients are needed to determine the value of these methods.

*Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

**Infectious Disease Unit, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

***Department of Virology, Armed Force Research Institute of Medical Sciences, Bangkok 10400, Thailand.

Implementation of Clinical Practice Policy on Continuous Intravenous Administration of Amphotericin B Deoxycholate

Pasri Maharom, M.D.,

Visanu Thamlikitkul, M.D.

Abstract

Background: The incidence of systemic fungal infection has significantly increased, and a mainstay of treatment is still amphotericin B deoxycholate (AmB-d). A limitation of using AmB-d includes infusion-related reactions and nephrotoxicity. A continuous infusion of AmB-d was found to reduce nephrotoxicity and infusion-related reactions.

Objective: To implement clinical practice policy on continuous intravenous administration of AmB-d in the patients hospitalized in general medical wards at Siriraj Hospital, Bangkok, Thailand.

Method: A one-page evidence-based clinical policy on continuous intravenous administration of AmB-d was prepared and distributed to all general medical wards at Siriraj Hospital. The information of the patients who received AmB-d treatment from March 2004 to March 2006 was collected. The data were analysed using the descriptive statistics, univariate analysis, and multivariate analysis as appropriate. A p-value of <0.05 was considered statistically significant.

Results: Of 166 courses of AmB-d treatment in 148 patients, 102 courses (61.4%) were given continuous intravenous administration of AmB-d (CI group) and

64 courses (38.6%) were given conventional 4-to-6-hour intravenous administration (RI group). The mean age of the patients in the CI group was significantly more than that in the RI group. The CI group had more patients with neutropenia and persistent fever whereas the RI group had more patients with HIV/AIDS and cryptococcal meningitis. The incidence of AmB-d-related nephrotoxicity was 27.5 percent in the CI group, compared with 39.1 percent in the RI group ($p=0.164$). Chills were observed in 6.9 percent of the patients in the CI group, compared with 26.6 percent in the RI group ($p=0.001$). Overall mortality at the end of treatment was significantly more than that in the CI group. However, most of the mortality in the CI group were unrelated to the fungal infections or AmB-d administration.

Conclusion: Continuous infusion of AmB-d was associated with a decrease in infusion-related reactions, and tended to have less nephrotoxicity than that in 4-to-6-hour infusion. However, the overall mortality in the CI group was higher. This observation might be due to more unfavorable characteristics of the patients who received continuous infusion of AmB-d rather than the method of infusion.

Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Received for publication: June 23, 2006.

Keyword: continuous-infusion, amphotericin B, nephrotoxicity, infusion-related reactions

Vancomycin Overuse in Siriraj Hospital

Pinyo Rattanaumpawan, M.D.*,

Visanu Thamlikitkul, M.D.*,

Kulkanya Chokepaibulkit, M.D.**,

Darin Lohsiriwat, M.D.***,

Nalinee Aswapokee, M.D.*

Abstract

Objective: An emergence of vancomycin-resistant organisms particularly vancomycin-resistant enterococci (VRE) has become a serious public health concern. For preventing and controlling the spread of vancomycin-resistant organisms, the prudent use of vancomycin is strongly recommended by the Hospital Infection Control Practices Advisory Committee (HICPAC).

Method: A 6-week prospective observational study of vancomycin use was conducted in hospitalized patients at Siriraj Hospital, Bangkok, Thailand, from February to March 2005. Indications of initiating and continuing vancomycin were categorized according to HICPAC recommendations. Factors related to the appropriateness of vancomycin use were also evaluated.

Results: At initiation, vancomycin was inappropriately and empirically prescribed for 37/222 times (16.7%) and 166/222 times (74.8%), respectively. After

microbiological results were obtained, the rate of inappropriate prescription continued to be 132/222 times (59.5%). Furthermore, an inappropriate use was significantly correlated with the type of department. There was a higher rate of an inappropriate use in the Department of Pediatrics, Surgery, and Ophthalmology when compared with that of the Department of Medicine ($p=0.001$), with topical formulation ($p<0.001$), with intravenous administration ($p=0.012$), and without consultation with infectious disease specialist ($p=0.001$). The overuse did not improve the clinical outcome.

Conclusion: A substantial rate of inappropriate use of vancomycin was found in our hospital. The intervention to improve an appropriateness of vancomycin use should be urgently implemented in order to prevent and control infections caused by vancomycin-resistant organisms.

*Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

**Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

***Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Received for publication: June 23, 2006.

Efficacy and Safety of Colistin for Therapy of Infections Caused by Multidrug-Resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in Siriraj Hospital

Pornpan Koomanachai, M.D.*,
Surapee Tiengrim, M.Sc.*,
Pattarachai Kiratisin, M.D.**,
Visanu Thamlikitkul, M.D.*

Abstract

Introduction: Infections due to *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, which are resistant to all available antibiotics in Thailand, have been increasing over the past five years, especially in a tertiary care hospital facility. The overall mortality rate, in patients infected with multidrug-resistant (MDR) *P. aeruginosa* and *A. baumannii* was approximately 80 percent. *In vitro* study of colistin against MDR *P. aeruginosa* and *A. baumannii* at Siriraj Hospital, Bangkok, Thailand, in 2002, revealed that all isolates were susceptible to colistin.

Objective: To determine the efficacy and safety of colistin produced by a local pharmaceutical company in Thailand for the treatment of infections caused by MDR *P. aeruginosa* and *A. baumannii*.

Patients and Methods: The patients hospitalized at Siriraj Hospital who had infections caused by MDR *P. aeruginosa* and *A. baumannii* were enrolled from January 2005 to March 2006. Colistin at a dosage of 2.5 to 5 mg/kg/d was given intravenously in two divided doses. The primary outcomes were the clinical response and overall mortality at 30 days after

initiation of colistin treatment. The secondary outcomes were microbiological response and adverse events.

Results: Eighty-seven patients infected with MDR *P. aeruginosa* and *A. baumannii* were enrolled. Seventy-two patients (65 *A. baumannii* and 7 *P. aeruginosa*) received colistin, and 15 patients (12 *A. baumannii* and 3 *P. aeruginosa*) received other antibiotics. The mean age, gender, underlying conditions, and severity of illness of the patients in both groups were not significantly different. In the colistin group, 59 patients (81.9%) had a favorable clinical response and 95 percent had a microbiological response. Overall mortality of the patients in the colistin and the non-colistin group was 47 percent and 80 percent, respectively. Nephrotoxicity was observed in 27 percent of the patients in the colistin group, and 12 of them had predisposing factors contributing to their renal dysfunction. No neurotoxicity was observed among 72 patients.

Conclusion: Locally produced colistin appears to be safe and effective for the treatment of infections caused by MDR *P. aeruginosa* and *A. baumannii* in Thai adult patients.

*Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

**Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Received for publication: June 23, 2006.

Impact of Antiretroviral Therapy on the Relapse of Cryptococcosis and Survival of HIV-Infected Patients with Cryptococcal Infection

Ubonvan Jongwutiwes, M.D.,
Sasisopin Kiertiburanakul, M.D.,
Somnuek Sungkanuparph, M.D.

Abstract

Background: Cryptococcosis is an opportunistic infection with substantial morbidity and mortality in HIV-infected patients. Impact of antiretroviral therapy (ART) on the relapse of cryptococcosis and survival of HIV-infected patients with cryptococcosis has not been well established.

Methods: A retrospective cohort study of HIV-infected patients with cryptococcosis during 1997 and 2005 was conducted. The relapse and survival rates with corresponding risk factors were determined.

Results: There were 149 patients with a mean age of 33.5 \pm 7.4 years, and 57 percent were male. The median CD4 cell was 22 cells/mm³. After exclusion of patients who died or were lost to follow-up during the first two weeks, 127 patients were eligible for the analysis of the effect of ART on the relapse and survival rates. Of 127 patients, 52 received ART. The demographic data between the two groups were

similar. The median time of ART initiation after diagnosis of cryptococcosis was 2.6 months. The most frequent ART used was nonnucleoside reverse transcriptase inhibitor (NNRTI)-based regimen (88.4%). The median CD4 change at six months of ART was 97 cells/mm³, and 87.9 percent achieved undetectable HIV RNA. The cumulative 75-percent survival (free) from relapse duration was 10.4 months in the no-ART group and 41.9 months in the ART group ($p < 0.01$). The 75-percent survival from cryptococcosis-related mortality in the no-ART and ART group was 6.4 months and > 54 months, respectively ($p < 0.01$). In Cox proportional hazards model, ART was the only factor associated with lower relapse and mortality rates ($p < 0.01$).

Conclusions: ART significantly reduced the relapse and mortality rates from cryptococcosis in HIV-infected patients. ART is strongly recommended in this population, and should not be delayed.

Isolated Antibody to Hepatitis B Core Antigen in HIV-1 Infected Patients and a Pilot Study of Vaccination to Determine the Anamnestic Response

Yogyuth Jongjirawisan, M.D.,
Prayut Ungulkraiwit, M.D.,
Somnuek Sungkanuparph, M.D.

Abstract

Background: Isolated antibody to hepatitis B core antigen (anti-HBc) is frequently observed in HIV-1 infected patients. There is no data of this entity in Asian population. This study aimed to determine the prevalence of and associated risk factors for the presence of isolated anti-HBc in Thai HIV-1 infected patients and the anamnestic response to hepatitis B vaccination in this population.

Methods: HIV-infected patients, who visited the Infectious Diseases Clinic in Ramathibodi Hospital, Bangkok, Thailand, from October 2005 to January 2006, were enrolled to determine hepatitis B serology. Subjects with isolated anti-HBc were given one-dose hepatitis B vaccine and tested for anti-HBs four weeks after vaccination.

Results: Of 140 patients, 28 (20%) had isolated anti-HBc and had undergone hepatitis B vaccination. Patients with isolated anti-HBc were more likely to have a history of intravenous drug use (25% vs 3.6%,

$p = 0.001$) and anti-HCV seropositivity (32.1% vs 6.6%, $p = 0.001$), compared to those without anti-HBc. In the multivariate analysis, a history of intravenous drug use (OR 30.8, $p < 0.001$) and HCV seropositivity (OR 6.7, $p = 0.002$) were the two independent risk factors associated with the presence of isolated anti-HBc. Among 28 patients with isolated anti-HBc and received hepatitis B vaccine, only two patients (7%) had a response to vaccination. Both subjects had high CD4 cell counts and undetectable HIV RNA.

Conclusions: The prevalence of isolated anti-HBc among Thai HIV-infected patients was 20 percent. The risk factors significantly associated with the presence of isolated anti-HBc were a history of intravenous drug use and positive anti-HCV seropositivity. Anamnestic response to hepatitis B vaccination in Thai HIV-1 infected patients with isolated anti-HBc was very low. Further large-scale study with strategies to improve the response of vaccination is needed.

Immunological Response to Hepatitis B Vaccine in Acquired Immunodeficiency Syndrome Patients with Virological Response to Highly Active Antiretroviral Therapy

Leilani Paitoonpong, M.D.,
Chusana Suankratay, M.D., Ph.D.

Abstract

Background: Acquired immunodeficiency syndrome (AIDS) patients who have hepatitis B virus (HBV) infection always have more adverse clinical course than seronegative patients. Prevention by immunization is necessary in this group. Several studies found that an immunological response to hepatitis B vaccine in AIDS patients was lower than normal population. AIDS patients with undetectable plasma human immunodeficiency virus (HIV) RNA after receiving antiretroviral therapy should have a restoration of the immune response. This group of patients may have a normal immunological response to hepatitis B vaccine.

Objective: To study the immunological response to hepatitis B vaccine in AIDS patients with virological response to highly active antiretroviral therapy (HAART).

Design: A descriptive study.

Study and Methods: AIDS patients with virological response to HAART (HIV RNA < 50 copies/mL) who

had no immunity to HBV were received three doses of intramuscular hepatitis B vaccine on day 0, 30, and 180. Anti-HBs level was measured one month after a complete immunization.

Results: There were 28 AIDS patients enrolled in our study. The overall response rate to hepatitis B vaccine was 71.4 percent. The vaccine responders had significantly higher CD4 counts at one month after a complete immunization than the nonresponders ($p=0.035$). The patients receiving efavirenz-containing HAART regimen had a better response than those without efavirenz-containing regimen ($p=0.030$). The responders had received a relatively longer duration of HAART. There was no statistical difference in the response between the patients with baseline CD4 count less and more than 350 cells/ μ L. No serious adverse reaction from immunization was observed.

Conclusion: AIDS patients with undetectable plasma HIV RNA have a good immunological response to hepatitis B vaccine.

Prevalence of Infections Caused by Community-Acquired Methicillin-Resistant *Staphylococcus aureus* at Siriraj Hospital, Bangkok, Thailand

Sripetcharat Mekviwattanawong, M.D.*,

Somporn Srifuengfung, Ph.D.**,

Kulkanya Chokepaibulkit, M.D.***,

Darin Lohsiriwat, M.D.****,

Visanu Thamlikitkul, M.D.*

Abstract

Background: Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections have emerged in many parts of the world over the past decade. To our knowledge, the prevalence of CA-MRSA infections in Thai patients is unknown.

Objective: To determine an epidemiology of CA-MRSA infections in hospitalized patients at Siriraj Hospital, Bangkok, Thailand.

Methods: The study was carried out at Siriraj Hospital from January to May 2005. The eligible patients were hospitalized patients whom *S. aureus* were isolated from their clinical specimens submitted to Department of Microbiology. *S. aureus* isolate were classified into infection or colonization. *S. aureus* infections were

further classified into MRSA or methicillin-susceptible *S. aureus* (MSSA) infections, and hospital-acquired (HA) or community-acquired (CA) infections. CA-MRSA infection is defined as the infection caused by MRSA isolated from the patient within 72 hours hospitalization, and has no features of healthcare-associated MRSA infections.

Results: There were 669 *S. aureus* isolates from 448 patients. 262 isolates (58.5%) were MSSA, and 186 (41.5%) were MRSA. CA-MRSA was found in three isolates (0.9% of total MRSA) from two patients.

Conclusion: The prevalence of CA-MRSA infections in hospitalized patients at Siriraj Hospital was uncommon, and these patients could probably be healthcare-associated MRSA infections.

*Division of Infectious Diseases and Tropical Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

**Division of Bacteria, Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

***Division of Infectious Diseases, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

****Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Received for publication: June 23, 2006.