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Original Article

Effectiveness of an early switch from intravenous to oral antimicrobial therapy for lower respiratory tract infection in patients with severe motor intellectual disabilities

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ABSTRACT

An early switch from intravenous to oral antimicrobial therapy is useful for reducing the duration of the hospitalization in adult patients with community acquired-pneumonia, whereas the efficacy of switch therapy for pediatric patients with community acquired (CA)-lower respiratory tract infection (LRTI) is uncertain. The aim of this study is to investigate the efficacy of switch therapy for LRTI in patients with severe motor intellectual disabilities (SMID). This retrospective study was performed on 92 patients with SMID who were admitted to the Department of Pediatrics at the Hospital of University of Occupational and Environmental Health, Japan from April 1, 2010 to March 31, 2017 for the suspicion of bacterial LRTI and were initially treated with an intravenous antimicrobial agent. Clinical outcomes were compared between patients with switch therapy (Switch therapy group) and conventional intravenous antimicrobial therapy (No switch therapy group). Thirteen and 79 in patients with SMID belonged to Switch thrapy group and No switch therapy group, respectively. Length of hospital stay in Switch therapy group was significantly shorter than that in No switch therapy group ($P = 0.002$). In the patients undergoing switch therapy, there was no patient who required re-treatment and/or re-hospitalization. Switch therapy for LRTI was useful for the reduction of length of hospital stay without increasing risk of re-treatment and re-hospitalization in patients with SMID.

1. Introduction

Community acquired (CA)-lower respiratory tract infection (LRTI) is one of the most common diseases in children [1]. It is important to confirm the involvement of bacterial pathogens in the treatment of CA-LRTI. Although the introduction of pneumococcal conjugate vaccine has reduced the number of pediatric patients with bacterial CA-LRTI [2–4], many patients who should be administrated intravenous antimicrobial agents are still hospitalized for the disease. Like other developed countries, the guideline for the treatment of pediatric respiratory infectious diseases has been used for the clinical practice in Japan [5,6]. The guideline recommends intravenous antimicrobial therapy for pediatric patients with severe or moderate bacterial pneumonia, in which the recommended duration of antimicrobial therapy is for 3–7 days whereas the route of the administration of the drugs is not stipulated clearly.

Several studies indicated that an early switch from intravenous to oral antimicrobial therapy was useful for reducing the duration of the hospitalization, cost saving and early rehabilitation in adult patients with community-acquired pneumonia [7–9]. On the other hand, the efficacy of switch therapy for pediatric patients with CA-LRTI is uncertain. Because previous reports indicated that oral and intravenous antimicrobial therapy had equivalent efficacy for the treatment of pneumonia in children without underlying diseases except for severe cases requiring intensive care [10,11], it might not be necessary to evaluate the efficacy of switch therapy in these children. On the other hand, patients with neuromuscular disorders are at a high risk of the development of severe CA-LRTI [12], and an intravenous antimicrobial agent is usually administrated as an initial treatment. Therefore, the evaluation of the efficacy of switch therapy for early discharge is needed in these patients.

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To investigate the efficacy of switch therapy in patients with severe motor intellectual disabilities (SMID) hospitalized for suspicion of bacterial LRTI, we compared the clinical course between patients treated with switch therapy and conventional intravenous antimicrobial therapy.

2. Materials and methods

2.1. Study population

A total of 343 patients were admitted to the Department of Pediatrics at the Hospital of University of Occupational and Environmental Health, Japan from April 1, 2010 to March 31, 2017 for the suspicion of bacterial LRTI and were initially treated with an intravenous antimicrobial agent. Of these patients, the number of patients with SMID was 98. The patients, who required intensive care (n = 2), received a diagnosis of Mycoplasma infection (n = 1), or were changed an initial antimicrobial agents because of no therapeutic effect (n = 3), were excluded from the present study. Ultimately, 92 with SMID were enrolled for our retrospective cohort study. LRTI was diagnosed when patients had cough and sputum production as clinical symptoms, accompanied by auscultatory findings of abnormal breath sounds, wheezes, or crackles [13]. Bacterial etiology of LRTI were suspected when a patient showed the increase in white blood cells (>15,000/μl) and/or the elevation of serum C-reactive protein (CRP) (>20 mg/L). In patients with leukocytosis and elevation of serum CRP levels, bacterial LRTI was diagnosed when phagocytized bacterial cells were seen on the Gram stain smear of the sputum sample. Clinical information on each patient was collected using a standardized case report form. Presence or absence of consolidation on the chest X-ray was assessed by two of the authors (T.H., K.K.). Our study was approved by the Institutional Review Board of the University of Occupational and Environmental Health, Japan (No. 281448).

2.2. Definition of a patient with severe motor intellectual disabilities

SMID was diagnosed according to the classical criteria (Oshima's criteria) [14]. We evaluated the psychomotor development for children under 5 years of age by developmental quotients (DQ) using the Enjoji Infant Analytic Developmental Test [15], and for those aged 5 years or older by intelligence quotients (IQ) using the Wechsler Intelligence Scale for Children. All children with SMID, classified as grade 1 or 2, were bedridden or unable to sit, crawl, or walk with support, and had IQ or DQ lower than 20.

2.3. Guideline of antimicrobial therapy for patients hospitalized for bacterial LRTI

In our hospital, an initial treatment of bacterial LRTI in children without underlying diseases conformed to Japanese guideline for the treatment of pediatric respiratory infectious diseases [5,6]. Ampicillin (100 mg/kg/day, maximal dose: 4 g/day) was initially administrated intravenously for these patients. Ampicillin/sulbactam was initially administrated intravenously for patients with SMID because *Moraxella catarrhalis* was a major causative pathogen of LRTI in these patients [16]. Patients with the suspicion of bacteremia were occasionally treated with third-generation cephalosporins. If an improvement in clinical symptoms was achieved promptly, an initial therapy was discontinued in around 5 days. When no therapeutic effect of an initial antimicrobial agents was shown after 2–3 days, we re-evaluated the diagnosis of the patient, and investigated the results of microbiological examinations. The change of treatment was considered after the re-evaluation.

2.4. Intravenous to oral switch of antimicrobial therapy

In 2013, a pediatric infectious disease specialist who was approved by the Japan Pediatric Society and the Japanese Association for Infectious Diseases began to work in the pediatric ward of our hospital, and started direct clinical intervention for infectious diseases [17]. Switch therapy for LRTI were actively performed for children without underlying diseases from April 1, 2013, and for patients with SMID from 2015. Switch therapy was considered to patients fulfilling the following conditions: (1) improving respiratory symptoms (e.g. dyspnea, tachypnea, sputum production), (2) absence of fever (38 °C) for more than 24 h, (3) improving oral intake or enteral feeding, and (4) intact gastrointestinal absorption. The oral antimicrobial agent used for switch therapy was the same kind of drug as the injectable agent used for the initial therapy. Total duration of antimicrobial therapy was around 5 days.

2.5. Sputum collection, bacteriological examination, and its evaluation

Sputum samples were obtained for the confirmation of bacterial infection. Macroscopic findings of all sputum samples were judged good quality (P2 or P3) for the presumption of causative pathogens by Miller and Jones' classification. The sputum collection and the judgment of their qualities using Geckler's classification were performed as previously described [16]. Smears, classified as Geckler's group 4 or 5, were judged to be suitable for bacterial examination. Only sputum samples suctioned through the tracheostomy orifice were judged to be suitable, even when they were classified as Geckler's group 6. When phagocytized bacterial cells were seen on the Gram stain smear of the sputum sample and corresponding bacterium was isolated later, it was identified as presumed bacterial pathogen.

2.6. Statistical analysis

The SPSS statistics software program (version 21; SPSS Inc., Chicago, IL, USA, and IBM, Armonk, NY, USA) was used for the analysis. Mann-Whitney *U* test was used to compare the differences between the quantitative values. Fisher's exact test was used for the comparison of the qualitative analysis. *P*-values less than 0.05 were considered to be statistically significant.

3. Results

The patients' clinical characteristics and laboratory data are shown in Table 1. Thirteen and 79 patients with SMID underwent switch therapy (Switch thrapy group) and conventional intravenous antimicrobial therapy (No switch therapy group), respectively. No significant differences in the demographic or clinical characteristics and laboratory findings on admission were seen between the 2 groups. Duration of intravenous antimicrobial therapy ($P < 0.001$) and length of hospital stay ($P = 0.002$) in Switch therapy group were significantly shorter than those in No switch therapy group (Table 2). No significant difference of total duration of antimicrobial therapy was seen between the 2 groups. In the patients undergoing switch therapy, there was no patient who required re-treatment and/or re-hospitalization (Table 2). These same results were also observed even when subjects were confined to patients with pneumonia confirmed in chest X-ray (data not shown).

The Japanese guideline for the treatment of pediatric respiratory infectious diseases recommends the administration of an intravenous antimicrobial agent as an initial treatment for patients with severe or moderate bacterial pneumonia [6]. We investigated the