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Antipyretic effect of Mao-to, a Japanese herbal medicine, for treatment of type A influenza infection in children

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Abstract

Mao-to is a Japanese traditional herbal medicine which has been used since ancient times for the treatment of influenza-like illness. This study was conducted to evaluate the effect of oral Mao-to administration in children with type A influenza, in comparison to Oseltamivir. We performed a controlled trial of 60 children, from 5 months through 13 years of age, with fever and influenza-like symptom of up to 48 h duration. Diagnosis of influenza type A was performed by virus isolation or detection of a viral gene by RT-PCR. Patients assigned into the following 3 groups: oral Mao-to powder (TJ-27) 0.06 g/kg body wt./dose three times daily ($n = 17$), Oseltamivir 2 mg/kg body wt./dose twice daily ($n = 18$) or both oral Mao-to plus Oseltamivir ($n = 14$). The median duration of fever after treatment was significantly shorter in the Mao-to and Mao-to plus Oseltamivir groups, compared with the Oseltamivir only group (15 h [95%CI 13.2–22.1] $p < 0.01$; 18 h[15.2–27.7] $p < 0.05$; 24 h[23.5–43.0], respectively). Oral Mao-to administration was effective in the control of fever due to type A influenza infection in children.

Keywords: Influenza; Mao-to; Japanese herbal medicine; Oseltamivir; Pediatrics

Introduction

The neuraminidase inhibitor Oseltamivir (-Ethyl[3*R*, 4*R*,5*S*]-4-acetamido-5-amino-3-[1-ethylpropoxy]cyclohex-1-ene-1-carboxylate monophosphate) (Fig. 1), a specific antiviral against type A and B influenza viruses, is effective in the treatment of influenza and is now used worldwide (Cooper et al., 2003). The drug is not, however, administered to infants under 1 year of age, because its safety for that population has not yet been established (Wooltorton, 2004). Furthermore, a recent report concerning the emergence of viruses resistant to this new drug (Gubareva, 2004; Kiso et al., 2004). It would therefore be advantageous to identify alternative strategies for treatment of influenza that do not rely on this drug.

Mao-to is a traditional herbal medicine that has been used in Japan for the treatment of influenza-like illness (high fever, headache, pain and cough) since ancient times and Ephedrae herba, one of component herbs of Mao-to has been reported to show an in vitro anti-influenza viral effect (Mantani et al., 1999). This study was conducted to investigate the efficacy of oral Mao-to administration, in order to evaluate this traditional medicine in comparison with modern treatment with the antiviral drug Oseltamivir in children with type A influenza, diagnosed based on virus isolation or detection of viral genes.

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Methods

Patients

The children enrolled in this study were between the ages of 5 months and 13 years who visited the outpatient clinic of the Department of Pediatrics, Self Defense Force Sendai Hospital from January to March 2004, suffering from influenza-like illness with fever [$\geqslant 38\,^{\circ}C$], at least two constitutional symptoms (headache, chill, or fatigue) and one respiratory symptom (cough or coryza) within 48 h duration of illness.

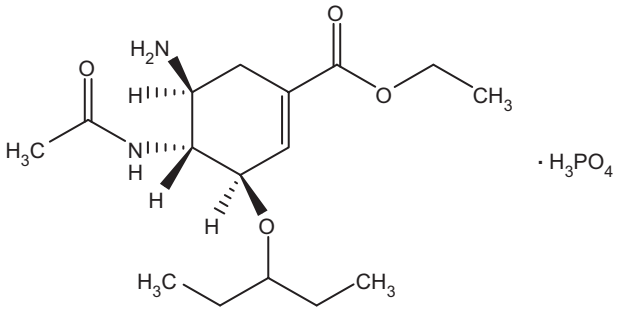

Fig. 1. Structure of Oseltamivir.

Study design

We did not exclude patients who had received vaccination for influenza that season. After physical examination and before treatment, nasal swabs or aspirates were collected from each patient for definitive diagnosis of type A influenza by isolation/detection of the virus. Patients were assigned to treatment groups based on their age and the results of a rapid influenza diagnosis kit test (Capilia FLU A, B; Nippon Becton Dickinson, Tokyo, Japan) (Fig. 2). Patients positive for the kit test and under the age of 1, or negative for the kit test, were assigned to the group which was administered only oral Mao-to powder (TJ-27. Tsumura&Co., Tokyo, Japan) at a dose of 0.06 g/kg body wt./dose three times daily (standard regimen for children), because they did not meet the criteria for Oseltamivir treatment in Japan. Those positive for the kit test and over the age of 1 year were randomized by two groups which received either oral Oseltamivir powder 2 mg/kg body wt./dose twice daily or both Mao-to 0.06 g/kg body wt./dose three times and Oseltamivir 2 mg/kg body wt./dose twice daily. TJ-27 contains extract from Ephedrae herba, Cinnamomi cortex, Armenicae cortex and Glycyrrhizae radix (Table 1). The three-dimensional HPLC profile of TJ-27 is shown in Fig. 3. Caregivers of

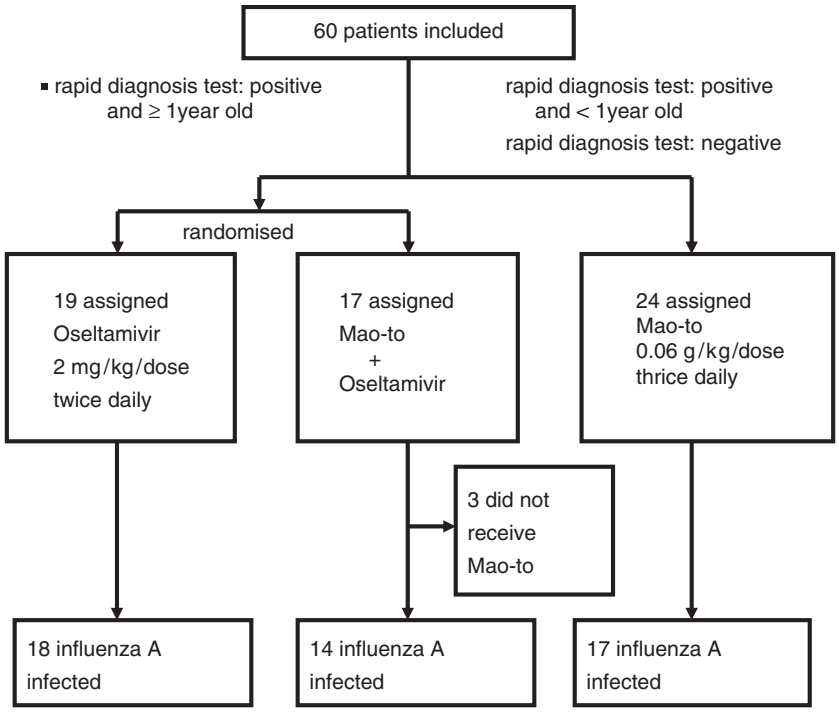

Fig. 2. Trial profile. Patients suffering from influenza-like illness were assigned to treatment groups based on their age and the results of a rapid influenza diagnosis kit test. Patients positive for the kit test and under the age of 1, or negative for the kit test, were assigned to the group which was administered only oral Mao-to powder (TJ-27) 0.06 g/kg/dose three times daily. Those positive for the kit test and over the age of 1 year were randomized by two groups which received either oral Oseltamivir powder 2 mg/kg/dose twice daily or both Mao-to and Oseltamivir. Patients who were confirmed to be infected with influenza virus by viral culture or RT-PCR were included in the analysis finally.