Vaccine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Significant circulation of influenza B viruses mismatching the recommended vaccine-lineage in South Korea, 2007–2014

Ji Yun Noh [a,b], Won Suk Choi [a,b], Joon Young Song [a,b], Han Sol Lee [c], Sooyeon Lim [c], Jacob Lee [d], Yu Bin Seo [d], Jin-Soo Lee [e], Seong-Heon Wie [f], Hye Won Jeong [g], Jung Yeon Heo [g], Young Keun Kim [h], Kyung Hwa Park [i], Shin Woo Kim [j], Sun Hee Lee [k], Jung Hwa Lee [l], Dong Hyun Kim [m], Sung Il Woo [n], Chae Seung Lim [o], Kyung Soon Cho [p], Hee Jin Cheong [a,b], Woo Joo Kim [a,b,c,*]

[a] Division of Infectious Diseases, Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea
[b] Asia Pacific Influenza Institute, Korea University College of Medicine, Seoul, South Korea
[c] Brain Korea 21 Plus for Biomedical Science, Korea University College of Medicine, Seoul, South Korea
[d] Division of Infectious Diseases, Department of Internal Medicine, Kangnam Sacred Heart Hospital, Hallym University School of Medicine, Chuncheon, South Korea
[e] Division of Infectious Diseases, Department of Internal Medicine, Inha University College of Medicine, Incheon, South Korea
[f] Division of Infectious Diseases, Department of Internal Medicine, The Catholic University of Korea, School of Medicine, St. Vincent's Hospital, Suwon, South Korea
[g] Division of Infectious Diseases, Department of Internal Medicine, College of Medicine, Chungbuk National University, Cheongju, South Korea
[h] Division of Infectious Diseases, Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, South Korea
[i] Division of Infectious Diseases, Department of Internal Medicine, Chonnam National University Medical School, Gwangju, South Korea
[j] Division of Infectious Diseases, Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, South Korea
[k] Division of Infectious Diseases, Department of Internal Medicine, Pusan National University School of Medicine, Busan, South Korea
[l] Department of Pediatrics, Korea University College of Medicine, Seoul, South Korea
[m] Department of Pediatrics, Inha University College of Medicine, Incheon, South Korea
[n] Department of Pediatrics, College of Medicine, Chungbuk National University, Cheongju, South Korea
[o] Department of Laboratory Medicine, Korea University College of Medicine, Seoul, South Korea
[p] Department of Food Science and Nutrition, College of Health, Welfare and Education, Tongmyong University, Busan, South Korea

ARTICLE INFO

Article history:
Received 29 November 2017
Received in revised form 10 July 2018
Accepted 11 July 2018
Available online xxxx

Keywords:
Epidemiology
Influenza B virus

ABSTRACT

We aimed to characterize the lineages of influenza B viruses obtained from clinical specimens during the 2007–2014 seasons in South Korea. RT-PCR for the partial hemagglutinin gene of influenza B virus was performed on laboratory-confirmed influenza B samples from the 2007–2008 season to 2013–2014 season. A phylogenetic tree was generated, and current influenza vaccine strains for the Northern Hemisphere were used as representative strains of Victoria and Yamagata lineages.

A total of 571 influenza B virus sequences were analyzed. During the 2009–2010 season, most of the circulating influenza B viruses matched the vaccine strain; 91.0% (91/100) of viruses belonged to the Victoria lineage. In the 2007–2008, 2011–2012, and 2013–2014 seasons, co-circulation of each influenza B lineage was found with a match ratio to the vaccine strain of 53.2% (42/79), 40.9% (63/154), and 58.3% (134/230), respectively. Overall, 41.7% (238/571) of the circulating influenza B viruses belonged to the lineage mismatching the vaccine strain.

During the seven influenza seasons, influenza B epidemics were substantial in four seasons in South Korea. Significant mismatches of the vaccine and lineage of the circulating influenza B viruses were found. The current trivalent influenza vaccine may not be fully suitable for effective protection against influenza B.

1. Introduction

Since 1985, two antigenically distinct lineages of influenza B viruses have been circulating worldwide: the Victoria lineage and Yamagata lineage represented by the prototype viruses B/Victoria/2/87 and B/Yamagata/16/88, respectively [1]. There is little or no cross-protection between these two influenza B lineages [2].

* Corresponding author at: Division of Infectious Diseases, Department of Internal Medicine, Korea University College of Medicine, Seoul, South Korea.
E-mail address: wjkim@korea.ac.kr (W.J. Kim).

https://doi.org/10.1016/j.vaccine.2018.07.021
0264-410X/

Current trivalent influenza vaccines (TIV) contain only one lineage of influenza B viruses. This situation leads to reduced effectiveness of the influenza vaccine, especially when the predominant circulating influenza B virus does not match the vaccine strain.

Although the proportion of influenza B among overall influenza varies by influenza season, region, and study populations, influenza B viruses are responsible for about 25% of influenza disease cases [3,4]. The overall number of deaths associated with influenza B was less than that with A/H3N2, but greater than with A/H1N1 influenza, and influenza-attributable mortality rates increased dramatically with age among the elderly [4]. Therefore, improvement in protection against influenza B and reduction of morbidity due to influenza B infection are important goals for public health.

In the United States (US), from the 2001–2002 season to 2010–2011 season, the dominant circulating influenza B lineage was different from the vaccine strain in five of the ten influenza seasons [1]. In Europe, the lineage of predominant influenza B virus and vaccine strain matched in four of the eight seasons between 2003 and 2004 and 2010–2011 [1].

In South Korea, influenza B viruses were likely to be a major cause of seasonal influenza epidemics every two years recently. According to the national influenza surveillance data from Korea Centers for Disease Control and Prevention from the 2000–2001 season through 2013–2014 season, influenza B was responsible for <1% to 64% of influenza positive samples [5]. On average, 27.7% of influenza samples during this period were positive for influenza B in South Korea. However, there is a lack of information about molecular characteristics of circulating influenza B viruses over several seasons. This study was aimed at investigating the proportion of the two lineages of influenza B viruses from 2007 to 2008 season through 2013–2014 influenza seasons in South Korea.

2. Materials and methods

2.1. Study samples

A total of 571 RNA samples of laboratory-confirmed influenza B cases diagnosed by RT-PCR from the 2007–2008 season through 2013–2014 season were used in this study. The samples were collected from the Korea University Guro Hospital, Seoul, the Busan Metropolitan City Institute of Health and Environment, Busan and the Hospital-based Influenza Morbidity & Mortality (HIMM) surveillance in Korea. The HIMM surveillance system is an influenza surveillance network in which 10 tertiary hospitals have participated. The surveillance scheme has been operated since the 2011–2012 influenza season. The subjects of surveillance are patients who visit emergency rooms with influenza-like illness or the hospitalised patients with influenza [6]. The subjects of surveillance are adult patients aged more than 18 years of age until the 2012–2013 season. Age of the surveillance subjects had been expanded to an all age group in the 2013–2014 season in three tertiary hospitals.

2.2. Molecular and phylogenetic analysis

Synthesis of cDNA was performed using primer Buni11w (AGCAGAAGCGS) (7). Partial nucleotides of the hemagglutinin (HA) gene was amplified by PCR as described elsewhere [7,8]. DNA sequences were determined in both directions using the Applied Biosystems Automatic Sequencer ABI 3730xl and ABI Prism BigDye® Terminator v3.1 sequencing system (Applied Biosystems, Foster City, CA). Phylogenetic classification was based on partial 238 bp- nucleotides of HA. Current influenza vaccine strains for the Northern Hemisphere were used as representative strains of the Victoria and Yamagata lineages: B/Brisbane/60/2008 (accession No.: CY115151) and B/Malaysia/2506/2004 (accession No.: EU124275) for the Victoria lineage; B/Massachusetts/2/2012 (accession No.: KC892118), B/Wisconsin/01/2010 (accession No.: CY115183), and B/Florida/4/2006 (accession No.: CY033876) for the Yamagata lineage. Sequence alignment was performed using Clustal W. A distance-based maximum likelihood phylogenetic tree was generated using MEGA software v.6 with 1000 bootstrap iterations. Same sequences from the same influenza season and the same region were not included in the phylogenetic analysis to avoid duplication.

2.3. Ethics approval

This study's protocol was approved by the Institutional Review Board of Korea University Guro Hospital (approval number: KUGH13222).

3. Results

Among 571 influenza B viral sequences during the 2007–2014 seasons, 296 (51.8%) samples belonged to the Victoria lineage and 275 (48.2%) samples were Yamagata lineage influenza B viruses. Only eight influenza B samples were available to be analyzed during 2008–2009 (2 viruses), 2010–2011 (1 virus), and 2012–2013 (5 viruses) season because influenza B epidemics were very low in those seasons (Fig. 1).

Among 79 samples in the 2007–2008 season, 42 (53.2%) samples belonged to the Victoria lineage and 37 (46.8%) samples were Yamagata lineage influenza B viruses (Fig. 2). Recommended influenza B virus for the influenza vaccine in the Northern Hemisphere in 2007–2008 season was B/Malaysia/2506/2004, which belonged to the Victoria lineage. During the 2009–2010 season, 91 (91.0%) samples belonged to the Victoria lineage among 100 samples. In the 2011–2012 season, partial HA sequences were obtained from 154 samples of laboratory-confirmed influenza B patients. More than a half of influenza B viruses (59.1%, 91/154) mismatched the lineage of the vaccine strain in the 2011–2012 season. During the 2013–2014 season, influenza B viruses which belonged to the Victoria lineage were 41.6% (96/230) and other samples (58.3%, 134/230) belonged to the Yamagata lineage influenza B virus. The overall match ratio of the circulating strains with the lineage of the vaccine strain was 58.3% (333/571) (Fig. 3).

4. Discussion

The disease burden of influenza B is significant, although influenza A is considered a more prevalent virus of seasonal influenza and the causative virus for all past pandemic influenza. The proportion of influenza B varies by season, location, study population, and surveillance methods. The proportion of influenza B ranged from 1% to 46% in the US and 2%-65% in the United Kingdom according to surveillance data from 1999 to 2013 [9]. In South Korea, influenza B accounted for <1% to 64% of all influenza viruses from 2000–2001 to 2013–2014 season [5]. The influenza-associated hospitalization rate was higher for influenza B than for influenza A/H1N1. The estimated influenza B-associated hospitalization rate for primary pneumonia and influenza was 37.7 per 100,000 person-years from the 1979–1980 through the 2000–2001 seasons in the US: 22.6 and 43.5 per 100,000 person-years for A/H1N1 and A/H3N2, respectively [10]. From 1990–1991 through 1998–1999, 14.5% of influenza-associated respiratory and circulatory mortality in the US was attributed to influenza B [4]. In Hong Kong, 24% of influenza hospitalisations were due to influenza B during 2000–2010 [11].

Please cite this article in press as: Noh JY et al. Significant circulation of influenza B viruses mismatching the recommended vaccine-lineage in South Korea, 2007–2014. Vaccine (2018), https://doi.org/10.1016/j.vaccine.2018.07.021