ORIGINAL ARTICLE

Severity of the two post-pandemic influenza seasons 2010-11 and 2011-12 in Northern Greece

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Abstract

Since the pandemic in 2009, the two following post pandemic influenza seasons have been associated with increased morbidity and mortality rates in Northern Greece. The scope of this short report is to provide relevant epidemiological information, an evaluation of the efficacy of the seasonal vaccine and antiviral drugs. Molecular analysis revealed the close match of A(H1N1) 2009 pandemic and post-pandemic 2010-11 viruses with the vaccine virus. However, a proportion of the influenza A(H3N2) and B viruses that circulated in 2011-12 differed from the vaccine strains, possibly explaining the high hospitalization and fatality rates. There is also a trend of new virus strains to accumulate amino acid changes. Only A(H1N1) viruses resistant to oseltamivir have been detected. Constant epidemiological and molecular surveillance is essential to monitor the efficacy of the vaccine and antiviral drugs and assess the severity of each influenza season. Hippokratia 2013, 17, 2: 150-152

Keywords: Influenza, molecular, vaccine, antiviral, post-pandemic, Northern Greece

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Since the pandemic in 2009, when the A(H1N1) 2009 pandemic virus appeared, the Northern Greek National Influenza Centre (NIC) in cooperation with Hellenic Centre for Disease Control and Prevention (HCIDCP) has been closely monitoring the influenza activity in Northern Greece[1]. Furthermore, molecular analysis of the haemagglutinin and neurnaminidase genes is routinely done on representative viruses, in order to assess the seasonal vaccine and the efficiency of the available antiviral drugs[2-5].

The two post pandemic influenza seasons 2010-11 and 2011-12 have been associated with increased morbidity and mortality rates in Northern Greece. The scope of this paper is to present relevant epidemiological information, an evaluation of the seasonal vaccine and of the most commonly used antiviral drug, oseltamivir.

During each influenza season, all of the examined cases range from mild Influenza-Like-Illness (ILI) to fatal cases. Nasopharyngeal swabs or aspirates sent to the NIC from the Sentinel system and outpatient hospital clinics, are all tested for influenza for diagnostic and surveillance purposes. During the pandemic in 2009, 32% of the 4391 examined samples were positive for influenza A(H1N1), 6.7% developed pneumonia and 2% of infections were fatal[6,7]. During the pandemic, a different infection pattern was observed, with two subsequent pandemic waves: a summer wave that initiated due to tourist importation and a second winter wave due to the widespread outbreak[6-8]. Influenza activity returned to the usual pattern during the two following seasons; in general it was low from September to December, increasing in January and ending in April. Epidemiological analysis revealed that the post-pandemic 2010-11 was more severe than the pandemic period, with a total of 1870 clinical samples tested for influenza A and B; 848 (45%) were found positive, 96.8% of which were infections caused by A(H1N1) 2009, and the remaining 1.53% and 1.65% were attributed to A(H3N2) and B viruses respectively. 11% severe pneumonia infections and 6.7% fatal cases were reported from A(H1N1)2009 (Table 1).

During 2011-12, another relatively severe influenza season, a total of 314 clinical samples were tested at the Northern Greek NIC for influenza, out of which 144 (46%) were positive for influenza viruses; 51% were A(H3N2) viruses and 49% were B influenza viruses. 32 (22%) patients positive for influenza, were transferred to intensive care units, out of which 13 (9%) were fatal. The hospitalization and fatality rates are unusually high during the last influenza season; however, it is important to note that there is a strong bias to this data, due to the altered policy of the HCIDCP to preferably examine severe influenza cases, rather than mild ILI cases (Table 1) .

The 2010/11 and 2011/12 influenza seasonal trivalent vaccine composition for the northern hemisphere included the same strains: influenza A(H1N1) 2009 pandemic strain A/California/07/2009, A(H3N2) (A/Perth/16/2009-

Table 1: Summary of results for influenza virus detection during 2009-2012. Total examined clinical specimens, positive for A(H1N1)2009, A(H3N2) and B influenza viruses and fatal influenza cases during the pandemic 2009-2010 and the post-pandemic period 2010-2011 and 2011-2012.

Influenza Season	2009-2010	2010-2011	2011-2012
Total examined	5173	1870	314
Total positive samples	1664	848	144
Positive influenza A(H1N1)	1645 (98.8%)	821 (96.8%)	0
Positive influenza A(H3N2)	17 (1.02%)	13 (1.53%)	73 (50.7%)
Positive influenza B	2 (0.12%)	14 (1.65%)	71(49.3%)
Fatal cases	33	55	13

like) and B (B/Brisbane/60/2008-like) strains. Phylogenetic analysis revealed a close relationship of the 2010-11 A(H1N1)2009 circulating viral strains to the vaccine virus, A/California/7/2009. Antigenic analysis also revealed that the circulating strains were antigenically homogeneous and closely related to the vaccine strain. Regarding the 2011-12 influenza season, a proportion of the circulating viruses did partially match the vaccine strains, A/Perth/16/2009 and B/Brisbane/60/2008. However, Northern Greek A(H3N2) circulating strains that grouped with a different phylogenetic clade, clustered with the WHO reference strains A/Finland/190/2011 and A/England/259/2011. Also half of the 2011-12 influenza B circulating viruses belonged to the Yamagata lineage, which was not included in the seasonal vaccine at all.

In 2010-11 the majority of influenza infections were attributed to A(H1N1) 2009 virus, causing a higher number of severe and fatal infections compared to the pandemic period, despite the fact that the circulating strains matched with the vaccine strain. Probably the high infection rate of unvaccinated individuals during the post pandemic period, was due to the fact that A(H1N1) 2009 was a newly identified antigenic virus variant and a high proportion of the Northern Greek population still had no previous immunity against this virus. The following season 2011-12, only influenza A(H3N2) and B viruses circulated in Northern Greece with a high proportion of severe and fatal infections. This can be explained by the co-circulation of antigenic variants of both A(H3N2) and B influenza viruses, and thus the low efficiency of the vaccine. These observations agree with those that WHO reported for the rest of Europe[9].

Molecular analysis of the haemagglutinin sequences of Northern Greek circulating strains revealed a number of variations. It is usually observed, that more than one strain of each influenza subtype co-circulate during the same influenza season. Additionally, there is a trend of the new influenza A virus strains to accumulate amino acid changes and form new phylogenetic clades[2,4]. Constant epidemiological and molecular surveillance is essential to assess the severity of each influenza season and monitor the efficacy of the vaccine. An important role of the Northern Greek National Influenza Centre is to contribute to the recommendations of WHO for the next season influenza virus vaccine selection, as well as to provide embryonated-egg isolates of antigenic viral variants as candidates for the manufacture of the seasonal vaccine.

As expected, WHO recommended an altered composition for the 2012-13 influenza seasonal vaccine to include the circulating antigenic variants. The WHO recommendation is: an A/California/7/2009(H1N1)pdm09-like virus, an A/Victoria/361/2011(H3N2)-like virus and a B/Wisconsin/1/2010-like virus[9].

Another important role of the NIC is to monitor the susceptibility of the circulating viruses to the antiviral drugs. The most commonly used antiviral drug in Greece is oseltamivir, commercially known as Tamiflu, which is a neuraminidase inhibitor. Molecular analysis of the neuraminidase gene of 34 influenza A(H1N1)2009 virus strains that circulated during 2010-2011 in Northern Greece showed that two possessed the known resistance mutation H275Y, whereas the rest were susceptible to oseltamivir[3]. The same number of resistant viruses was detected during the pandemic period[10]. According to a previous study and to the WHO report, the resistance mutation is mostly induced by the use of oseltamivir to the patient, rather than spontaneously occurring and persisting to the viral population[3,9]. No A(H3N2) resistant viruses have been detected. This result agrees with a previous study from 2004-2008 A(H3N2) viruses isolated in Northern Greece[5].

Constant and timely epidemiologic and molecular analysis of circulating viruses is important to assess the severity of the influenza season, and evaluate the vaccine and antiviral drugs, our first line of defense against the influenza virus epidemics and pandemics.

Conflict of Interest

There is no conflict of interest.

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