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REVIEW PAPER

A Brief Review about Swine Flu: Pharmacology and Pharmacovigilance Study in the Present Time

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ABSTRACT

In this review the main focus is to provide the more information about the Swine flu (H1N1), virus which is basically a type of the Influenza virus of subdivision of A and B which were firstly identified in Mexico, Canada and the US in 2009. In this report, information about its pharmacological study of the swine flu and some pharmacovigilance studies done on it is to be described and also provide the what prevention and treatment should be preferred against the swine flu.

Keywords: Swine flu, pharmacology, pharmacovigilance, prevention, treatment

INTRODUCTION

In April 2009, the first cases of human influenza (‘swine flu’) were identified in Mexico, Canada and the US [1]. The virus spread rapidly to other parts of the world and a global flu pandemic was declared in June 2009 by the World Health Organization (WHO). The rapid development of H1N1 vaccines to prevent further morbidity and mortality became a public health priority and the first vaccines were licensed in October 2009. A mass vaccination programme for high risk groups was introduced in the UK from late October 2009 onwards. In Scotland, the vaccination programme was launched on 21 October 2009. The people initially offered vaccination included frontline health and social care workers, people over 6 months and up to 65 years in the seasonal flu vaccine clinical at-risk groups (e.g. heart, lung, kidney disease), all pregnant women, household contacts of people with compromised immune systems and people aged 65 years and over in the existing seasonal flu vaccine clinical at-risk groups. In a second phase of the programme, young children aged over 6

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months and up to 5 years of age were also prioritized for vaccination between December 2009 and March 2010 [2]. Around 500000 people in Scotland were vaccinated against H1N1 influenza between November 2009 and April 2010 (>5 million in the UK) [3].

WHO has the experience, knowledge, and foundation upon which to build further structures, core capacities, and pandemic preparedness plans, worldwide. Today, there is unprecedented opportunity to undertake appropriate protective actions; given the alarming increase in emerging and re-emerging diseases, now is the time to strengthen collaboration for the sake of global health security worldwide [4].

On 25 April 2009, the Director-General of the World Health Organization (WHO) announced a Public Health Emergency of International Concern. The emergence and rapid spread of a novel influenza virus, influenza A (H1N1), posed a pandemic threat. The 2009 influenza pandemic spread internationally with unprecedented speed and pandemic viruses were reported in all WHO regions in less than six weeks. As of 1 August 2010, worldwide more than 214 countries and overseas territories or communities reported laboratory-confirmed cases of pandemic influenza H1N1 2009, including over 18449 deaths [4].

In early August 2010, the World Health Organization officially announced the end of Phase 6 of the Influenza Pandemic Alert, with a global shift into the post-pandemic period. On behalf of the WHO, an Emergency Committee of external scientists met to review the epidemiological situation around the world. They noted that the H1N1 virus began to take on the behavior of a regular seasonal flu virus, and that pandemic flu disease activity largely returned to levels normally seen for seasonal flu, thus fulfilling the criteria for declaration of the post-pandemic phase. During this phase of the virus, the UN Medical Services, including WHO Health and Medical Services and Regional Medical Services, continues to remain vigilant, maintain surveillance, evaluate previous responses, and revise pandemic preparedness plans accordingly. Annex Two contains a diagram of the pandemic phases. From the initial outbreak in April 2009 to the recent shift into the post-pandemic period, WHO has emphasized adequate surveillance, good patient care, and appropriate risk communication as the basis for reducing the health impact of the pandemic [4]. WHO response to H1N1 involved all levels of the organization, working in close collaboration with partners. The overarching goal was to mitigate the impact of the pandemic by coordinating essential global

activities and strengthening the readiness and response capacities of countries and communities, particularly the world's most vulnerable populations. This innovative, cross-cutting, and dynamic functional approach was effectively adapted to the evolving pandemic situation. Most national health systems were able to cope with the onset of H1N1. However, in some countries, outpatient, emergency and intensive-care services have been severely stressed during peak periods of activity. From the outset of the pandemic it was feared that the people in the least-resourced countries would be most affected because of the higher prevalence of risk factors, including limited capacities of health systems and the relative difficulty in accessing recommended vaccines and antiviral medicines. In particular, greater-than-usual numbers of patients with acute respiratory problems have placed significant stress on intensive-care support systems, even in developed countries [4].

As such, in consultation with its partners, UN agencies, and other relevant stakeholders, WHO developed and implemented strategic action plans to support Member States' capacity to cope, specifically in least resourced countries, and to lessen the impact of pandemic A (H1N1) overall.

Possible source of the virus

The outbreak was probably detected in Mexico City first, where surveillance began picking up a surge in cases of influenza-like illness starting on March 2009. The surge was assumed by Mexican authorities to be late-season flu, which usually coincides with a mild influenza-virus B peak, until middle April, when CDC alert concerning two isolated cases of a novel swine flu was reported in the media. An international team of researchers suggested that the H1N1 strain responsible for the current outbreak first evolved around September 2008 and circulated in the human population for several months before the first cases were detected [5].

There is a scenario in which an industrial pig farm in the central Mexican state of Veracruz may be the likely source of the virus. The virus seems to have evolved to a stronger form because of the abuse of antibiotics, which have been used to keep the pigs alive in the extreme conditions needed to maximize profit. However, many researchers believe that currently the proximate source of the virus is unknown [6].

Classification

Influenza viruses A, B and C are the 3 genera of influenza viruses that can cause human flu. Among these viruses, type A is common in pigs, type C is rare and type B has not been reported in pigs [7]. Within A and C, the

strains found in pigs and humans are largely distinct, WHO, a pandemic can start when three conditions have been met:

a) Emergence of a disease new to a population,

b) Agents infect humans causing serious illness,

c) Agents spread easily and sustainably among humans [8, 9].

Historical context

Influenza constitutes a zoonosis of pigs that was first recognized during the Spanish influenza pandemic of 1918–1919. Swine influenza in humans was initially described as illness resulting in frequent outbreaks of influenza in families immediately followed by illness in their swine herds and vice versa [10,11]. Influenza virus was first isolated from pigs in 1920-'30's, with the virus isolated from humans several years later. However, the first isolation of a swine influenza virus from a human occurred in 1974, confirming the speculation that swine-origin influenza viruses could infect humans [12].

Swine influenza is known to be caused in pig's mainly by 3 influenza A subtypes H1N1, H3N2 and H1N2 [13]. The 2009 flu outbreak is due to a new strain of subtype H1N1 not previously reported in pigs. The new strain was initially described as apparent re assortment of at least 4 strains of influenza A virus subtype H1N1, including one strain endemic in humans, one endemic in birds, and two endemic in swine. Subsequent analysis suggested it was a re assortment of only two strains, both found in swine. Although initial reports identified the new strain as swine influenza, its origin is unknown [14].

Spread

H1N1 viruses do not spread by food. Eating properly handled and cooked pork or pork products are safe. In addition, tap water pre-treated by conventional disinfection processes does not likely pose a risk for transmission of influenza viruses. Free chlorine levels typically used in drinking water or recreational water pre-treatment is adequate to inactivate highly pathogenic influenza viruses. Currently, there are no documented human cases of influenza caused by exposure to influenza-contaminated drinking water or swimming pool water [15,16].

Clinical symptoms

The symptoms of this S-OIV influenza in people are similar to the symptoms of regular human flu and include fever, cough, sore throat, body aches, headache, chills and fatigue. A significant number of people who have been infected with S-OIV also have reported diarrhea and vomiting. In a recent analysis of 642 confirmed cases, the commonest clinical symptoms were fever in 94% of patients, cough in 92%, sore throat in

66%, diarrhea and vomiting in 25%, respectively [17,18]. Unfortunately, severe illness and death has occurred as a result of infection by S-OIV [19,20]. In seasonal flu, there are certain people that are at higher risk of serious flu-related complications. These include young children, pregnant women, people with chronic medical conditions and people 65 years and older. At this time it is unknown whether certain groups of people are at greater risk of serious flu-related complications from infection due to S-OIV. However, in a recent study, 60% of patients were <18 years of age suggesting that children and young adults may be more susceptible to S-OIV infection than are elderly persons [20]. This observation may be due to differences in social networks resulting to a delayed transmission to older persons. In addition, it is also possible that older persons may have some level of cross-protection from pre existing antibodies against S-OIV infection [20].

Diagnosis

Clinicians should consider swine influenza as well as seasonal influenza virus infections in the differential diagnosis for patients who have febrile respiratory illness and who: 1) live in USA, Mexico and all other countries with several confirmed cases or traveled to these countries 2) are residents of a country without confirmed or probable case but have recently traveled to USA, Mexico and all other countries with several confirmed cases, 3) have been in contact with persons who had had febrile respiratory illness and had been in one of the above countries during the 7 days preceding their illness onset. Any unusual case of febrile respiratory illness elsewhere also should be investigated [6,21]. Currently, no Food and Drug Administration (FDA)-cleared tests specifically for the S-OIV strain exist in the US or elsewhere. CDC has developed the real-time reverse transcription-polymerase chain reaction (rRT-PCR) [22].

The case definition for infection due to S-OIV is presented in Table 1.

Table 1: Case definitions for infection due to swine-origin influenza A (H1N1) virus (S-OIV)

Confirmed case	An individual with acute febrile respiratory illness and laboratory-confirmed S-OIV infection by one or more of the following tests: • real-time reverse transcription-polymerase chain reaction (rRT-PCR), and/or • viral culture, and/or • four-fold rise in swine influenza A (H1N1) virus specific neutralizing antibodies
Probable case	An individual with a clinically compatible illness: • with an influenza test that is positive for influenza A, but is unsubtypable by reagents used to detect seasonal influenza virus infection, and/or • who died of an unexplained acute respiratory illness who is considered to be epidemiologically linked to a probable or confirmed case

Suspected case	Acute febrile respiratory illness in a person: • with onset within 7 days of close contact with a person who has a confirmed or probable case of SOIV infection, or • with onset within 7 days of travel to a country, which has one or more confirmed S-OIV cases, or • who resides in a community without confirmed or probable case, but has traveled to a country, within 7 days, where there are one or more confirmed or probable S-OIV influenza cases have occurred

Prevention and treatment

There is currently no vaccine available to protect against S-OIV influenza. Recommendations to prevent infection by the virus consist of the standard personal precautions against influenza [23]. These include

a) Frequent washing of hands with soap and water or with alcohol-based hand solutions, especially after touching potentially contaminated items

b) Covering the nose and mouth with a tissue during cough or sneeze and avoiding touching eyes, nose or mouth, because germs spread this way; avoiding close contact with sick people and staying home during illness for 7 days after symptoms begin or until symptom-free for 24 hours, to keep from infecting others and spreading the virus further.

Finally, following public health advice regarding school closures and avoidance of crowds and other social distancing measures is necessary action.

For the treatment and prophylaxis of S-OIV influenza, oseltamivir and zanamivir can be used. The S-OIV is resistant to amantadine and rimantadine [24]. Oseltamivir is FDA-approved for treatment and prevention of influenza in adults and children aged ≥1 year. Zanamivir is FDA approved for treatment of influenza in adults and children aged ≥7 years who have been symptomatic for <2 days, and for prevention of influenza in adults and children aged ≥5 years. In the case of S-OIV influenza, oseltamivir can be used for treatment in children aged <1 year and for prevention in children aged 3 months-1 year. Under the scope and conditions of current pandemic, mass dispensing of both antiviral medications will be allowed.

Pharmacovigilance case studies

1. During pandemics, health authorities may be uncertain about the spread and severity of the disease and the effectiveness and safety of available interventions. This was the case during the swine flu (H1N1) pandemic of 2009–2010, and governments were forced to make decisions despite these uncertainties. While many countries chose to implement wide scale vaccination programs, few accomplished their vaccination goals. Many research studies

aiming to explore barriers and facilitators to vaccine uptake have been conducted in the after math of the pandemic, including several qualitative studies [25].

- To explore public attitudes to the swine flu vaccine in different countries through a review of qualitative primary studies.
- To describe and discuss the implications drawn by the primary study authors.

2. Personalized and precision vaccination requires consideration of an individual's sex and age. This article proposed systematic methods to study individual differences in adverse reactions following vaccination and chose trivalent influenza vaccine as a use case. Data were extracted from the Vaccine Adverse Event Reporting System from years 1990 to 2014 [26].
3. During the global H1N1 influenza A (swine flu) pandemic 2009–2010, swine flu vaccines were expeditiously licensed and a mass vaccination programme for high risk groups, including pregnant women, was introduced in the UK. This pilot active safety surveillance study was performed to establish the feasibility of rapidly monitoring the new swine flu vaccines in large patient numbers receiving or offered the vaccination under normal conditions of use within a short time frame [27]. Overall, no significant safety issues were identified. The methodology and use of modern technologies to collect safety data from large numbers of patients was successful and could be used again in similar safety studies [27].

Conclusion

Response actions against S-OIV must be aggressive, although may vary across countries and communities depending on local circumstances. Communities, businesses, places of worship, schools and individuals can all take action to slow the spread of this outbreak. Information is insufficient to make recommendations on the use of the antiviral in prevention and treatment of S-OIV infection. In addition, until a new vaccine against S-OIV becomes available, avoidance of viral spreading is the most appropriate way to prevent a new pandemic.

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