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The comparison of pandemic H1N1 IgG levels between H1N1 influenza-vaccinated healthcare workers and unvaccinated healthcare workers

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Background/aim: To compare pandemic H1N1 (pH1N1) IgG antibody levels between healthcare workers who were vaccinated with the pH1N1 influenza vaccine and the unvaccinated healthcare workers who were selected as the control group.

Materials and methods: A total of 68 healthcare workers were included in this study. Of those, 53 were adults vaccinated with the H1N1 influenza vaccine and 15 were unvaccinated. Serum samples were parsed and stored at -40 °C until they were examined.

Results: Of the total 53 vaccinated healthcare workers, 16 (30.1%) were positive for IgG antibodies (titer > 11), 17 (32.0%) were negative for IgG antibodies (titer < 9), and 20 (37.7%) were borderline (titer: 9–11). Of the 15 unvaccinated healthcare workers, 1 (6.6%) was positive for IgG antibodies, 11 (73.3%) were negative for IgG antibodies, and the remaining 3 (20.0%) had borderline values (P = 0.014, P < 0.05). In both groups, there was no statistically significant difference between IgG-negative, IgG-positive, and borderline subjects in terms of age or sex.

Conclusion: The IgG antibody level was higher in the vaccinated healthcare workers than among the unvaccinated healthcare workers.

Key words: H1N1 vaccination, healthcare workers, H1N1 IgG antibody level

1. Introduction

Pandemic influenza H1N1 (pH1N1) infection emerged for the first time in April 2009 in Mexico and spread from there throughout the world. A total of 128 cases were reported in Turkey, which were confirmed between May and July 2009. The only way to terminate a pandemic is to immunize society. Natural immunity is possible by contracting the illness. However, vaccines are superior for creating immunity before contracting the illness (1). According to data from the Ministry of Health of the Republic of Turkey, a total of 207,580 health workers have been immunized with the pH1N1 vaccine.

The purpose of this study was to compare the IgG antibody levels against the H1N1 virus in 53 healthcare workers who were vaccinated with the vaccine during the H1N1 pandemic influenza and 15 healthcare workers, selected as the control group, who were not vaccinated with the H1N1 vaccine.

2. Materials and methods

A total of 68 healthcare personnel were included in this study. There were 53 adult healthcare personnel (39 males, 14 females; mean age: 43 years) to whom the H1N1 vaccine was administered and 15 healthcare personnel (8 males, 7 females; mean age: 45 years) to whom the vaccine was not administered. The approval of the ethics committee and patient consent forms from the healthcare personnel were obtained for the study. Approximately 3 months after vaccination, blood samples were taken simultaneously from the healthcare personnel who were vaccinated and from the healthcare personnel who were not vaccinated. Serum samples were parsed and stored at -40 °C until they were examined.

The IgG antibody levels against H1N1 influenza vaccine in the healthcare personnel who were and were not vaccinated were analyzed with the New Influenza Commercial Pandemic IgG Original ELISA Kit (Genzyme Virotech, Germany), in accordance with

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the recommendations of the manufacturer. This study considered IgG antibody titration of >11 AU (arbitrary units) to be positive, IgG antibody titration of <9 AU (arbitrary units) to be negative, and IgG antibody titration of 9–11 AU (arbitrary units) as a borderline value (<http://www.sekisuivirotech.com>).

In the statistical analysis, independent sample t-test and Pearson chi-square were carried out with SPSS 15. Values of $P < 0.05$ were considered statistically significant.

3. Results

Of the 53 vaccinated health personnel, H1N1 IgG antibodies (titration > 11) were positive in 16 (30.1%), negative (titration < 9) in 17 (32.0%), and borderline (titration: 9–11) in 20 (37.7%). Of the 15 healthcare workers who were not vaccinated, 1 (6.6%) was positive, 11 (73.33%) were negative, and 3 (20.0%) had borderline values.

There was a statistically significant difference between the positive, negative, and borderline IgG antibody levels for those who were vaccinated and those who were not vaccinated, thus being selected as the control group ($P = 0.04$, $P \leq 0.05$).

The mean antibody levels were detected at 10.63 ± 3.39 in the vaccinated group and 8.40 ± 2.11 in the unvaccinated group. There was a statistically significant difference between the antibody levels ($P = 0.04$ and $P \leq 0.05$, respectively).

In both groups, there was no statistically significant difference between H1N1 IgG antibody-positive, antibody-negative, and borderline subjects in terms of age or sex ($P > 0.05$).

4. Discussion

Around the world, as well as in Turkey, influenza is an important health problem, especially in the winter and autumn seasons. H1N1 influenza, which emerged in 2009, caused a pandemic throughout the world, including Turkey. An effective vaccination program is the most economic and practical method to prevent infection from the influenza virus (1,2).

The target population for the vaccine is considered to be pregnant women, individuals who became infected at home, caregivers of children younger than 6 months, healthcare and emergency service workers, children between the ages of 6 months to 18 years, adults between the ages of 19 to 24 years, and individuals between the ages of 25 and 64 who are at risk for complications from influenza (2).

In the literature, different data are available on the effectiveness of the pH1N1 influenza vaccine. In a study conducted by Simpson et al. (3) in Scotland, it was reported that the effectiveness of the H1N1 influenza

vaccine in preventing diseases associated with influenza in emergency departments was 19.5%, and the laboratory-confirmed effectiveness of the vaccine in preventing influenza was 77%.

In a study conducted by Noah et al. (4), in 20 (25.5%) of 47 HIV-positive patients and in 2 (2.8%) of 71 healthy individuals, a sufficient IgG antibody response was not detected after vaccination. Four weeks after vaccination, the antibody response in healthy subjects and HIV-positive individuals were 16.8 ± 2.4 virotech units (VU) and 13.8 ± 5.3 VU, respectively; the antibody response in healthy individuals was higher than in HIV-positive patients.

In the study by Dikow et al. (5) performed with 291 patients undergoing hemodialysis, 64 of 169 patients were vaccinated with a single dose of vaccine and 105 patients were vaccinated with 2 doses of vaccine. The control group comprised 123 patients who did not accept vaccination. Pandemic influenza IgG levels in the patient and control groups were determined by ELISA, and 11 AU was accepted as a positive response. Quantitative IgG antibody titers were examined 3 months after vaccination in vaccinated patients and control subjects. In the study, a protective IgG antibody response developed in 41 (64.1%) of the 64 patients vaccinated with a single dose of pH1N1 influenza vaccine, in 93 (88.6%) of the 105 patients with 2 doses of vaccine, and in 43 (34.9%) of the 123 patients who did not receive the vaccine. The antibody response was higher in the group that received the vaccine compared to the control group.

In the study of Lagler et al. (6), which evaluated seroconversion and seroprotection rates of inactivated H1N1 vaccine in 79 HIV-infected adults by standard hemagglutination inhibition (HAI) test, the H1N1 IgG antibody levels were also evaluated via the ELISA method. Tolerance after vaccination was evaluated 1 month after the second dose of the vaccine. Initially, it was determined that, in 55 of 79 patients, HAI was $\geq 1:40$, and IgG positivity was detected in 2 patients.

The seroconversion rate was 31% after the first vaccine and increased to 41% after the second vaccine. The seroprotection rates after the first and second vaccine were 92% and 83%, respectively. ELISA IgG antibody levels after the first and second vaccine were positive, at 25% and 35%, respectively. As a result, it was reported that inactivated H1N1 vaccine in HIV-infected individuals was well tolerated and generated a measurable immune response.

Although Dikow et al. (5) and Lagler et al. (6) found H1N1 IgG-antibody positivity rates at about 90% after vaccination, in our study it was found to be about 30.1% among the healthcare personnel after vaccination. H1N1 IgG-antibody positivity was found to be about 6.6% among unvaccinated healthcare personnel. This figure was nearly 4 times less than the figure we found among the vaccinated

healthcare personnel. No serious adverse effects as a result of the vaccine were observed, and in 43 (86.4%) of 169 patients, mild or moderate local side effects were observed. In conclusion, those authors reported that pH1N1-adjuvanted vaccine was immunogenic, safe, and effective in patients undergoing hemodialysis. In the present study, with the exception of local symptoms such as pain, redness, and increased temperature, which were observed in a very small segment of the healthcare personnel after vaccination, other side effects were not observed.

In a study carried out by Temiz et al. (7) on 70 hemodialysis patients from Turkey, the cut-off value was regarded as 1.503. The figures above this value were accepted as positive in terms of preventive antibody levels, while the figures under this value were accepted as negative. They found the rates of positivity similar in hemodialysis patients and in the healthy control group after vaccination ($68/70 = 97.1\%$, $19/20 = 95\%$, respectively). These rates were similar to the findings of Lagler et al. (6) and Dikow et al. (5). As a result, they decided that H1N1 vaccination was reliable and effective for hemodialysis patients.

In a nonrandomized observational study conducted by Meyer et al. (8) on 47 patients that underwent heart transplantation, antibody titers against an inactivated, adjuvanted H1N1 vaccine were evaluated using the HAI test and a pandemic influenza A H1N1 IgG ELISA kit. Antibody titers measuring 1:40 and higher after vaccination were detected in 15 patients as positive, and it was determined that this corresponded to a 32% seroprotection rate. The sensitivity, specificity, positive predictive values, and negative predictive values of the H1N1 influenza IgG ELISA kit used in this study were 80.0%, 68.8%, 54.5%, and 88%, respectively. As a result, the authors reported that a single dose of inactivated adjuvanted vaccine caused a considerable proportion of immunosuppressive antibody response in patients with heart transplantation and an immunosuppressive seroprotective antibody response caused by pandemic H1N1 influenza A.

The IgG commercial kit has limited clinical use. Sayan et al. (9) observed using ELISA an antihemagglutinin exchange of antibodies in 50 vaccines in 50 patients with chronic obstructive pulmonary disease and asthma, who

were vaccinated with the influenza vaccine before the 1994–1995 influenza season, and compared the sensitivity and specificity of this method with the HAI method. The seroconversion of IgG antibodies was detected for the sixth month as 64%, 52%, and 40% for a subtype of H1N1, subtype of H3N2, and the B-type, respectively, and the sensitivity and specificity of the ELISA method was 76% and 88%, respectively. This study revealed that the ELISA method was time-efficient and relatively sensitive and specific, and could be used to monitor seroconversion and infection.

Sun et al. (10), in their study, examined specific antibody responses after vaccination using the HAI test and ELISA by analyzing IgG levels in 58 volunteers who were vaccinated with the pandemic H1N1 vaccine (2009 A/H1N1). It was reported that protective IgG antibody levels developed at the earliest within 10 days, and the antibody response continued for 60 days without a decrease.

As a result, IgG antibody positivity was approximately 30.1% in health personnel vaccinated with the H1N1 vaccine, whereas this rate was 6.6% in healthy individuals who were not vaccinated. The IgG antibody level was approximately 4 times higher in patients who were administered the H1N1 vaccine, compared to individuals who did not receive the vaccine. However, one limitation of this study was the fact that borderline (limit-value) IgG values were obtained in both vaccinated and unvaccinated individuals and could not be evaluated as positive or negative. The IgG antibody response against the H1N1 vaccine was determined in medical staff, with the exception of those with borderline values (between 9 and 11 titers), as approximately 30%. When the borderline values were included, this rate was approximately 68%.

The H1N1 IgG ELISA method is a very practical method to determine the immune response to the H1N1 vaccine compared to the HAI test. The current study is one of the few studies in Turkey that investigates IgG titers against the H1N1 vaccine using ELISA.

To exactly determine the importance of IgG response (humoral immune response) against the H1N1 vaccine, other controlled studies comparing IgG levels against the H1N1 influenza virus between vaccinated groups and individuals who were naturally infected are needed.

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