Russian Journal of Infection and Immunity = Infektsiya i immunitet
2024, vol. 14, no. 1, pp. 125–132

Инфекция и иммунитет
2024, Т. 14, № 1, с. 125–132

SAFETY AND EFFECTIVENESS OF SINGLE- VERSUS DOUBLE-DOSE OF SEASONAL INFLUENZA VACCINE IN KIDNEY TRANSPLANT RECIPIENTS: A RANDOMIZED CLINICAL TRIAL

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Abstract. *Introduction*. Influenza virus poses significant risks to immunocompromised individuals such as those who have received organ transplants and are undergoing immunosuppressive treatment to prevent transplant rejection. Therefore, annual influenza vaccination is recommended for these individuals. This study aimed to comparison of safety and effectiveness of single- versus double-dose of seasonal influenza vaccine in kidney transplant recipients. *Materials and methods*. This randomized clinical trial involved 50 kidney transplant recipients at Imam Khomeini Hospital. Participants were randomly assigned to two groups: those receiving a single dose (standard dose) and those receiving a double dose of the seasonal flu vaccine. Serum samples were collected before and 4 weeks after vaccination to measure influenza A&B-related antibodies. Sixteen patients were excluded from the study. The trial focused on evaluating the vaccine safety and immunogenicity, as well as documenting any local and systemic side effects following vaccination. *Results*. The results indicated no significant difference in gender, age, and type of immunosuppressive drug used between the single- and double-dose groups ($p > 0.05$). No significant difference in post-vaccination adverse effects, such as injection site pain ($p = 0.21$) between the two groups. The seroconversion rates (change from IgG < 9 IU/μL to IgG >11 IU/μL) for IgG Influenza A were 12.5% (n = 2) in the single-dose group and 26.7% (n = 4) in the double-dose group, and for IgG Influenza B, they were 11.8% (n = 2) and 21.4% (n = 3), respectively. *Conclusion*. A double dose of the influenza vaccine slightly enhanced the immune response in kidney transplant patients without causing any adverse side effects.

Key words: *influenza vaccine, transplant recepients, double dose, immunogenecity, effectiveness, single dose.*

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Для цитирования:
Мейдани М., Хатами М., Абдоллахи А., Мирзапюр П., Каримян Э., СейедАлинаги С. Безопасность и эффективность однодозовой и двудозовой вакцины от сезонного гриппа у реципиентов трансплантации почки: рандомизированное клиническое исследование // Инфекция и иммунитет. 2024. Т. 14, № 1. С. 125–132. doi: 10.15789/2220-7619-SAE-17550

Citation:
Meidani M., Khatami M., Abdollahi A., Mirzapour P., Karimian E., SeyedAlinaghi S. Safety and effectiveness of single- versus double-dose of seasonal influenza vaccine in kidney transplant recipients: a randomized clinical trial // Russian Journal of Infection and Immunity = Infektsiya i immunitet, 2024, vol. 14, no. 1, pp. 125–132. doi: 10.15789/2220-7619-SAE-17550

DOI: http://dx.doi.org/10.15789/2220-7619-SAE-17550

БЕЗОПАСНОСТЬ И ЭФФЕКТИВНОСТЬ ОДНОДОЗОВОЙ И ДВУДОЗОВОЙ ВАКЦИНЫ ОТ СЕЗОННОГО ГРИППА У РЕЦИПИЕНТОВ ТРАНСПЛАНТАЦИИ ПОЧКИ: РАНДОМИЗИРОВАННОЕ КЛИНИЧЕСКОЕ ИССЛЕДОВАНИЕ

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Резюме. *Введение.* Вирус гриппа представляет значительный риск для лиц с ослабленным иммунитетом, например, для реципиентов трансплантации органов и получающих иммуносупрессивное лечение для предотвращения отторжения трансплантата. Поэтому таким лицам рекомендуется проведение ежегодной вакцинации против гриппа. Целью настоящего исследования было сравнение безопасности и эффективности однократной и двудозовой вакцины против сезонного гриппа у реципиентов трансплантата почки. *Материалы и методы.* В рандомизированном клиническом исследовании приняли участие 50 реципиентов почечного трансплантата в больнице Имама Хомейни, которые случайным образом были разделены на две группы: получившие однократную дозу (стандартную дозу) и получившие двойную дозу вакцины против сезонного гриппа. Образцы сыворотки собирали до после вакцинации и через 4 недели после нее для измерения антител против антигенов вакцинных вирусов гриппа A и B. Шестнадцать пациентов были исключены из исследования. Исследование было сосредоточено на оценке безопасности и иммуногенности вакцины, а также на документировании любых местных и системных побочных эффектов после вакцинации. *Результаты.* В ходе исследования не были отмечены существенные различия по полу, возрасту и типу иммунодепрессанта, используемого между группами, получавшими однократную и двойную дозу ($p > 0,05$). Между двумя группами не обнаружено существенных различий в побочных эффектах после вакцинации, таких как боль в месте инъекции ($p = 0,21$). Частота сероконверсии (изменение от IgG < 9 МЕ/мкл до IgG > 11 МЕ/мкл) для IgG против гриппа A составила 12,5% ($n = 2$) в группе однократного приема и 26,7% ($n = 4$) в группе двудозовой вакцинации, а для IgG против гриппа B они составили 11,8% ($n = 2$) и 21,4% ($n = 3$) соответственно. *Заключение.* Двойная доза противогриппозной вакцины незначительно усиливала иммунный ответ у реципиентов трансплантата почки, без развития каких-либо побочных эффектов.

Ключевые слова: *вакцина против гриппа, реципиенты трансплантата, двойная доза, иммуногенность, эффективность, однократная доза.*

Introduction

The influenza virus is the main cause of seasonal influenza, which is generally associated with symptoms such as fever, myalgia and respiratory symptoms. In healthy people, this disease can improve without any medication [1]. Influenza is still considered as an infectious disease with high prevalence in the society. According to the statistics announced by World Health Organization (WHO), this virus infects between 5–10% of adults and 20–30% of children annually [2]. In America, it is estimated that this virus causes 36 000 deaths annually and leads to approximately 200 000 hospitalizations [1].

Most experts concur that influenza virus particles are transmitted through coughing, sneezing, and talking, potentially infecting those in close proximity to an infected individual. In some cases, the influenza infection in children and people with compromised immune systems might experience prolonged influenza infections, necessitating an extended duration of monitoring for pathogenicity [3]. Chronic medical conditions, such as heart disease, lung disease, diabetes, renal disease, rheumatologic disease, dementia, and stroke are identified as risk factors for influenza. Regardless of age, having underlying diseases can increase the chances of hospitalization and death upon contracting influenza [4, 5].

In a study of 616 transplant recipients (477 organs and 139 bone marrow), suffering from influenza, the most reported clinical symptoms were cough in 85% and fever in 64%, and pneumonia in 22.1% of patients. Eleven percent required intensive care unit (ICU) admission, with some also reporting headache, body pain, gastrointestinal symptoms, myocarditis, and myositis [6]. In another study conducted in Europe, invasive Aspergillus was detected in 83 cases out of 432 cases of severe influenza that were hospitalized for an average of 3 days in ICU. Notably, organ transplantation is recognized as

a common risk factor for invasive Aspergillus infection [7, 8, 9]. Another study in the USA showed that out of 237 transplant patients with influenza, approximately 70% were hospitalized, 16% required ICU care, and 4% succumbed to respiratory failure [6, 7, 8, 10]. Another U.S. study on adult hematopoietic cell transplant recipients found that systemic reactions were comparable between groups following both injections during the study [11].

Some clinical studies emphasize the beneficial effects of the flu vaccine in people who have undergone transplants. Seasonal flu vaccines are widely recognized as the most important strategy in combating influenza virus. Consequently, it is strongly recommended that organ transplant recipients receive an annual the influenza vaccination [3, 10]. However, given the significance of care and treatment for kidney transplant patients and existing research in this domain, further comprehensive studies are warranted. So, due to the lack of research in the field of evaluates the effectiveness of two different influenza vaccination and more emphasis on the kidney transplant recipients, we consider it necessary to conduct more studies in this field. Therefore, in the present study, we evaluated and compared the safety and effectiveness of single- (standard) versus double-dose of seasonal influenza vaccine in kidney transplant recipients.

Materials and methods

Study setting. This study was a randomized, open-label clinical trial involving 50 kidney transplant recipients at Imam Khomeini Hospital in Tehran in 2019. We included all the individuals who had undergone a kidney transplant and visited Imam Khomeini Hospital to receive their annual influenza vaccine. After administering the vaccine, the immune response and possible side effects of the vaccine in were measured and monitored.

Participants selection. Eligible participants were kidney transplant recipients, aged at least 18 years old, who regularly attended the transplant outpatient clinic of Imam Khomeini Hospital for follow-up visits. In order to be eligible to receive the vaccine, at least 3 months should have passed from their transplant. Providing informed consent was necessary to participate in the study. Exclusion criteria were as follows:

1. Undergoing treatment for acute transplant rejection;
2. Experiencing any febrile illness within the two weeks before the vaccine administration;
3. A history of threatening reactions to previous vaccines (such as Guillain-Barré syndrome);
4. Presence of an active autoimmune disease;
5. Those transplanted less than 3 months prior.

Study design. At the beginning of the study, the participants were randomly divided into two groups: one received a single dose (standard does) and other a double dose of FLUVAC 2020/2021 quadrivalent influenza vaccine at 1:1 ratio. Patients in the single-dose group received one intramuscular injection (15 μg of HA antigen for each strain) in the deltoid muscle of the non-dominant arm, while patients in the double-dose group received two simultaneous intramuscular injections, one in each deltoid muscle (30 μg of antigen for each strain), sourced from the similar influenza vaccine.

Data collection. The serum samples were collected before and 4 weeks after vaccination, then stored at minus 70 degrees Celsius for further influenza antibody measurement. The immune response was assessed using the Spanish Vircell brand IgM/IgG antibody assay kit with 95% sensitivity and 89% specificity. IgM/IgG antibody levels below 9 against influenza A&B were considered negative. Furthermore, IgM antibody level was measure to rule out acute influenza infection.

According to previous studies on the side effects of influenza vaccine, patients were asked to report local side effects (pain, redness and swelling) and systemic side effects (fever, headache, tiredness, nausea or vomiting, muscle and joint pain) within the first 3 days' post-vaccination. Patients were followed up for the occurrence of vaccination complications 3 days after receiving the vaccine. Systemic side effects were recorded as none, mild (no interference with normal daily activities), moderate (some interference with normal daily activities) or severe (patient unable to perform normal daily activities). Pain at the injection site was assessed as none, mild (pain on touch), moderate (pain when moving the limb) or severe (spontaneous pain). Redness and swelling at the injection site were assessed as none, mild (more than 5 mm), moderate (more than 20 mm) or severe (more than 50 mm) according to the measured diameter. Fever was defined as a body temperature more than 38 degrees Celsius. In case of flu-like symptoms, patients were advised to visit the outpatient clinic [12, 13].

Four weeks after vaccination, the immune response was assessed by comparing post-vaccinnation serum antibody levels with those before vaccination. Based on the used kit, seroprotection was defined as IgG antibody titer less than 11 IU/μL. In addition, seroconversion was measured by GMT (mean antibody titer after vaccination) and IgG production. Based on the used kit, converting values were assigned as > 9 IU/μL and > 11 IU/μL against influenza type A and B.

Ethical considerations. This research has been approved by Tehran University of Medical Sciences with ethical code (IR.TUMS.IKHC.REC.1399.333). In addition, in all stages of the research, justification and obtaining permission from all patients was done by filling out a written consent form, and no financial costs were imposed on the patients and all subjects

for the research. The collection of information from the files was done without mentioning the names of the patients and completely confidentially.

Statistical analysis. Quantitative variables were presented using mean and standard deviation, while categorical variables were described with percentages and frequencies. T-test or Mann–Whitney, and Chi-square (χ^2) test were used to compare the immune response between two groups. All analyzes were done with SPSS software version 26. A significance level of less than 0.05 was considered significant.

Results

In this study, participants were divided into two groups; one receiving single dose (standard dose) and the other receiving a double dose of seasonal influenza vaccine. Serum samples from 50 patients were collected prior to vaccination. Four weeks post-vaccination, 34 patients (17 patients in the single-dose group and 17 patients in the double-dose group) were attended the follow up visit and samples were collected for the measurement of IgG&IgM antibodies

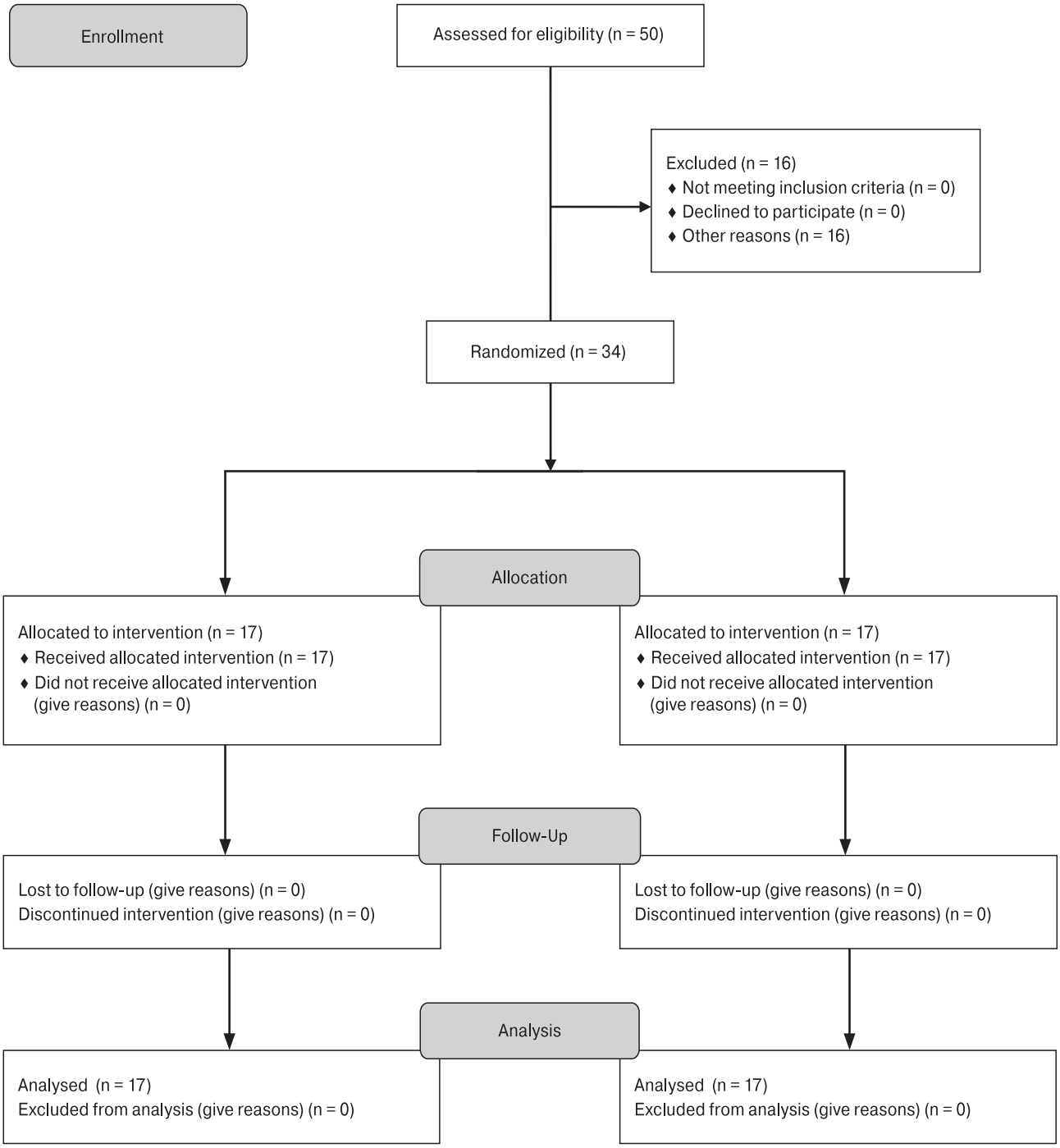

Figure. CONSORT 2010 Flow Diagram

Table 1. Demographic and clinical information of the studied patients

Variable		Recipient of two doses of vaccine, n (%)	Recipient of a vaccine dose, n (%)	P-value
Age, mean (SD)		45.4 (10.59%)	44.76 (14.74%)	0.86
Gender	Male (n, %)	10 (40%)	13 (52%)	0.40
	Female (n, %)	15 (60%)	12 (48%)	
History of receiving vaccines (n, %)		16 (64%)	20 (80%)	0.21
Injection site pain (n, %)		4 (16%)	4 (16%)	> 0.9
Prograf drug use (n, %)		19 (76%)	19 (76%)	> 0.9
Myfortic drug consumption (n, %)		21 (84%)	20 (80%)	> 0.9
Prednisolone drug use (n, %)		25 (100%)	25 (100%)	> 0.9
Cyclosporine drug use (n, %)		1 (4%)	1 (4%)	> 0.9
Time since transplantation, mean (SD) (months)		55.64 (54.51%)	49.33 (34.52%)	0.63

against influenza A&B. Patients, on average, were undergoing immunosuppressive treatment, with daily doses ranging from 2.5–5 mg of Prednisolone, 75 mg of Cyclosporine, 1 mg of Prograf, and 1 gram of Myfortic These doses were determined by their respective attending physicians. Additionally, any local and systemic side effects were recorded in follow up visit post-vaccination. More details about the randomization process are provided by the CONSORT 2010 Flow Diagram (Fig.).

Table 1 presents the demographic and clinical information of the patients in two groups. The average age for patients receiving a single dose was 44.14±76.74 years and for patients receiving two doses of vaccine was 45.10±4.59 years. There was no statistically significant difference between the average age in the two groups ($p = 0.86$). In the single-dose group, 52% ($n = 13$) were men, compared to 40% ($n = 10$) in the double-dose group. The difference in gender distribution between the groups was not statistically significant ($p = 0.4$). In the group receiving one dose of vaccine, 20 people (80%) and in the group receiving two doses of vaccine 16 people (64%) had a history of receiving vaccine. There was no significant difference between these two groups in terms of history of receiving vaccines ($p = 0.21$). The injection site pain was not significantly different in both groups ($p = 0.9$). No statistically significant difference was observed regarding the use of Prograf, Myfortic, Prednisolone and Cyclosporine drugs ($p = 0.9$). The time since transplantation in the group receiving one dose of vaccine was 49.34±33.52 months and in the group receiving two doses of vaccine was 55.54±64.51 months, and there was no significant difference between the two groups in terms of the time since transplantation ($p = 0.63$).

It shows the rate of seroconversion and the cases where the average IgG antibody titer < 9 IU/μL after 4 weeks changed to the average IgG antibody titer > 11 IU/μL in the two studied groups. It is worth mentioning the cases where the average antibody titer $9 < IgG < 11$ IU/μL was based on the kit used, it was considered unclear and due to the need to repeat the test and the lack of patient referrals for re-examination, it was not considered in the results. The average titer of IgGA antibody was less than 9 IU/μL before injection in the single-dose and two-dose groups, respectively, 72% ($n = 18$) and 72.7% ($n = 16$). The amount of seroconversion IgGA average antibody titer changed by 12.5% ($n = 2$) and 26.7% ($n = 4$) respectively after injection in single dose and two dose groups. The average titer of IgGB antibody values less than 9 IU/μL before injection in the single dose and two dose groups were 81% ($n = 17$) and 76% ($n = 19$), respectively. The rate of seroconversion of IgGB after injection in the single-dose and two-dose groups was 11.8% ($n = 2$) and 21.4% ($n = 3$), respectively. In terms of systemic side effects, no complications were observed after the injection of the vaccine. For local side effects, pain at the injection site was reported in four patients post-vaccination which was resolved after 48 hours. No significant difference in side effects were observed between the two groups (Table 2).

Discussion

In this clinical trial study, we evaluated and measured the immunogenicity and safety of one dose (15 μg) versus two doses (30 μg) of the influenza vaccine in kidney transplant patients. Overall, the vaccine response across the entire study population was suboptimal. Nevertheless, a heightened response rate and a trend towards increased immunogenicity were noted in participants receiving two doses compared to those given a single dose (Table 2).

Table 2. Seroconversion rate in the two studied groups, %

Variable	Single dose n (%)	Double dose n (%)
IgGA (IU/μL)		
Before injection (IgG < 9)	18 (72%)	16 (72.7%)
After injection (IgG > 11)	2 (12.5%)	4 (26.7%)
IgGB (IU/μL)		
Before injection (IgG < 9)	17 (81%)	19 (76%)
After injection (IgG > 11)	2 (11.8%)	3 (21.4%)

According to a previous clinical trial study, the administration of high-dose influenza vaccines and booster doses appeared to be the most effective strategies for enhancing the immunogenicity of the influenza vaccine in organ transplant recipients [14]. In a study by Natori et al., involving 161 transplant recipients, revealed that a high dose of the influenza vaccine (60 μg) significantly improved the seroconversion rate (79%) compared to the standard dose (56%). Notably, among the cases showing an enhanced immune response to the vaccine, the Myfortic drug intake was under 2 grams per day. In our study, patients, on average, received 1 gram of Myfortic daily [15]. However, due to the limited sample size and concurrent use of various immunosuppressive treatments, it was challenging to ascertain their distinct impacts on the immunological response within the cohort studied.

In another study conducted in 2018 on 37 kidney transplant patients in the USA, it was found that a 60 μg dose of the influenza vaccine significantly improved the seroconversion rate for influenza A. Despite the small sample size of this study, the results suggest that a higher antigen dose from the vaccine might enhance the immune response in transplant recipients. However, 60 μg influenza vaccines are not commercially available outside of North America. Additionally, administering four simultaneous doses of a 15 μg vaccine in medical centers appears impractical and could result in patient dissatisfaction with the vaccination process [16].

In another large clinical trial study conducted by Cordero et al. in Spain involving 499 transplant recipients, the administration of a booster dose 5 weeks after the initial dose significantly increased the seroconversion rate of all influenza virus strains. It is important to note that the injection of a booster dose of influenza vaccine in patients who underwent organ transplantation brings serious challenges. For instance, to receive the booster, patients must return to the medical facility, posing potential risks for this vulnerable population. Another study by Mombelli et al. in 2018, which evaluated 79 kidney and liver transplant recipients, found that a double dose (30 μg) of influenza vaccine caused no serious side effects. Similar to our study, the response to the vaccine was suboptimal in this study. However, in contrast to our findings, there was a significant increase in seroconversion rates for all virus strains post-vaccination [13]. Previously, the efficacy of a double influenza vaccine dose was assessed in HIV patients. During the 2009 influenza pandemic, 192 HIV patients were randomized to receive either the standard dose (15 μg) or a double dose (30 μg) of the vaccine. Notably, both doses were given concurrently. The seroconversion rate was markedly higher for those who received the double dose (68.5% vs 47.8%). In the 2022 another study by Paget J. et al., it was found that the lack of improved efficacy of the intervention vaccines is unlikely to be explained by additional protection against the B strain (Yamagata) included only in the standard quadrivalent vaccine because influenza B/Yamagata strains were not identified in Switzerland and Spain during the period. Unlike in our study, there was a significant difference in seroconversion rates between the two groups. This could be attributed to the larger sample size and absence of immunosuppressive treatment.

In the 2015 study by GiaQuinta et al., the safety of the triple influenza vaccine was compared in the standard-dose group (15 μg) and the high-dose group (60 μg), and no abnormal side effects were reported. However, in the group that received a high dose of influenza vaccine more fatigue and body pain were reported as compared to standard-dose group. Additionally, arm pain was more frequent in high-dose group. However, all of these side effects were mild to moderate and resolved within 3 days after injection similar to our study [6]. In our study, both the single and double doses of the influenza vaccine were well-tolerated, with no serious side effects reported. All adverse reactions were mild to moderate, and no severe side effects were observed in any patient from either group

Strengths and limitations

In this study, administrating a double dose of influenza vaccine was associated with an increased immune response in kidney transplant recipients without inducing serious side effects. Double dose of flu vaccine can be considered as a suitable alternative where high dose vaccines are not available. Some limitations, however, should be considered in interpreting the results of the present study. First, the sample size of the study was small, in part due to its concurrent timing with the COVID-19 pandemic and also because some patients did not return for re-serum sampling after 4 weeks. Second, without a comparison of the post-vaccination immunological response in a healthy population, we cannot conclusively discuss the vaccine's immunological effects

and thirdly, due to the heterogeneity of immunosuppressive treatment in our study population, the relationship between the immunological response and Immunosuppressive drugs could not be accurately evaluated.

Conclusion

Compared to the standard dose, the double dose of influenza vaccine was associated with an increase in immunological response in kidney transplant patients. Although the difference was not statistically significant but it could be clinically relevant as a double dose of influenza vaccine did not cause any serious side effects. It is suggested that more studies with a larger sample size and longer follow-up along with examining the clinical response to the vaccine and comparing the immunological and clinical response across population and with healthy individuals. Additionally, future research should compare the effects of various immunosuppressive treatment regimens on the immunological response after administering both the standard and double doses of the seasonal influenza vaccine to kidney transplant recipients.

References

1. Chong P.P., Handler L., Weber D.J. A systematic review of safety and immunogenicity of influenza vaccination strategies in solid organ transplant recipients. *Clin. Infect. Dis., 2018, vol. 66, no. 11, pp. 1802–1811. doi: 10.1093/cid/cix1081*
2. Control CfD, Prevention. Seasonal influenza: flu basics. *URL: http://www cdc gov/flu/about/disease/index htm [Last accessed: 2017, Feb 20]. 2014.*
3. Cordero E., Pérez-Romero P., Moreno A., Len O., Montejo M., Vidal E., Martín-Dávila P., Fariñas M.C., Fernández-Sabé N., Giannella M., Pachón J.; Novel influenza A(H1N1) Study Group of Spanish Network for Research in Infectious Diseases (REIPI). Pandemic influenza A(H1N1) virus infection in solid organ transplant recipients: impact of viral and non-viral co-infection. *Clin. Microbiol. Infect., 2012, vol. 18, no. 1, pp. 67–73. doi: 10.1111/j.1469-0691.2011.03537.x*
4. Cordero E., Roca-Oporto C., Bulnes-Ramos A., Aydillo T., Gavaldà J., Moreno A., Torre-Cisneros J., Montejo J.M., Fortun J., Muñoz P., Sabé N., Fariñas M.C., Blanes-Julia M., López-Medrano F., Suárez-Benjumea A., Martinez-Atienza J., Rosso-Fernández C., Pérez-Romero P.; TRANSGRIPE 1–2 Study Group. Two doses of inactivated influenza vaccine improve immune response in solid organ transplant recipients: results of TRANSGRIPE 1-2, a randomized controlled clinical trial. *Clin. Infect. Dis., 2017, vol. 64, no. 7, pp. 829–838. doi: 10.1093/cid/ciw855*
5. El Sahly H.M., Davis C., Kotloff K., Meier J., Winokur P.L., Wald A., Johnston C., George S.L., Brady R.C., Lehmann C., Stokes-Riner A., Keitel W.A. Higher antigen content improves the immune response to 2009 H1N1 influenza vaccine in HIV-infected adults: a randomized clinical trial. *J. Infect. Dis., 2012, vol. 205, no. 5, pp. 703–712. doi: 10.1093/infdis/jir837*
6. GiaQuinta S., Michaels M.G., McCullers J.A., Wang L., Fonnesbeck C., O'Shea A., Green M., Halasa N.B. Randomized, double-blind comparison of standard-dose vs. high-dose trivalent inactivated influenza vaccine in pediatric solid organ transplant patients. *Pediatr. Transplant., 2015, vol. 19, no. 2, pp. 219–228. doi: 10.1111/petr.12419*
7. Iuliano A.D., Roguski K.M., Chang H.H., Muscatello D.J., Palekar R., Tempia S., Cohen C., Gran J.M., Schanzer D., Cowling B.J., Wu P., Kyncl J., Ang L.W., Park M., Redlberger-Fritz M., Yu H., Espenhain L., Krishnan A., Emukule G., van Asten L., Pereira da Silva S., Aungkulanon S., Buchholz U., Widdowson M.A., Bresee J.S.; Global Seasonal Influenza-associated Mortality Collaborator Network. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. *Lancet, 2018, vol. 391, no. 10127, pp. 1285–1300. doi: 10.1016/S0140-6736(17)33293-2*
8. Izurieta H.S., Thompson W.W., Kramarz P., Shay D.K., Davis R.L., DeStefano F., Black S., Shinefield H., Fukuda K. Influenza and the rates of hospitalization for respiratory disease among infants and young children. *N. Engl. J. Med., 2000, vol. 342, no. 4, pp. 232–239. doi: 10.1056/NEJM200001273420402*
9. Kumar D., Ferreira V.H., Blumberg E., Silveira F., Cordero E., Perez-Romero P., Aydillo T., Danziger-Isakov L., Limaye A.P., Carratala J., Munoz P., Montejo M., Lopez-Medrano F., Farinas M.C., Gavalda J., Moreno A., Levi M., Fortun J., Torre-Cisneros J., Englund J.A., Natori Y., Husain S., Reid G., Sharma T.S., Humar A. A 5-year prospective multicenter evaluation of influenza infection in transplant recipients. *Clin. Infect. Dis., 2018, vol. 67, no. 9, pp. 1322–1329. doi: 10.1093/cid/ciy294*
10. Kumar D., Michaels M.G., Morris M.I., Green M., Avery R.K., Liu C., Danziger-Isakov L., Stosor V., Estabrook M., Gantt S., Marr K.A., Martin S., Silveira F.P., Razonable R.R., Allen U.D., Levi M.E., Lyon G.M., Bell L.E., Huprikar S., Patel G., Gregg K.S., Pursell K., Helmersen D., Julian K.G., Shiley K., Bono B., Dharnidharka V.R., Alavi G., Kalpoe J.S., Shoham S., Reid G.E., Humar A.; American Society of Transplantation H1N1 Collaborative Study Group. Outcomes from pandemic influenza A H1N1 infection in recipients of solid-organ transplants: a multicentre cohort study. *Lancet Infect. Dis., 2010, vol. 10, no. 8, pp. 521–526. doi: 10.1016/S1473-3099(10)70133-X*
11. Manuel O., Estabrook M.; American Society of Transplantation Infectious Diseases Community of Practice. RNA respiratory viral infections in solid organ transplant recipients: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin. Transplant., 2019, vol. 33, no. 9: e13511. doi: 10.1111/ctr.13511*
12. Miskulin D.C., Weiner D.E., Tighiouart H., Lacson E.K. Jr., Meyer K.B., Dad T., Manley H.J. High-dose seasonal influenza vaccine in patients undergoing dialysis. *Clin. J. Am. Soc. Nephrol., 2018, vol. 13, no. 11, pp. 1703–1711. doi: 10.2215/CJN.03390318*
13. Mombelli M., Neofytos D., Huynh-Do U., Sánchez-Céspedes J., Stampf S., Golshayan D., Dahdal S., Stirnimann G., Schnyder A., Garzoni C., Venzin R.M., Magenta L., Schönenberger M., Walti L., Hirzel C., Munting A., Dickenmann M., Koller M., Aubert J.D., Steiger J., Pascual M., Mueller T.F., Schuurmans M., Berger C., Binet I., Villard J., Mueller N.J., Egli A., Cordero E., van Delden C., Manuel O. Immunogenicity of high-dose versus MF59-adjuvanted versus standard influenza vaccine in solid organ transplant recipients: the swiss/spanish trial in solid organ transplantation on prevention of influenza (STOP-FLU Trial). *Clin. Infect. Dis., 2024, vol. 78, no. 1, pp. 48–56. doi: 10.1093/cid/ciad477*

14. Mombelli M., Rettby N., Perreau M., Pascual M., Pantaleo G., Manuel O. Immunogenicity and safety of double versus standard dose of the seasonal influenza vaccine in solid-organ transplant recipients: a randomized controlled trial. *Vaccine, 2018, vol. 36, no. 41, pp. 6163–6169. doi: 10.1016/j.vaccine.2018.08.057*
15. Natori Y., Shiotsuka M., Slomovic J., Hoschler K., Ferreira V., Ashton P., Rotstein C., Lilly L., Schiff J., Singer L., Humar A., Kumar D. A double-blind, randomized trial of high-dose vs standard-dose influenza vaccine in adult solid-organ transplant recipients. *Clin.Infect. Dis., 2018, vol. 66, no. 11, pp. 1698–1704. doi: 10.1093/cid/cix1082*
16. Paget J., Caini S., Del Riccio M., van Waarden W., Meijer A. Has influenza B/Yamagata become extinct and what implications might this have for quadrivalent influenza vaccines? *Euro Surveill., 2022, vol. 27, no. 39: 2200753. doi: 10.2807/1560-7917.ES.2022.27.39.2200753*

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Поступила в редакцию 11.12.2023
Отправлена на доработку 10.01.2024
Принята к печати 25.02.2024

Received 11.12.2023
Revision received 10.01.2024
Accepted 25.02.2024