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The Effect of Adjuvant H1N1 Influenza Vaccine on Allograft Kidney Function

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ABSTRACT

Introduction. Administration of the adjuvant influenza vaccine has been suspected to increase the risk of allograft rejection; however, not much is known about the effect of adjuvant H1N1 vaccination on allograft kidney function. The aim of this study was to evaluate the effect of adjuvant H1N1 vaccine on allograft kidney function.

Methods. A total of 78 stable kidney transplant recipients were enrolled in the study. These patients were vaccinated with a pandemic adjuvant H1N1 inactivated intramuscular influenza vaccine. Local and systemic adverse reactions occurring for 2 weeks after vaccination were recorded. Serum creatinine, creatinine clearance, and 24-hour urine proteinuria were measured before and 1 and 3 months and 2.5 years after vaccination.

Results. Mean patient age was 45 ± 14 years (range, 21–78 years). Serum creatinine, creatinine clearance, and 24-hour urine proteinuria levels were not significantly different between before and 1 month after vaccination (1.3 ± 0.35 vs 1.3 ± 0.5 mg/dL, 83 ± 28 vs 78 ± 31 mL/min, and 356 ± 437 vs 293 ± 307 mg, respectively). Serum creatinine level did not differ significantly between before and 2.5 years after vaccination (1.3 ± 0.35 vs 1.4 ± 0.39 mg/dL; $P > .05$). No rejection episodes occurred during 2.5 years of follow-up. Reported adverse reaction frequencies included pain (20%), muscle aches (4%), fever (2.6%), and headache (1.3%).

Conclusions. The use of pandemic adjuvant H1N1 influenza vaccination is safe in patients after kidney transplantation. However, larger cohort studies with longer follow-up periods are needed to confirm this issue.

THE APPEARANCE of a novel influenza A H1N1 virus in March and April 2009 resulted in the progression of a novel pandemic influenza vaccine.[1] Pandemic H1N1 is associated with severe disease in patients after organ transplantation[2]; therefore, the administration of H1N1 vaccination is recommended in recipients of kidney transplants.[3]

Few studies have examined the efficacy of H1N1 vaccination after kidney transplantation.[4,5] However, there are concerns regarding the effect of H1N1 vaccine on renal function. Adjuvant influenza vaccination resulted in the development of anti–human leukocyte antigen (HLA) antibody in the kidney allograft; however, no rejection episodes were reported during the 3 months of follow-up.[6] Some studies do not recommend the use of adjuvant vaccinations in patients after organ transplantation until its safety in this population is determined.[7]

The aim of our study was to evaluate the effect of adjuvant H1N1 vaccine use on allograft kidney function.

PATIENTS AND METHODS

This single-center prospective observation cohort study was performed from May to July 2010. A total of 78 stable kidney transplant recipients older that 18 years of age were enrolled in the study. Pregnant women were excluded. This study was approved by the local ethics committee. All patients provided written informed consent.

A single dose of the vaccine was administered by intramuscular injection into the deltoid muscle. Each patient revived a 0.5-mL dose of a monovalent adjuvant vaccine (Omnivest, Fluval P, Budapest, Hungary). One dose (0.5 mL) contains 6 μg of antigen

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0041-1345/13/$–see front matter
http://dx.doi.org/10.1016/j.transproceed.2013.09.008

Table 1. Allograft Function and Biochemical Parameters Before and After Vaccination

	Before Vaccination (n = 78)	1 Month After Vaccination (n = 78)	3 Months After Vaccination (n = 78)	*P*
Creatinine (mg/dL)	1.3 ± 0.35	1.3 ± 0.5	1.2 ± 0.47	NS
Creatinine clearance (mL/min)	83 ± 28	78 ± 31	83 ± 33	NS
24-h Urine protein (mg)	356 ± 437	293 ± 307	291 ± 307	NS
Acid uric (mg/dL)	5.5 ± 1.57	5.7 ± 1.44		NS
Hemoglobin (g/dL)	13.2 ± 1.59	13.1 ± 1.75		NS
Leukocytes (10^3/mm)	7.8 ± 2	7.7 ± 1.9		NS

Abbreviation: NS, not significant.

(A/California/7/2009 (H1N1)v-like strain) and aluminum phosphate as an adjuvant.

Local (pain, erythema, and induration) and systemic (fever [auxiliary temperature >38°C], myalgia, headache, and vomiting) adverse reactions during the first 2 weeks after vaccination were recorded.

Serum concentrations of hemoglobin, alanine aminotransferase, aspartate aminotransferase, uric acid, and creatinine, creatinine clearance, 24-hour urine protein excretion, and other biochemical profiles were measured at enrollment and at 1 month after vaccination. Moreover, serum creatinine levels, creatinine clearance, and 24-hour urine protein excretion were again estimated 3 months and 2.5 years after vaccination.

Creatinine clearance was calculated using the Modification of Diet in Renal Disease equation.

Statistical Analysis

Data are presented as means ± SD. A paired Student *t* test, repeated measures test, and Friedman test were used and statistical significance was defined as $P < .05$.

RESULTS

All of the patients received transplants from living donors. The mean patient age was 45 ± 14 years (range, 21–78 years). Twenty-seven (39%) of the patients were women. Time since transplantation was 71 ± 41 months (range, 8–176 months). Table 1 shows data about the renal allograft function and other biochemical parameters before and 1 month and 3 months after vaccination.

Serum creatinine levels did not differ significantly between before and 2.5 years after vaccination (1.3 ± 0.35 vs 1.4 ± 0.39 mg/dL; $P > .05$). No rejection episodes occurred in any patients during the 2.5-year follow-up period.

Pain was the most commonly reported local reaction (20%). Myalgia was the most common systemic reaction (4%), followed by fever (2.6%), headache (1.3%), and vomiting (1.3%). No serious adverse events such as anaphylactic reactions were reported.

DISCUSSION

We administered 1 dose of adjuvant pandemic influenza vaccine to recipients of kidney transplants with stable graft function. In our country, only adjuvant H1N1 vaccine was available at the peak of the novel influenza H1N1 2009 pandemic. Adjuvants are used to augment cellular and humoral responses by attracting greater numbers of antigen-presenting cells to the vaccination site. Therefore, theoretical concerns have been raised about adjuvant use increasing the risk of allograft rejection. We found that allograft function remained stable during the 3-month follow-up period, and no increases in proteinuria levels were observed during that time. No episodes of acute rejection occurred even 2.5 years after vaccination.

Not much is known about the effect of adjuvant H1N1 vaccination on allograft kidney function.

Crespo et al[8] showed that serum creatinine levels, glomerular filtration rate, and proteinuria remained stable during the first month after adjuvant H1N1 vaccination in kidney transplant recipients. An open-label, randomized clinical trial in pediatric kidney transplant recipients receiving a single pandemic H1N1 adjuvant vaccine revealed no kidney rejection during the 8-week follow-up.[9]

The use of adjuvant vaccines is associated with up-regulation of HLA alloantibodies following kidney transplantation. Katherine et al[6] reported that 7.3% and 11.9% of kidney transplant recipients in 2 cohorts had increased HLA alloantibody levels after administration of the adjuvant H1N1 vaccine. De novo anti-HLA antibody was reported in 1.1% of allograft kidney recipients by Broeders et al.[10] However, they did not record increased acute rejection rates during the 1-month follow-up. Nevertheless, anti-HLA and donor-specific antibody (DSA) are associated with adverse outcomes of graft survival in long-term follow-up.[11] We did not measure DSA and anti-HLA levels. However, acute rejection did not occur during 2.5 years of follow-up.

The local reactions to the adjuvant vaccine were moderately higher than those to the nonadjuvant vaccine.[12] However, in our study, only 20% of patients reported local pain after administration of the adjuvant vaccination.

In summary, the data of the current study showed that administration of the pandemic adjuvant H1N1 influenza vaccination is safe after kidney transplantation. However, larger cohorts studies with longer follow-up periods are needed to confirm these findings.

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