MAJOR ARTICLE

Randomized, Double-Blind, Controlled Trial of Pneumococcal Vaccination in Renal Transplant Recipients

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Renal transplant recipients are at increased risk for developing invasive pneumococcal disease but may have a poor response to pneumococcal polysaccharide vaccine (PPV23). For them, pneumococcal conjugate vaccine (PCV7) may be more immunogenic. Patients were given a single dose of PPV23 or PCV7 in our randomized, controlled, double-blind trial. Immunogenicity was assessed 8 weeks after vaccination by serotype-specific enzyme-linked immunosorbent assay (ELISA) and opsonophagocytic assay (OPA). Baseline demographics, renal function, time since transplantation, and immunosuppression were comparable. In the PCV7 group, the vaccine response rate was improved for serotypes 23F ($P = .046$) and 6B ($P = .067$), and mean fold increases in antibody titer were higher for serotypes 23F ($P = .046$) and 9V ($P = .09$). The response rate and mean fold increase in OPA titers were not significantly different between groups. There was a trend toward enhanced immunogenicity for PCV7 by ELISA. However, functional antibody responses were not different.

Streptococcus pneumoniae is a major cause of infectious complications, including bacterial pneumonia, bacteremia, and meningitis, in renal transplant recipients. The risk of invasive pneumococcal disease among renal transplant recipients is ~1%/year or 28 infections/1000 patient-years—this is >60 times higher than the rate in the general population [1, 2]. Pneumococcal polysaccharide vaccine (PPV23), a 23-valent vaccine derived from the capsular polysaccharides of *S. pneumoniae*, is routinely recommended for this population [3]. However, the use of immunosuppressive medications such as cyclosporine, prednisone, and mycophenolate mofetil (MMF) may impair these patients' response to vaccination. Studies that assessed the immunogenicity of polysaccharide vaccine in renal transplantation have demonstrated variable protective efficacy but, collectively, have produced suboptimal responses when functional antibody responses have been assessed.

Recently, conjugate pneumococcal vaccines have been developed, whereby the immunogenicity of capsular polysaccharides is enhanced by covalent conjugation with carrier proteins. The currently available conjugate pneumococcal vaccine (PCV7) contains 7 capsular polysaccharides (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F). These serotypes are known to cause 80% of pneumococcal disease in the general population [4].

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Written, informed consent was obtained from all patients for participation in the study. The human experimentation guidelines of our institution were followed in the conduct of the clinical research. The study protocol was approved by the research ethics boards of the Toronto General Hospital, Toronto, and St. Joseph's Hospital, Hamilton, Canada. The study also received approval from the Health Protection Branch of Health Canada.

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PCV7 elicits a T cell–dependent response, which, in turn, induces the T helper cell to stimulate polysaccharide-specific B cells to mature into either antibody-producing plasma cells or memory cells [5, 6]. Conjugate vaccine results in increased antibody production, and the antibodies produced are of high avidity. The efficacy of conjugate vaccine has been demonstrated in infants. Enhanced immunogenicity has also been found in patients with sickle-cell disease, Hodgkin's lymphoma, and human immunodeficiency virus (HIV) infection who were primed with a dose of conjugate vaccine prior to receiving polysaccharide vaccine [7–9].

Conjugate vaccine may have enhanced immunogenicity in transplant recipients as well, but it has not been assessed in this population. The goal of our study was to compare the quantitative and functional antibody responses of PPV23 with those of PCV7 in adult renal transplant recipients in a randomized, double-blind, controlled trial.

PATIENTS, MATERIALS, AND METHODS

Study population. Patients were recruited at 2 adult renal transplant centers in Ontario, Canada, from September to December 2001. Patients were eligible if between 3 months and 3 years had passed since their kidney transplant and if they had stable allograft function, as evidenced by a creatinine level $\leqslant$250 μmol/L, for 1 month prior to enrollment. Exclusion criteria included previous splenectomy, pneumococcal vaccination within the preceding 5 years, ongoing treatment for an episode of allograft rejection, any acute febrile illness in the 2 weeks prior to or at the time of enrollment, and use of intravenous immunoglobulin within the preceding 6 months. No changes to the current immunosuppression protocols were made for the study. Patients were generally receiving triple immunosuppression (usually cyclosporine, prednisone, and MMF) or double immunosuppression (usually cyclosporine and prednisone) therapy. Prednisone dosing was not based on weight, and MMF levels were not routinely tested. Patients did not routinely receive antilymphocyte antibody induction therapy. For most patients, cyclosporine dosing was based on peak levels done 2 h after the dose, and tacrolimus dosing was based on trough levels. No patients were taking azathioprine.

Study design and vaccines. This was a randomized, double-blind, controlled trial. Eligible patients were randomly assigned to receive a single 0.5-mL intramuscular dose of PCV7 or PPV23 in the deltoid muscle. PCV7 (Prevnar; Wyeth-Ayerst Canada) is composed of 2 μg of capsular antigen from each of serotypes 4, 9V, 14, 18C, 19F, and 23F and 4 μg of serotype 6B individually conjugated to diphtheria carrier protein CRM_{197}. PCV7 induces a T cell–dependent immune response that results in protective levels of antibody in infancy, as well as inducing a booster response with subsequent doses. This vaccine is approved in the United States for immunization of infants as early as age 6 weeks for protection against invasive pneumococcal disease. PPV23 (Pneumovax; Merck) is composed of 25 μg each of 23 pneumococcal serotypes, including those in the conjugate vaccine. This vaccine contains the individually extracted and purified capsular polysaccharides, which are combined into the final vaccine product. Polysaccharide vaccines are indicated for use in adults and children aged >2 years who are at high risk for pneumococcal disease, but these vaccines are not immunogenic in children aged <2 years. Participants were enrolled into the study by the principal investigator. The vaccine was assigned, by telephone, from a computer-generated randomization schedule, immediately before administration. Patients were randomly assigned to blocks of 4 each, to ensure equal numbers in each group. Vaccine was drawn up by personnel not related to the study. The administrator of the vaccine and the patient were blinded to the type of vaccine given. Patients were instructed to record local reactions (e.g., redness, swelling, and tenderness) and systemic reactions (e.g., fever, nausea, and vomiting). Patients were contacted by telephone 24–48 h after vaccination, for the evaluation of adverse events. Serum samples were obtained immediately before and 8 weeks after vaccination, for measurement of antibody concentration and functional antibody assessment.

Antibody concentrations. Antibody levels to each of the 7 serotypes contained in the conjugate vaccine were measured at baseline and 8 weeks after vaccination by an ELISA method [8] (Focus Technologies). Serum samples were assayed for antibody concentration to serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F. Round-bottom microtiter plates were coated with specific pneumococcal polysaccharide. Patient serum samples were absorbed with a 1:50 dilution of 10 mg/mL cell-wall polysaccharide (Statens Seruminstitut), and goat anti–human IgG–alkaline phosphatase conjugate was added, followed by phosphatase substrate. The assay was performed using a standard reference serum (89-SF) and quality control serum (Food and Drug Administration). The standard antibody values present in the reference serum had been previously determined, as published elsewhere [10]. The lower limit of detection for this test was 0.5 μg/mL. Titers <0.5 μg/mL were assigned a value half that of the lower limit of detection. Values greater than the upper limit of detection of the assay were ascribed the upper limit values.

Opsonophagocytic assay (OPA). A flow-cytometric OPA for each of the 7 serotypes was performed using methods described elsewhere [11, 12] (Flow Applications). This assay uses the HL-60 promyelocytic leukemia cell line as effector cells and viable carboxyfluoroscein–labeled *S. pneumoniae* as the target cells. Rabbit serum was used as a source of complement. Controls were HL-60 cell controls that contained only cells and bacteria, 3 complement controls with all reagents except patient serum, and a postvaccination serum sample with a known op-

Table 1. Demographics and characteristics of patients in the 2 vaccine groups.

Characteristic	Polysaccharide vaccine (n = 30)	Conjugate vaccine (n = 30)
Age, mean years ± SD	47.7 ± 12.7	47.5 ± 13.7
Sex, male:female	16:14	18:12
Race		
White	16 (53)	19 (63)
Black	5 (17)	4 (13)
Other	9 (30)	7 (24)
No. of days after transplantation, mean ± SD	461 ± 289	414 ± 311
History of rejection	6 (20)	2 (7)
Baseline creatinine level, mean μmol/L ± SD	147 ± 43.1	132 ± 43.7
Immunosuppression		
Prednisone	30 (100)	29 (96.7)
Prednisone dose, mean mg/day ± SD	7.2 ± 1.5	7.4 ± 2.9
MMF	23 (76.7)	25 (83.3)
MMF dose, mean mg/day ± SD	1370 ± 568	1640 ± 569
Triple immunosuppression	23 (76.7)	25 (83.3)
History of pneumococcal vaccination >5 years	3 (10)	5 (16.7)
Retransplant	4 (13.3)	2 (6.7)

NOTE. Data are no. (%) of subjects unless otherwise specified. P was not significant for all comparisons. MMF, mycophenolate mofetil.

sonophagocytic titer. Titers were reported as the reciprocal of the highest serum dilution yielding ⩾50% of maximum phagocytic uptake. The lowest measurable titer was 1:8, and titers lower than this were given a value of 4. The laboratory personnel were blinded to patient vaccine assignment.

Definitions and statistical methods. All patients were included in the analysis. The intent-to-treat and per-protocol groups were the same, because all patients completed the required follow-up. A vaccine response by ELISA was defined as a 2-fold increase in prevaccination titer and an absolute postvaccination value of at least 1 μg/mL. A vaccine response by OPA was considered to be a 4-fold increase in titer and an absolute value >1:8. Variables, including vaccine response and demographic data, were compared between the 2 study groups. The study was powered to detect an improvement in vaccine response with conjugate vaccine in any of the 7 serotypes. The study had a power of 80% to detect a 35% improvement in the response rate for a given serotype. Categorical variables were analyzed using a χ^2 or Fisher's exact test, and continuous variables were analyzed by the Mann-Whitney U test for nonnormally distributed data. Antibody levels are reported as geometric mean concentrations. ELISA and OPA responses were correlated using Pearson's correlation coefficient. All statistics were done using SPSS (version 10.0; SPSS).

RESULTS

Patients

A total of 60 of 174 screened patients were recruited for the study from both transplant centers from September to December 2001. Of these, 30 patients were randomly assigned to receive PPV23 and 30 were assigned to receive PCV7. The vaccines were prepared in a masked fashion for those who administered it. Among the 114 screened patients who were not enrolled, 70 had received the vaccine within the preceding 5 years, 24 did not consent to the study, and 20 were not enrolled for other reasons. Follow-up serum samples at 8 weeks were obtained from all recruited patients. Patients were monitored for 6 months after enrollment for the development of pneumococcal disease. The 2 groups were similar in demographics and clinical characteristics, as shown in table 1. The groups were also similar with respect to comorbid illness and underlying kidney disease (data not shown).

Reactions to the Vaccine and Other Adverse Events

There were no statistically significant differences between vaccine reactions caused by the PCV7 and PPV23 at 24 h after vaccination (table 2). Most reactions were local and generally mild. All were self-limited, with resolution in 2 days. One person in each group became febrile within 24 h. Pneumococcal pneumonia developed in 1 patient in the PPV23 group 4 months after vaccination. This isolate was determined to be serotype 23F. Two patients in the PCV7 group developed infections caused by a herpesvirus within 4 months after vaccination (localized varicella zoster in 1 patient 4 days after vaccination and cytomegalovirus colitis in 1 patient 70 days after vaccination). The serum creatinine level (mean ± SD) in the PPV23 and PCV7 groups was comparable at baseline

Table 2. Local and systemic reactions to vaccine at 24 h after vaccination.

Adverse event	Polysaccharide vaccine (n = 30)	Conjugate vaccine (n = 30)
None	16 (53.3)	14 (46.7)
Local tenderness	11 (36.7)	14 (46.7)
Erythema	2 (6.7)	0
Fever	1 (3.3)	1 (3.3)
Nausea	2 (6.7)	0
Fatigue	0	1 (3.3)

NOTE. Data are no. (%) of subjects. Patients may have had >1 adverse event. P was not significant for all comparisons.

Table 3. Concentration of serotype-specific antibodies before and after vaccination with polysaccharide and conjugate vaccines.

Serotype	Polysaccharide vaccine		Conjugate vaccine	
	Baseline	8 weeks	Baseline	8 weeks
4	0.98 (0.25–8.7)	1.71 (0.25–11.1)	1.00 (0.25–20)	2.16 (0.25–20)
6B	2.97 (0.5–12.4)	3.91 (0.7–30)	2.43 (0.5–30)	4.55 (0.6–30)
9V	1.06 (0.25–33.6)	1.70 (0.25–40)	0.84 (0.25–13.9)	2.86 (0.25–40)[a]
14	14.1 (3.3–40)	19.9 (5.6–40)	12.1 (2.6–40)	18.1 (3.3–40)
18C	1.33 (0.25–22.1)	2.71 (0.25–30)	1.20 (0.25–19.4)	3.93 (0.25–30)
19F	5.98 (0.5–40)	6.96 (0.6–40)	4.61 (1.4–40)	7.20 (1.6–40)
23F	0.83 (0.25–13.4)	1.15 (0.25–40)	0.45 (0.25–4.4)	1.49 (0.25–40)[b]

NOTE. Data are geometric mean concentrations (range), in micrograms per milliliter.

[a] $P = .09$, for fold increase at 8 weeks, vs. polysaccharide vaccine (Mann-Whitney *U* test).

[b] $P = .046$, for fold increase at 8 weeks, vs. polysaccharide vaccine (Mann-Whitney *U* test).

(146.8 ± 44.0 vs. 131.5 ± 43.0 μmol/L, respectively; $P = .28$). There were no episodes of allograft rejection or potential vaccine-related rejection in the 8 weeks after vaccination. The mean (±SD) serum creatinine level between the 2 groups at the 8-week follow-up was significantly different (PPV23, 152.7 ± 44.8 μmol/L vs. PCV7, 124.4 ± 41.9 μmol/L; $P = .008$). However, at 6 months after vaccination, the mean serum creatinine levels were not significantly different between the 2 groups (PPV23, 146.6 ± 42.8 μmol/L vs. PCV7, 131.9 ± 39.0 μmol/L; $P = .20$).

Immunogenicity

Antibody response. Geometric mean concentrations before and after vaccination for each of the serotypes, assayed by the ELISA method, are shown in table 3. Fold increases in ELISA titers were determined by dividing the postvaccination titer by the prevaccination titer. The fold increase between baseline and 8 weeks was not significantly different between the PPV23 and PCV7 groups for serotypes 4, 6B, 14, 18C, and 19F. For serotype 23F, the PCV7 group had a 16.8 mean (range, 0.8–160) fold response, versus a 2.2 (range, 0.4–23.5) fold response in the PPV23 group ($P = .046$). A trend toward an improved response was also seen for serotype 9V (PCV7, 17.0-fold; range, 0.53–160 vs. PPV23, 2.6-fold; range, 0.57–18; $P = .09$). Response to a given serotype was defined by a 2-fold increase in antibody titer and a value of at least 1 μg/mL after vaccination. The number of patients responding to each serotype is shown in figure 1. A response to at least 1 serotype was seen in 16 (53.3%) of 30 patients who received PPV23 and 22 (73.3%) of 30 patients who received PCV7 ($P = .11$). The median number of serotypes responding in the PPV23 versus the PCV7 group was 1.0 versus 2.5, respectively ($P = .069$). The number of patients who responded to PCV7 for serotypes 4, 9V, 18C, and 19F was greater than the number who responded to PPV23, but this did not reach statistical significance. However, the number of patients who responded to PCV7 was significantly greater for serotype 23F (PCV7, 40% vs. PPV23, 16.7%; $P = .046$). In addition, there was a trend toward significance for serotype 6B (PCV7, 33.3% vs. PPV23, 13.3%; $P = .067$), a serotype that has been considered to be less immunogenic. There was no correlation of serological response with dose of prednisone or MMF or peak cyclosporine or trough tacrolimus levels (data not shown). The median number of serotypes responding in patients who were taking MMF was 1.0 versus 2.0

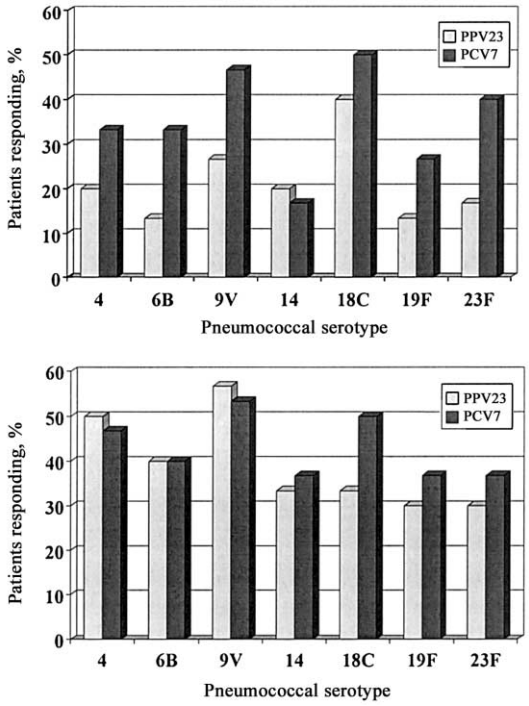

Figure 1. *Top,* Percentage of subjects responding to each serotype in the 2 groups when compared by the quantitative antibody response. *Bottom,* Percentage of subjects responding to each serotype in the 2 groups when compared by the opsonophagocytic response. PCV7, 7-valent pneumococcal conjugate vaccine; PPV23, 23-valent pneumococcal polysaccharide vaccine.

serotypes for patients not taking MMF ($P = .13$). Patients for whom >1 year had elapsed since their transplant seemed to have similar responses to those for whom <1 year had elapsed since their transplant (median, 2 serotypes responding in each group; $P = .45$).

OPA. Geometric means of the inverse of OPA titers before and after vaccination for each of the serotypes are shown in table 4. The fold increase between baseline and 2 months was not significantly different between groups for all 7 serotypes. An OPA response to a serotype was defined as a 4-fold increase in titer. Using this method, a response to any serotype was achieved in 25 (83.3%) of 30 and 24 (80%) of 30 patients receiving PPV23 and PCV7, respectively (*P,* NS). The median number of serotypes responding in the PPV23 group versus the PCV7 group was 2.0 versus 3.0, respectively (*P,* NS). The percentage of patients responding to each serotype is shown in figure 1. No significant differences in response rates were observed for any of the 7 serotypes. There was no correlation of OPA responses with prednisone or MMF dose or peak cyclosporine or trough tacrolimus levels (data not shown).

Correlation of antibody response and OPA. Postvaccination values for serotype-specific antibodies were correlated with $\log_2$ values of postvaccination titers obtained by OPA. There were moderate but significant correlations seen in all serotypes ($r = 0.40$–0.60; $P < .001$ for all correlations) except 14 ($r = 0.18$; $P = .17$). The overall serological response was significantly correlated with the overall OPA response ($r = 0.635$; $P < .001$).

DISCUSSION

This randomized, double-blind, controlled study was done to evaluate the comparative immunogenicity of pneumococcal polysaccharide vaccine versus a 7-valent conjugate vaccine in a renal transplant population, a group at high risk for invasive pneumococcal disease. We have found that PCV7 is immunogenic in the renal transplant population, with 73% of patients responding to at least 1 serotype, as tested by ELISA, and that serotypes 23F and possibly 6B and 9V show greater responses and greater fold increases in antibody concentrations in the PCV7 group. However, the overall response rates to each individual serotype were poor for each group, 13%–40% for PPV23 and 17%–50% for PCV7. Also, opsonophagocytic studies for functional antibody production showed similar response rates and fold increases in the 2 groups. Response rates for individual serotypes by OPA were 30%–57% for PPV23 and 37%–53% for PCV7. Fold increases of OPA titer were not significantly different between the 2 arms for all 7 serotypes.

Pneumococcal polysaccharide vaccination has become the standard of care for several population groups, including elderly persons and patients with HIV infection, hematologic malignancy, chronic renal failure, and solid-organ transplants [3]. The vaccine induces serotype-specific antibodies that enhance the opsonization and killing of pneumococci. However, capsular polysaccharides have properties of T cell–independent type 2 antigens that only induce a restricted IgG response and result in the poor generation of memory B cells [5, 6]. The conjugate vaccine induces a T cell–dependent response, which, in turn, induces the T helper cell to stimulate polysaccharide-specific B cells to mature into either antibody-producing plasma cells or memory cells. There is increased antibody production, and the antibodies produced are of high avidity. The creation of this immunologic memory may be crucial in immunocompromised organ transplant recipients, in whom immunity to pneumococcus wanes quickly after polysaccharide vaccination [13].

There have been no previous studies that have evaluated conjugate vaccine in solid-organ transplant recipients. Results from studies that have assessed the response to polysaccharide vaccine have been somewhat mixed. Linnemann et al. [14] showed that mean antibody levels after vaccination in renal transplant recipients were lower than those in the healthy population and in patients undergoing hemodialysis. The same authors subsequently documented vaccine failures due to a 3-fold decrease in antibody levels over 2 years [13]. However, in

Table 4. Titer of opsonophagocytic assay for serotype-specific functional antibody before and after vaccination with polysaccharide and conjugate vaccines.

Serotype	Polysaccharide vaccine		Conjugate vaccine	
	Baseline	8 weeks	Baseline	8 weeks
4	49.6 (4–1024)	172.8 (32–1024)	45.3 (4–256)	207.9 (32–2048)
6B	70.2 (8–512)	198.6 (32–4096)	70.2 (8–2048)	294.1 (32–4096)
9V	14.3 (4–256)	78.8 (4–1024)	16.0 (4–128)	82.5 (4–8192)
14	70.2 (8–1024)	203.3 (4–2048)	111.4 (8–1024)	238.9 (4–4096)
18C	30.6 (4–1024)	86.4 (4–2048)	19.7 (4–512)	119.4 (4–2048)
19F	49.6 (8–256)	111.4 (16–1024)	58.4 (4–4096)	147.0 (8–2048)
23F	12.4 (4–128)	28.5 (4–512)	16.8 (4–1024)	64.0 (4–2048)

NOTE. Data are geometric mean titer (range).

contrast, other studies have shown relatively good responses to the polysaccharide vaccine. Cosio et al. [15] showed that 80% of allograft recipients had a 2-fold increase in antibody concentration after vaccination, and Silberman et al. [16] demonstrated that renal transplant recipients with stable allograft function are able to mount an antibody response comparable to that of healthy control subjects. Although these studies were done prior to the era of modern immunosuppression, a more recent noncomparative study did find a significant increase in antibody titers after polysaccharide vaccination in 20 of 21 renal transplant recipients [17]. Studies of polysaccharide vaccine in other organ transplant types have also demonstrated some degree of immunogenicity [18].

Our study shows a much lower rate of response to PPV23. This may be the result of several reasons. First, in our study, we used a standardized ELISA with adsorption of serum with cell-wall polysaccharide for antibody measurement, as opposed to RIA. RIA may give falsely elevated titers because of nonprotective C-polysaccharide antibodies [19]. Second, patients were receiving modern, more-potent immunosuppressive regimens (calcineurin-based plus MMF). Finally, our study population included patients who were at a relatively early stage after transplant (as soon as 3 months), a time at which immunosuppression is greatest.

To substantiate our findings, we also performed the OPA. There was a modest, but not perfect, correlation between OPA findings and ELISA data. Other studies that have evaluated functional antibody production with polysaccharide vaccines are more limited. Bortolussi et al. [20] measured functional antibody levels using chemiluminescence methods and found that, although there was a 10.2- and 2.9-fold increase in antibody to serotypes 3 and 6A, respectively, there was no statistically significant increase in opsonic activity. Arnold et al. [21] measured opsonizing antibody level by chemiluminescence to serotypes 5, 12F, and 14. Serotypes 12F and 14 elicited a functional antibody response in 59% and 76% of patients, whereas no response was seen for serotype 5. We measured opsonic activity against many serotypes and found that, overall, OPA responses were comparable to serological responses, although no significant differences were seen between the 2 vaccine groups.

Our study had several limitations. First, the sample size was relatively small, such that small effects and differences in long-term infection rates may have been missed. However, because responses to all 7 serotypes were measured by both ELISA and OPA, this increased the overall amount of data accrued. Moreover, well-defined criteria for pneumococcal vaccine response are lacking in the literature. To overcome this, we used rather strict criteria for response to compare the 2 vaccines ($\geq$1 μg/mL and 2-fold response for serological testing and a 2-tube or 4-fold response for opsonophagocytic activity) and also analyzed the antibody titer as a continuous variable (increase from baseline). Although the protective levels of antibody for invasive pneumococcal disease have not been well defined, we estimated the minimum protective level to be 1 μg/mL on the basis of animal data and the literature [22–24]. Finally, the period of follow-up was short. Data on waning immunity in this population are limited. We have speculated that serological and opsonic responses to PCV7 may last longer than responses to PPV23. Longitudinal follow-up of this group of patients to determine the rate of waning immunity to the 2 vaccines is ongoing at our center.

The strengths of our study include the study design (a randomized, blinded trial), which is the first, to our knowledge, to have assessed pneumococcal conjugate vaccine in adult solid-organ transplant recipients. Also, although many of the previous immunogenicity studies with PPV23 in renal transplantation have been done using RIA, indirect hemagglutination, or chemiluminescence assays, we used a standardized ELISA with C-polysaccharide absorption, which may be a more accurate method of measuring the serotype-specific pneumococcal antibody response [19]. Finally, we incorporated an assessment of functional antibody response using a standardized flow-cytometric OPA [11, 12]. The OPA provides another measure of vaccine immunogenicity and may correlate better with clinical protection [22].

In conclusion, we have shown that pneumococcal conjugate vaccine is immunogenic in renal transplant recipients and, for certain serotypes, demonstrates a trend toward greater immunogenicity by quantitative antibody measurements, compared with polysaccharide vaccine. However, when assessed using functional antibody response by OPA, there does not appear to be a substantial difference between the 2 vaccines. Overall response rates were generally suboptimal for both groups, but this could potentially be overcome with repeat dosing schedules or, perhaps, higher doses of vaccine. Another strategy would be to use conjugate vaccine to prime the immune system and then give a booster dose of the polysaccharide vaccine. This may result in an even greater response than a single vaccine dose and has shown promise in other groups of immunocompromised patients [7–9]. Further studies of transplant recipients are required to determine an optimal vaccination strategy.

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