Use of Intravenous Immune Globulin and Rituximab for Desensitization of Highly HLA-Sensitized Patients Awaiting Kidney Transplantation

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Background. We have shown that high-dose intravenous immune globulin (IVIG; 2 g/kg ×2 doses) + rituximab (1 g ×2 doses) was effective in lowering anti-human leukocyte antigen (HLA) antibodies and improving rates of transplantation. The aim of this report was to evaluate the efficacy of IVIG + rituximab on reduction of anti-HLA antibodies to a level that was permissive for living donor (LD) or deceased donor (DD) transplantation without incurring the risk of antibody-mediated rejection and immediate graft loss.

Methods. From July 2006 to February 2009, 76 HLA-sensitized (HS) patients who met strict sensitization criteria received kidney transplants after desensitization using IVIG 2 g/kg (days 1 and 30) + rituximab (1 g, day 15). Parameters evaluated included rates of transplantation, previous transplants, panel reactive antibodies, donor specific antibody, crossmatches (CMXs), patient and graft survival, acute rejection, serum creatinines, and infections.

Results. Seventy-six HS CMX+ treated patients (31 LD/45 DD) were transplanted. For LD and DD recipients, significant reductions were seen in T-cell flow cytometry CMXs from pretreatment (T cell 183.5 ±98.4 mean channel shifts (MCS) for LD and 162.8 ±41 MCS for DD) to time of transplant (T cell 68.2 ±58 MCS for LD [P<0.00006] and 125 ±49 for DD [P=0.05]), respectively. Time on wait list for DD recipients was reduced from 95±46 months to 4.2±4.5 months after treatment. Twenty-eight patients (37%) experienced acute rejection (29% C4d+/8% C4d−). Patient and graft survival up to 24 months was 95% and 84%, respectively. The mean serum creatinines, at 12 and 24 months were 1.5±1.1 and 1.3±0.3 mg/dL, respectively. Viral infections were seen in six patients.

Conclusions. IVIG and rituximab seems to offer significant benefits in reduction of anti-HLA antibodies allowing improved rates of transplantation for HS patients, especially those awaiting DD, with acceptable antibody-mediated rejection and survival rates at 24 months.

Keywords: Rituximab, IVIG, Highly sensitized, Alemtuzumab, Antithymocyte globulin, Daclizumab, Acute cell-mediated rejection, Acute antibody-mediated rejection, Kidney transplant.

Renal transplantation has long been recognized as the treatment of choice for end-stage renal disease, because it offers improved quality of life and survival (1–3). As a result, the demand for donor kidneys continues to outpace the supply. Currently, there are more than 86,079 end-stage renal disease patients on the deceased donor (DD) waiting list, and almost 32,000 new patients register annually; yet, fewer than 18,000 kidney transplants are performed each year (based on Organ Procurement and Transplantation Network data as of September 7, 2009) (4). Because the demand for organs continues to exceed the supply, the number of days spent waiting for a kidney transplant increases exponentially, particularly for the patients who are difficult to match secondary to the presence of broadly reactive human leukocyte antigen (HLA)-specific alloantibodies. Recent data obtained from the United Network for Organ Sharing (2001–2008) (5) shows that the rates of transplantation for living donor (LD) and (DD) by panel reactive antibody (PRA) status are less than...
16% per year for patients with PRAs 10% to 80% and less than 8% for patients with PRAs more than 80%. Thus, patients with any level of sensitization are difficult to transplant.

Our group recently reported on the use of a combination of intravenous immune globulin (IVIG) and rituximab to reduce the levels of anti-HLA antibodies and improve the transplantation rates in highly HLA-sensitized (HS) patients. This was an open label, single-center, phase I/II study that aimed to evaluate the effectiveness of IVIG+rituximab in reducing PLA levels and T-cell crossmatches (CMXs) to improve the transplant rates. This study enrolled 20 HS adults who were awaiting kidney transplantation. The results of this study indicated that the combination of IVIG+rituximab reduced PLA values, improved CMX results, and allowed for transplantation of 80% of entered patients. The patient and graft survival were 100% and 94%, respectively, at 1 year (6).

It is important to note that the sensitization level of these patients would have prevented them from ever receiving a kidney transplant without this therapy at our center. The protocol required two 1 g doses of rituximab. However, during routine monitoring, we noted that excellent depletion of B cells was achieved after a single 1 g dose.

The aim of this report was to evaluate the efficacy of IVIG+rituximab on reduction of anti-HLA antibodies to a level that was permissive for LD or DD transplantation without incurring the risk of antibody-mediated rejection (AMR) and immediate graft loss. Here, we report on a modified approach to desensitization using IVIG (2 g/kg x 2 doses) + rituximab (1 g) in HS patients awaiting kidney transplantation.

PATIENTS AND METHODS

Between July 2006 and February 2009, 76 HS patients awaiting LD or DD transplantation who met the following criteria for desensitization were evaluated. All patients had flow cytometry PRAs more than 30% (75% of patients were >80%). All patients had significant sensitizing risks such as multiple blood transfusions, pregnancies, and previous transplants. All had positive pretransplant T-cell flow cytometry CMXs (FCMXs) with prospective donors or had donor-specific antibodies (DSAs). Patients who had positive pretransplant B-cell FCMXs only were eliminated from this analysis. These patients received IVIG and rituximab therapy as described later (6–8).

IVIG/Rituximab Desensitization Protocol

All HS patients received IVIG 10% (2.0 g/kg maximum 140 g per dose) on days 1 and 30 and rituximab (1 g administered on day 15). A donor-specific FCMX was performed pretransplant. An acceptable CMX is defined as a negative complement-dependent cytotoxicity (CDC), at least at a 1:2 dilution of sera. A positive T- and B-cell FCMX with a shift of less than 250 channel shifts (CS) was also acceptable (negative: <100 mean channel shifts [MCS] for B cell and <50 MCS for T cell). Solid-phase antibody analysis was also used to define the specificity of the antibodies detected, to follow the effect of desensitization, and the strength of DSA as reported previously (7). B-cell FCMX data obtained before June 2008 were not valid because of the presence of rituximab in test samples. However, pronase-treated B-cell CMXs have been obtained in test samples. Hence, pronase treatment of CMXs was performed after that time. Insufficient numbers of pronase-treated B-cell CMXs have been obtained to date, and therefore, these data are not included in this study. Thus, a heavier reliance on T-cell FCMX data and DSA values (<1,000,000 standard fluorescence intensity [SFI] units) was used as the primary determinants of CMX acceptability as described previously (7).

This strategy was also used in HS DD transplant candidates who were on the United Network of Organ Sharing list for more than 5 years who received frequent DD offers with positive CMXs. After completion of the desensitization protocol, patients usually waited 4 to 6 months for acceptable CMX offers. Because the half-life of IVIG is only 30 days, an additional IVIG dose was given at the time of transplant. All transplanted patients received an additional dose of IVIG (2 g/kg, maximum dose 140 g) 10 to 14 days post-transplant. We believe that the additional dose of IVIG helps to prevent rebound AMR and has a positive influence on patient and graft outcomes long term.

Data were gathered before and after each IVIG infusion at the time of transplant and at months 1, 6, 12, and 24 posttransplant. Safety data included monitoring patients for infusion-related side effects (such as fever, headache, and shortness of breath during and immediately after infusion), viral infections, and central nervous system-related side effects. The patients were followed up to determine the proportion with reductions in anti-HLA antibodies that subsequently obtained and retained a viable and functioning kidney allograft. The monitoring protocols were similar to those reported previously (6).

All IVIG doses were infused during a 4-hr hemodialysis session as described previously (8). Rituximab infusions were administered in an outpatient infusion center during a 6-hr period with frequent monitoring of vital signs. To reduce the frequency of infusion-related side effects, all patients were pretreated with intravenous methylprednisolone (40–125 mg), acetaminophen (650 mg orally), and diphenhydramine (50 mg orally) 30 to 60 min before scheduled IVIG and rituximab infusions.

Donor-Specific Crossmatching and Anti-HLA Antibody Analysis

The FCMX and CDC were performed as described previously (11). Three-color FCMXs were performed according to the method of Bray and coworkers (9), using FACSscan cytometer (Becton-Dickinson, San Jose, CA). T-cell FCMXs were considered positive at more than 50 MCS, and B-cell FCMXs were considered positive at more than 100 MCS. B-cell CMXs were always positive after rituximab therapy for up to 6 months or longer. These B-cell CMX results were considered invalid. To address this issue, pronase-treated B- and T-cell CMXs have been performed since June 2008 (11). The negative cutoff values for pronase-treated cells is 70 MCS for T cells and 130 MCS for B cells.

The binding level of DSA was determined by the multianalyte bead assay performed on the Luminex platform. The single antigen Luminex bead assay was standardized with Quantiplex beads (One Lambda Inc., Canoga Park, CA), and the results were expressed as SFI as reported previously (7). These data were obtained on sera from patients treated after June 2007. Flow PRA Screening was performed per manufacturer’s instructions as described previously (12). Briefly, 25 μL patient serum was mixed with 5 μL of FlowPRA screening beads (One Lambda Inc.). Any significant shift of the bead population to the right of the negative control marker more than 50% is considered as positive. The percentage of Flow PRA Screening was calculated from the positive reactivity bead population.

Posttransplant Induction Protocol and Maintenance Immunosuppression

Transplanted patients received either a single dose of alemtuzumab (30 mg subcutaneously) (n=50) or daclizumab 1 mg/kg (maximum 100 mg) (n=22) or antithymocyte globulin 1.5 mg/kg (maximum 6 mg/kg) (n=4) as induction therapy immediately posttransplantation (13, 14). Maintenance immunosuppression consisted of prednisone with a rapid taper to 5 mg per day by 2 to 4 weeks, mycophenolate mofetil (500–750 mg twice daily), and tacrolimus to maintain a target level of 8 to 10 ng/mL for the first 3 months, 7 to 9 ng/mL for months 3 to 5, and 7 to 10 ng/mL after 6 months.

Treatment of Allograft Rejection Episodes

Biopsy-proven rejection episodes were treated with “pulse” methylprednisolone (10 mg/kg/day for 3 days) and antithymocyte globulin for cell-mediated rejection episodes. Those patients who experienced episodes of AMR that were C4d positive (Banff AMR grade I or II) (15, 16) were initially given pulse methylprednisolone (10 mg/kg/day for 3 days), IVIG (2 g/kg once) and rituximab (375 mg/m²). Those patients experiencing severe AMR (Banff grade III) or thrombotic microangiopathy received plasmapheresis (three to five sessions) followed by repeat IVIG (2 g/kg) and rituximab (375 mg/m²) (16).
Infection Prophylaxis Protocols

All transplanted patients, regardless of their cytomegalovirus (CMV) status, received IV ganciclovir while inpatients and valganciclovir as outpatients for 6 months, with dose adjustments for renal function. Fungal prophylaxis was accomplished with nystatin (10 mL four times daily for 1 month), which was recently replaced with fluconazole 100 mg daily for 1 month. Pneumocystis carinii pneumonia and bacterial prophylaxis was accomplished with trimethoprim 80 mg and sulfamethoxazole 400 mg daily for 6 months.

Monitoring for Viral Infections Posttransplant

Viral polymerase chain reaction assays for CMV, Epstein Barr virus, Parvovirus B-19, and for Polyoma virus BK were performed on HS kidney transplant patients monthly for 6 months posttransplantation. Methodologies used for monitoring viral replication have been described previously (12).

Monitoring for Adverse Events or Serious Adverse Events

There are significant infusion-related adverse events described for rituximab (IV injection; Biogen Idec Inc. and Genentech USA, Inc., South San Francisco, CA). Because of this, careful attention to rates of infusion and monitoring of known infusion-related side effects, such as shortness of breath, hypotension and allergic reactions, were performed hourly with each infusion.

There are also concerns regarding the use of rituximab, because it has been reported to induce the reactivation of polyoma JC virus with resultant progressive multifocal leukoencephalopathy in patients with systemic lupus erythematosus and rheumatoid arthritis. (http://www.fda.gov/cder/drug/advisi-ory/rituximab.htm). All patients were monitored for onset of neurologic symptoms such as motor deficits and sensory loss.

Statistical Analysis

Statistical analysis was performed using the paired Student’s t test. Different parameters, including patients and graft survival, mean serum creatinines (Scr), primary or multiple transplants, acute rejection (AR) episodes (C4d+ and C4d+), and transplant by CMX/PRA and DSA status were analyzed. Differences were considered significant at the two-sided 0.05 level. The relationship between DSA levels and graft loss and patient and graft survival were analyzed using chi-square methods.

RESULTS

Success of Desensitization

Seventy-six HS patients who met criteria for desensitization were successfully transplanted (31 LD/45 DD). The mean follow-up time was 18.8 ± 10.3 months. Forty percent of patients had 24 months follow-up (Table 1). All patients in this group were deemed to have high immunologic risk (54% had more than one previous transplant, 25% had PRA 30%–75%, and 75% had PRA ≥80% [Table 2]).

Effects of Desensitization on calculated Panel Reactive Antibody (cPRA), Crossmatch, and DSA Results

The effect of desensitization on flow cytometry PRA determinations was performed on a subset of 39 HS patients. These data show that the mean pretreatment class I PRA was 79.7% ± 25.6% versus posttreatment 67.1% ± 28.6% (P = 0.0001). The mean pretreatment class II PRA was 59.7 ± 29.2% versus posttreatment 49.7 ± 27.8 (P = 0.01). This reduction is less than reported previously (6). Reasons for this difference include a change in technique from cytotoxicity-based PRA determinations to solid-phase antibody testing using flow cytometry and luminex bead technologies. Both cytotoxicity and solid-phase assays are susceptible to interference from IVIG but only for a period of less than a week after IVIG administration. The CDC assay (CDC-CMX) can be inhibited by high-dose IVIG given less than 7 days before performance of this assay. This is likely due to IVIG inhibition of complement and idiotype/antidiotype blockade by antibodies in the IVIG (17, 18). This effect is not usually seen after 7 days because of rapid equilibration of IgG molecules from the IVIG to the extracellular fluid. The luminescent bead assay can give false-positive results in patients receiving IVIG less than 7 days before performance of this assay. This is likely due to nonspecific binding of IgG molecules to the beads (19). Twenty-five percent of treated patients experienced a reduction in flow cytometry PRA of 25% or greater. Analyses of transplantation and outcomes by flow cytometry PRA (class I or II) and donor type are shown in Figure 1. Seventy-five percent of patients had flow cytometry PRA more than or equal to 80% (19 LD/38 DD) before desensitization. However, there was no significant difference in AMR episodes or graft survival by PRA status posttransplant. A significant reduction was seen in FCMX positivity against donor T cells for patients receiving LD and DD transplants after desensitization (Fig. 2A and B). Figure 2A shows the MCS results for T-cell FCMXs for all 31 individual LD recipients on whom data were available. Figure 2A shows the mean values for MCS pretreatment and at transplant. Briefly, T-cell FCMX were significantly reduced from 183 ± 98 MCS before therapy to 68 ± 58 MCS at the time of transplant (P < 0.000006). T-cell FCMX data for DD recipients pretreatment and at transplant are shown in Figure 2B. Briefly, a significant reduction in mean T-cell FCMX was seen after desensitization in DD recipients (162 ± 41 MCS pretreatment versus 125 ± 49 MCS at transplant [P = 0.05]).

An analysis of AR (cell mediated rejection [CMR] and AMR) during the 24-month observation period is shown in

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<th>TABLE 1. Demographics for highly sensitized patients desensitized with IVIG and rituximab (N=76)</th>
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<td><strong>Total transplants</strong></td>
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<td><strong>Other (GN, Alports, OU, CIN)</strong></td>
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IVIG, intravenous immune globulin; DD, deceased donor; LD, living donor; Tx, transplantation; ESRD, end-stage renal disease; HTN, hypertension; FSGS, focal and segmental glomerulosclerosis; SLE, systemic lupus erythematosus; GN, glomerulonephritis; OU, obstructive uropathy; CIN, chronic interstitial nephritis.
Table 3. Briefly, 37% of patients had AR episodes (8% CMR and 29% AMR). There was a significant association of AMR risk with the presence of DSA more than 100,000 SFI Units at the time of transplant (17/29 with DSA >100,000 had AMR, whereas only 5/42 with DSA <100,000 experienced AMR). There is no significant association between DSA more than 100,000 or less than 100,000 SFI units with graft loss to AMR. The data also include two patients who developed late AMR (>12 months) because of noncompliance, both with graft losses.

Outcomes of Highly HLA-Sensitized Patients Transplanted After Desensitization

Patient and graft survival, AR episodes, infectious complications, and renal function were monitored after transplantation. A summary of the patient demographics, immunologic profiles, and infectious complications is shown in (Tables 1 and 2). Patients who received DD transplants waited 95\(\pm\)46 months on the transplant waitlist before receiving desensitization with IVIG/rituximab, but waited only 4.2\(\pm\)4.5 months after treatment for transplantation. Patients who received DD transplants did not receive additional points toward transplantation for participation in this protocol.

Patient and Graft Survival

Patient and graft survival (nondeath censored) up to 24 months were 95% and 84%, respectively (LD [100%/90%] vs. DD [91%/80%]) (Fig. 3A and B). Graft losses occurred in nine patients: AMR (6), nonadherence (2), and surgical complications (1). Four deaths occurred posttransplant: 1 at 1 month because of donor-transmitted fungal sepsis, 1 at 6 months because of bacterial sepsis, and 2 at 12 months because of myocardial infarctions. Data are summarized in Table 2. No significant differences in outcomes were seen among the three induction regimens used.

Acute Rejection Episodes

AR episodes occurred in 37% of transplanted patients. Twenty-nine percent (22/76) of AR episodes were C4d+...
antibody-mediated rejections (AMR) (Table 3). Most rejection episodes occurred within the first month posttransplant (18/22 [82%]) and were reversible with treatment. Seven graft losses were because of AMR: 4 at 1 month, 1 at 6 months, and 2 at 12 months. All but one patient who lost their allografts to AMR showed progressive elevations in DSAs.

Renal Function

Mean serum creatinine values at 1, 6, 12, and 24 months were 1.9±1.5 (n=76), 1.3±0.4 (n=76), 1.5±1.1 (n=76), and 1.3±0.3 (n=30) mg/dL, respectively.

Adverse Events, Serious Adverse Events, and Infections

No patients to date have developed neurologic symptoms suggestive of progressive multifocal leukoencephalopathy. Viral infections were seen posttransplant in six patients (8%) who were treated with IVIG and rituximab for desensitization: two CMV, three Polyoma BK (PBK) viremia, and one CMV/Parvovirus B-19 (PVB)19 (Table 2). No patient developed BK nephropathy. One patient died of donor transmitted fungal infection at 1 month posttransplant, and another patient died of bacterial sepsis after prolonged bowel obstruction at 1 year posttransplant. Both had normal renal function at death. Minimal infusion-related side effects were noted (shortness of breath in several patients requiring additional methylprednisolone 125 mg×one dose). Lack of significant infusion-related side effects is likely due to the premedication regimen used before infusion and the long infusion times (6).

DISCUSSION

Data from our group and others suggest that IVIG therapy given to highly sensitized patients results in reduced allosensitization, reduced ischemia-reperfusion injuries, fewer AR episodes, and higher successful long-term allograft outcomes for cardiac and renal allograft recipients (8, 20–24). We and others have confirmed that pretreatment with IVIG results in reduction of anti-HLA antibodies, and it is effective in treatment of allograft rejection episodes (15, 25–27). We have also shown that IVIG is effective in reducing anti-HLA antibody levels and significantly improving transplant rates in highly HS patients in a controlled clinical trial (8). Despite these observations, the use of high-dose IVIG alone for desensitization was not always effective and often took several months to lower antibodies to acceptable levels. Considering these problems, we developed a protocol using high-dose IVIG with rituximab. The data from the initial phase I/II trial were reported recently (6). From this work, we believe that the use of two doses of rituximab (1 g) and two doses of IVIG...
of dendritic cell, B-cell, and T-cell functions (29–31) and associated with reduction in DSA (32), bullous skin diseases and chronic allograft nephropathy associated with reduction in DSA (36, 37). These types of benefits have been described recently for IVIG and rituximab and include the induction of regulatory T cells and the suppression of dendritic cell, B-cell, and T-cell functions (18, 38).

The primary objective of our approach to desensitization using IVIG + rituximab was to lower anti-HLA antibody levels to a point that would produce an "acceptable" FCXM pretransplant (6, 7). These ranges are less than 250 CS for T- and B-cell FCXMs with a CDC CMX negative at 1:2 dilution. It is important to understand that some of our patients had T-cell, B-cell, or T- and B-cell FCXMs before transplant that were below these levels. Transplant would normally not proceed with pretreatment levels of more than 50 for T-cell FCXM or more than 100 MCS for B cell FCXM without desensitization. In addition IVIG + rituximab treatment of the DD recipients was based on having a PRA more than 30% with a significant history of sensitization. Thus, some HS DD recipients received well-matched grafts after desensitization, so the pretreatment FCXMs were less than the 250 MCS cut-off. This was just a matter of chance. However, 63% of patients with PRA 30% to 79% and 84% of patients with PRA more than or equal to 80% had positive FCXM at transplant. It is important to recognize that this protocol is unlikely to produce a true negative CMX, but reduction of antibody to this range prevents hyperacute rejection and is associated with an acceptable rate of AMR 10 to 14 days posttransplant. This is likely due to a suppressive effect on anamnestic immune responses posttransplant.

We believe that the data presented here, using a combination of IVIG and rituximab in 76 HS patients who were at high risk for AMR without treatment, are encouraging and support further analysis of this approach in a randomized, controlled trial.

Although transplantation was accomplished in 76 HS patients, we found that those most at risk for AMR had persistently high-DSA (>100,000 SFI units) at time of transplant and maintained high levels during the posttransplant period. These data suggest that the titer of antibody is important and that reductions below a critical level could prevent AMR from occurring. Our current practice (7) is to use the DSA levels to

![Graph A: Patient and graft survival for 76 highly sensitized patients who were desensitized with intravenous immune globulin + rituximab.](image)

![Graph B: Patient and graft survival for donor type living donor (LD) and deceased donor (DD) for the same period.](image)

**FIGURE 3.** (A) and (B) Nondeath censored patient and graft survival values at 0, 1, 6, 12, and 24 months for 76 highly sensitized patients who were desensitized with intravenous immune globulin + rituximab. (A) Patient and graft survival for all patients up to 24 months posttransplant. (B) Patient and graft survival by donor type living donor (LD) (n = 31) and deceased donor (DD) (n = 45) for the same period. The number of patients evaluated at each time point is shown at the bottom of the graphs.
determine whether a kidney meets acceptable CMX criteria, especially for DD candidates.

Another important observation in the present protocol is that those patients who received DD transplants had been on the United Network of Organ Sharing waitlist for a mean of 95±46 months but received transplants within 4 months (4.2±4.5M) after IVIG + rituximab treatment.

A critical and ongoing issue to consider is the interpretation of PRA and CMX results after use of IVIG and rituximab. Rituximab results in long-term (up to 6 months) positivity of B-cell CDC and CMX results. This interference results in false-positive CMXs that are not due to DSA and are thus invalid. Although rituximab does not affect the solid phase PRA determinations, we now use pronase treatment of donor cells to remove CD20 antigen and to reduce or eliminate the "rituximab interference" from these CMXs. We have also noted that the use of solid-phase assays to determine antibody specificities is susceptible to interference for the first week after IVIG treatment. Thus, solid-phase and CMX assays (CDC and CMX) are performed with sera after that time period to minimize these effects. In addition, we have noted that these assays, due to their greater sensitivity, show lesser degrees of PRA changes immediately after desensitization compared with cytotoxicity PRA assays. At this point, we believe that the benefits of this protocol are best analyzed 1 to 2 months after completion and may carry the added benefit of modulation of cellular immunity to the allograft.

These observations have important implications for HS patients awaiting transplantation and is especially true for those awaiting DD transplantation. Currently, we use a paradigm assessing the CDC T-cell, CMX T-cell, pronase-treated B-cell CMX, and DSA levels as described previously to determine whether the organ will be accepted for transplantation. We are comfortable that our current paradigms for assessing the efficacy of desensitization allows for transplantation to occur without the risk of hyperacute rejection. In addition, the incidence of AMR (29% with 8% graft loss) is acceptable to also support this approach.

From our viewpoint, this protocol offers hope to many sensitized individuals who would never otherwise be transplanted. The "best" candidates for this protocol seem to be sensitized patients who are awaiting DD transplantation and have extended wait times without an acceptable CMX offer. We have had success with this group as reductions of anti-HLA antibody levels results in a significant increase in chances for transplantation with a donor where an acceptable CMX is obtained. This protocol gives a patient the opportunity to receive a transplant without the risk of hyperacute rejection and an acceptable rate of AMR. Clearly, patients with lower levels of DSA seem to benefit most, but none of the available desensitization protocols deals well with patients who have high levels of DSA. Thus, expectation for success of desensitization should be tempered in relationship to the breadth and strength of the HS patients’ DSA levels.

In conclusion, we have demonstrated that the combination of IVIG + rituximab seems to be safe and effective as a desensitization protocol for highly HS patients awaiting DD and LD transplantation. Outcomes for these patients are similar to those observed in nonsensitized patients and are far superior to outcomes for the patients who remain on dialysis for extended periods of time (4).

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REFERENCES


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