Efficacy of IVIG for Treatment of De-Novo Donor Specific Antibodies in Renal Transplant Recipients

Abstract

Development of Donor Specific Antibodies (DSA) is linked to worsened outcomes in renal transplant recipients. Intravenous immunoglobulin (IVIG) is an immune-modulator utilized in treatment of antibody mediated rejection. A retrospective review of kidney transplant cases at Lehigh Valley Health Network (LVHN) from January 2009 to June 2014 was performed to evaluate the efficacy of IVIG in treatment of new DSAs. All patients undergoing renal transplant at LVHN are cross-match compatible at the time of procedure. Desensitization is not utilized. All highly sensitized patients (PRA>50%) receive prophylactic IVIG monthly x 4 months post-transplant. Study patients that tested positive for DSA post-transplant were treated with additional IVIG (0.5g/kg monthly). 95 patients were treated with IVIG during the study period. Of 55 patients with newly positive DSA, 24 of these cleared the DSA after IVIG treatment. IVIG was more effective in clearance of class I than class II DSA. Highest rates of graft loss occurred in patients that tested positive for both a class I and class II DSA. Conclusion: 1. IVIG can be a useful in eliminating DSA post-renal transplant. 2. IVIG is effective in eliminating Class I DSA. 3. Class II DSA can be difficult to eliminate and requires further investigation.

Background

Intravenous immunoglobulin (IVIG) is a medication that has emerged as a useful tool in modulating immunity, treatment of antibody mediated rejection (AMR), and in desensitization protocols. IVIG serves as a mediator of the immune system and as a regulator of inflammation. DSAs specifically target the transplant donor organ. The presence of DSAs has been linked to significantly worse graft survival. In patients with AMR, therapy with IVIG paired rituximab and plasmapheresis (PP) can increase graft survival by more than 40% and suppress DSAs. (1) Studies have still not demonstrated optimal regimens for treatment of new DSA. The purpose of this study was to investigate the effectiveness of IVIG in elimination of DSAs.

Methodology

A retrospective chart review was performed of all kidney transplant patients at Lehigh Valley Health Network who were treated with IVIG post transplantation from January 2009 to June 2014. All patients were cross match compatible (no DSA presence at time of transplant) and had not undergone desensitization protocols. All highly sensitized patients (PRA greater than 50%), were prophylactically treated with 0.5g/kg of IVIG monthly for four doses beginning at the time of transplant per the center's protocol. These patients had monthly DSA tests for at least one year. Nonsensitized patients (PRA less than 50%) did not receive prophylactic IVIG. These patients were checked for DSAs after 1, 6, and 12 months and when symptoms arose (elevated creatinine, proteinuria).

Patients that tested positive for DSA post-transplant were treated monthly with 0.5g/kg of IVIG until clearance of DSA. These patients also underwent renal transplant biopsy at discovery of DSA. Successful treatment was considered elimination of DSA for greater than 1 month. Time to DSA clearance, dates of graft loss, AMR, and development of Class I versus Class II DSA were noted.

Results

Of the 293 patients who received kidney transplantation at Lehigh Valley Health Network in the study period, 95 were treated with IVIG. 55 patients that were treated with IVIG had a positive DSA (57.8%). 24 (43.6%) of those patients cleared the DSA after treatment with IVIG. Of the remaining 31 patients, 28 did not clear the DSA and 3 patients expired during the study interval.

61 of the 95 (64.2%) patients received prophylactic IVIG. Out of those, 41/61 (67.2%) never developed a DSA while 20/61 (32.8%) did. Out of the 20 that developed a DSA, 9 cleared the DSA. 34 non-sensitized patients (12% total non-sensitized transplants) developed DSAs and then received treatment with IVIG.

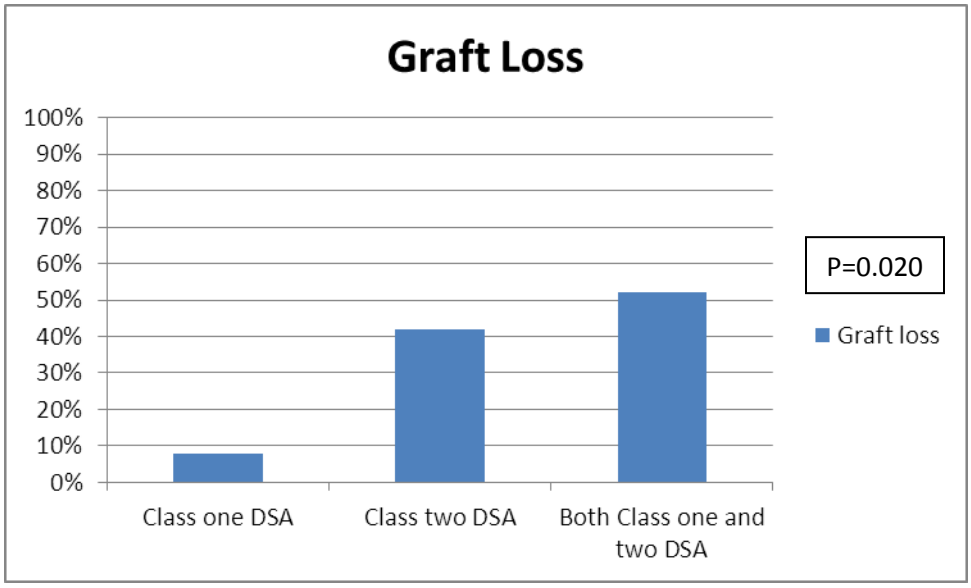
Outcomes Sensitized versus Non-sensitized Patients Treated with IVIG

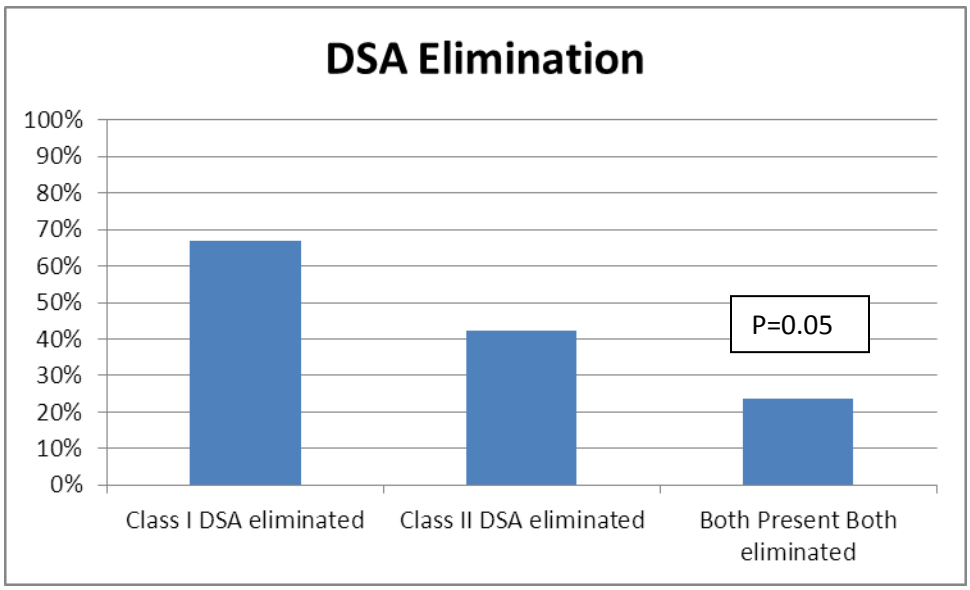
	Prophylactic IVIG (Sensitized patients)	Non Prophylactic patients (nonsensitized)
Total Patients	61/95	34/95
Total percent	64.20%	35.80%
New DSA	32.8% (20)	100%
DSA clearence	45% (9/20)	44.1% (15/34)
AMR	35% (7/20)	64.7% (22/34)

Outcomes of Class I versus Class II DSAs Treated with IVIG

DSA	Cleared DSA	%	Average days positive	Graft loss but patient alive	Death while graft functional	AMR
Class I (12)	Yes	66.7% (8/12)	164	12.5% (1/8)	0% (0/8)	37.5% (3/8)
	No	33.3% (4/12)	544	0% (0/4)	0% (0/4)	0% (0/4)
Class II (26)	Yes	42.3% (11/26)	85	9% (1/11)	0% (0/11)	18.2% (2/11)
	No	57.7% (15/26)	883	20% (3/15)	6.7% (1/15)	60% (9/15)
Class I and Class II	Both	23.5% (4/17)	739	28.6% (2/7)	28.6% (2/7)	100% (7/7)
	Neither	29.4% (5/17)	613	33.3% (4/12)	16.7% (2/12)	100% (4/4)
	Class I only	41.2% (7/17)	1039	20% (1/5)	40% (2/5)	80% (4/5)
	Class II only	6% (1/17)	*66	0% (0/1)	100% (1/1)	0% (0/1)

IVIG was more effective in the clearance of class I DSA's than class II. Following treatment with IVIG, 8/12 (66.7%) of the Class I DSAs cleared and 11/26 (42.3%) of the class II DSAs cleared (p=0.05). Clearance rates were lower in patients starting with both Class I and II antibodies, but Class I cleared more frequently. In only one case, the patient cleared the class II DSA first, however this patient expired only two months later while the class I was still present. Lowest rates of graft loss occurred in patients with a class I DSA, followed by class II, and lastly if a patient had both (p=0.02).





Conclusions

1. IVIG can be a useful in eliminating DSA post-renal transplant.

2. IVIG is effective in eliminating Class I DSA.

3. Presence of Class II DSA is associated with higher rates of graft loss. Class II DSA can be difficult to eliminate and requires further investigation, possibly in combination with biologic agents.

4. Limited numbers of patients at this time make statistically significant results difficult to achieve. Further investigation is necessary.

References

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