Does the Effectiveness of Thymoglobulin as Measured by T-Cell Depletion Correlate with the Incidence of Acute Rejection Post Kidney Transplant?

Makenzie O'Brien

Tara Stansbury

Michael J. Moritz MD
Lehigh Valley Health Network, Michael.Moritz@lvhn.org

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Does the Effectiveness of Thymoglobulin as Measured by T-Cell Depletion Correlate with the Incidence of Acute Rejection Post Kidney Transplant?

Makenzie O'Brien, Tara Stansbury, Michael Moritz, MD

Lehigh Valley Health Network, Allentown, Pennsylvania

BACKGROUND

- Thymoglobulin® is one of two standards for immunosuppression induction agents for renal transplantation and is antibodies derived from rabbits against human T-cell markers including CD2 and CD3[1].
- CD2 and CD3 are different pan-T cell markers on cell surfaces, quantifiable by flow cytometry[3,4].
- T lymphocytes are the primary mediator in recognition of foreign antigen so their depletion post transplantation reduces acute cellular graft rejection[5].
- Grades of kidney graft rejection are defined using the Banff 2017 classification of antibody-mediated rejection (AMR) and acute-cell mediated rejection (ACR)[9].

OBJECTIVE

- The purpose of this study was to evaluate the relationship between the effectiveness of Thymoglobulin® as measured by T lymphocyte depletion in preventing rejection.

METHODS

- A retrospective review of 425 kidney only transplant recipients from March 2012 to October 2017.
- From a complete transplant database the following data was extracted: date of transplant, transplant status, severity of rejection, CD2 and CD3 measurements from the first week and Ascending grades of rejection (Borderline, 1A, 2B, 2A, 2B).

Received a total of 5mg/kg of Thymoglobulin® over 3 daily doses and 1.25g of methylprednisolone → Blood samples were take to measure CD2 and CD3 counts → Protocol biopsies were performed 1,6 and 12 months post-transplantation

OUTCOMES

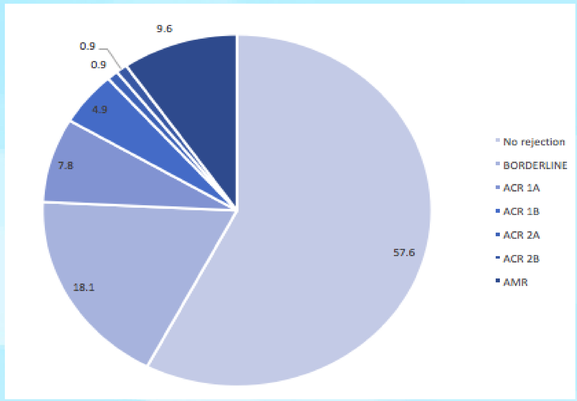

Figure 1: Break down of worst pathology for each patient. Ascending grades of rejection represent increasing inflammation in the biopsy.

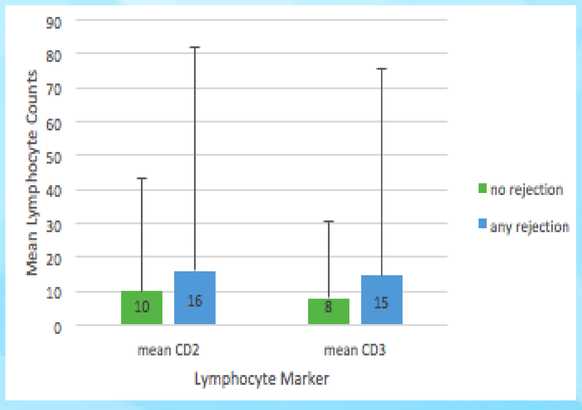

Figure 2: Patients with no rejection had lower mean CD2 and CD3 counts than patients with any type of rejection

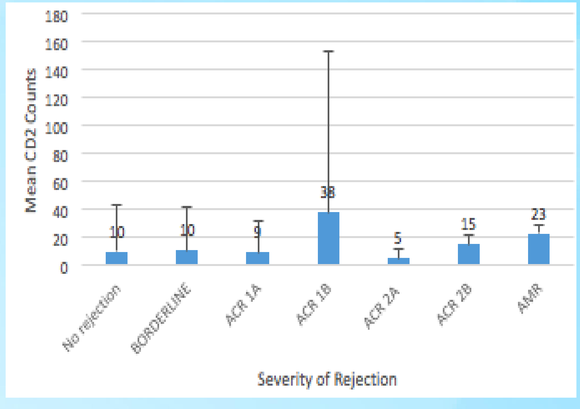

Figure 3: There was no relationship between mean CD2 or CD3 counts and each grade of rejection.

RESULTS

- Mean CD2 and CD3 counts before Thymoglobulin® were 1258.5 ± 545.7 and 1162.0 ± 501.9 cells/mm^3.
- The mean CD2 and CD3 counts after Thymoglobulin® were 10± 33.6 and 8.0± 22.5 in patients with no rejection (N=245) and 16 ± 65.6 and 15 ± 60.9 in patients with any level of rejection (N=180).
- No association between rejection grade and lymphocyte depletion.

CONCLUSIONS

- Higher post treatment CD2 and CD3 counts are associated with increased risk of graft rejection in the first post-transplant year
- CD2/CD3 counts are not associated with severity of rejection.
- Future studies should look into if additional Thymoglobulin® to lower CD2/CD3 counts in patients with higher counts would result in these patients having fewer rejections.

REFERENCES

1. Peddi, V. R., Bryant, M., Roy-Chaudhury, P., Woodle, E. S., First, M. R. (2002). Safety, efficacy, and cost analysis of thymoglobulin induction therapy with intermittent dosing based on cd3 lymphocyte counts in kidney and kidney-pancreas transplant recipients. *Transplantation, 73*(9), 1514-1518. doi:10.1097/00007890-200205150-00025
2. CD2 CD2 molecule [Homo sapiens (human)] - Gene - NCBI. (2018, July 8). Retrieved July 17, 2018, from https://www.ncbi.nlm.nih.gov/gene/914
3. Chetty, R. and Gatter, K. (1994), CD3: Structure, function, and role of immunostaining in clinical practice. J. Pathol., 173: 303-307. doi:10.1002/path.1711730404
4. Issa, F., Schiopu, A., & Wood, K. J. (2010). Role of T cells in graft rejection and transplantation tolerance. *Expert Review of Clinical Immunology,6*(1), 155-169. doi:10.1586/eci.09.64
5. Haas, M., Loupy, A., Lefaucheur, C., Roufosse, C., Glotz, D., Seron, D., . . . Mengel, M. (2018). The Banff 2017 Kidney Meeting Report: Revised diagnostic criteria for chronic active T cell-mediated rejection, antibody-mediated rejection, and prospects for integrative endpoints for next-generation clinical trials. *American Journal of Transplantation,18*(2), 293-307. doi:10.1111/ajt.14625

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