Incidence and risk factors associated with leukopenia in transplant recipients: a retrospective medical record audit

Author: Ms. Winnie Zhao *(BPharm, GradCertPharmPrac, MClinPharm)*[1]

Ms. Elaine Chan - Renal Specialist Pharmacist[1]
Ms. Michelle Lee- Renal Specialist Pharmacist, [1]
Ms. Kathy Kable – Renal Transplant Nurse Practitioner [2]
Dr. Ankit Sharma – Nephrologist [2]
Prof. Lisa Pont – Associate Professor in the Discipline of Pharmacy[3] and Academic Pharmacist[1]

[1] Department of Pharmacy Westmead Hospital
Westmead NSW
Australia

[2] Department of Renal Medicine
Westmead Hospital
Westmead NSW
Australia

[3] Graduate School of Health at the University of Technology Sydney
Australia

Background

Kidney transplant (KTx) has been widely utilised as a treatment for patients with end-stage kidney failure (ESKF). (1) Patients with Type 1 diabetes and ESKF may also be offered a pancreas transplant either simultaneously or at some stage after the KTx. (2) The success of transplant is reliant on a complex regimen of immunosuppressive medications. This regimen is successful in reducing the risk of graft rejection however the risk of infection and cancer due to bone marrow suppression and leukocyte abnormalities is inherently increased. (1)

Leukopenia is frequently observed post KTx; however its epidemiology and natural history remains poorly defined. (1, 3). Complicating matters further, transplant or immunosuppression related comorbidities and infections can also cause leukopenia. Other factors suggested in increasing the risk of leukopenia include kidney impairment and baseline body mass index (BMI). (1,4) There is a need to better understand the risk factors associated with leukopenia as infections of various aetiologies are reported to be the second most common cause of death post KTx. (1)

Objective

To identify the incidence and factors associated with leukopenia in the first 6 months post-transplantation.

Methods

A retrospective audit of a longitudinal cohort of patients who underwent a kidney and/or pancreas transplant at a large quaternary hospital in Sydney Australia was conducted.

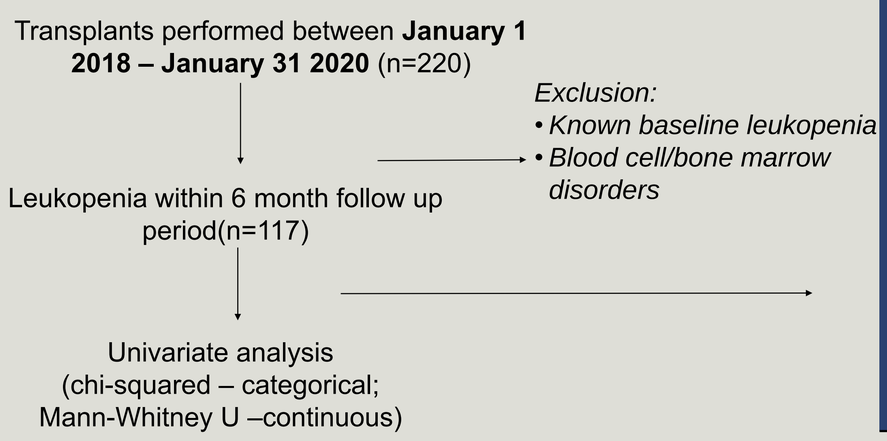

Table 1. Demographic and clinical parameters of study population (n=117)

Patient characteristics and factors associated with leukopenia		Leukopenia (n=58)	No leukopenia (n=59)
Patient Details	Age (Mean 48.2 ± 13.6)		
	Gender		
	Female	29 (50.0%)	20 (33.9%)
	Type of Transplant		
	Kidney Transplant (KTx)	51 (87.9%)	53 (89.8%)
	Simultaneous Kidney and Pancreas (SPK) or Pancreas Only Transplant	7 (12.1%)	6 (10.2%)
	Previous immunosuppression for underlying kidney disease		
	Yes	8 (13.8%)	4 (6.8%)
	Baseline CrCl (mL/min) (Mean 58.96 mL/min ± 21.09 mL/min)		
	CrCl 15 to 29 mL/min	3 (5.2%)	4 (6.8%)
	CrCl 30 to 44 mL/min	14 (24.1%)	22 (37.3%)
	CrCl 45 to 59 mL/min	12 (20.7%)	18 (30.5%)
	CrCl 60 to 89 mL/min	22 (37.9%)	23 (39.0%)
	CrCl over 90 mL/min	7 (12.1%)	3 (5.1%)
	Baseline BMI (Mean 28.2 kg/m^2± 5.5 kg/m^2)		
	Underweight (less than 18.5)	1 (1.7%)	2 (3.4%)
	Normal (18.5 to 24.5)	14 (24.1%)	16 (27.1%)
	Overweight (25 to 29.9)	22 (37.9%)	20 (33.9%)
	Obese (over 30)	21 (36.2%)	21 (35.6%)
Donor Details	Type of donor		
	Deceased	47 (81.0%)	45 (76.3%)
	Living	11 (19.0%)	14 (23.7%)
Medications	Induction immunosuppression		
	Basiliximab	42 (72.4%)	49 (83.1%)
	Antithymocyte globulin (rabbit)	15 (25.9%)	9 (15.3%)
	Other	1 (1.7%)	1 (1.7%)
	Maintenance immunosuppression		
	Standard	47 (81.0%)	51 (86.4%)
	Other	11 (19.0%)	8 (13.6%)
	Pneumocystis pneumonia (PCP) Prophylaxis		
	Pentamidine	2 (3.4%)	0 (0.0%)
	Trimethoprim and sulfamethoxazole	56 (96.6%)	59 (100.0%)

Results

- A total of 220 transplants were performed, 117 participants met the inclusion/exclusion criteria and included in the study. The majority of transplants were kidney transplants (88.9%; n=104).
- Females accounted for 41.9% (n=49)
- Over half of the study population (53.8%; n=63) were less than 50 years of age with a mean of 48.2 years (SD=13.6 years).
- Patients were generally overweight (mean baseline BMI 28.2kg/m2; SD 5.5kg/m2)
- Mild renal impairment was common with 38.5% (n=45)
- On univariate analysis, no patient characteristics or risk factor were identified that were significantly associated with leukopenia. Although females were noted to have a 95% increased odds of leukopenia compared with males (OR= 1.950; 95% CI 0.925-4.109).
- In the multivariate model (age and gender included), gender had a borderline significant association with leukopenia with women found to have approximately double the odds of experiencing leukopenia in the first 6 months post-transplant compared with men (OR=2.132, 95% CI=0.990-4.589, p=0.053).

Discussion

The results found an incidence of 49.6% of leukopenia post KTx which mirrors the estimates from the literature with reports ranging 20-60%. (3, 5) The wide variability of the reported incidence is likely due to differences between prescribed regimens due to adverse effects, antimicrobial resistance trends and clinician experience. The results also found a borderline significant association with women more than twice as likely to develop leukopenia compared to males (p=0.053). Review of the literature has found no significant association between gender and leukopenia post kidney and/or pancreas transplant. Interestingly, a study conducted by Wu et al found females were significantly associated with leukopenia (p=0.037) in the 6-month follow up period post lung transplant. (6) Given that medication regimens are similar between different solid organ transplants, larger cohort studies are required to establish the association of female gender as a predictor of new onset leukopenia post transplant. Current evidence also suggests a high baseline BMI with being associated with an increased risk of leukopenia, and higher CrCl with being significantly associated with a decreased risk. (4) Kidney dysfunction or overestimation may lead to suboptimal estimated clearance of bone marrow suppressive medications used hence increasing risk of leukopenia. (4) Whilst the results from this study did not find any discernible association with BMI and CrCl on leukopenia, perhaps this is a testament to the appropriate renal dose adjustment of post-transplant medication regimens prescribed in the study site. It is however noted that a major limitation of the study is the relatively small sample size and is likely to have been underpowered.

CONCLUSION

This study highlights that leukopenia remains a significant complication post kidney and/or pancreas transplant and whilst there are no significant risk factors found to be associated with leukopenia from this small cohort study, the concerns and complications resulting from leukopenia in the immunocompromised remains. Larger cohort studies are required to better establish the potential causality between risk factors such as gender, BMI and CrCl on leukopenia.

CONTACT

Winnie Zhao, Clinical Lead Pharmacist
Westmead Hospital
Email: Winnie.zhao@health.nsw.gov.au

References

1. Kidney Disease Improving Global Outcomes. KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation. 2009;9:S97 -S101.
2. ADA. Pancreas Transplantation for Patients with Type 1 Diabetes. Diabetes Care. 2003;26:s120-s.
3. Khalil MAM, Khalil MAU, Khan TFT, Tan J. Drug-Induced Hematological Cytopenia in Kidney Transplantation and the Challenges It Poses for Kidney Transplant Physicians. Journal of Transplantation. 2018;2018:9429265.
4. Liang X, Famure O, Li Y, Kim SJ. Incidence and Risk Factors for Leukopenia in Kidney Transplant Recipients Receiving Valganciclovir for Cytomegalovirus Prophylaxis. Prog Transplant. 2018;28(2):124-33.
5. Yang Y, Yu B, Chen Y. Blood disorders typically associated with renal transplantation. Frontiers in Cell and Developmental Biology. 2015;3(18).
6. Wu G, Ganesh S, Forrester K, G.M.Liebler. Characteristics of Patients who Develop Leukopenia After Lung Transplant. Am J Respir Crit Care Med. 2020;201.