Issues with Medication Adherence in Transplant Recipients

Molly E. Henry, PharmD, BCTXP
Clinical Pharmacist Practitioner
Solid Organ Transplant

Nebraska Medicine

1

Disclosure

I have no actual or potential conflict of interest in relation to this program/presentation.

2

2

Objectives

1. Discuss post-transplant outcomes associated with poor medication adherence
2. Identify potential barriers to medication adherence
3. Describe strategies recommended to overcome barriers to medication adherence

3

Medication Adherence

World Health Organization Definition:

- "The extent to which a person's behavior (taking medications, following a recommended diet, and/or executing lifestyle changes) corresponds with the agreed recommendation of a health care provider"

ABC Taxonomy of Medication Adherence:

- "The process by which patients take their medication as prescribed"
  - Three quantifiable phases: initiation, implementation, persistence

Kuypers, Dirk RJ. "From nonadherence to adherence." *Transplantation* 104.7 (2020): 1330-1340

4

Medication Nonadherence (MNA) in Solid Organ Transplant

- Can be challenging for both patient and healthcare team
  - Patient: perception of complex medical regimen
  - Healthcare team: barriers to monitoring and improving adherence
- Changes over time after transplantation
- Associated with increased risk of poor clinical outcomes

5 Dew, Mary Amanda et al. "Posttransplant Medical Adherence: What Have We Learned and Can We Do Better?." *Current transplantation reports* vol. 5,2 (2018): 174-188. doi:10.1007/s40472-018-0195-8

5

Prevalence of MNA Post-Transplant

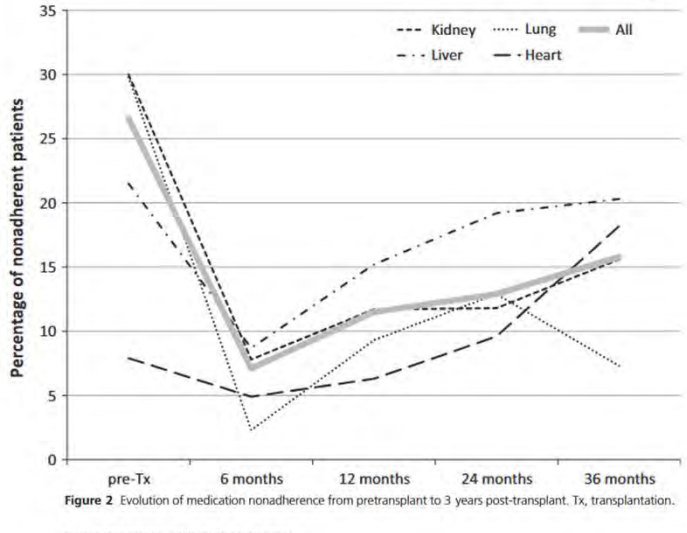


Figure 2 Evolution of medication nonadherence from pretransplant to 3 years post-transplant. Tx, transplantation.

6 De Geest, Sabina, et al. "Describing the evolution of medication nonadherence from pretransplant until 3 years post-transplant and determining pretransplant medication nonadherence as risk factor for post-transplant nonadherence to immunosuppressives: The Swiss Transplant Cohort Study." *Transplant international* 27.7 (2014): 657-666.

6

Clinical Outcomes Associated with Medication Nonadherence (MNA)

- Increased risk for:
  - Acute graft rejection
  - Chronic rejection and long-term graft abnormalities
  - Graft failure
  - Patient mortality
  - Higher rehospitalization rates
  - Increased healthcare costs

7 Dew, Mary Amanda et al. "Posttransplant Medical Adherence: What Have We Learned and Can We Do Better?." *Current transplantation reports* vol. 5,2 (2018): 174-188. doi:10.1007/s40472-018-0195-8

7

Risk factors for MNA

Condition-Related	Treatment-Related	Psychosocial	Sociodemographic	Health System
• Time since transplant • Physical limitation	• Increase number of medications • Increased frequency of medication dosing times • Bothersome side effects	• Past non-adherence • Low health literacy • Poor social support • Cognitive impairment	• Younger age • Minority race/ethnicity • Male sex	• Insurance status • Access to care • Provider-patient communication • Transition from pediatric to adult transplant program

8 Dew, Mary Amanda et al. "Posttransplant Medical Adherence: What Have We Learned and Can We Do Better?." *Current transplantation reports* vol. 5,2 (2018): 174-188. doi:10.1007/s40472-018-0195-8

8

Identifying Medication Nonadherence

Proactive approach	Reactive approach

• Adherence assessment completed at first pretransplant evaluation and subsequent visits
  • Review compliance with scheduled visits and maintenance medications
  • Assess patient's expectations of transplantation and how they concur with the care team
	• Review adherence with validated tools in patients who have displayed nonadherence or have risk factors for nonadherence

9

TRAMM Tool - Created by Transplant Pharmacy Adherence Consortium (TPAC). October 2023. Contributors: Nohely Castro, Paige Dunton, Kayla Evans, James Fleming, Haley Gutstein, Jennifer Iuppa, Tiffany Kaiser, Karen Khalil, Mary Leick, Abbie Leino, Holly Mansell, Jeong Park, TrisAnn Rendulic, Christina Ruggia-Check, Rahul Samudralwar, Tricia Suarez, David Taber, Kimi Ueda

9

HME0

Transplant recipient adherence monitoring and management (TRAMM) tool

	Definition	Pros	Cons
Self-Report	Questions directly investigating adherence	-Inexpensive -Customizable	-Burdensome for patients and providers -Subjective
Pill Counts	Objective measure to count number of pills not taken by patient	-Inexpensive -Simple -Objective	-Calculation relies on dispense date and rate
Lab and Appointment	Comparison of visits completed to the expected	-Inexpensive -Objective -Data in EHR	-EHR may lack accuracy -Difficult to standardize definitions
Immunosuppressant Levels	Proportion of drug levels measured within range	-Objective -Data in EHR	-Complex calculations -Potentially expensive
Refill Records	Review of refill history to estimate percent of time patient had enough medication	-Inexpensive -Objective -Time consuming	-Provides no data on how medication is ingested
Biomarker Monitoring	Serial assessment of biomarkers- i.e. DSA	-Objective -Noninvasive	-No specific data to support adherence monitoring -May involve third part

10

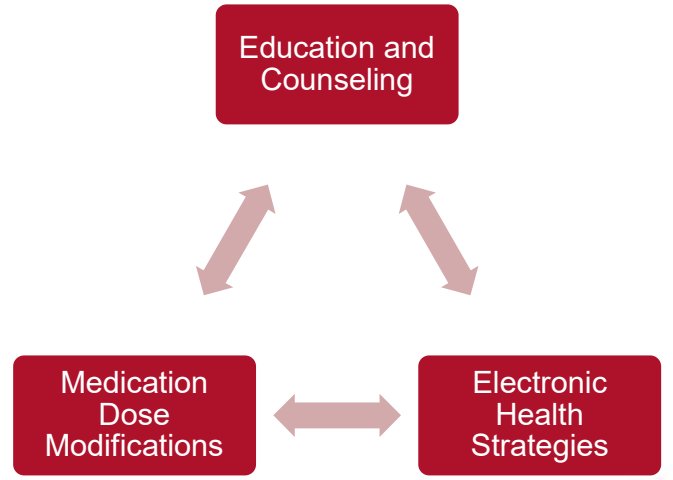
TRAMM Tool - Created by Transplant Pharmacy Adherence Consortium (TPAC). October 2023. Contributors: Nohely Castro, Paige Dunton, Kayla Evans, James Fleming, Haley Gutstein, Jennifer Iuppa, Tiffany Kaiser, Karen Khalil, Mary Leick, Abbie Leino, Holly Mansell, Jeong Park, TrisAnn Rendulic, Christina Ruggia-Check, Rahul Samudralwar, Tricia Suarez, David Taber, Kimi Ueda

10

Slide 10

HME0 This slide with a summary versus the next two slides
Henry, Molly E, 2024-02-19T21:39:17.632

Strategies to Overcome MNA



11

11

Education and Counseling

Multimodal:

- Use of both written and visual educational materials

Interdisciplinary:

- Pharmacist, nurse coordinators, etc…

Timing:

- Regular intervals
  - Education at time of pretransplant assessment
    - Instruction on importance of immunosuppressive drug adherence
  - Post-transplant education program

Strategies:

- Motivational interviewing and active listening

12 Dew, Mary Amanda et al. "Posttransplant Medical Adherence: What Have We Learned and Can We Do Better?." *Current transplantation reports* vol. 5,2 (2018): 174-188. doi:10.1007/s40472-018-0195-8

12

Medication Adherence Enhancing Intervention in Transplantation (MAESTRO-Tx Trial)	
Objective	Evaluate average daily proportions of patients with correct dosing and timing at baseline, at the conclusion of the 6 months intervention period, and 5 years
Methods	Randomized controlled trial (RCT) -Patients: heart, liver, and lung transplant recipients >1 year post-transplant on tacrolimus twice daily -After 3-month run=in, patients randomly assigned 1:1 -All patients had visits at month 0, 3, 6, 9, and 15 -Intervention group (IG): Received implementation of adherence techniques at month 3, 6, and 9 -Control group (CG): standard visits where no medication adherence was addressed
Results	-205 adult heart, liver, and lung recipients IG: n= 103, CG: n= 102 -Baseline average daily proportions of patients with correct dosing (82.6% IG, 78.4% CG) and timing adherence (75.8% IG, 72.2% CG) were comparable -Post-intervention dosing adherence was 16% higher in IG group (95.1% IG, 79.1% CG; p<0.001) -Post-intervention timing adherence was higher 20% higher in the IG group (92% IG, 72% CG; p<0.0001) -Effect was sustained at end of follow-up -5-year clinical event-free survival was comparable (82.5% IG, 72.5% CG; p=0.18)
Conclusion	Studied interventions were efficacious and sustainable in improving adherence

13 Dobbels, Fabienne, et al. "Efficacy of a medication adherence enhancing intervention in transplantation: the MAESTRO-Tx trial." *The Journal of Heart and Lung Transplantation* 36.5 (2017): 499-508

13

Medication Adherence Enhancing Intervention in Transplantation (MAESTRO-Tx Trial)	
Objective	Evaluate average daily proportions of patients with correct dosing and timing at baseline, at the conclusion of the 6 months intervention period, and 5 years
Methods	Randomized controlled trial (RCT) -Patients: heart, liver, and lung transplant recipients >1 year post-transplant on tacrolimus twice daily -After 3-month run=in, patients randomly assigned 1:1 -All patients had visits at month 0, 3, 6, 9, and 15 -Intervention group (IG): Received implementation of adherence techniques at month 3, 6, and 9 -Control group (CG): standard visits where no medication adherence was addressed
Results	-205 adult heart, liver, and lung recipients IG: n= 103, CG: n= 102 -Baseline average daily proportions of patients with correct dosing (82.6% IG, 78.4% CG) and timing adherence (75.8% IG, 72.2% CG) were comparable -Post-intervention dosing adherence was 16% higher in IG group (95.1% IG, 79.1% CG; p<0.001) -Post-intervention timing adherence was higher 20% higher in the IG group (92% IG, 72% CG; p<0.0001) -Effect was sustained at end of follow-up -5-year clinical event-free survival was comparable (82.5% IG, 72.5% CG; p=0.18)
Conclusion	Studied interventions were efficacious and sustainable in improving adherence

14 Dobbels, Fabienne, et al. "Efficacy of a medication adherence enhancing intervention in transplantation: the MAESTRO-Tx trial." *The Journal of Heart and Lung Transplantation* 36.5 (2017): 499-508

14

Electronic Health Strategies

- Electronic tools available for patients to help improve education and monitoring of medication adherence
  - Enhance patient education and improve patient's understanding of medication regimen
  - Improve medication reconciliation within healthcare facilities
  - Improve medication adherence
  - Improve continuity of care between inpatient and outpatient settings
  - Reduce readmissions related to medication errors/medication nonadherence
- Examples: Mobile applications, telehealth integration
- Limitations: Access to technology

15

15

Effectiveness of mobile health-based self-management application for posttransplant cares: A systematic review	
Objective	Review the consideration to mobile health applications (m-Health apps) used in transplantation
Methods	A systematic search of MEDLINE from inception to November 2020 -MeSH terms: m-health, empowerment, self-management, and transplantation -Two independent reviewers screened titles and abstracts for inclusion -Eligible studies: original research articles that included posttransplant care and mobile phone-based applications
Results	62.5% of studies demonstrated that the use of m-health improved medication adherence and self management in transplantation
Conclusion	The use of m-Health apps for self-management after transplant as shown promising feasibility and acceptability and there is modest evidence to support the efficacy of these interventions

16

Abasi, Sanaz, et al. "Effectiveness of mobile health-based self-management application for posttransplant cares: A systematic review." *Health Science Reports* 4.4 (2021): e434.

16

Effectiveness of mobile health-based self-management application for posttransplant cares: A systematic review	
Objective	Review the consideration to mobile health applications (m-Health apps) used in transplantation
Methods	A systematic search of MEDLINE from inception to November 2020 -MeSH terms: m-health, empowerment, self-management, and transplantation -Two independent reviewers screened titles and abstracts for inclusion -Eligible studies: original research articles that included posttransplant care and mobile phone-based applications
Results	62.5% of studies demonstrated that the use of m-health improved medication adherence and self management in transplantation
Conclusion	The use of m-Health apps for self-management after transplant as shown promising feasibility and acceptability and there is modest evidence to support the efficacy of these interventions

17

Abasi, Sanaz, et al. "Effectiveness of mobile health-based self-management application for posttransplant cares: A systematic review." *Health Science Reports* 4.4 (2021): e434.

17

Medication Dose Modifications

- Simplify, simplify, simplify
  - Number of tablets/capsules patient takes each day
  - Frequency of administration times
  - Dose changes

18

18

Improved Adherence to Tacrolimus Once-Daily Formulation in Renal Recipients: A Randomized Controlled Trial Using Electronic Monitoring (ADMIRAD Study)	
Objective	Compare medication adherence between once-daily tacrolimus and twice-daily tacrolimus regimens
Methods	Randomized controlled trail (RCT) -Patients: Adult renal transplant patients treated with tacrolimus twice daily -3 month run-in: all patients took twice daily tacrolimus -2:1 randomization to either switch from BID to QD formulation (study arm) or remain on BID (control arm)
Results	-219 stable patients were randomized -Study arm: n= 145; control arm: n=74) -6 months after randomization, 88.2% of the QD group and 78.8% of the BID group (P=0.001) took the prescribed number of daily doses -Timing adherence (defined as day-to-day percentage of patients who dosed consistently within 2 hours) was higher in the QD group compared to BID (83.7% versus 73.4%; P=0.001) -No difference in clinical outcome (acute rejection, graft loss, patient survival) were observed
Conclusion	Implementation of once daily regimen is superior to the more common twice-daily regimen

19

Kuypers, Dirk RJ, et al. "Improved adherence to tacrolimus once-daily formulation in renal recipients: a randomized controlled trial using electronic monitoring." *Transplantation* 95.2 (2013): 333-340

19

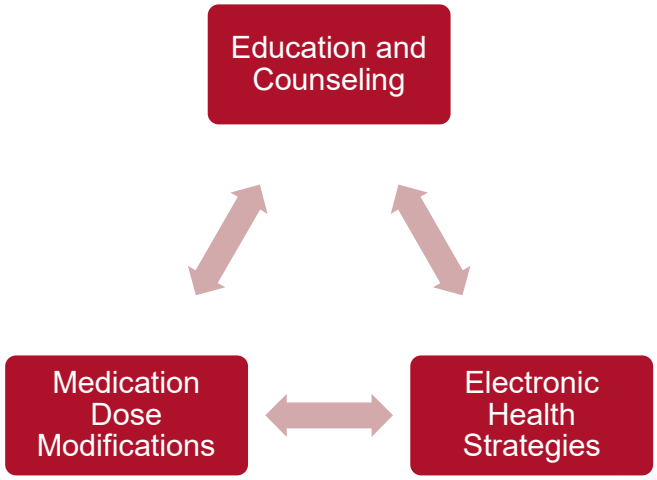
Improved Adherence to Tacrolimus Once-Daily Formulation in Renal Recipients: A Randomized Controlled Trial Using Electronic Monitoring (ADMIRAD Study)	
Objective	Compare medication adherence between once-daily tacrolimus and twice-daily tacrolimus regimens
Methods	Randomized controlled trail (RCT) -Patients: Adult renal transplant patients treated with tacrolimus twice daily -3 month run-in: all patients took twice daily tacrolimus -2:1 randomization to either switch from BID to QD formulation (study arm) or remain on BID (control arm)
Results	-219 stable patients were randomized -Study arm: n= 145; control arm: n=74) -6 months after randomization, 88.2% of the QD group and 78.8% of the BID group (P=0.001) took the prescribed number of daily doses -Timing adherence (defined as day-to-day percentage of patients who dosed consistently within 2 hours) was higher in the QD group compared to BID (83.7% versus 73.4%; P=0.001) -No difference in clinical outcome (acute rejection, graft loss, patient survival) were observed
Conclusion	Implementation of once daily regimen is superior to the more common twice-daily regimen

20

Kuypers, Dirk RJ, et al. "Improved adherence to tacrolimus once-daily formulation in renal recipients: a randomized controlled trial using electronic monitoring." *Transplantation* 95.2 (2013): 333-340

20

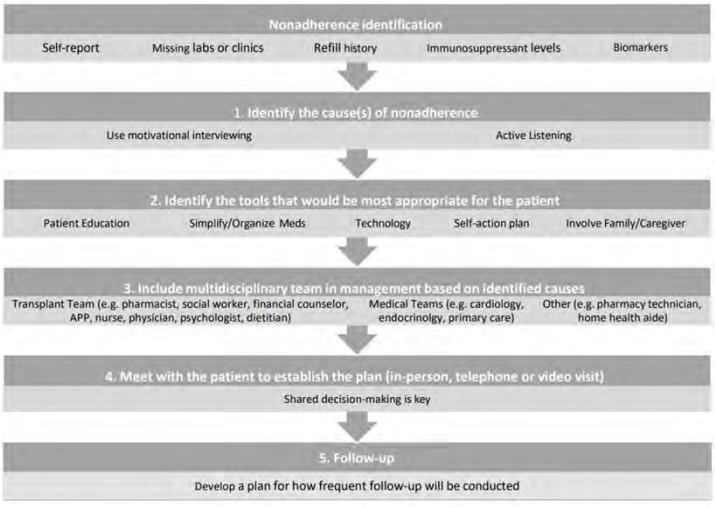
Strategies to Overcome MNA



21

21

Implementation



22

TRAMM Tool - Created by Transplant Pharmacy Adherence Consortium (TPAC). October 2023

Contributors: Nohely Castro, Paige Dunton, Kayla Evans, James Fleming, Haley Gutstein, Jennifer Iuppa, Tiffany Kaiser, Karen Khalil, Mary Leick, Abbie Leino, Holly Mansell, Jeong Park, TrisAnn Rendulic, Christina Ruggia-Check, Rahul Samudralwar, Tricia Suarez, David Taber, Kimi Ueda

22

Future directions

- Patient-friendly technology
  - Mobile applications
    - MedActionPlan PRO®
- Artificial intelligence (AI)
  - Education and monitoring
- Information technology (IT) integration
  - Electronic medical records (EMR) for monitoring and identification

23

23

Summary

- High rates of medication nonadherence (MNA) are associated with poor clinical outcomes post transplant
  - Increased risk of graft dysfunction, graft loss, and mortality
- Close monitoring for barriers to medication adherence can help identify need for early intervention
  - Condition-related, treatment-related, psychosocial, sociodemographic, and health-system related
- Implementation of timely, multimodal, and interdisciplinary strategies can help overcome MNA
  - Education and Counseling, Electronic Health Strategies, Medication Dose Modifications

24

24


Issues with Medication Adherence in Transplant Recipients
Molly E. Henry, PharmD, BCTXP
Clinical Pharmacist Practitioner
Solid Organ Transplant
Nebraska Medicine

25