Post-Transplant Patient Education and Medication Adherence

Texas Kidney Foundation
Spring Symposium
April 28, 2017

Alex de la Vega, PharmD, BCPS
Diana Luong, PharmD, BCPS
Objectives

At the end of this presentation, you will be able to:

• Understand post-kidney transplant medication education and counseling
• Discuss the importance of medication adherence and compliance
• List and describe risk factors and potential barriers to medication nonadherence and noncompliance
• Identify various interventions and strategies to prevent nonadherence
• Examine current and future Medicare immunosuppressant drug coverage
Overview of Kidney Transplantation

• Most patients with end-stage renal disease (ESRD) stem from conditions such as:
  • Diabetes (diabetic nephropathy)
  • Hypertension (hypertensive nephrosclerosis)
  • Glomerular disease

• Transplantation is the primary treatment option for most ESRD patients

• Transplant patients live an average of 10 to 15 years longer than patients on dialysis\textsuperscript{1}
Management of Transplant Patients

• Immunosuppressive therapy is most important component
• Complex regimen of drugs
• Lifelong immunosuppressive
• Primary cause of kidney transplant failures
  ➢ Lack of adherence to immunosuppressive medications
Patient Education Workflow

Pre-transplant education sessions
- Living donors
- Deceased donors

Post-transplant nurse coordinators
- Education booklet
- Wound care
- Appointment follow ups
- Medication delivery/pillbox

Inpatient and Outpatient Transplant Pharmacists
- UNOS Bylaws
- See next slides
UNOS Bylaws: Transplant Clinical Pharmacist

**Pre**
- Evaluates, screens and identifies medication related issues for potential transplant recipients

**Peri**
- Educates transplant recipients and their family members on transplant medications and adherence to medication regimen
- Prepares and assists with discharge planning for all transplant recipients
- Acts as liaison between patient and patients’ families and other health care team members regarding medication issues

**Post**
- Evaluates transplant recipient medication regimens
- Communicates all transplant recipient medication issues and concerns to appropriate members of the transplant team
- Assists with designing, implementing, and monitoring of comprehensive care plans with other team members (i.e. transplant coordinators, financial coordinator, social worker, dietician, etc.)

UNOS= United Network for Organ sharing
• Transplant pharmacist counseling
  • Importance of medications
  • Side effects
  • Pain control
  • Duration of anti-infective prophylaxis
  • Drug-drug, drug-food interactions
  • Medication reconciliation
Transplant Patient Education

• Medication List
  • Every patient should have an up-to-date medication list that includes:
    • Names and doses of medications
    • Indications/Frequency
    • Name of prescriber
    • Allergies
    • Medication conditions
  • Bring med list to every clinic appointment

• Medication Pillbox
Transplant Patient Education

• Why patients need these medications
  • Anti-rejection medications
    • Lowers body’s natural defense (immune system) against illness and new organ
    • When the body’s immune system fights against organ/allograft, it is known as rejection
    • Thus, these medications stop the body from rejecting the new organ

• Anti-infective medications
  • Anti-rejection medications increases risk of becoming sick from infections due to the decrease in immune system
  • Taking an antibacterial and antiviral can help prevent certain potential infections
Transplant Patient Education

• **Cytomegalovirus (CMV)** ³
  • Related to herpes virus
  • Most people have previously been exposed to CMV
  • Latent virus may become active
    • Can affect many organ systems
      • Eyes
      • Lungs
      • GI tract
      • Liver
    • May increase risk of rejection
  • Symptoms of nausea, vomiting, and diarrhea, abdominal pain

• **BK virus (polyomavirus)** ⁴
  • Very common in general population, but infection is not manifested
  • Virus attaches to urothelial cells
  • ~ 40-50% develop BKV infection during the 1st year
  • BK viruria
  • BK viremia
  • BKV nephropathy
Typical Post-Transplant Medication Regimen

- Anti-rejection medications
- Anti-infective medications
- Other medications
  - Anti-hypertensives
  - Anti-hyperglycemics
Mycophenolate REMS program\(^5\)

<table>
<thead>
<tr>
<th>Acceptable Contraception Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Option 1</strong></td>
</tr>
<tr>
<td>Methods to Use Alone</td>
</tr>
<tr>
<td>- Intraterine devices (IUDs)</td>
</tr>
<tr>
<td>- Tubal sterilization</td>
</tr>
<tr>
<td>- Patient’s partner had a vasectomy</td>
</tr>
<tr>
<td><strong>OR</strong></td>
</tr>
<tr>
<td><strong>Option 2</strong></td>
</tr>
<tr>
<td>Choose One Hormone Method <strong>AND</strong> One Barrier Method</td>
</tr>
<tr>
<td>Hormone Methods choose 1</td>
</tr>
<tr>
<td>- Estrogen and Progesterone</td>
</tr>
<tr>
<td>- Oral contraceptive pill</td>
</tr>
<tr>
<td>- Transdermal patch</td>
</tr>
<tr>
<td>- Vaginal ring</td>
</tr>
<tr>
<td>- Progesterone-only</td>
</tr>
<tr>
<td>- Injection</td>
</tr>
<tr>
<td>- Implant</td>
</tr>
<tr>
<td><strong>Barrier Methods choose 1</strong></td>
</tr>
<tr>
<td>- Diaphragm with spermicide</td>
</tr>
<tr>
<td>- Cervical cap with spermicide</td>
</tr>
<tr>
<td>- Contraceptive sponge</td>
</tr>
<tr>
<td><strong>AND</strong></td>
</tr>
<tr>
<td>- Male condom</td>
</tr>
<tr>
<td>- Female condom</td>
</tr>
<tr>
<td><strong>OR</strong></td>
</tr>
<tr>
<td><strong>Option 3</strong></td>
</tr>
<tr>
<td>Choose One Barrier Method</td>
</tr>
<tr>
<td>from each column (<strong>must choose two methods</strong>)</td>
</tr>
<tr>
<td><strong>Barrier Methods choose 1</strong></td>
</tr>
<tr>
<td>- Diaphragm with spermicide</td>
</tr>
<tr>
<td>- Cervical cap with spermicide</td>
</tr>
<tr>
<td>- Contraceptive sponge</td>
</tr>
<tr>
<td><strong>AND</strong></td>
</tr>
<tr>
<td>- Male condom</td>
</tr>
<tr>
<td>- Female condom</td>
</tr>
</tbody>
</table>
Immunizations Post Kidney Transplant

• Only “inactivated” vaccines
• No “live” vaccines for the rest of your life
• Always ask/inform PCP or pharmacist prior to vaccination
• Avoid vaccinations for the first 6 months (Consider when at minimal maintenance immunosuppression post 6 months)
• Exception: Prior to or during flu season
  ➢ Influenza vaccine can be given at least 1 month post transplant
Why is medication adherence so important?

- Patients are on life-long immunosuppressive regimens
- Non-adherence and non-compliance is associated with a 60% increased risk of kidney transplant failure\(^7\)
  - Increase graft rejection episodes
  - Increase hospitalizations
  - Increase costs
  - Increase poor long-term kidney outcomes

Good patient compliance and adherence means taking the right drugs, on time and in the proper doses
Non-adherence

Intentional

Non-intentional

Missing doses*

Altering doses*

Forgetting doses
WHO classification of risk factors for non-adherence

<table>
<thead>
<tr>
<th>Socio-economic factors</th>
<th>Patient- / disease-related factors</th>
<th>Treatment-related factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Health beliefs/behaviors</td>
<td>Patient symptoms</td>
</tr>
<tr>
<td>Gender</td>
<td>Vaccination status</td>
<td>Side effects of medications</td>
</tr>
<tr>
<td>Nationality</td>
<td>Smoking history</td>
<td></td>
</tr>
<tr>
<td>Live alone/with others</td>
<td>Alcohol use</td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Perceived adequacy of one’s financial situation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td>Lack of health insurance or health benefits</td>
</tr>
</tbody>
</table>

WHO = World Health Organization
Factors affecting NON-ADHERENCE

- Poorly perceived treatment benefits
  - Greater distances to travel
  - Poor transportation
- Higher medication side effects
- Patients without diabetes
- Poor social support
- Complex medical regimens
- Lack of education
- Unemployment
- Increased time period since transplant
- Poorly perceived benefits
  - Age < 25
  - Males
  - Non-Caucasian
- Patients without diabetes
  - Age < 25
  - Males
  - Non-Caucasian
Additional factors

• Influence of personal characteristics
• Predictor of health-related behavior
• Previous dialysis-dependent patients
• Perceived susceptibility to rejection
• Frequency of drug dosing  
  • Once vs Twice daily
Patient Survey Responses on Medication Non-adherence\textsuperscript{10}
Measuring nonadherence

- Electronic medication monitoring\(^9\)
  - Gold standard
  - Limitations:
    - Lack of certainty that med or correct dose was taken
- Self-reporting
- Drug levels
- Compliant with medications prior to known lab draw
  - Patient may have missed a dose or two
- Difficult to quantify nonadherence
  - Inconsistent methodology
  - Honest disclosure of self reporting
<table>
<thead>
<tr>
<th>Study, duration</th>
<th>Number of participants</th>
<th>Interventions</th>
<th>Measurement</th>
<th>Results</th>
<th>Measurement</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chisholm(^1) (2001) 21 months</td>
<td>C: n = 12 \n I: n = 12 \n Usual care (C) vs intervention (I)</td>
<td>Informational: verbal or written instructions \n Behavioral: Monthly face-to-face sessions with pharmacist</td>
<td>Pharmacy refill records</td>
<td>Mean compliance rates</td>
<td>Serum drug concentrations of IS</td>
<td>% patients within target serum levels</td>
</tr>
<tr>
<td>Chisholm-Burns (^2) (2013) 15 months</td>
<td>C: n = 74 \n I: n = 76</td>
<td>Informational: non-adherence consequences \n Behavioral: identify tools/strategies Patient motivation</td>
<td>Pharmacy refill records</td>
<td>t-test Adherence score 6 months: \n I: 0.89 \n C: 0.80 \n 9 months: \n I: 0.91 \n C: 0.81</td>
<td>Monthly healthcare screening questionnaire</td>
<td>% patients requiring hospitalization</td>
</tr>
</tbody>
</table>
Overcoming Nonadherence/Noncompliance

A combination of interventions via team approach is the most helpful long-term strategy

- Pharmacist-led medication counseling
- Individualized and patient-tailored education
- Open-ended questions regarding adherence
- Repetitive teaching
- Developing good communication and good relationships between patient and healthcare provider
- Medication scheduling
- Weekly pillboxes
- Refill reminders
Other considerations

• Steroid free protocols
• Calcineurin-inhibitor (CNI) minimization
• Valganciclovir (Valcyte®) mini-dosing\(^\text{13}\)
• Once vs Twice daily dosing
  • Drug holidays
• Generics vs Brand medications
• Belatacept (Nulojix™)
• Pipeline transplant medications
• Novel technology: New ingestible sensor system\(^\text{14}\)
Barriers to Medication Adherence

• Access to immunosuppressive agents
  • Financial
  • Medicare benefits
  • Direct relationship between loss of insurance coverage and allograft failure
Disparities in Kidney Transplant Outcomes

Risk Factors for Worse Graft Function

<table>
<thead>
<tr>
<th>Sociocultural</th>
<th>Socioeconomic</th>
<th>Geographic</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>Lower Income</td>
<td>Living in Poor Areas</td>
</tr>
<tr>
<td>Male</td>
<td>Less Insurance Coverage</td>
<td>Living Further from Transplant Center</td>
</tr>
<tr>
<td>Older Age</td>
<td>Medicare or Medicaid</td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>Low Socioeconomic Status</td>
<td></td>
</tr>
<tr>
<td>Less Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Disparities in Kidney Transplant Outcomes

• Immunological risk factors
• Non-immunological risk factors
  ➢ Comorbidities
  ➢ Time on dialysis
  ➢ Donor characteristics and organ characteristics
  ➢ Socioeconomic status
  ➢ Medication adherence
  ➢ Access to care and health policies
Medicare Coverage of Immunosuppressant drugs
Social Security Amendments of 1965 established Medicare and Medicaid

- >65 age, people with disabilities, and poor families

92nd Congress: H.R. 1 as section 2991 of the Social Security Amendments of 1972 providing disease specific Medicare benefits for eligible patients with ESRD

- Part A and B coverage of the costs of dialysis and renal transplantation but not immunosuppressive drug coverage

Omnibus Budget Reconciliation Act 1986

- Authorized payment through Part B benefits for immunosuppressive medications for 1 year after a Medicare covered renal transplant

Medicare Part B History
Medicare Part B History

1993-95 Medicare and Medicaid services gradually extended coverage
  • 3 years after kidney transplantation

2011-Present
  • Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients Act
Fascinating Tidbit of Information

• Extension of Medicare’s immunosuppressive medication coverage from 1 to 3 years post-transplant:
  ➢ Associated with a significant improvement in kidney transplant survival among lower-income recipients
  ➢ 27% relative improvement in graft survival among lower-income patients
Current Medicare Part B after kidney transplant

You have Part A

Qualify for Medicare based on age and disability

ISD covered for a lifetime

Transplant in Medicare-covered facility

ISD = immunosuppressive drugs
Current Medicare Part B after kidney transplant

You have Part A

Entitled to solely Medicare because of ESRD

Transplant in Medicare covered facility

ISD covered for a limited time
Medicare Part B

Part B Premiums

• The standard Part B premium amount in 2017 is $134 (or higher depending on your income)

• If you pay your Part B premium through your monthly Social Security benefit, you’ll pay less ($109 on average).

Part B deductible & coinsurance

• You pay $183 per year for your Part B deductible

• After your deductible is met, you typically pay 20% coinsurance
Medicare Part B: What does this all mean?

<table>
<thead>
<tr>
<th>Medication</th>
<th>30-d AWP $ Based on avg. dose</th>
<th>Annual AWP $</th>
<th>20% copay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrolimus</td>
<td>856</td>
<td>10,272</td>
<td>$2,054.00</td>
</tr>
<tr>
<td>Mycophenolate Mofetil</td>
<td>942</td>
<td>11,304</td>
<td>$2,260.00</td>
</tr>
<tr>
<td>Prednisone</td>
<td>3</td>
<td>36</td>
<td>$7.00</td>
</tr>
</tbody>
</table>

$4,321 total per person
Economic Impact of ESRD care and ISD coverage

Medicare Part D ~ $305 million
Medicare Part B ~ $460 million

Prograf
Cellcept
Myfortic

All Rx coverage

ESRD = End Stage Renal Disease
<table>
<thead>
<tr>
<th>2010 rank by total Medicare expenditures</th>
<th>Brand name(s)</th>
<th>Condition(s) treated</th>
<th>Spending on Medicare beneficiaries (dollars in millions)</th>
<th>Spending on total U.S. insured population (dollars in millions)</th>
<th>Percentage spent on Medicare beneficiaries (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>Myfortic</td>
<td>Prevent transplant kidney rejection; treat Crohn’s disease</td>
<td>$80</td>
<td>$86</td>
<td>92.2%</td>
</tr>
<tr>
<td>18</td>
<td>Prograf</td>
<td>Prevent transplant organ rejection; treat fistulizing Crohn’s disease</td>
<td>267</td>
<td>290</td>
<td>92.1%</td>
</tr>
<tr>
<td>52</td>
<td>Brovana</td>
<td>Symptoms of chronic obstructive pulmonary disease</td>
<td>70</td>
<td>77</td>
<td>91.3%</td>
</tr>
<tr>
<td>22</td>
<td>Pulmicort</td>
<td>Prevent wheezing, shortness of breath, and troubled breathing in asthma and lung disease patients</td>
<td>245</td>
<td>273</td>
<td>89.6%</td>
</tr>
<tr>
<td>33</td>
<td>Aranesp (ESRD use)</td>
<td>Anemia in end-stage renal disease (ESRD) patients</td>
<td>162</td>
<td>182</td>
<td>88.7%</td>
</tr>
<tr>
<td>45</td>
<td>Primacor, in Dextrose</td>
<td>Acute decompensated heart failure</td>
<td>87</td>
<td>101</td>
<td>85.6%</td>
</tr>
<tr>
<td>40</td>
<td>Cellcept</td>
<td>Prevent transplant organ rejection; treat Crohn’s disease</td>
<td>113</td>
<td>133</td>
<td>84.9%</td>
</tr>
</tbody>
</table>

Source: GAO analysis of Centers for Medicare & Medicaid Services and RED BOOK data. | GAO-16-594
Medicare Part D

- Voluntary prescription drug coverage program available to all people with Medicare.
- If you have Part B and Part D, Part B will cover the immunosuppressant.
- Covers drugs not covered by Part B (i.e., antihypertensives).
- Part D went into effect in 2006 and has been administered by private health plans.
Medicare Part D

Entitled to Medicare solely because of ESRD

Medicare effective date is AFTER month of transplant

Transplant in Medicare covered facility

ISD covered by Part D
Medicare Part D

• Routine medications may always have $4 copays

• Class IV and V medications without Extra Help:
  ➢ Copays may range between 25 and 50%
  ➢ $200, $500, $900, $1800 are possible
  ➢ Valcyte® class V, will temporarily have high copay

• Class IV and V medications WITH Extra Help
  ➢ Copays between $4 and $8
Medicare Part D Gap

Total costs reach About ~ $3,000
Future

• Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients Act “Immuno Bill”
• Affordable Care Act (ACA)
• Assistance Programs
Immuno Bill

• S.1454/H.R. 2969 was first introduced in 2011 (112th congress)
• Proposed to amend Medicare to extend ISD coverage beyond 36 mo
• Would allow individuals to be eligible for Medicare Part B solely for the purpose of drug coverage
• Has “died” in the senate finance committee twice
• Recently re-introduced in House 9/22/16 and the Senate 11/30/16
  ➢ H.R. 6139 and S.3487
  ➢ Bill was not enacted
“Immuno Bill”

• A “no brainer”

• Medicare expenditures on 1st year transplant vs. dialysis

Kidney transplant $32,914
PD $66,751
HD $87,561
Total Medicare ESRD Expenditures, by modality, 2004-2014

Data Source: USRDS ESRD Database. Total Medicare costs from claims data for period prevalent ESRD patients. Abbreviation: ESRD, end-stage renal disease.
Total Medicare ESRD expenditures per person per year, by modality, 2004-2014

Data Source: USRDS ESRD Database; Reference Tables K.7, K.8, & K.9. Period prevalent ESRD patients; includes all claims with Medicare as primary payer only. Abbreviation: ESRD, end-stage renal disease.
Immuno Bill

Why the hesitation?

- The financial health of Medicare programs will be partly determined by cost savings associated with the ACA over the next decade.
- Political pressure/lobbyists from industry has opposed any shifting of payment away from dialysis to transplant antirejection drugs.
- Additional expenditures and disease-specific ESRD entitlement have been questioned by some policymakers when other disease-specific programs lack similar benefits.

ACA = Affordable Care Act
Affordable Care Act

• Market Place
  - Prevents pre-existing condition exclusions
  - Requires qualified health plans sold through the health insurance marketplaces to cover immunosuppressive drugs.

• Competitive bidding for drugs

• ACA plans
  - Prescription costs: but pay full price until the deductible is met
  - Deductible ranges from $500-$5000

• Medicaid expansion
  - Texas did not expand
Can we off set some of the cost burden?

• Medicare Supplement Insurance (Medigap)
  ➢ Medigap policies sold after 1/1/06 aren’t allowed to include Rx drug coverage

• Medicare Advantage plan (“Part C”)— Avoid
  ➢ Prior to developing ESRD
  ➢ Successful kidney transplant and you still qualify for Medicare benefits

• Medicare Savings Plan

• Medicaid
  ➢ Texas : Never expanded Medicaid under the ACA
  ➢ Traditional Medicaid will cover only 3 Rx a month
  ➢ Medicaid alone may not be adequate coverage
Can we off set some of the cost burden?

• Extra Help Program
  - Help with Medicare prescription drug plan costs

• Part D Catastrophic coverage
  - Spend a total of $4,950 in True Out-of-Pocket Part D drug costs in 2017
  - Automatically leave the “Gap”
  - Pay a small coinsurance amount or copayment for covered drugs for the rest of the year
Medication Assistance Programs

• Texas Kidney Health Care Program
• Rx Assist, RxHope, Together Rx Access Card
• AZ&Me Prescription Savings Program
• Drug Company prescription assistance programs: e.g. Valcyte® Co-Pay Card and GENENTECH® ACCESS TO CARE FOUNDATION (GATCF)
  ➢ https://www.kidney.org/patients/resources_Prescription
• A Charitable Life- MSTH
Conclusion

• Recognizing patient’s risk factors for non-adherence and overcoming financial barriers may significantly impact long term kidney transplant outcomes

• Social worker/case manager/RN/dietician/pharmacist

• Pre-transplant screening is of utmost importance

• Passing Legislation/law similar to the Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients
References


2. The United Network of Organ Sharing Bylaws. Attachment 1 to Appendix B of the UNOS Bylaws; Designated Transplant Program Criteria. UNOS-Appendix B-Attachment I--XIII-93 June 28-29, 2011


