Dietary Influences on Mycophenolate Related Diarrhea in Kidney Transplant Recipients

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Background and Quality Issue

- Diarrhea is a common side effect of mycophenolate in renal transplant patients
- Dose reductions are frequently done to treat mycophenolate related diarrhea
- Dose reductions are associated with increased acute rejection and graft failure

22% experience clinically significant diarrhea

Dose reduction > 50% → **Graft failure OR = 2.36[1]**

Discontinuation → **Graft failure OR = 2.72[1]**

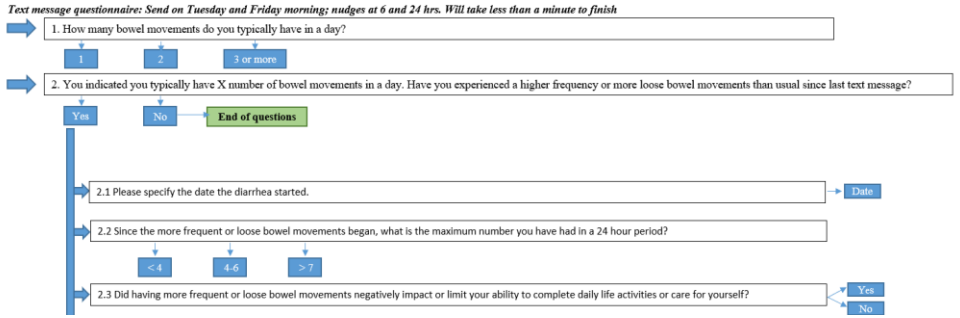
- Dietary effects on mycophenolate related diarrhea have not been well studied
- Polyols, including sorbitol and mannitol, have been associated with diarrhea in the general public due to their osmotic effects
  - Component of FODMAP
  - FODMAP avoidance improves IBS symptoms
  - Could polyol avoidance improve mycophenolate relate diarrhea?

Aim

- To determine if polyol intake is associated with mycophenolate related diarrhea
  - Inform future prospective intervention
    - Find treatment that does not require mycophenolate alterations
  - Ultimately, to improve outcomes for patients

Methods

- 25 subjects – up to 6 months post transplant
- Bi-weekly text surveys
  - Allowed for categorization of diarrhea based off of CTCAE V 5.0



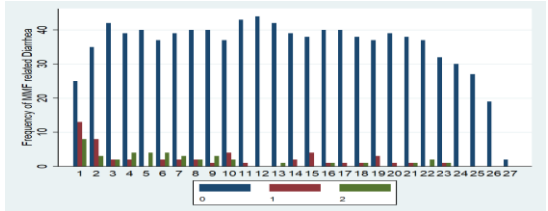
- Participants completed 48 hour food recalls using provided food diaries
- Analyzed with Nutrition Data System for Research (NDSR)
- Results assessed for correlation with episodes of diarrhea

Results

	No CTCAE grade 2 diarrhea (n=14) Mean (95% CL Mean)	Developed CTCAE grade 2 diarrhea (n=11) Mean (95% CL Mean)	P-value (t-test)
Fiber (g/day)	20 (12-27)	16 (13-18)	0.33*
Soluble Fiber (g/day)	6 (4-8)	5 (4-6)	0.49*
Insoluble Fiber (g/day)	14 (8-19)	11 (9-13)	0.32*
Mannitol (g/day)	0.32 (0.06-0.59)	0.4 (0.12-0.68)	0.66
Sorbitol (g/day)	0.26 (-0.05 – 0.57)	0.12 (-0.01 – 0.24)	0.37*
Fructose (g/day)	14 (6-22)	19 (9-29)	0.39
Lactose (g/day)	9 (3-14)	21 (5-37)	0.13*
Percent Calories from Fat (%)	37 (32-42)	33 (28-39)	0.32
Percent Calories from Protein (%)	16.9 (14.4-19.4)	17.8 (16.3-19.3)	0.53
Poly-Sat fat ratio	0.9 (0.55-1.24)	0.72 (0.51-0.93)	0.36*

Results

- Total of 1,147 biweekly surveys filled out by the 25 subjects
  - 22/25 met CTCAE criteria for diarrhea at some point
  - 54 reports of CTCAE Grade 1 diarrhea
    - Increase < 4 stools/day
  - 42 reports of CTCAE Grade 2 diarrhea
    - Increase of 4-6 stools/days
- No correlation between sorbitol or mannitol ingestion and diarrhea



Discussion

Conclusions

- Mannitol and sorbitol ingestion were not associated with mycophenolate related diarrhea
- Other FODMAP categories and fiber also showed no correlation with diarrhea
- Reasons for no correlation?
  - Truly no effect
  - Reliance on dietary recall
  - Too many confounders

Future Directions

- Other potential factors in mycophenolate related diarrhea
  - Microbiome
  - Interactions with other medications

Reference:

1. Bunnapradist S, Lentine KL, Burroughs TE, Pinsky BW, Hardinger KL, Brennan DC, et al. Mycophenolate mofetil dose reductions and discontinuations after gastrointestinal complications are associated with renal transplant graft failure. Transplantation. 2006;82(1):102-7.