



Dietary Influences on Mycophenolate Related Diarrhea in Kidney Transplant Recipients

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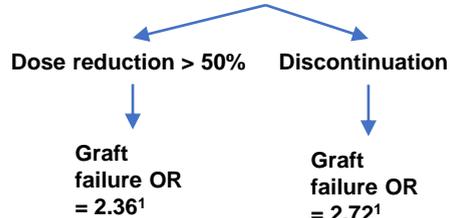
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Driven to DiscoverSM

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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



- 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 low-FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet
 - FODMAP avoidance improves IBS symptoms
 - Could polyol avoidance improve mycophenolate related diarrhea?

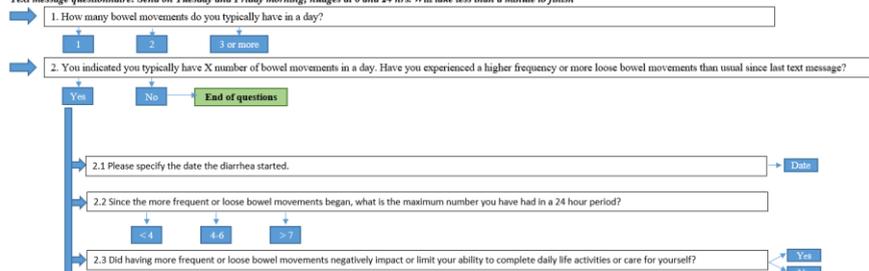
Aim

- 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

- Subjects recruited for MISSION study – prospective observational study of the microbiome in kidney transplant patients taking mycophenolate
- 25 subjects – followed-up for up to 6 months post transplant
- Twice weekly text surveys
 - Allowed for categorization of diarrhea based off of CTCAE V 5.0

Text message questionnaire: Sent on Tuesday and Friday morning; nudges at 6 and 24 hrs. Will take less than a minute to finish



- Participants completed 48-hour food recalls using provided food diaries at 21 days, 2 months, 4 months and 6 months
- Nutrient content analyzed with Nutrition Data System for Research (NDSR)
- Results assessed for correlation with episodes of diarrhea collected using MOSIO

Results

- Total of 1,147 twice weekly surveys filled out by the 25 subjects
 - 22/25 met CTCAE criteria for diarrhea at any time-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 dietary sorbitol or mannitol and 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 or Satterthwaite* when unequal variance)
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*

Discussion

Conclusions

- Dietary intake of mannitol and sorbitol was not associated with mycophenolate related diarrhea
- Other FODMAP affiliated nutrients and fiber were not correlated with diarrhea
- Reasons for no correlation?
 - Truly no effect
 - Reliance on dietary recall
 - Too many confounders (e.g. liquid medications)

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.