Maternal Prenatal Use of Reflux Medication and the Development of Food Protein-Induced Allergic Proctocolitis in Offspring

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Abstract

Rationale: Recent studies have linked exposure to prenatal acid suppressive medications with the development of allergic diseases early in life, but associations with food protein-induced allergic proctocolitis (FPIAP) have not been well-studied. We hoped to evaluate the association between FPIAP and prenatal exposure to acid suppressive medication.

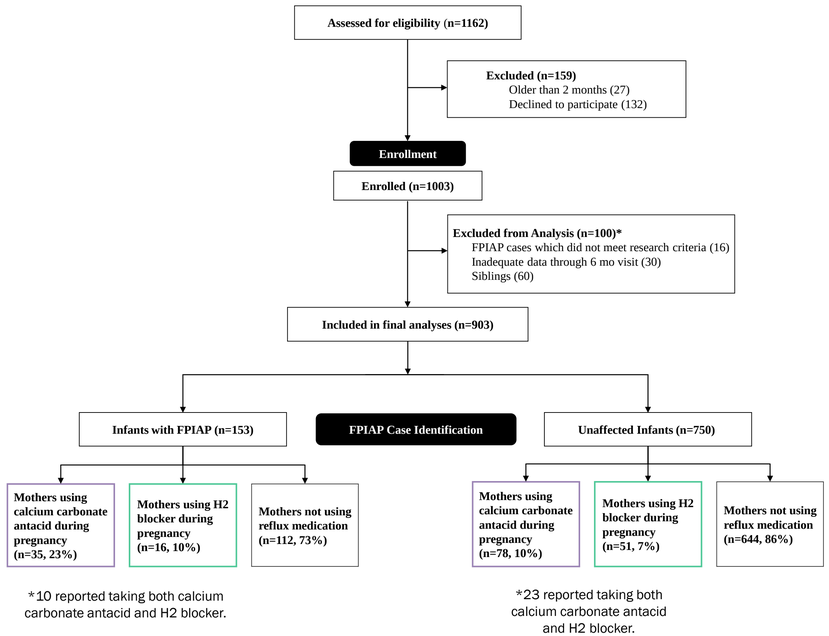
Methods: The Gastrointestinal Microbiome and Allergic Proctocolitis (GMAP) Study is an ongoing prospective observational cohort study of 1003 healthy newborn infants enrolled at their first well visit. Mothers disclosed whether they took acid suppressive medications during pregnancy in a comprehensive initial visit questionnaire administered at study enrollment and prior to the development of FPIAP. The diagnosis of FPIAP was made by the treating pediatrician. Investigators reviewed each case to confirm prespecified inclusion criteria, including documented gross or occult blood in the stool. Associations were tested using univariable and multivariable logistic regression.

Results: Of 903 infants that were analyzed, 153 (17%) were identified as cases. 67 mothers (7%) took a histamine-2 receptor antagonist and 113 mothers (13%) took a calcium carbonate antacid during pregnancy. FPIAP was associated with prenatal exposure to calcium carbonate antacids (OR 2.56, 95%CI [1.64, 3.98], p<.001) but not associated with prenatal exposure to a H2 blocker (OR 1.60, 95%CI [.89, 2.89], p=.12). This association between prenatal calcium carbonate antacid exposure and FPIAP remained significant after adjusting for sex, race, maternal proton-pump inhibitor and H2 blocker use, and relevant family history. Results also remained significant using a stricter FPIAP diagnosis criteria requiring gross blood or mucus in stool.

Conclusion: We found a novel association between prenatal exposure to calcium carbonate antacids and FPIAP development in offspring. More research should be conducted to explore this potential association.

Methods

Figure 1. GMAP Study Consort Diagram

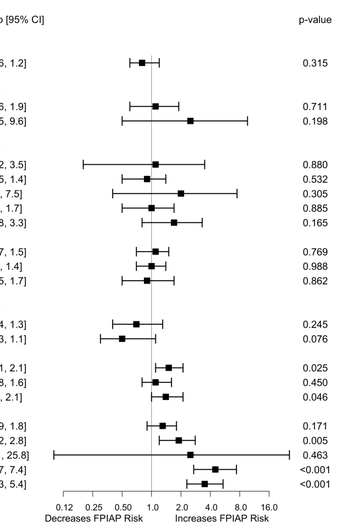


*10 reported taking both calcium carbonate antacid and H2 blocker.

*23 reported taking both calcium carbonate antacid and H2 blocker.

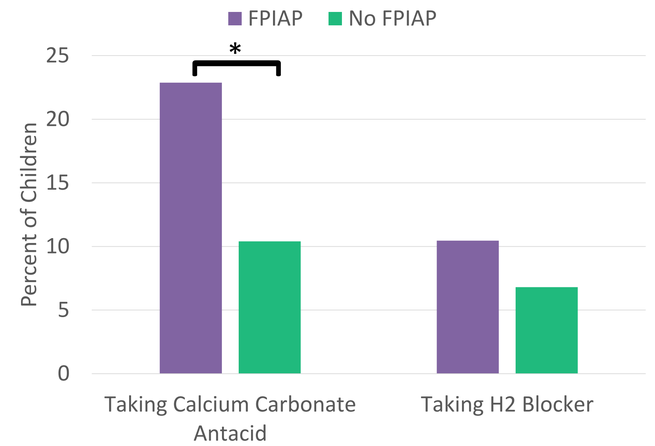
Table 1. GMAP Study Population Demographics

	Cohort: n (%) 903	FPIAP: n (%) 153	Unaffected: n (%) 750	Odds Ratio [95% CI]	p-value
Demographics					
Female	417 (46)	65 (42)	352 (47)	0.8 [0.6, 1.2]	0.315
Gestational Age					
>37 weeks	806 (89)	134 (88)	672 (90)	*	
33-37 weeks	88 (10)	16 (10)	72 (10)	1.1 [0.6, 1.9]	0.711
25-32 weeks	9 (1)	3 (2)	6 (1)	2.5 [0.5, 9.6]	0.198
Race					
White	601 (69)	104 (70)	497 (68)	*	
Black	16 (2)	3 (2)	13 (2)	1.1 [0.2, 3.5]	0.880
Asian	164 (19)	25 (17)	139 (19)	0.9 [0.5, 1.4]	0.532
Other	10 (1)	3 (2)	7 (1)	2 [0.4, 7.5]	0.305
Multiple Race	84 (10)	14 (9)	70 (10)	1 [0.5, 1.7]	0.885
Hispanic or Latino	41 (6)	11 (9)	30 (5)	1.7 [0.8, 3.3]	0.165
Delivery Characteristics					
C-section	286 (32)	50 (33)	236 (31)	1.1 [0.7, 1.5]	0.769
Maternal Antibiotics at Delivery	449 (50)	76 (50)	373 (50)	1 [0.7, 1.4]	0.988
Infant Perinatal Antibiotics	80 (9)	13 (9)	67 (9)	0.9 [0.5, 1.7]	0.862
Initial Diet					
Formula	59 (7)	14 (9)	45 (6)	*	
Breastmilk	558 (62)	98 (64)	460 (61)	0.7 [0.4, 1.3]	0.245
Mixed	286 (32)	41 (27)	245 (33)	0.5 [0.3, 1.1]	0.076
Other Characteristics					
Eczema	366 (44)	78 (52)	288 (42)	1.5 [1.1, 2.1]	0.025
First child	423 (47)	76 (50)	347 (46)	1.1 [0.8, 1.6]	0.450
Pets	334 (41)	70 (48)	264 (39)	1.4 [1, 2.1]	0.046
Family History (1st Degree Relative)					
Family History of Atopy	409 (45)	77 (50)	332 (44)	1.3 [0.9, 1.8]	0.171
Family History of Food Allergies	138 (15)	35 (23)	103 (14)	1.9 [1.2, 2.8]	0.005
Family History of EoE	3 (0)	1 (1)	2 (0)	2.5 [0.1, 25.8]	0.463
Family History of Bloody Stools	76 (8)	33 (22)	43 (6)	4.5 [2.7, 7.4]	<0.001
Family History of Diet Intolerance	121 (13)	44 (29)	77 (10)	3.5 [2.3, 5.4]	<0.001



Results

Figure 2. Association between FPIAP Development and Prenatal Reflux Medication



*The asterisk refers to P value < .05 calculated with binomial logistic regression.

Table 2. Associations Between Prenatal Reflux Medication and Food Allergic Manifestations

FPIAP	Odds Ratio	95% Confidence Interval	P value
Calcium Carbonate Antacid	2.56	1.64, 3.98	<.001
H2 Receptor Antagonist	1.60	.89, 2.89	.12
IgE-Mediated Food Allergy	**Odds Ratio**	**95% Confidence Interval**	**P value**
Calcium Carbonate Antacid	1.00	.44, 2.26	1.00
H2 Receptor Antagonist	.96	.34. 2.73	.94

*All measures calculated with binomial logistic regression. Odds ratios are unadjusted; adjusting for sex, race, maternal proton-pump inhibitor and H2 blocker use, and relevant family history did not affect significance.

Key Findings

- Prenatal calcium carbonate antacid but not H2 blocker use significantly associated with FPIAP development
- No association between prenatal reflux medication and IgE-mediated food allergy
- Further study needed to better understand the relationship between prenatal reflux mediation and FPIAP

Acknowledgments

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References

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