#224: First real-world effectiveness analysis of preschool peanut oral immunotherapy

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Background

- In 2017, Vickery et al demonstrated that peanut oral immunotherapy (P-OIT) was effective and safe in 37 preschool-aged children; 85% of children on 300mg daily P-OIT maintenance for a median of 29 months were desensitized, there were no severe reactions during build-up, and only one child required epinephrine at home during build-up.
- In 2019, our group of community and academic allergists from across Canada who initiated 'Canadian Preschool Peanut Oral Immunotherapy' (CPP-OIT), a quality improvement (QI) project published safety of P-OIT for the first 270 preschoolers; only 0.4% of patients experienced a severe reaction, and 4.1% received epinephrine, during build-up.
- In contrast, in older children, a recent systematic review and meta-analysis by Chu et al noted a higher rate of anaphylaxis (16.5%) during P-OIT compared with avoidance (2.70%), and concluded that avoidance is safer than P-OIT. Similarly, Grzeskowiak et al's 2020 systematic review and meta-analysis reported a 7.6% rate of reactions requiring epinephrine during P-OIT.
- Efficacy of P-OIT in older children appears to be lower than in preschoolers, according to the meta-analysis by Grzeskowiak et al, reporting a 68.9% likelihood of passing the exit OFC (range: 41.9% to 92.3%) based on 17 studies.
- The current study aimed to evaluate the effectiveness of real world P-OIT in preschoolers after a median of 12 months on maintenance.

Methods

- This is a Canada-wide quality improvement project of academic and community allergists.
- Patients aged 9-70 months old were included in this analysis based on the following inclusion criteria:
  1. a history of an allergic reaction to peanut (at home or at the optional baseline OFC to a cumulative dose <300mg peanut protein), AND either a positive skin prick test (SPT) ≥3 mm or peanut-specific Immunoglobulin E (ps-IgE) ≥0.35 kU/L.
  2. If no peanut ingestion history and no baseline OFC, a ps-IgE ≥5 kU/L was required, regardless of SPT size.
  3. If grade 1 (mild) history only (according to the WAO criteria published in our previous paper) and no baseline OFC, a baseline ps-IgE ≥2 kU/L and a peanut SPT ≥7 mm were required.(11)
  4. At least one allergic reaction temporally associated with dosing during OIT build-up, or a positive baseline OFC to a cumulative dose below 300mg.
- Some patients underwent an optional open OFC to peanut according to Bird et al's protocol.
- For build-up, increasing doses of peanut were administered in-clinic every two weeks up to 300mg peanut protein daily maintenance, with daily doses at home, according to one of three CPP-OIT protocols published previously (Peanut flour-only, Bamba®-only (Osem Group, Israel) and Hybrid.
- Symptoms were graded according to the World Allergy Organization Subcutaneous Immunotherapy Reaction Grading System, with adaptations specific to allergic reactions in infants (1 mildest, 5 most severe).
- After approximately 12 months on OIT maintenance, patients were invited to participate in an open peanut OFC to a cumulative dose of 4000mg peanut protein following the Bird et al protocol. Patients on maintenance for 18 months were considered eligible to receive the follow-up OFC.
- Means, percentages, and 95% confidence intervals (Cis) were calculated for categorical variables; median and interquartile range (IQR) were calculated for continuous variables.
- Patients who underwent a follow-up OFC after 12 months on OIT maintenance were compared with patients who did not receive the follow-up OFC to determine whether there were any characteristics associated with not receiving the follow-up OFC. The two-sample test of proportions was used for these statistical comparisons, and the results were considered statistically significant (indicated with an asterisk* in the tables) if the 95% confidence interval of the difference between the proportions did not cross zero/null.
- Data were analyzed using Stata 15.
- We received a waiver for ethics from the Research Ethics Board at The University of British Columbia/British Columbia Children's Hospital since CPP-OIT is a Quality Improvement project.

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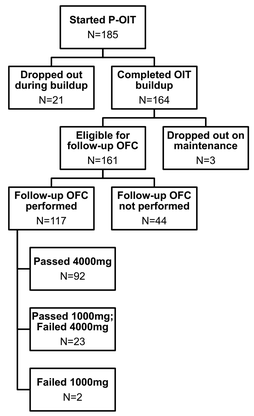
Results

- Of 185 eligible patients who started P-OIT between April 2017 and December 2018, 164 reached maintenance, 21 (11.4%) dropped out during build-up, and 3 (1.83%) dropped out during maintenance. Figure 1 shows a flow diagram of patients.

Figure 1: Flow diagram of patients



- Those who did and did not receive the follow-up OFC were similar in terms of baseline characteristics, and likelihood of experiencing moderate/severe reactions or requiring epinephrine during build-up and maintenance. However, baseline SPT and IgE levels were higher in those who did not receive the follow-up OFC (Table 1).

Table 1: Comparison of characteristics of patients who received the follow-up OFC, and who were eligible for the follow-up OFC but did not receive it

	Received follow-up OFC	Did not receive follow-up OFC
Total	N=117	N=44
Age (in months) at entry into OIT, mean (95%CI)	25.0 (22.5, 27.4)	28.6 (24.5, 32.7)
Baseline peanut SPT (mm), mean (95%CI)	7.08 (6.62, 7.54)* *based on data from 112 patients*	8.95 (7.83, 10.1)* *based on data from 42 patients*
Baseline peanut sIgE (kU/L), mean (95%CI)	12.0 (7.34, 16.7)* *based on data from 80 patients*	30.6 (18.7, 42.6)* *based on data from 35 patients*
Build-up data	N=117	N=80
Highest grade of rxn, n (%)		
Rxn at baseline OFC only	12 (10.3)	4 (9.10)
1 (Mild)	61 (52.1)	18 (40.9)
2 (Moderate)	44 (37.6)	22 (50.0)
Received Epinephrine, n (%)	2 (1.70)	4 (9.10)
Maintenance data	N=105	N=19
Highest grade of rxn, n (%)		
No reaction	95 (90.5)	16 (84.2)
1 (Mild)	8 (7.60)	2 (10.5)
2 (Moderate)	2 (1.90)	1 (5.30)
Received Epinephrine, n (%)	1 (0.90)	1 (5.30)

CI=Confidence interval; OFC=oral food challenge; OIT=oral immunotherapy; SPT=skin prick test
*Statistically significant difference between those who did and did not receive the follow-up OFC.

Effectiveness of peanut oral immunotherapy in preschoolers

- 117 of 161 (72.7%) patients underwent the follow-up OFC after a median of 12.2 months on maintenance (IQR: 11.5, 13.1).
- 92 of the 117 (78.6%) of patients who underwent the follow-up OFC tolerated at least 4000mg peanut protein without symptoms.
- 115 0f the 117 (98.3%) tolerated at least 1000mg peanut protein without symptoms, more than enough to protect against an accidental exposure.
- Of those who did not pass the 4000mg OFC, their symptoms were mild (68.0%) to moderate (32%), with no severe reactions (Table 2).

Table 2: Grade of reaction and cumulative dose for patients who failed the follow-up OFC

Cumulative dose	Grade 1	Grade 2	Grade 3	Total
300	1	1	0	2
2000	3	0	0	3
3000	0	1	0	1
2600	1	0	0	1
4000	12	5*	1**	18
Total	17	7	1	25

Note: there were no grade 4 or grade 5 reactions during the follow-up OFC.
*One patient required epinephrine.
**One patient required epinephrine and went to the emergency department.

Conclusions

- We are the first group to describe the effectiveness of preschool peanut OIT in a real-world, multi-center setting. We confirm with a sample of 117 preschool children that the treatment is effective, with 78.6% of patients tolerating 4000mg of peanut protein without symptoms after a median of 1 year on maintenance
- What may be a more meaningful outcome for families is the protection from accidental exposures (to 1000mg protein) that peanut OIT provided for 98.3% of preschoolers in our study.
- Effectiveness in our study is slightly lower than Vickery et al (78.6% vs. 85%), which could be due to a shorter time on maintenance in our study (1 year vs. 2.5 years), or random chance.
- Effectiveness in our study is higher than Blumchen et al (78.6% vs. 41.9%), which could be due to age (median 23 months vs. 7.9 years), study selection criteria, maintenance dose (300mg vs 125mg), time on maintenance (12 months vs 9.5 weeks).
- The PALISADE trial reported that 67.2% of patients who received active treatment (300mg peanut protein maintenance) were able to ingest an eliciting dose of 600mg (cumulative dose 1043mg) peanut protein without symptoms at their exit food challenge. This is substantially lower than in our study population, where 98.3% of patients tolerated at least 1000mg. In comparison to our study population, participants in PALISADE were older (4-17 years vs. 9-70 months), had more significant symptoms to peanut based on prior reaction history, and the time on maintenance was shorter (6 months vs. 12 months).
- Limitations include lack of baseline OFCs on all patients due to resource limitations which would prevent many allergists from participating in OIT outside of the research setting. However, given the real-world nature of this study with the majority of patients recruited in the community, these results likely reflect what similar centers might experience.
- With long-term safety data, this treatment could be offered to preschool children to prevent potential long-term consequences of living with food allergy, including anxiety, poor quality of life, social isolation, and lower safety and effectiveness if OIT is attempted at an older age.
- *Note: the results we present in this poster are a subset of the results from a manuscript which will be submitted shortly.*

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