Clinical Communications

Weighing peanut candies used for oral immunotherapy mitigates variable peanut protein dose

Douglas P. Mack, MSc, MD[a], Gary A. Foster, PhD[b], Jacob D. Mack[c], Lauren C. Mack[c], and Mariam A. Hanna, MD[a]

Clinical Implications

- Some allergists use peanut candies for oral immunotherapy (OIT). Dose variability has been hypothesized to contribute to reactivity during OIT. Although peanut candies contain variable peanut amounts, use of a predetermined candy weight dose range may improve accuracy, especially at higher doses.

Peanut allergy affects approximately 2% of population and is a significant cause of morbidity, anxiety, and limitation.[1,2] Although oral immunotherapy (OIT) for peanut with a standardized product is Food and Drug Administration approved, many allergists use candies such as M&Ms for dosing.[3-5] A recent study reported that peanuts in M&Ms were smaller than typical peanuts, variable in size, and that visual assessment did not reliably predict peanut dose.[6] Others have demonstrated variability amongst other nonstandardized products currently used for OIT.[7] We used statistical modeling to evaluate whether weight-based selection could mitigate peanut candy shell and peanut weight variability in M&Ms for 2 commonly used doses, 300 and 3000 mg protein.

Briefly, 294 peanut M&Ms (Mars Chocolate, Hackettstown, NJ) from 2 lots were weighed using Salter Digital Scale Model 1250BKEF. After weighing, each candy had the shell carefully removed leaving the peanut. Two investigators weighed and tabulated the peanut kernel. We assumed approximately 25% protein content based on historical values but were unable to determine actual protein content of the peanuts. We did not evaluate candies containing peanut butter.

After tabulation, modeling of all possible combinations (86,436) of 2 M&Ms was generated and the candy characteristics were computed for each pair. Ten thousand bootstrapped samples of 19 M&Ms were modeled. The linear relationship between full candy weight and protein amount was determined graphically and was used to inform the acceptable range of candy for obtaining an appropriate protein amount from 2 and 19 candies.

There was considerable variability in the weight of individual candies. The mean (standard deviation [SD]) of candy weights and protein amount for M&Ms was 2.78 g (0.39) and 158.4 (38.7) mg, respectively. Fourteen (4.8 %) candies contained no, partial, or multiple peanuts and 1 almond. Candy color was associated with significant differences in candy weight and shell weight.

Two protein amounts commonly used for OIT were evaluated, approximately 300 and 3000 mg. The random selection of 2 and 19 M&M candies (normally distributed) was made to approximate these protein amounts (Table I). The mean (SD) protein concentration of all pairs of M&Ms was 316.7 (54.6) mg, and bootstrap combinations of 19 M&Ms had a mean (SD) of 3008.3 (176.3) mg (Figure E1, available in this article's Online Repository at www.jaci-inpractice.org).

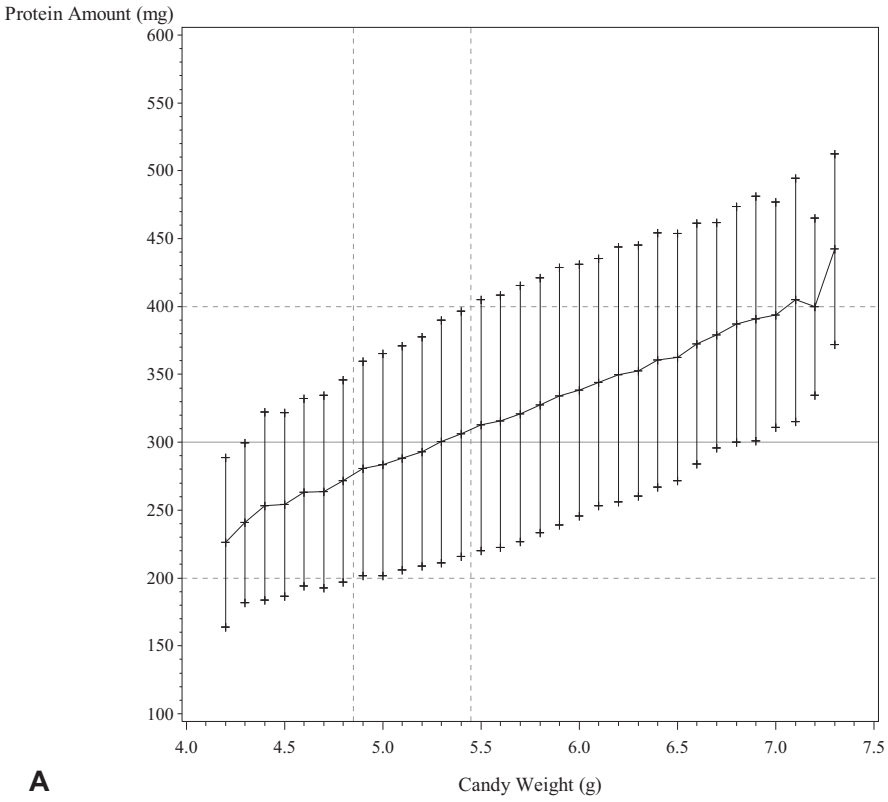
Figure 1 illustrates the relationship between the weight of M&Ms, with the shell on, and the protein amount for 2 and 19 candies, respectively. To approximate a 300 mg dose, if 2 M&Ms weigh approximately 5.3 g, the protein content varies between 211 and 390 mg for 95% of the samples (Figure 1, *A*). Practically, if a parent wants to keep the protein amount between 200 and 400 mg (±33%), the total weight of 2 M&Ms should not exceed 5.4 g and should not go below 4.9 g. To approximate a 3000 mg protein dose, if the combined weight of 19 M&Ms equals 52.5 g, the protein content varies between 2733 and 3270 mg for 95% of the samples (Figure 1, *B*). Practically, to obtain a target protein amount between 2700 and 3300 g (±10%), the total weight of the 19 M&Ms should fall between the target range 52.0 and 52.5 g.

We observed significant variability in the weight of peanuts found in M&M candy. Not only were the individual peanuts variable in size, the amount of candy/chocolate coating was also inconsistent. The presence of an almond is concerning for almond-allergic patients. Leroux et al[6] suggested that a visual assessment was not an acceptable method to select candies for OIT. A more reasonable alternative to reduce inconsistency in

TABLE I. Comparison of random selection vs total candy weight selection of 2 and 19 M&Ms to achieve target dose with prespecified dose limits

Target dose (mg)	Peanut protein dose range ± % (mg range)	Chance of random selection within observed dose range (%)	M&M candy weight range to achieve dose range with 95% accuracy (g)
300	5 (285-315)	23.3	NA
	10 (270-330)	42.3	NA
	16.7 (250-350)	61.8	NA
	33 (200-400)	92.2	4.9-5.4
3000	5 (2850-3150)	63.8	NA
	10 (2700-3300)	93.1	52.0-52.5
	16.7 (2500-3500)	99.7	49.5-56.5
	33 (2000-4000)	100	49.5-57.5

NA indicates that the candy weight range cannot be achieved with 95% accuracy prespecified dose range.



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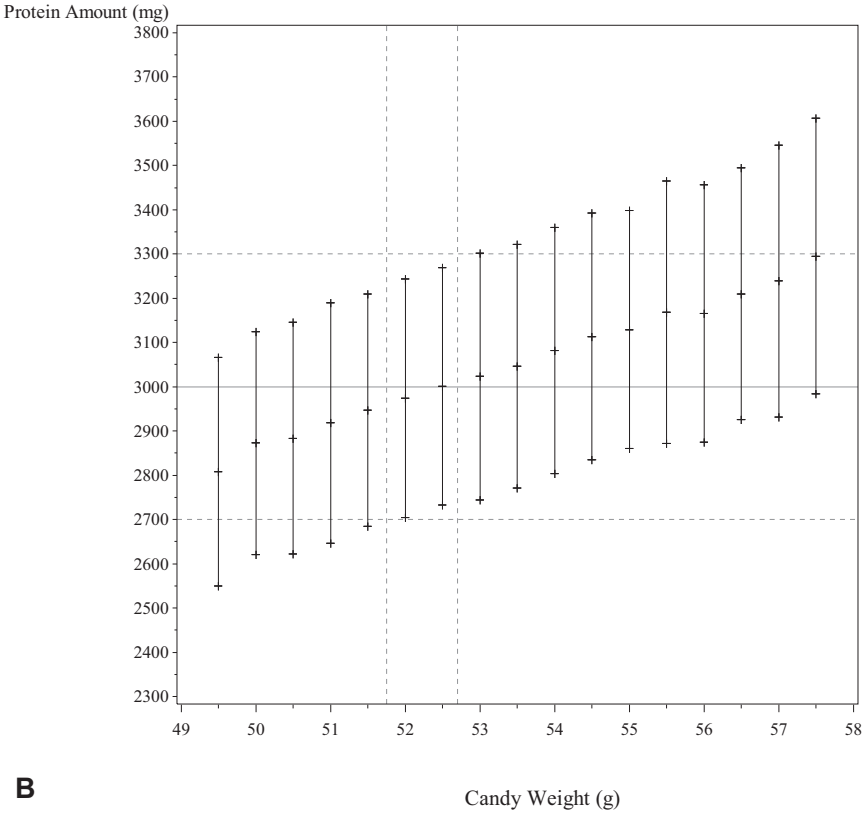

B

FIGURE 1. Peanut protein by M&M weight category. Bands are ±1.96 SD. **A**, From all bootstrapped pairs of M&Ms. The horizontal line represents 300 mg dose target. The horizontal hatched lines represent ±33% dose limits as an example. The vertical hatched lines represent corresponding candy weight limits from which peanut combinations should be selected. **B**, From 10,000 bootstrapped samples of 19 M&Ms. The horizontal line represents 3000 mg dose target. The horizontal hatched lines represent ±10% dose limits as an example. The vertical hatched lines represent the corresponding candy weight limits from which peanut combinations should be selected. *SD*, Standard deviation.

peanut content would be to weigh candies and to target a particular total weight range. This weight-based approach accounts for variability in both shell and peanut weight to give a more accurate dose.

As expected, the dose variability became smaller as the dose increased. Dose ranges for 3000 mg could be measured with greater accuracy than for 300 mg (Table I). Although the 3000 mg dose is commonly used in private practice,[8] the commercial product dose is 300 mg.[5] At this low dose, significant irregularity is expected and it is difficult to measure doses precisely.

Whether the variability in peanut weight/peanut protein dose is clinically relevant is difficult to determine as many allergists have been successful using these products during OIT.[3] In a highly sensitive patient, this dose inconsistency may theoretically result in a clinical reaction. For example, in the PALISADE Phase 3 trial,[5] an increase in cumulative dose of less than 50% in an oral challenge was sufficient to cause a reaction in a small percentage of participants after 6 months of maintenance. This dose inconsistency may be more clinically relevant shortly after a dose increase or in the setting of sleep deprivation, viral illness, or even exercise (despite taking recommended precautions during illness or exercise). Dua et al[9] recently demonstrated that thresholds of reactivity to peanut in patients dropped by 45% with exercise or sleep deprivation, consistent with OIT clinical practice. Future studies could evaluate the use of premeasured candies versus standardized products during OIT to evaluate differences in reactivity.

Our clinical experience suggests that patients who dislike the taste of peanuts select the smallest available candy, resulting in a significantly lower dose. This potential for underdosing may have safety implications when a patient routinely receiving a protein dose of 200 mg is suddenly given a dose of 400 mg protein or more.

Many providers use M&Ms and other candies to improve palatability. We recommend standardizing the dose of M&Ms based on weight rather than directing families to use a specific number of candies or by using a visual assessment, especially at lower doses. This approach accounts for the variability in shell weight and peanut weight resulting in a statistically predictable dose range. Weighing candies also helps to ensure that patients who prefer smaller candies will receive a peanut protein dose closer to the target dose. Even with these precautions, OIT providers and patients must be aware of the dose variability in M&Ms and similar peanut candy products.

[a]Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada
[b]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, Ontario, Canada
[c]Halton Pediatric Allergy, Burlington, Ontario, Canada

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Corresponding author: Douglas P. Mack, MSc, MD, Halton Pediatric Allergy, 5500 North Service Road, Suite 106, Burlington, Ontario L7L 6W6, Canada. E-mail: dougpmack@gmail.com.

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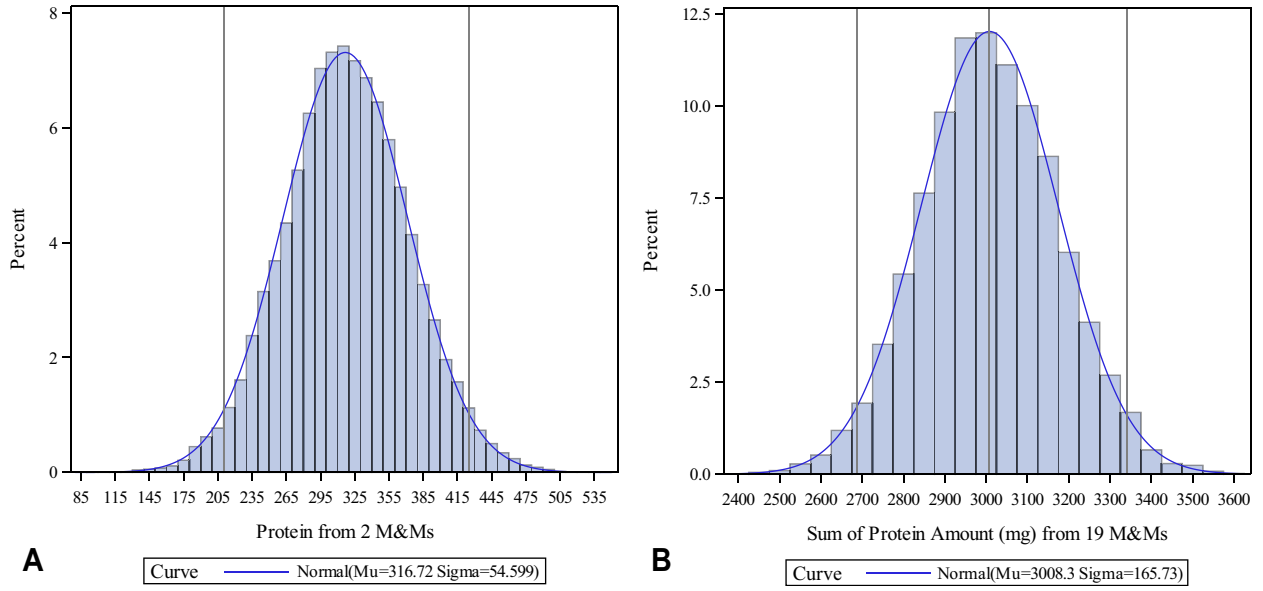

FIGURE E1. A, Normal and observed distribution of calculated protein content from all pairs of M&Ms. **B**, Normal and observed distribution of calculated protein content from 10,000 bootstrapped samples of 19 M&Ms.