The Safety of Formula Switching for Infants

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Funded by PBM Nutritionals, LLC

Introduction

Pediatricians often advise parents/guardians to switch between infant formulas for a variety of infant behavioral issues including colic, frequent spit-up and loose stools. In otherwise healthy infants these formula switches may act as a placebo therapy. The most common switch is between National Brands of cow milk-based infant formula.

All infant formulas are highly regulated by the U.S. Food and Drug Administration (FDA) and must meet nutritional and quality requirements stipulated by the Infant Formula Act of 1980. The purpose of this act is to ensure the safety and nutrition of infant formulas. The act authorizes the FDA to promulgate appropriate regulations defined under 21 CFR 106 and 107 under section 412c.

There are no switch studies in the literature that include Store Brand infant formula and a "sham switch" (same formula to same formula). And there are no studies of the optimal method of switching between formulas.

Objective

The primary objective of this study was to demonstrate that there is no difference in formula tolerance between a Store Brand milk-based infant formula and the equivalent National Brand milk-based infant formula (Parent's Choice infant formula, Similac Advance and Enfamil Premium). Tolerance variables measured were increases in spit-up, burping, gas, crying and irritability.

The secondary objective was to assess the method in which parents/guardians transitioned from one formula to another.

Materials & Methods

A total of 67 infants were randomized in groups of 3 from the formula they were on to an alternative formula or the same formula (sham switch). Each infant was observed over a 4 day interval followed by a 3 day washout during which time the infants were switched to the different formula or same formula (SHAM). Caregivers either transitioned over the 3 day period or switched immediately to the blinded formula. An additional 4 day observation interval on the alternative formula or the sham formula was performed (Figure 1). Caregivers kept a diary scoring the tolerance variables (spit-up, burping, gas, crying, irritability) as relative to normal where 0=none; 1=less than average; 2=average; 3=more than average and 4=excessive.

Caregivers were also asked to document the protocol used to switch infants from one formula to the new formula.

The formulas used in this study were Similac Advance milk-based infant formula (Abbott Nutritionals), Enfamil Premium milk-based infant formula (Mead Johnson Nutritionals) and Parent's Choice milk-based infant formula (Wal-mart Store Brand).

Wilcoxon Signed Ranked Test was used as a non-parametric equivalent to paired sample t-test to provide evidence of a difference between period 1 and period 2 tolerance within each of the three subgroups. And to provide evidence of a difference between period 1 and period 2 in spit-up, burping, gas, crying and irritability within each of the three subgroups.

Results

Tolerance measures were analyzed within each of the three subgroups. There were no statistically significant differences in tolerance measures between the National Brand to different National Brand (p=0.164) and from the National Brand to the Store Brand (p=0.148). However, there was a statistically significant difference in the National to same National Brand (p=0.001(SHAM)). The analysis suggested that one of the National Brands had the increase tolerance variables between period 1 and period 2 (see Figure 2). The reason for this difference may have been parental/guardian anxiety or an increased sensitivity to infant behavior.

Further analysis was performed to determine the difference between period 1 and period 2 in spit-up, burping, gas, crying and irritability within each of the three subgroups.

Figure 3 demonstrates that there were no statistically significant differences between period 1 and period 2 with spit-up (p=0.153), burping (p=0.674), gas (p=0.212), crying (p=0.305) and irritability (p=0.288) in the group of infants that were switched from National to different National Brand infant formula.

Figure 4 depicts the analysis of the infants that were switched from National Brand to same National Brand (SHAM). In this group there was no statistically significant difference between period 1 and 2 in spit-up (p=0.097). There was, however, a statistically significant difference between period 1 and 2 in burping (p=0.008), gas (p=<0.001), crying (p=0.002) and irritability (p=0.11).

In the National to Store Brand infant group there were no statistically significant differences between period 1 and 2 in burping (p=0.204), gas (p=0.636), crying (p=0.348) and irritability (p=0.203). There was a statistically significant difference between the two periods with the reports of spit-up (p=0.038). See figure 5.

Further analysis of infants that were switched (n=44), compared period 1 vs period 2 for all tolerance variables and the combined tolerance variable (Figure 6).

This shows that there is a statistically significant increase in the combined tolerance variable from period 1 to period 2 (p=.039). Some of the individual tolerance variables show statistically significant increases, while others do not. However, there were no statistically significant differences in tolerance variables across the three groups in period 1 and while the tolerance variables increased in all three groups, there are no statistically significant differences in tolerance variables across the three groups in period 2.

These results demonstrate that there were no tolerance variables when switching from National Brand to different National Brand or from National Brand to Store Brand. And that there was an increase of burping, gas, crying and irritability in a small subset of infants in the SHAM study group. In addition, there were no differences in tolerance variables across the three groups in period 1 and an increase in tolerance variables in all three groups in period 2.

While tolerance variables increased in all three groups, no statistically significant differences in tolerance variables were detected across the three groups in period 2.

Conclusion

The objective of this study was to collect data to support the safety of switching infant formulas. National Brand formulas are more expensive than Store Brand formulas such as Parent's Choice. This study was performed to provide data to assure parents and caregivers that they can safely switch to a less expensive Store Brand formula. All infant formulas sold in the United States are nutritionally equivalent and are required to meet stringent quality and nutritional requirements. Since they are used as sole source nutrition it is important to have economical options available to families. Reports have surfaced of caregivers diluting infant formula to save money. This poses a public health risk since it reduces the amount of nutrients an infant requires.

Switching between different brands of infant formula is safe. Formula tolerance is similar between standard milk-based infant formulas in healthy, term infants. And there is no statistically significant difference in tolerance variables if infants are gradually switched to a new infant formula or immediately switched (data not shown).

References

1. Lloyd, B., Halter, R.J., Kuchan, M.J., Baggs, G.E., Ryan, A.S. and Masor, M.L. (1999). "Formula tolerance in postbreastfed and exclusively formula fed infants." Pediatrics 1999; 103;e7.
2. Berseth, C.L., Mitmesser, S.H., Ziegler, E.E., Marunycz, J.D. and Vanderhoof, J. (2009). "Tolerance of a standard intact protein formula versus a partially hydrolyzed formula in healthy term infants." Nutrition Journal 2009, 8:27.

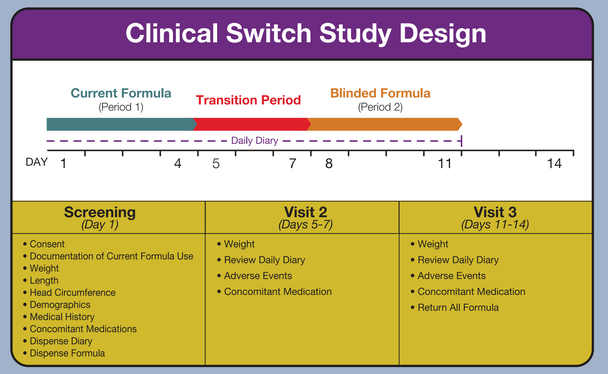

Figure 1 Schematic of Switch Study Design. Infants were screened on Day 1. Visit 2 included physical exam and review of diary. Visit 3 included physical exam and review of diary.

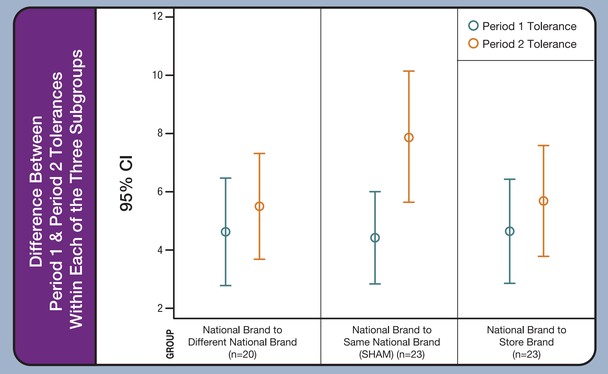

Figure 2 Wilcoxon Signed Rank Test analysis between period 1 and period 2 tolerance within each of the three subgroups.

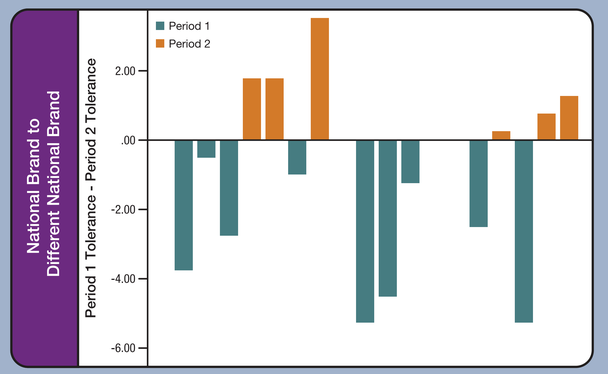

Figure 3 Wilcoxon Signed Rank Test analysis of difference between Period 1 and 2 in each tolerance variable. National Brand to different National Brand.

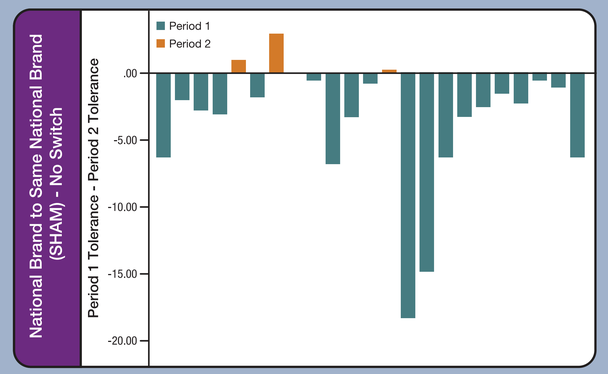

Figure 4 Wilcoxon Signed Rank Test analysis of difference between Period 1 and 2 in each tolerance variable. National Brand to same National Brand (SHAM).

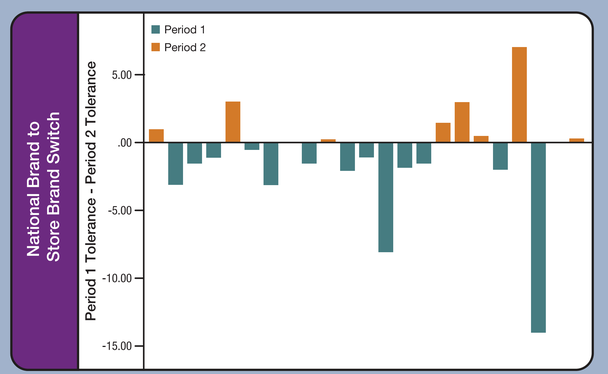

Figure 5 Wilcoxon Signed Rank Test analysis of difference between Period 1 and 2 in each tolerance variable. National Brand to Store Brand.

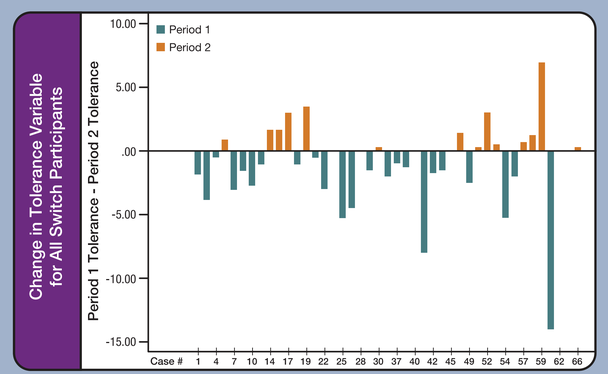

Figure 6 Wilcoxon Signed Rank Test analysis of difference between Period 1 and 2 in each tolerance variable. All switch participants.