Report of an RCT for gum gel impacts on attachment loss and pocket depth

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Introduction

This is a report of a randomized control trial investigating the relationship of a new gum gel on gum disease. The trial’s population was recruited from southwestern dental clinics and the baseline sample size included 130 participants with 103 completing the trial. At baseline, pocket depth and attachment loss at sites across the mouth was collected along with some demographic information. Participants were randomized to receive one of five treatments and asked to rub the gel on their gums twice daily. The treatment groups included a control group, a placebo, low active substance of gel, medium active substance of gel, and high active substance of gel. The outcomes, attachment loss and pocket depth, were again one year later. The study’s primary hypothesis was that treatment would result in different whole-mouth average attachment loss and whole-mouth average pocket depth in one year across the five treatment groups. The hypotheses tested in this report are as follows: 1.) Exposure to one of the five treatment groups results in a significant attachment loss change from baseline to one year 2.) Exposure to one of the five treatment groups results in a significant pocket depth change from baseline to one year.

Methods

Beginning data management steps were limited in this analysis plan but included changing all missing values from ‘NA’ to blank in order to be read as a missing value in SAS. All other coding of variables stayed the same as described by the principal investigators. Two new variables were created as the main outcome variables. Both these variables assessed the average attachment loss and pocket depth (pd) change between baseline whole mouth averages and one-year whole mouth averages. The difference between pdbase and pd1year is ‘pd\_change’ and ‘attach\_change’ is the difference between attachbase and attach1year.

Descriptive statistics were performed first to examine potential demographic differences across the treatment groups. For Table 1, a t-test was used for numerical variables (age and sites) and for categorical variables (sex, race, smoking) Chi-Squared Test was conducted for all variables with counts greater than five in each cell of their respective frequency tables. Otherwise, a Fisher’s Exact Test was conducted to account for low cell numbers in categorical variables. P-values greater than .1 were considered not significantly different between treatment groups and therefore variables were successfully randomized. Bivariate descriptive statistics were then preformed with pd and attachment loss baseline, one-year, and change outcome variables across treatment groups. Histograms and scatter plots were examined to ensure outcomes did not violate assumptions of linear regression.

Two multiple linear regression analyses were performed to assess both statistical hypotheses. Treatment groups were dummy coded and put in as exposures in linear regression model to examine crude estimates of attachment loss and pd changes. Control group was used as the reference group but all treatment group estimates were tested for meaningful differences between estimates using *test* statements in *proc reg*. Multiple linear regression was picked for the analysis to get separate estimates for treatment group as a categorical variable, while the outcomes were continuous. The *test* statement was one of three options listed in BIOS 6602 for changing the reference group and making comparisons. Control group was picked for the reference because it was the only treatment in which there was no treatment behavior, so it appeared to be the most likely to reflect actual population attachment loss and pd change.

Potential covariates were assessed individually using linear regression and the outcome variables. Even though randomization controls for confounding in clinical trials, there could still be precision variables or interactions. The covariates examined were age, sex, race, smoking, sites, pd at baseline, and attachment loss at baseline. Each covariate was assessed for a meaningful and clinically significant change in the intercept. If the covariate met criteria for being a precision variable it was added to the adjusted model and reported. Statistical significance was .05 and the software used was SAS.

Results

Demographics are summarized overall and across treatment groups in Table 1. There were no significant differences across treatment groups. The majority of treatment groups were white with a mean age of 50.

Table 1: Demographics

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Overall  (n=130)** | **Control (n=26)** | **Placebo (n=26)** | **Low (n=26)** | **Medium (n=26)** | **High (n=26)** | **Pvalue** |
| Age (SD) | 49.94 (10.03) | 50.75 (9.89) | 47.11 (8.61) | 51.92 (10.78) | 49.01 (9.49) | 50.82 (11.2) | 0.3788 |
| Male (%) | 54  (42.54) | 10  (38.46) | 11  (42.31) | 11  (42.31) | 11  (42.31) | 11 (42.31) | 0.9981 |
| Race (%) |  |  |  |  |  |  | 0.2163 |
| Native American | 4  (3.08) | 1  (3.85) | 0 | 1  (3.85) | 0 | 2  (7.69) |  |
| African American | 9  (6.92) | 1  (3.85) | 2  (7.69) | 5  (19.23) | 0 | 1  (3.85) |  |
| Asian | 3 (2.31) | 1 (3.85) | 1 (3.85) | 0 | 1 (3.85) | 0 |  |
| White | 114 (87.69) | 23  (88.46) | 23  (88.46) | 20  (76.92) | 25  (96.15) | 23 (88.46) |  |
| Smoker (%) | 48  (37.21) | 9  (34.62) | 11  (42.31) | 8  (30.77) | 11  (44.00) | 9 (34.62) | 0.8452 |

Table 2 compares the crude model to the adjusted model for change in attachment loss estimates. The final analyses included 103 participants, with high treatment having the least amount of participants. The overall crude model of the change in attachment loss showed that treatment groups have a significant effect on attachment loss (p=.0451). The low treatment group had an average 0.20 (SD= 0.08) less attachment loss when compared to the control group (p=0.0134). The medium treatment group had an average 0.215 (0.08) less attachment loss when compared to the control group (p=0.0101). The adjusted multiple linear regression analysis includes baseline attachment loss as a precision variable. Once this variable was included the overall model was more significant (p=<.0001). The medium treatment group had the least amount of attachment loss decreasing 0.17 (0.076) when compared to the control group (p=0.0232). The low treatment group was the second least for attachment loss with an average 0.14 (0.076) less than control, however this relationship failed to meet statistical significance (p=0.0573).

Table 2: Change in Attachment Loss

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model Variables** | **Model 1: Crude Betas** | | **SD** | **P-value** | **Model 2:**  **Final Betas** | **SD** | **P-value** |
| Intercept  (Control- 23) | | 0.222 | 0.056 | **0.0001** | -0.107 | 0.093 | 0.2527 |
| Placebo  (23) | | -0.135 | 0.079 | 0.09180 | -0.042 | 0.076 | 0.5824 |
| Low  (21) | | -0.204 | 0.081 | **0.01340** | -0.146 | 0.076 | 0.0573 |
| Medium  (20) | | -0.215 | 0.082 | **0.01010** | -0.176 | 0.076 | **0.0232** |
| High  (16) | | -0.057 | 0.087 | 0.51590 | -0.027 | 0.081 | 0.7425 |
| Attach Base | |  |  |  | 0.129 | 0.030 | **<0.0001** |

Table 3 compares the crude and adjusted estimates for change in pocket depth across treatment groups. The overall crude model of treatment groups and change in pocket depth was not significant (p=0.0899). There were no individual significant relationships when compared to the control group. When using test statements the estimates between the low and medium treatment groups were significant (p=0.0456) and the estimates between medium and high treatment groups was significant (p=0.0436). The adjusted multiple linear regression for pocket depth change includes pocket depth at baseline as a precision variable. Although sex was significantly related to the outcome pocket depth change (p=0.0286), it was not included in the final analysis because it did not decrease the variance and increased the degrees of freedom. The overall final model including pocket depth baseline was significant (p=0.0339). The low treatment group had the least amount of pocket depth loss and the medium group the second least, but neither treatment met statistical significance requirements.

Table 3: Change in Pocket Depth

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Model 1: Crude Betas** | **SD** | **P-value** | **Model 2: Final Betas** | **SD** | **P-value** |
| Intercept  (Control) | 0.33817 | 0.05466 | **<.0001** | -0.03344 | 0.19164 | 0.8618 |
| Placebo | 0.01152 | 0.0773 | 0.8818 | 0.03285 | 0.07684 | 0.67 |
| Low | -0.132 | 0.07912 | 0.0984 | -0.12484 | 0.07799 | 0.1127 |
| Medium | -0.13562 | 0.08015 | 0.0938 | -0.10844 | 0.08006 | 0.1787 |
| High | 0.04413 | 0.08534 | 0.6063 | 0.05622 | 0.08424 | 0.5061 |
| PD Base |  |  |  | 0.11303 | 0.05594 | **0.0461** |

Conclusions

The results of this randomized control trial suggest that medium treatments may result in lower whole-mouth attachment loss. Even though results are not significant, the general direction of estimates suggest that medium or low treatments may be more beneficial forms of treatment than control treatment for attachment loss and pocket depth. Future studies should aim to recruit more participants to account for participant drop out. The final results included 103 participants, with the high treatment group having 16 total. There are not enough participants to make correct inferences and this could be skewing the high results closer towards the null hypothesis. A power analysis prior to starting could assist in creating trial recruitment goals.

Reproducible research information

https://github.com/BIOS6623-UCD/bios6623-delgoulding/tree/master/Project0