Safety and efficacy of RF-utilizing toothbrush for the reduction of plaque, calculus and gingival inflammation

DO116537A

ToothWave™ (Model H7001) Clinical study report

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1. SUMMARY

Objective:

To evaluate the effect of ToothWave™ a novel RF-utilizing toothbrush on plaque, calculus and gingival inflammation as compared to a control standard ADA-approved powered toothbrush.

Methods:

This was a single-blind double arm prospective study, including 4 clinical visits that were conducted every two weeks. Subjects were randomized to one of two study groups, receiving either the Silk'n ToothWave™ or control toothbrush, and performed twice daily brushing during a test period of 6 weeks. Plaque, calculus, gingival inflammation and bleeding were assessed using the RMNPI, V-MI, MGI, and GBI measures, at baseline and after 4 and 6 weeks (visits 3 and 4 respectively) of brushing. Results (mean scores) were compared within each group between the different visits and between the groups; delta values (reduction from baseline) of each score were also compared between the groups. Statistical analyses were conducted using the Mann Whitney non-parametric model.

Results:

A total of 85 subjects (44 in the treatment group and 41 in the control) completed the study, having fully evaluable data. At baseline, the test groups did not differ significantly in the efficacy measurements mean scores ($p \geq 0.165$). Following 6 weeks of brushing the test group showed significant reductions in all the tested measures as compared to the control group. In addition, the reduction from baseline of all measured scores were significantly greater in the treatment group as compared to the control ($p \leq 0.001$). Both toothbrushes were well-tolerated and no device related adverse events were reported during the study.

Conclusions:

The Silk'n ToothWave™ RF-utilizing toothbrush produced significant benefits in reduction of plaque, calculus, gingivitis and bleeding as compared to a control, ADA-approved powered toothbrush.

2. INTRODUCTION

Gingivitis is an inflammation of the gums and a treatable initial stage of gum disease [1]. The direct cause of gingivitis is plaque, which is a soft, colorless film of bacteria that forms constantly on the teeth and gums. In cases where the plaque is not removed efficiently by daily brushing, it produces toxins that can irritate the gum tissue, causing gingivitis. At this early stage in gum disease, damage can be reversed by improving the oral hygiene, since the bone and connective tissue that hold the teeth in place are not yet affected. Left untreated, however, gingivitis can become periodontitis and cause permanent damage to the teeth and gums [1].

Calculus or tartar is a form of hardened dental plaque, caused by precipitation of minerals from the saliva on the teeth. This rough and hardened substance provides an ideal surface for further plaque formation, which leads to calculus buildup, and impairs gingival health. Calculus can form both along the gumline (supragingival), and within the narrow sulcus that exists between the teeth and the gingiva (subgingival) [2].

Previous publications exhibit the efficacy of power toothbrush in reducing supragingival plaque, gingival inflammation, and gingival bleeding following a several-week period of twice-daily brushing at home [3]. However, once the calculus is formed, it is firmly attached to the teeth surface and is too hard to be removed with a regular toothbrush; thus, in the conventional way, calculus build-up can be removed with ultrasonic tools or dental hand instruments (such as a dental scaler) [2].

Home Skinovations LTD. (Yokneam, Israel) has developed the Silk'n ToothWave™, a novel toothbrush intended to remove impurities that are attached to the teeth surface, such as plaque and calculus, and to promote the reduction of bleeding and gingival inflammation. ToothWave™ utilizes radiofrequency (RF) energy that streams between two electrodes and over a silicon barrier, and reaches the teeth surface during brushing. RF is an alternating electric current that oscillates at radio frequencies in the range of 3kHZ-300GHz. It has been used in medicine for several decades for many different applications, from surgical to aesthetic, providing various effects, depending on the specific parameters of the device in use [4].

Figure 1 below provides a schematic representation of the toothbrush head; *Figure 2* exemplifies the process of RF streaming through the toothpaste as it reaches the tooth surface.

The current clinical study aims to evaluate the safety and efficacy of the Silk'n ToothWave™ in reduction of plaque, calculus and gingival inflammation, as compared to a standard powered toothbrush that is approved by the American Dental Association (ADA).

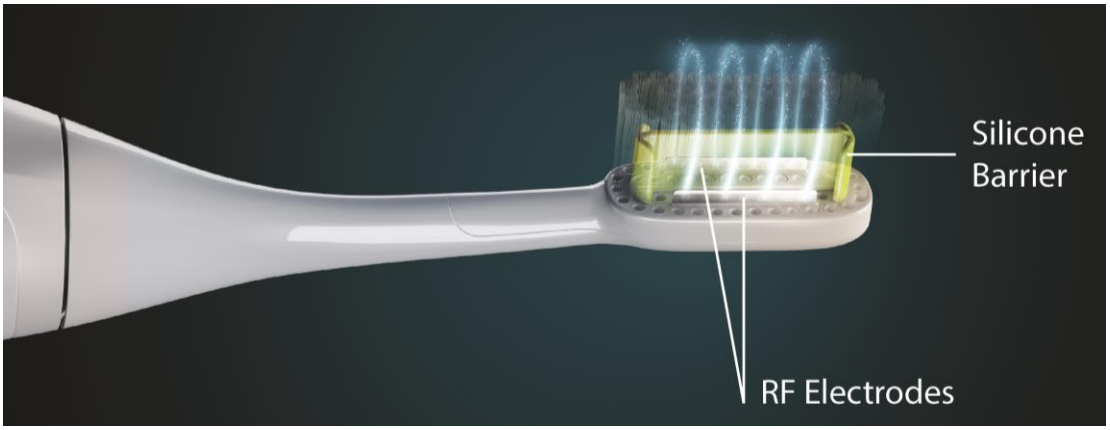

Figure 1 - *a graphic representation of the ToothWave™ brush head*

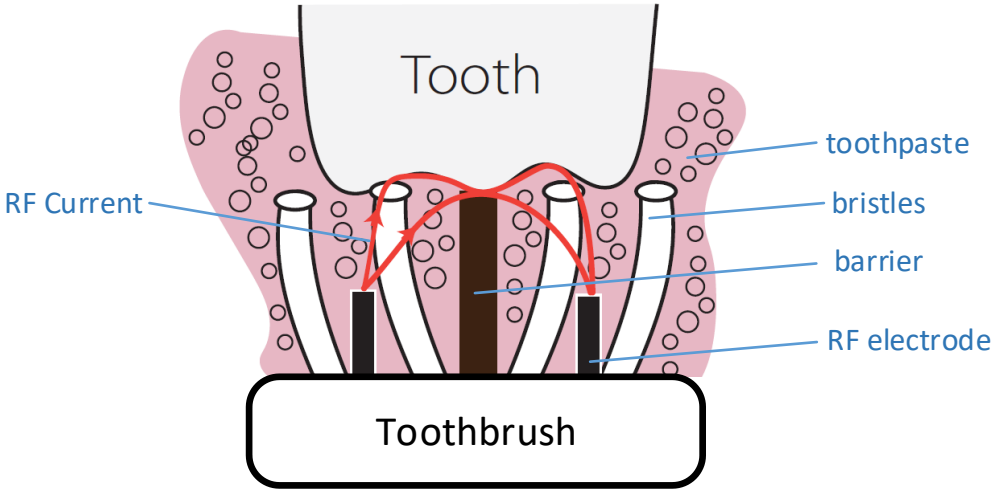

Figure 2 - *schematic representation of the RF current that streams in proximity to the tooth surface*

3. METHODS

A randomized single-blind double arm prospective study was conducted, in order to evaluate the safety and efficiency of the RF-utilizing toothbrush (*ToothWave™, Manufactured by Home Skinovations LTD, Yokneam, Israel*), as compared to a reference powered toothbrush (Smilesonic® Pro Advanced Clean, Manufactured by Ranir, LLC, Grand Rapids, MI 49512). The protocol and consent form were approved by the U.S. Institutional Review Board (U.S.IRB2019SRI/03) before study initiation, and verbal and written consent were obtained from all subjects.

Participants

Screened subjects received an oral soft tissue (OST) examination. Gingival status was evaluated using the Modified Gingival Index (MGI) and the Gingival Bleeding Index (GBI) [5, 6], plaque examination was performed using the Rustogi Modified Navy Plaque Index (RMNPI) [7], and the calculus present on the lingual surfaces of the lower six anterior teeth was measured using the Volpe-Manhold Index (V-MI) [8].

Recruited subjects were 18-70 years of age, with baseline MGI score of at least 1.80, baseline GBI score equal to or greater than 1 on at least 20 sites, an overnight (12 to 18 hour abstention from any oral hygiene) dental plaque (mean) score greater than 0.6 according to the RMNPI Index, and lingual calculus total score greater than 7 on the lower anterior teeth according to V-MI. Exclusion criteria were composed of current or history of oral cavity cancer or oropharyngeal cancer, any active electrical implant anywhere in the body, pregnant or nursing, and any active condition or surgery in the oral cavity within 3 months prior to treatment. Subjects that do not brush regularly were also excluded.

Study procedures

Eligible study participants were provided with regular, marketed Crest® Cavity Protection Cool Mint Gel (0.243% Sodium Fluoride, Procter & Gamble, Cincinnati, OH 45202), and a toothbrush (either the ToothWave™ or control brush). Participants were randomized and assigned to study group in accordance with a randomization schedule generated by an independent statistics agency prior to the start of the study, using validated software (SPSS Version 25.0). Participants were stratified according to their age and ethnicity. Randomization numbers within each stratum were assigned in ascending numerical order according to

appearance at the study site on the day participants were randomized. Participating subjects were instructed to brush at home twice-daily (morning and evening) with a full brush head of toothpaste for two timed minutes. The study included 6 weeks of test phase, during which 4 pre-scheduled face-to-face visits were performed every 2 weeks. Each use was recorded in a provided diary.

The first brushing session was carried out under supervision at the study site. Participants brushed for 2 timed minutes in their usual manner with the standard fluoride toothpaste (Crest® Cavity Protection Cool Mint Gel). Participants continued to use their assigned study treatment twice-daily (morning and evening) for the next 6 weeks, recording each brushing in the diary provided. Participants returned to the study site every two weeks over the 6-week study period, bringing their study kit so that the toothpaste be weighed to verify study compliance. Diaries were checked to assess compliance. The participants undertook a supervised brushing during the second visit as was conducted at the first visit, in order to make sure brushing is conducted according to the instructions.

Assessments

Clinical efficacy was evaluated at visits 3 and 4 (following 4 and 6 weeks of brushing, respectively). A full mouth gingival assessment was performed based on the Lobene et al. (1986) Modified Gingival Index [3]. The gingiva was segmented into 6 sites per tooth (distobuccal, buccal, mesiobuccal and distolingual, lingual, mesiolingual surfaces), and the gingival inflammation was recorded at each tooth site on a scale of 0 to 4, where 0 denotes Normal (absence of inflammation), 1 denotes Mild inflammation (slight change in color, little change in texture) of any portion of the gingival unit, 2 denotes Mild inflammation of the entire gingival unit, 3 denotes Moderate inflammation (moderate glazing, redness, edema, and/or hypertrophy) of the gingival unit, and 4 denotes Severe inflammation (marked redness and edema/hypertrophy, spontaneous bleeding, or ulceration) of the gingival unit.

A full mouth bleeding assessment was performed based on the Gingival Bleeding Index [4]. The gingiva was gently dried and lightly swept with a 0.5 diameter periodontal probe (to be used for each subject for all visits). The probe was engaged approximately 1 millimeter (mm) into the gingival crevice at an angle to the tooth. A moderate pressure was used while sweeping from interproximal to interproximal along the sulcular epithelium. The gingiva was segmented into 6 sites per tooth (distobuccal, buccal, mesiobuccal and distolingual, lingual,

mesiolingual surfaces). Bleeding or the absence of bleeding was assessed at each tooth site on a scale of 0 to 3, where 0 denoted no bleeding after 30 seconds, 1 denoted bleeding upon probing after 30 seconds, and 2 denoted immediate bleeding observed. Subjects with less than 20 bleedings sites at Visit 1 was dismissed from the study.

Plaque examinations was performed using the Rustogi Modified Navy Plaque Index (RMNPI) [7]. Subjects' swished with 5 ml of a disclosing solution for 10 seconds and expectorate followed by 10 ml of water for 10 seconds. After disclosing, the plaque on each tooth was evaluated as present (1) or absent (0). Mean plaque score for each subject was calculated using the total number of tooth sites with plaque present divided by the total number of tooth sites scored.

The supragingival calculus present on the lingual surfaces of six mandibular anterior teeth was calculated using the V-MI [8]. After drying the teeth with a stream of air and using a standard periodontal probe graduated in millimeters, the examiner placed the instrument on the most inferior border of the visible calculus, and measurements were obtained on the following three planes:

1) Bisecting the center of the lingual surface;

2) Diagonally through the mesial-incisal point angle of the tooth through the area of greatest calculus height; and

3) Diagonally through the distal point angle of the tooth through the area of the greatest calculus height.

The examiner assigned a score to each measurement plane, with measurements made in 0.5 mm increments starting at 0.5. A score of zero (0) denoted that there was no calculus present at a measurable site. The V-MI was calculated for each subject by summing the millimetre scores over all sites graded.

Safety

For safety, a thorough evaluation of the oral soft tissues was conducted at each visit, by way of a visual examination of the oral cavity, including the gingiva (free and attached), hard and soft palate, oropharynx/uvula, buccal mucosa, tongue, floor of the mouth, labial mucosa, mucobuccal/mucolabial folds, lips, and perioral area. A trained dental evaluator performed intraoral examinations at each study visit. All adverse events (AEs) were recorded and monitored throughout the study. The AEs and any observed abnormalities noted during the

OST examination were transcribed beginning at the screening visit until 5 days after the final use of study product. The investigator determined the causal relationship of each AE using their clinical experience and selected the appropriate severity descriptor as mild, moderate, or severe. Treatment-emergent AEs were reported for the safety population, which included all randomized participants who received study product.

Data analysis

A sufficient number of participants were to be screened in order to randomize at least 90 participants (approximately 45 to the Test, and 45 to the Control groups) to ensure 84 evaluable participants completed the entire study. The sample size in this the study provided 80% power to detect a significant difference in the scores improvements, with type 1 error of 5%. Safety analysis was carried out on a modified intent-to-treat (ITT) population, defined as all randomized participants who conducted at least one treatment. Efficacy analysis was conducted on the per-protocol (PP) population included all participants in the ITT population who had no protocol deviations deemed to affect efficacy.

Summary statistics (e.g., count, mean & SD, Median, 25th and 75th percentile) of the demographic characteristics and the efficacy measurements were calculated for each group and study visit. Normality distribution of measures was evaluated using Shapiro and Wilk test; as the majority of measures deviate from normal distribution, non-parametric approach was implemented.

Friedman's test followed by Dunn's test was used to evaluate the change over time (the time effect) within each group.

The Mann Whitney test was used to compare the improvement after 4 and 6 weeks between the groups; the improvement was calculated as

$$Delta = Score_{Week_i} - Score_{Baseline}$$

Significance level was defined as α=0.05. Analyses were carried out using SPSS version 25.0.

4. RESULTS

A total of 94 subjects provided informed consent and were enrolled to this study, and 88 of these met the entrance criteria. Two subjects self-selected to withdraw during the first visit, 86 subjects were randomized at baseline to receive either the ToothWave™ or the control powered toothbrush. One subject in the treatment group discontinued study participation prior to study end, with 85 subjects (90.4%) completing and deemed fully evaluable at the trial's conclusion. As shown in ***Table I***, the mean age of the randomized study population was 45.4 years, with a range of 18 to 70 years; thirty (66.7%) of the subjects were female.

Table I exemplifies the demographic baseline values, indicating that the study population was well-balanced with respect to all baseline demographic variables ($p \geq 0.339$).

Efficacy

The treatment and control groups' average baseline scores are shown in *Table II*. The test groups did not differ significantly in the efficacy measurements mean scores ($p \geq 0.165$).

Figure 3 summarizes the changes in the bleeding index scores of the control and treatment groups over time, indicating a statistically significant reduction in the treatment group ($p<0.001$), as compared to a mild, non-significant reduction in the control ($p=0.147$).

Figure 4 exemplifies the changes in MGI scores over time, indicating a significantly lower MGI score in the treatment group as compared to the control following 6 weeks of brushing ($p=0.003$).
Figure 5 exhibits the mean plaque scores over time, showing a lower plaque score in the treatment group as compared to the control following 6 weeks of brushing ($p=0.051$).

Figure 6 exhibits the changes in V-MI scores over time, showing a significant decrease in the treatment group (*$p<0.001$*) following 6 weeks of brushing vs calculus accumulation in the control. The final V-MI scores were found to be significantly higher in the treatment group as compared to the control, both at week 4 ($p=0.009$) and week 6 ($p=0.028$).

Table III summarizes the median delta values (difference from Baseline) of all efficacy measures, following 6 weeks test phase. Negative delta values represent an improvement in the measured score, having scores that are decreased with time; a greater negative value represents a greater improvement. Although an improvement in GBI, MGI, and Plaque was obtained in both groups, as indicated by the negative delta values, the improvements reported in the treatment group are significantly greater than those calculated for the control group following 6 weeks of brushing

($p \leq 0.001$). A negative delta value was obtained in the V-MI score of the treatment group as well, indicating on calculus reduction in week 6 as compared to baseline. Furthermore, the V-MI scores of the control group exhibits a positive delta value, indicating calculus accumulation in week 6 as compared to baseline. Similar to the other measures, the V-MI reduction in the treatment group was found to be significantly different from the control (p=0.001).

Safety

Both toothbrushes were well-tolerated and no device-related adverse events or any side effects were reported during the study. There were medical incidents, which led to discontinuation of treatment or withdrawal from the study.

Subject satisfaction

At the last study visit, participants were asked a series of questions designed to explore the level of satisfaction regarding the device operation and treatment results. Five questionnaire items were scored on a 5-point scale from 1 to 5 with '1' begin 'very dissatisfied' and '5' being 'very satisfied'. One questionnaire item was an open question, designed to collect data on device aspects that can be improved in view of the user's experience. Results are summarized in ***Table IV***. The average score of all items was 4.52 (±0.70), indicating the participants were satisfied with the treatment performance and results. All study participants (44, 100%) were satisfied or highly satisfied with the safety of brushing with ToothWave™, and the vast majority of the participants (42 of 44, 95%) were satisfied with the ease of treatment. Most of the participants were satisfied with the extent of calculus reduction (36 of 44, 82%) and with the improvement in their oral hygiene (38 of 44, 86%).

Table I - Demographic characteristics

characteristic	*ToothWave™ N=45*	*control N=41*	*overall*
mean age (SD)	44.9 (14.42)	46 (11.52)	45.4(13.05)
age range	18-70	23-66	18-70
Male (%)	15 (33.3%)	13 (31.7%)	28 (32.6%)
Female (%)	30 (66.7%)	28 (68.3%)	58 (67.4%)
Caucasian (%)	36 (80%)	35 (85.4%)	71 (82.6%)
Black, Non-Hispanic (%)	6 (13.3%)	4 (9.8%)	10 (11.6%)
Asian Pacific Islander (%)	2 (4.4%)	1 (2.4%)	2 (2.3%)
American Indian/Alaskan Native (%)	1 (2.2%)	1 (2.4%)	2 (2.3%)

Table II - Baseline efficacy measures

Measure	*Group*	*Mean*	*SD*	*P25*	*Median*	*P75*	*P value*
GBI	Control*	37.2	13.7	36.0	26.0	44.0	0.167
	Treatment§	41.6	15.7	41.0	29.0	49.0	
MGI	Control	2.5	0.3	2.6	2.3	2.8	0.222
	Treatment	2.6	0.4	2.7	2.4	2.9	
Plaque	Control	0.8	0.1	0.9	0.7	0.9	0.165
	Treatment	0.9	0.1	0.9	0.8	0.9	
VMI	Control	16.1	5.3	14.5	12.5	18.5	0.846
	Treatment	16.4	6.0	16.3	12.5	18.8	

*n=41; §n=44

Table III - Calculated difference (delta) from baseline after 6 weeks of twice daily brushings

		25 Percentile	*Median*	*75 Percentile*	*P value**
GBI	Treat[¥]	-19.0	-26.5	-4.0	<0.001
	Control[£]	-1.0	-13.0	8.0	
MGI	Treat	-1.3	-1.5	-0.9	<0.001
	Control	-0.8	-1.0	-0.5	
Plaque	Treat	-0.2	-0.3	-0.1	<0.001
	Control	-0.1	-0.2	-0.1	
VMI	Treat	0.0	-2.0	2.3	0.001
	Control[§]	2.0	0.5	3.5	

[¥]n=44

[£]n=41

*representing significance level comparing the difference from BL in treatment vs control.

[§]calculus index increased in the control group but decreased in the treatment group during 6 weeks of brushing.

Table IV - Satisfactory questionnaire results

Question	Average score (±SD)
Over all, how satisfied are you with the Silk'n ToothWave Toothbrush device?	4.45(±0.76)
What are some aspects of the device that can be improved?	No change needed - 50%. Other suggestions included the following changes: Changing the location of the power button (13.6%) Changing Stiffness or movement of the bristles (11.4%) Improving the handle grip (4.5%) Strengthening the indication vibrations (6.8%).
How satisfied are you with the safety of using the Silk'n ToothWave Toothbrush?	4.75 (±0. 44)
How satisfied are you with the ease of treatment with Silk'n ToothWave Toothbrush?	4.73 (±0. 54)
How satisfied are you with the level of improvement in oral hygiene after brushing with Silk'n ToothWave Toothbrush?	4.37 (±0. 82)
How satisfied are you with the level of improvement in calculus (tartar) after using the Silk'n ToothWave Toothbrush?	4.28 (±0. 77)
Average	**4.52 (±0.70)**

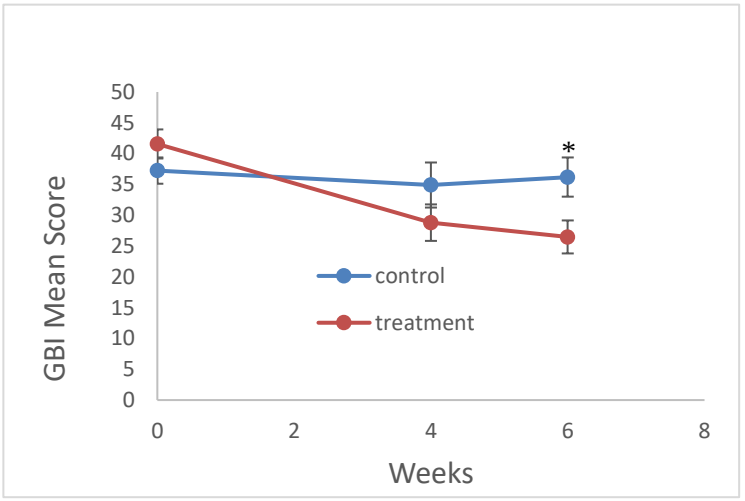

Figure 3 *- GBI scores are significantly lower in the treatment group as compared to the control group following 6 weeks of brushing (*p=0.023)*

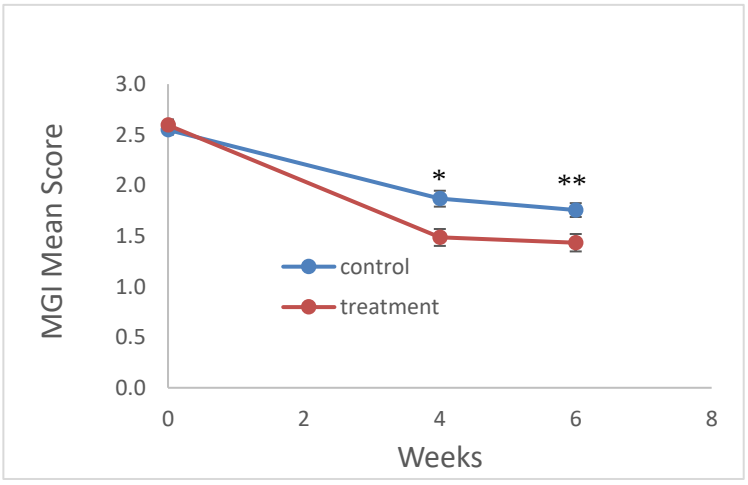

Figure 4 *- MGI scores are significantly lower in the treatment group as compared to the control group following 4 and 6 weeks of brushing (*p=0.001, **p=0.003)*

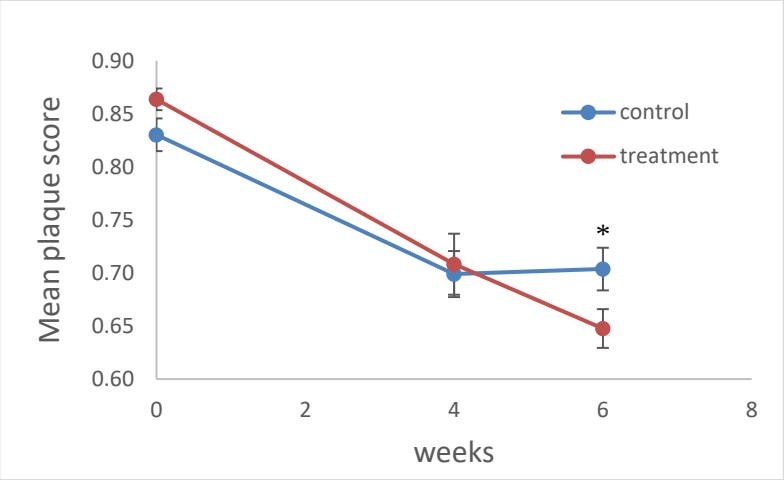

Figure 5 *- Plaque score in the treatment group is significantly lower as compared to the control group following 6 weeks of brushing (*p=0.051)*

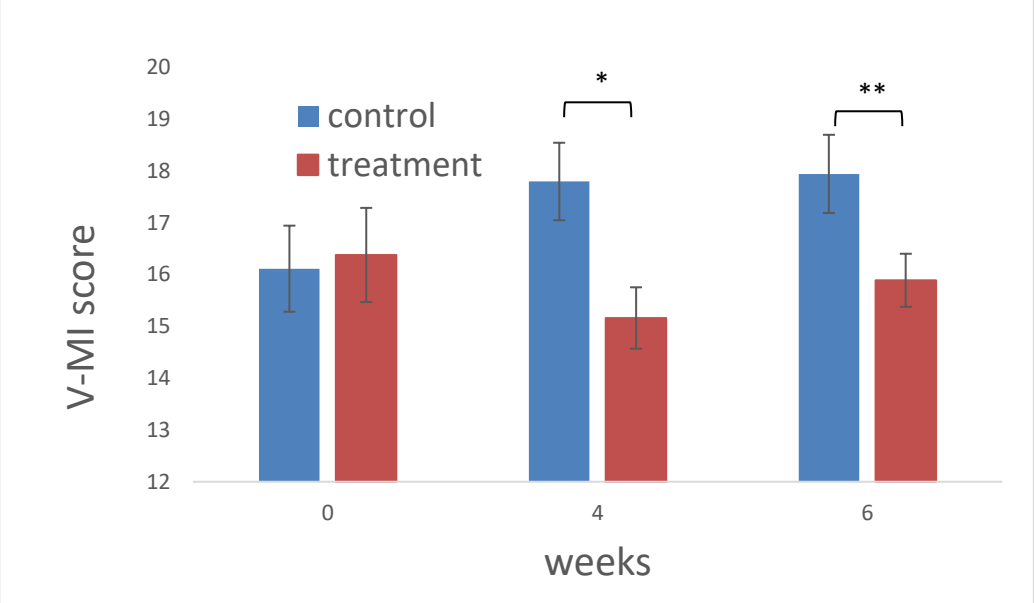

Figure 6 *- The amount of calculus was reduced in the treatment group and was increased in the control group during the test phase of the study (*p=0.009; **p=0.028)*

5. DISCUSSION

Plaque is a gel-like material forming on the teeth pellicle (a thin biofilm, coating the teeth, gums and tongue) and is composed of bacteria, polysaccharides and glycoproteins. Within 2 to 14 days of plaque formation, the plaque deposits will bond with minerals in the saliva to form a calcified deposit called calculus, more commonly known as tartar [9].

Stains and calculus that are attached to the teeth surface, can rarely be removed by regular brushing, either with manual or powered toothbrush; however, in the current study we show that the ToothWave™ provides a significant reduction in plaque and calculus, as well as in gingival inflammation and bleeding. The improvement seen in all the efficacy measures was found to be significantly greater in the ToothWave™ group as compared to the control; and specifically, the significant calculus reduction in the treatment group compared to calculus accumulation in the control group.

The Silk'n ToothWave™ utilizes an alternating low power electric current that oscillates at a frequency of 3MHz. During brushing, the current streams through the toothpaste, while air bubbles are formed and increase the surface area available for streaming. RF current tends to flow along the surfaces of electrical conductors, which is known as the "skin effect" [10]. In addition, the Silk'n ToothWave™ includes an electro-mechanical silicon barrier, which is located between the electrodes. Both the "skin effect" and electro-mechanical barrier steer the current to the desired direction and provide alternating current fluency around the tooth. In addition, the electric current is able to effectively reach hidden areas like the ones between the teeth or along the gum line; these areas and surfaces would otherwise be difficult to reach using mechanical means (i.e. powered or manual toothbrush).

Since the alternating current streams close to the tooth, it brings the charged molecules that are present in the toothpaste close to the tooth surface and changes the chemical environment around it. Once charged molecules accumulate near the tooth surface, the chemical balance may be shifted towards the removal of the attached compounds, replacing them by other, non-staining charged substances, which might have greater affinity to the surface area (for instance fluoride).

We hypothesize that by changing the local charges around the tooth the alternating electrical current is able to activate, speed up, or inhibit chemical reactions that could take place at the tooth surface and remove substances (i.e., calculus) that are otherwise attached strongly to the enamel layer.

Our hypothesis is based on the assumption that the electrically charged toothpaste ingredients take part in the process that occurs on the teeth surface. Toothpastes are water based complex mixtures of abrasives and surfactants, humectants, binders, and other active ingredients. All available toothpastes contain charged organic and inorganic molecular compounds that once the RF is activated, act as electrolytes in the medium and stream along the tooth surface, and are able to achieve the desired effect.

6. CONCLUSIONS

The Silk'n ToothWave™ (model H7001) novel toothbrush is shown to produce a significant reduction in plaque, calculus, gingivitis and gum bleeding following 6 weeks of brushing. These benefits were shown to be significantly greater as compared to a control powered toothbrush and are attributed to the RF feature that is uniquely utilized by the ToothWave™ brush.

7. REFERENCES

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