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THE EFFECTS OF AN ANTI-INFLAMMATORY DIET ON GINGIVAL HEALTH IN CHILDREN (RANDOMIZED CONTROLLED TRIAL)

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ABSTRACT

Background: Several studies observed that only under western diet condition, there was a link between improper plaque control measures and gingival inflammation. Therefore, the aim of this clinical trial was to study the effects of an anti-inflammatory diet on the clinical and serological parameters in children with gingivitis.

Subjects and methods: Forty children were randomly allocated to test and a control group. The participants within a test group were instructed to change their usual diet to anti-inflammatory diet that is rich in vitamin C, antioxidants, omega-3 fatty acids, plant nitrates, vitamin D, fibers and contain a low amount of processed carbohydrates for 4 weeks. While patients within the control group followed their usual dietary habit until the termination of the study. Gingival index and Plaque index were recorded at baseline and after 4 weeks for all children in both groups. Salivary samples were taken at baseline and after 4weeks for quantification assessment of serological parameters for all participants.

Results: While**,** all patients in both groups showed an increase in the mean values of plaque index. Children within the test group showed a significant decrease in the mean values of Interleukin-6 (IL-6), gingival index, and Tumor Necrosis Factor-α (TNF-α) from baseline to the end. This reduction was statistically significant when compared to a control group.

Conclusion: Anti-inflammatory diet can significantly reduce serological parameters and gingival inflammation in children.

KEY WORDS: Anti-inflammatory diet; Interleukin-6; Gingivitis; Tumor Necrosis Factor-α

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INTRODUCTION

Chronic periodontitis (CP) is considered as one of the most prevalent oral diseases, which occurs within 50% of the adult population throughout the world[1]. Lang and coworkers reported that Gingivitis is a prerequisite to initiate periodontal disease and is associated with long-range tooth loss [2].

Improper plaque control was considered as the main cause of gingivitis and this link between the effect and cause was also reported in the 2018 classifications, where plaque-induced gingivitis was used to describe the main part of gingivitis [3]. However, many studies suggest that the observed relationship between gingivitis and plaque accumulation might be true only with Western diet situation [4].

The Western diet contains a low amount of fiber and micronutrients, high content of trans-, saturated-, and omega-6 fatty acids, and high level of processed carbohydrates (such as white flour and white rice) [5]. Van Woudenbergh and co-workers[6] reported that in addition to cariogenic impacts of Western diet, its components promote both systemic inflammation and plaque accumulation. In the absence of plaque control measures, over 4 weeks it was observed that diet is important in the development or control of gingivitis [7].

Many dietary recommendations to improve the periodontal health can be established, such as an additional intake vitamin C, Omega-3 fatty acids, vitamin D, fiber, antioxidants and reduction in carbohydrates [8]. The study of Woelber et al. [4] observed that the anti-inflammatory diet (AID) was able to significantly decrease gingival inflammation despite constant plaque levels. However, no further assessments regarding microbiome or serological variables were done in this study. In spite of these very promising results, there is a fundamental lack of dietary-interventional trials in randomized controlled conditions [8]. Therefore, the aim of the present clinical study was to assess the effects of AID on gingival health and serological parameters in children participants.

MATERIAL AND METHODS

Sample size

Gingival index (GI) [9] was used in the current study as the primary outcome for sample size calculation. Based on the former trial [10], the change between the studied groups in the mean value of GI was 5% with a standard deviation (SD) of 5. Counting on these data sample size of 15 participants per group assured α =0.05 with a power of 80%. The total sample size in this study was 40 patients to compensate for the dropout rate during the study.

Patients and study design

The present study was a single-blinded, randomized, controlled trial. It was conducted on 40 children in two parallel groups. The follow-up period was 4 weeks. The current study was designed following the CONSORT guidelines. Participant's parents/ caregivers signed the informed consent whereas the informed ascent was signed by Adolescents. Ethical approval of the study was obtained from the Research Ethics Committee, Faculty of Dentistry; Kafrelsheikh University where the study was conducted.

The patients were selected from attendants of Pediatric Outpatients Clinic, Faculty of Dentistry, Kafrelsheikh University and from Kafrelsheikh University Hospital between January 2019 and March 2019. Following the informed consent and checking the inclusion and exclusion criteria, the mean plaque value was measured for each patient using the plaque index (PI) [11]. Following measuring of the baseline plaque values for all patients and pseudonymization. The randomization of the patient data was done by means of statistical software version 13.1 (STATA 13.1, Stata Corp, Texas, USA) for equal allocation to the test and control group using plaque values. The allocation ratio in the current study was1:1.

Inclusion criteria

- Age from 10-14 years
- Mean value of (GI) ≥ 0.5
- Both gender
- No cognitive disorders

Exclusion criteria

- Presence of severe or life-threatening medical disorders
- Intake of antibiotics during the period of study or within 6 months prior to study
- Handicapped children
- Uncooperative children
- Intake of drugs that can affect bleeding and gingival inflammation (e.g., anticoagulants and corticosteroids)

Intervention protocol

The patients in the test group were instructed to change their diet to AID protocol for a study period (4 weeks). While there was no change in usual dietary habits within a control group. A detailed verbal data about AID protocol was received to each patient and participant's parents/ caregivers in a test group by specialized in nutritional medicine. In addition participant's parents/ caregivers were instructed to contact this specialist for any help regarding this dietary protocol. All participants in this study were instructed not to use any interproximal cleaning aids throughout the study period In order to not affect possible inflammation.

In this study, GI and PI were used for quantitative recording of gingival bleeding and plaque for all participants in both studied groups. PI assesses the quantity of plaque according to tooth area covered. Regarding this method, the four gingival sites for each tooth is evaluated and scored from 0 to 3. Total tooth score was obtained by adding a score for the four areas and divided by four, and then all total scores for teeth were collected and divided by the number of examined teeth to assess the patient's PI.

GI evaluates the severity of gingival inflammation. Regarding this index, each of the four tooth gingival sites is assessed and scored from 0 to 3. The GI calculation is similar to that for the PI calculation. Bleeding is assessed using a periodontal probe (Hu-Friedy, Chicago, IL, USA).

Saliva collection and assay

Non-stimulated whole saliva (5ml) sample was collected from each child, using a sterile container; children were advised to refrain from drink and food for at least 1 h prior to saliva collection. Immediately, samples were frozen, centrifuged for 5 minutes, and finally, samples were stored at -20°**C** until analysis.

Salivary samples were centrifuged again prior to assay for 1 min at 5000 rpm to prevent possible contamination with oral mucosal cells or food debris.

In this study, a Bio-Plex Multiplex System (Bio-Rad Laboratories, Hercules, CA, USA) according to manufacturer's recommendation, was used to assay Tumor Necrosis Factor α (TNF-α) and Interleukin-6 (IL-6). The concentration of salivary TNF-α and IL-6 were expressed as pg/mL.

The clinical and serological variables were recorded for all patients in the two studied groups at baseline and after 4 weeks.

AID protocol

In the current study, the dietary recommendations within the test group were mainly based on that in a study of Woelber et al. [10], but with some modifications. Dietary model in the test group included the following components:

Macronutrients

- Low carbohydrates diet by reduction of the daily intake from carbohydrates to level <130 g/ day [12]. This includes a reduction in the amount of sugar, soda, white rice, sweetened beverages,

and white flour. Regarding vegetables and fruits, there were no restrictions.

- A reduction in the amount of omega-6 fatty acids (such as margarine, safflower oil, corn oil, sunflower oil, sesame oil, etc.).
- Decrease the amount of industrial animal proteins (such as processed meat products and industrial dairy) as far as possible.
- A reduction in the quantity of trans-fatty acids (such as French fries, fried meals, croissants, crisps, donuts, etc.) as far as possible.
- Daily intake of supplements of omega-3 fatty acids (such as two spoons of flaxseed oil, a portion of the sea fish, etc.).
- A fatty fish meal at least two times weekly such as mackerel, anchovies, sardines, salmon, tuna and herring.
- Daily intake of vegetables such as tomatoes, broccoli, carrots, spinach, sweet potatoes, beets, cabbage, and beans.
- Daily intake of fruits such as orange, cherries, blueberries, strawberries, cantaloupe, watermelon, avocados, and kiwifruit.
- Almonds and walnuts.
- Gluten-free whole grains.
- Olive oil and Soy-based foods.
- Herbs and spices such as garlic and Curcuma.

Micronutrients

- Vitamin C intake on a daily basis (such as one orange, one pepper, two kiwis, etc.).
- Daily intake of vitamin D by exposure to the sun unprotected for 15 min or diet such as fatty fishes, orange juice, soy milk, etc.
- Daily intake of nitrate (for examples beet and spinach).
- Daily intake of fiber (such as legumes, vegetables, bran, and fruits).
- Daily intake of antioxidants (for example a cup of green tea, one pinch of Curcuma, coffee without milk, and ginger).

Study outcomes

In this clinical trial, the primary outcome was GI while PI and serological variables were the secondary outcomes.

Statistical analyses

Data were collected, coded, and analyzed by means of SPSS version 23 under Mac OS. Mean and standard deviation was used for simple descriptive analysis (age and sex). A paired *t*-test was computed to detect general changes within each group throughout the follow-up periods. A student t test was used to assess changes between studied groups. *P*-value of 0.05 was considered as a level of significance.

RESULTS

In the present study, all participants (40 patients) in the two groups attended until the termination of the study (4 weeks). Throughout study duration, there were no significant changes in physical activity within the study population in both groups. The test group consisted of 20 children with 11 girls (55%) and 9 boys (45%). In this group, the mean age was 11.90 ± 1.410 years, ranging from 10 to 14 years. The control group included 12 girls (60%) and 8 boys (40%) with mean age 11.75±1.410 years, ranging from 10 to 14 years. A flow chart of a clinical trial was presented in Fig. 1.

Data regarding GI and PI are demonstrated in Table 1 and 2. In the test group, the mean values of GI were significantly decreased from baseline to 4 weeks while within the control group, the mean values of GI were significantly increased from baseline to the end of the study and the difference between the two groups was statistically significant

at 4 weeks. Within both studied groups, the mean values of PI were increasing with the time of measurements. However, differences between these groups at different follow-up periods were not found significant.

Results regarding serological outcomes are showed in Table 3 and 4. The test group showed a significant decrease in the mean values of serological parameters (TNF-α and IL-6) from baseline to week 4, which were also significant compared to those within the control group at week 4. It was found that in a control group the mean values of TNF-α and IL-6 were significantly increased throughout the duration of the study.

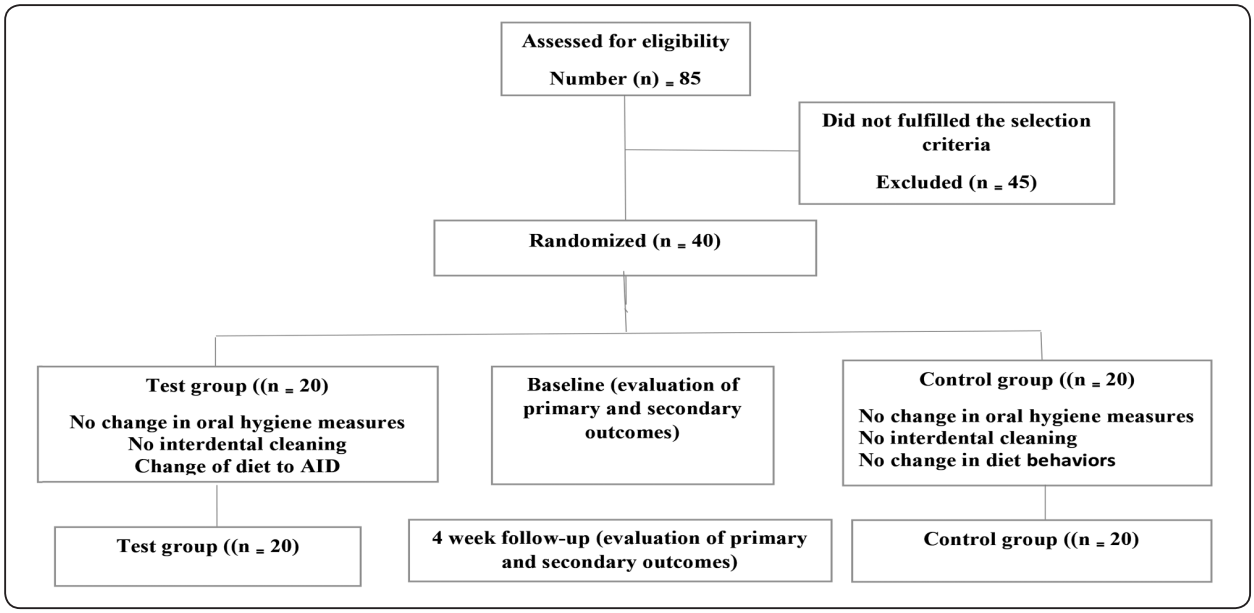

Fig. (1) Flow diagram of study procedures

TABLE (1): Comparison of gingival index among studied groups

	Control group (n = 20)	Test group (n =20)	t	*Inter-p*-value (Control VS. test)
At baseline:				
Mean	1.445	1.450	0.038	0.970
SD	0.4084	0.4335		
At 4 weeks:				
Mean	1.660	1.145	-3.951	0.000 *
SD	0.3775	0.4443		
t	-6.015	8.171		
Intra p-value (baseline VS.4 weeks)	0.000 *	0.000 *		

Significant, Standard deviation (SD), Number (n)

TABLE (2): Distribution of Plaque index among studied groups

	Control group (n = 20)	Test group (n =20)	t	*Inter-p*-value (Control VS. test)
At baseline:				
Mean	1.540	1.550	0.043	0.966
SD	0.7051	0.7585		
At 4 weeks:				
Mean	1.655	1.560	-0.422	0.676
SD	0.6589	0.7618		
t	-3.708	-0.346		
Intra p-value (baseline VS.4 weeks)	0.001 *	0.733		

Significant, Standard deviation (SD), Number (n)

TABLE (3): Comparison between the two groups regarding Tumor Necrosis Factor-α

	Control group (n = 20)	**Test group (n =20)**	**t**	***Inter-p*-value (Control VS. test)**
At baseline:				
Mean	7.410	7.460	0.439	0.663
SD	0.3669	0.3530		
At 4 weeks:				
Mean	7.650	7.235	-3.549	0.01 *
SD	0.3502	0.3884		
t	-6.208	4.436		
intra p-value (baseline VS.4 weeks)	0.000 *	0.000 *		

Significant, Standard deviation (SD), Number (n)

TABLE (4): Distribution of studied groups in relation to Interleukin-6

	Control group (n = 20)	**Test group (n =20)**	**t**	***Inter-p*-value (Control VS. test)**
At baseline:				
Mean	2.970	2.980	0.079	0.938
SD	0.4131	0.3915		
At 4 weeks*:*				
Mean	3.110	2.810	-2.125	0.04 *
SD	0.4399	0.4529		
t	-3.907	3.569		
intra p-value (baseline VS.4 weeks)	0.01 *	0.002 *		

Significant, Standard deviation (SD), Number (n)

DISCUSSION

The goal of this study was to assess the effect of AID on clinical and serological parameters. In the present study GI according to Loe and Silness [13], was utilized because it has been used frequently for intervention clinical studies and its reproducibility and sensitivity is good. The follow-up period in this study was 4 weeks. This is in an agreement with Baumgartner et al. [7], and Woelber et al. [10]. In accordance with Granger et al. [14], passively drooled unstimulated whole saliva sample was used in the current study.

This technique for saliva collection is highly reliable because it provides a huge amount of saliva and prevents the contamination that may occur when products or devices are used for salivary collection or stimulate salivary flow. In addition, this technique proves to be suitable for adults, adolescents, and children above the age of 6 [14].

Data from the present clinical trial showed that AID can decrease gingival inflammation without any modifications in oral hygiene performance. This is in agreement with Baumgartner et al. [7], who conclude that without oral hygiene measures dietary factors are important for the development or control of gingivitis.

The control group in this study showed a significant increase in PI throughout the period of the study. While the test group demonstrated slightly insignificant increase in PI. This can be explained by the absence of interdental hygiene throughout the study. This in contrast to observations of Woelber et al., [10] who found a significant decrease in values of plaque within studied groups. In accordance with Woelber et al. [4], the test group in the current study demonstrated a significant reduction in GI compared with their values at baseline.

The results of this trial questioning the positive association between gingivitis and plaque in different dietary situations. In agreement with Marsh and Devine [15], our results emphasize the important role

of host modulation and the host reaction in gingival inflammation.

Based on the observations of Sheiham and Watt[16], the AID protocol can provide a reduction in both gingival bleeding and weight using one intervention approach. In addition to the dietary effects of micro- and macronutrients, it is also associated with better gingival and periodontal health [17].

In the present trial, the serological parameters (TNF-α and IL-6) within a test group showed a significant reduction after 4 weeks. This observation coincided with Ruth et al.[18], who showed a significant improvement in systemic inflammatory markers after 12 weeks from a dietary intervention. This is in contrast to observations of Woelber et al. [10] who stated that there was no significant change observed regarding the inflammatory parameters after 4 weeks in an experimental group.

In total, the results from our study support the assumptions that a dietary lifestyle that contains a high Omega-6 and a lot of refined carbohydrates promotes inflammatory processes [19].

The relationship between gingival inflammation and carbohydrate consumption has been evaluated in many clinical trials, also with impressive effects[20]. Based on the literature are many possible explanations for the link between inflammatory response and carbohydrates. Firstly, high glycemic index carbohydrates can enhance inflammation via oxidative stress[21], activation of nuclear factor-kappa B [22], and higher levels of C-reactive protein[23]. Secondly, weight gain and its associated consequences such as inflammation, caused by raise in adipokine secretion[24]. Furthermore, the results from the current study are in line with Sidi and Ashley[25], who observed a significant higher gingival bleeding in patients on a high sugar diet compared with those on a low sugar diet, without any changes regarding the level of plaque between studied groups.

The data from this study raise several questions on the role of dental plaque for the development of gingival/periodontal diseases and its effect on treatment. When the oral examination reveals signs of gingivitis or periodontitis, the host-factors such as dietary factors should be primary checked [26].

Limitations of the present study were a relatively low number of patients, which is not a representative sample, a limited range of study variables (such as microbiome analysis), and a short study follow-up period.

CONCLUSIONS

Within the previous limitations, our clinical study concluded that AID was able to significantly decrease serological inflammatory parameters (TNF-α and IL-6) and gingival inflammation, while there was no effect on PI.

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