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Crosstalk between oral and general health status in e-smokers

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Abstract

Electronic cigarette (e-cigarette) simulates the act of tobacco smoking by vaporizing a mixture of propylene glycol, nicotine, and flavoring agents. e-cigarette has been proposed as a product able to aid to stop smoking. The aim of the study is to verify the clinical variations of periodontal health induced by e-cigarettes use and, moreover, to investigate about the awareness of the e-smokers about their health variations and about their hypothetical need to turn back to smoke combustible cigarettes.

This clinical observational pilot study involved 110 out of 350 smokers, who switched to e-cigarette. Patients were subjected to oral examinations. A questionnaire to self-assess the variations of some parameters of general health, and to self-assess the need to smoke combustible cigarettes, was distributed to such subjects involved in the study.

At the end of the study, we registered a progressive improvement in the periodontal indexes, as well as in the general health perception. Finally, many patients reported an interesting reduction in the need to smoke.

In the light of this pilot study, the e-cigarette can be considered as a valuable alternative to tobacco cigarettes, but with a positive impact on periodontal and general health status.

Abbreviations: BI = bleeding index, CO = carbon monoxide, e-cigarette = electronic cigarette, e-smoker = electronic smoker, PBI = papillary bleeding index, PI = plaque index.

Keywords: nicotine, prevention, tobacco

1. Introduction

Tobacco smoking is the largest preventable cause of death in the world today[1]; the estimated overall prevalence of active smokers in high-income countries, according to the World Mental Health Surveys, ranges between 20% and 30% of the population, against the 5% to 35% observed among the middle-income and low-income countries[2]; thus, making the cigarette smoking one of the major worldwide public health issues.[3] Although it is well known that cigarette smoking is a risk factor for cardiovascular diseases,[4] pulmonary diseases, cancer,[5] and other systemic pathologies, the area of human body directly exposed to tobacco smoke effects is the oral cavity.[6–10] Neoplastic and preneoplastic conditions take a particular attention among oral diseases induced by tobacco smoking, because of the importance that early diagnosis can have with such clinical pictures.[11] Cigarettes smoking is also one of the most important known cofactor in the development of oral leukoplakia,[12] palatal leukokeratosis and melanosis,[13] and of the modifications of the oral microenvironment which can lead to several opportunistic pathologies, such as oral candidiasis and hairy tongue.[14] Furthermore, tobacco smoking represents a high risk factor for periodontal diseases,[15] enhancing the loss of gingival attachment,[16] and the increase of gingival regression,[17] with the final result of a severe progression of periodontal inflammation.

As reported in literature, wound healing after periodontal scaling was significantly altered in smokers,[18] with an increased risk of dental implant failure.[19]

Quit smoking entails a clear reduction of the smoke-related diseases,[20] and a decreased exposure to the risk to develop oral cancer[21] and periodontal diseases.[13] A strong addiction to nicotine can make it very hard to stop smoking: in this case, a therapy with nicotine substitutes, such as the transdermal patches,[22] can help to reduce the consumption of tobacco cigarettes.

A new alternative therapy is the electronic cigarette, also known as e-cigarette.[23] This device simulates the act of tobacco smoking, by vaporizing a mixture of propylene glycol, nicotine, and flavoring agents.[24,25]

E-cigarette companies propose their product as a smoking cessation aid; however, some clinical studies failed to demonstrate a complete stop of the consumption of combustible cigarettes by the electronic smokers (e-smokers)[26] and failed to demonstrate a better efficacy of e-cigarettes with respect to other nicotine substitutes.[27]

Our study was aimed to assess the variations of oral and general health status in a population of randomized smokers who switched to e-cigarette. Particular attention has been paid to the periodontal health status, by analyzing the plaque index (PI) and

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periodontal bleeding index (BI). Furthermore, we provided to the enrolled patients a self-assessment questionnaire to evaluate the awareness of patients involved in this study about the changes in their general health status, induced by the switching from combustible cigarette to e-cigarette.

2. Materials and methods

This clinical observational study was carried out at the Unit of Periodontology and Oral Hygiene of Calabrodental Clinic (Crotone, Italy). The Ethics Committee specifically required by Calabrodental approved this study and the related procedures (Prot. July-2012/Res005). Written informed consent was obtained from the patients by filling in a specific form. The study followed the "Ethical principles for medical research involving human subjects" of the Helsinki Declaration. The study was conducted in accordance with Italian laws and regulations. The study complies with the STROBE Guidelines.

2.1. Patients selection

This study was conducted for 120 days on each patient. Clinical examinations were performed at 3 different check-points: T_0 (baseline), T_1 (after 60 day), and T_2 (after 120 days).

A total of 350 e-smokers were randomly recruited for this study. The 1st selection was performed by choosing those subjects which started to use e-cigarette approximately from 4 ± 1 months, before the start of the study. We also asked if they would like to stop smoking and if they would like to participate to a clinical study aimed to assess their oral health. Exclusion criteria were pregnancy and the presence of any clinical condition requiring any premedication (cancer, respiratory, cardiovascular, and/or any severe oral disease). Smokers were divided into 2 groups, according to the number of years of smoking by each of them: group 1 (less than 10 years of tobacco smoking), group 2 (more than 10 years of tobacco smoking). All subjects were asked to abstain from tobacco cigarettes for the entire duration of the study; they were asked to report on a personal diary, properly created and provided to patients by the Calabrodental teamwork, if they were able to fulfill the indications suggested by our researchers, or, conversely, if they smoked during this specific period, and how many tobacco cigarettes they smoked. To avoid the possibility that the outcomes of this study could be influenced by the Hawthorne effect,[28] patients were asked not to change their oral hygiene habits during the observational time.

Only 110 e-smokers (89 men and 21 women, average age 31 ± 9; group 1 = 60 subjects, group 2 = 50 subjects) out of 350 were included in the final stage of the study, as shown in Fig. 1.

2.2. Nicotine consumption

All the recruited patients, who switched to the e-cigarettes, reported that they have previously smoked only combustible cigarettes with high amount of nicotine (among 0.8–1 mg per cigarette).

All patients included in our study stated that they use e-cigarettes with an average content of 0.25 mL of liquid containing a total amount of nicotine equivalent to 18 mg: each cycle of use of the e-cigarette contains on average 4.5 mg of nicotine, although the calculation should not consider the dispersed nicotine part, equal to about half of the basic content. The subjects enrolled in the study said they had smoked in the past an average of 20 cigarettes a day, absorbing an average of 16 mg of nicotine per day. With the e-cigarette, if subject smokes the same number of cigarettes in a day it would be absorbed approximately 7 mg of nicotine.

2.3. Intraoral examinations

The oral cavity was divided in 4 areas: upper right and upper left jaw, lower right and lower left jaw. Each patient underwent an accurate oral examination to investigate the following parameters: PI (according to Silness and Loe; 1964), BI (according to Carter and Barnes; 1974), and papillary bleeding index (PBI; according to Muhleman; 1977). All the measurements were taken by using a periodontal probe that measures to one tenth millimeter, according to the commonly used standardized techniques, and with the aid of the digital radiology and of the software for image analysis.

Mean (±standard deviation) values for PI and PBI were calculated and graphically represented on a chart. In order to avoid potential bias, all the procedures were standardized, and the operators who performed the measurements were not fully aware about the final aim of the study.

2.4. Self-assessment questionnaire

At the end of the observational period, patients were asked to answer a self-assessment questionnaire of 5 entries: general health status; smell perception; taste perception; frequency of respiratory diseases; and need to smoke. All entries were associated to a rating scale. The answers were properly archived and analyzed.

2.5. Smoke Check-meter assay

To ensure the reliability of this research, we asked to all the involved patients to sign at the end of the study a declaration assessing their strict adherence to the indications of the physicians, particularly regarding the stop smoking of combustible cigarette. Moreover, we randomly selected a sample of 20% among the enrolled patients (22 patients, 18 men and 4 women) and we asked them to undergo to a breath-test with the Smoke Check-meter assay. With this test, we analyzed the exhaled breath carbon monoxide (CO): this test allows to know whether patient has smoked combustible cigarettes in the last period or not; we asked to these patients, randomly selected by a casual numbers generator, to carry out Smoke Check-meter test at T_o, T_1, and T_2.

The Smoke Check meter is a technology used for the analysis of exhaled breath CO. Smoke Check meter detects the CO eventually present in exhaled breath in parts per million (ppm) and it is used to check the smokers aiming to stop smoking: the CO values obtained from this examination are particularly accurate in detecting not smoking for at least 24 hours.

3. Results

3.1. Evaluation of general and oral health status at T_0

All subjects came from the macroregion of the Southern Italy; they belonged to different social classes, and they had an average age of 31 ± 9 years. Patients involved in this study were clinically examined to assess their general health status at T_0. No respiratory and cardiovascular diseases were reported by any subject of both groups. No missing data were reported for any of the subjects involved at the end of the study. Dental decay of

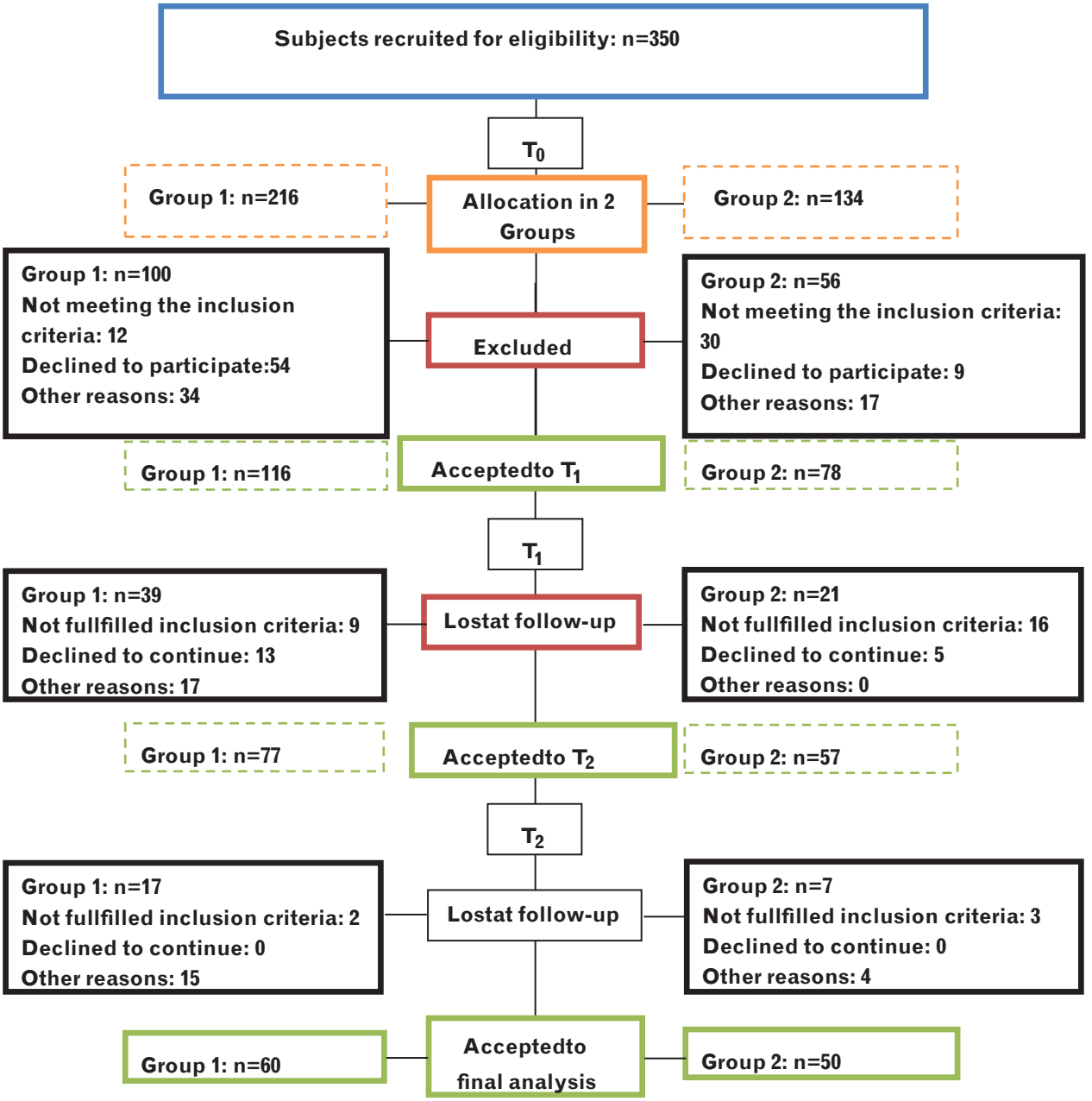

Figure 1. Flowchart of participation to the study. Only 110 smokers (89 men and 21 women, average age 31 ± 9; group 1 = 60 subjects, group 2 = 50 subjects) out of the initially recruited 350 were included in the final stage of the study. The flowchart describes, for each timepoint, the number of patients excluded or withdrawn from the study.

several degrees and nicotine induced dental pigmentation have been reported in 45 subjects of group 1 and in all subjects of group 2.

3.2. Plaque index at T_0, T_1, and T_2

At T_0 85% of subjects of group 1 showed PI scores equal to 1; only in 15 subjects it was found PI score equal to 0 (no plaque) (Table 1). In group 2, 73% of subjects were found with a PI score equal to 2, while PI scores of 1 or 3 were assigned to 12% and 15% of the remaining subjects, respectively (Table 1).

At T_1 slight changes started to be appreciable. In group 1 the percentage of patients with PI score of 0 increased to 54%, while a thin plaque film persisted in the rest of the subjects of this group (PI score equal to 1) (Table 1). A more noticeable improvement (PI score equal to 0 or 1) was observed in 81% of the subjects, with the remaining percentage still showing a PI score of 2 (Table 1).

The final observation at T_2 revealed an overall improvement of the PI among nearly the totality of subjects of group 1 (PI score equal to 0 in 92% of subjects) (Table 1). Similarly, a remarkable plaque regression was observed in the 87% of subjects of group 2 (Table 1).

We calculated the mean value of PI scores in the 2 groups to show the variations of plaque accumulation on a chart. In group 1, PI decreased from a mean value of 0.9 ± 0.3 (T_0) to 0 (T_2);

Table 1

PI, BI, and PBI distribution in the 2 groups.

PI					BI		PBI			
Group 1 (% value)	0	1	2	3	Yes	No	0	1	2	3
T_0	15	85	–	–	61	39	66	34	–	–
T_1	54	46	–	–	55	45	84	16	–	–
T_2	92	8	–	–	8	92	98	2	–	–
Group 2 (% value)	0	1	2	3	Yes	No	0	1	2	3
T_0	–	12	73	15	65	35	60	5	25	10
T_1	41	40	16	3	48	52	76	24	–	–
T_2	87	13	–	–	2	98	100	–	–	–

BI = bleeding index, PBI = papillary bleeding index, PI = plaque index.

however, the decrease was more evident in group 2 with PI score going from 2.13 ± 0.5 (T_0) to 0.25 ± 0.45 (T_2) (Fig. 2).

3.3. Bleeding index at T_0, T_1, and T_2

At T_0 many subjects of group 1 showed a gingival bleeding response after probe stimulation. Similarly, a bleeding response was observed in the most of subjects of group 2 (Table 1).

An improving trend was recorded at T_1 for both groups: more precisely, in almost the half of the subjects of group 1 the presence of bleeding was clinically reduced while, in group 2, gingival bleeding was persisting in slightly less than half of the subjects (Table 1).

At T_2 a noteworthy improvement of the periodontal status, with no bleeding reaction after stimulation with a probe, was

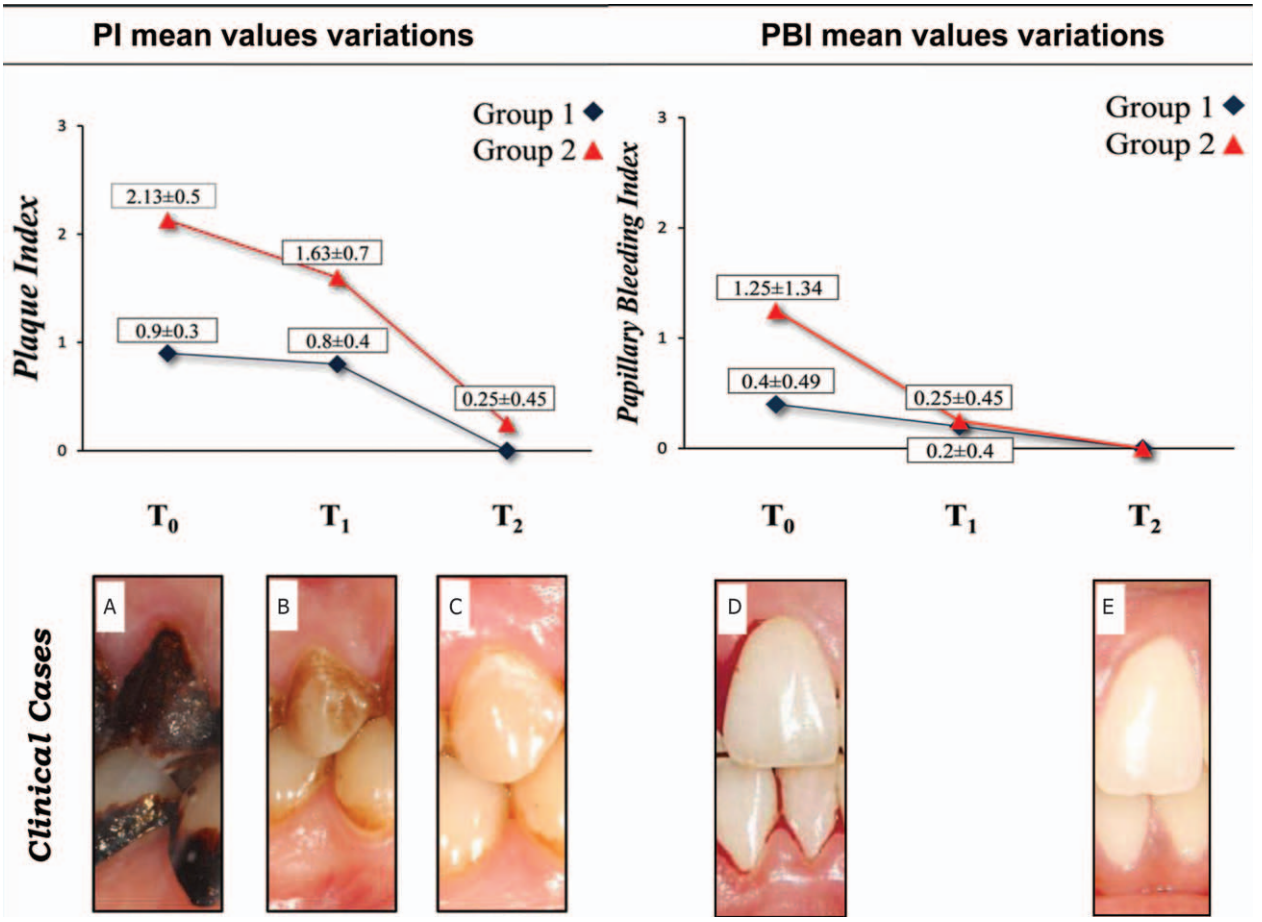

Figure 2. Comparison of PI and PBI values from T_0 to T_2. Group 1 (blue line) shows a PI that remains rather constant between T0 and T1, instead, group2 (red line) shows a PI that tends to decrease homogeneously from T0 to T2. On the other hand, the PBI shows a trend rather comparable between the 2 groups, of course, starting from different values at baseline. PI and PBI values are expressed as mean ± standard deviation. Clinical cases represent the appearance of the clinical conditions at different time points: (A–C) show the variation of PI from T_0 to T_2; (D, E) show the variation of PBI from T_0 to T_2. PBI = papillary bleeding index, PI = plaque index.

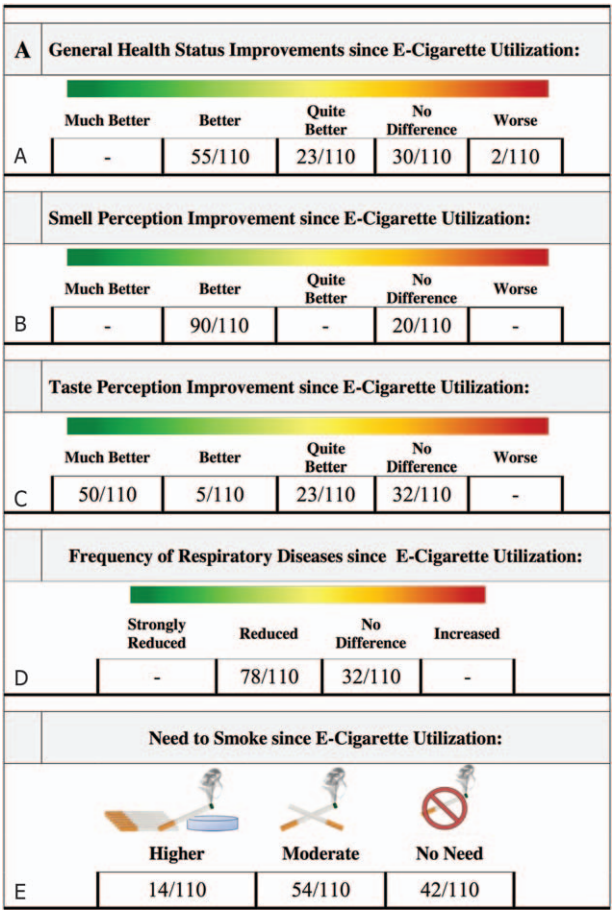

Figure 3. Self-awareness questionnaire used in the study. This questionnaire was filled by patients enrolled and maintained into the study protocol until its conclusion. Five questions were reported on questionnaire: they ranged from the general health status to the smell perception, the taste perception, the respiratory clinical conditions, and up to the need to return to smoke the classic cigarettes. Each indicator was assessed after having analyzed the replies collected by the patients: the reported data were based on the subjective evaluation of the parameter investigated.

observed in over the 90% of subjects of both groups (92% for group 1 and 98% for group 2, respectively) (Table 1).

3.4. Papillary bleeding index at T_0, T_1, and T_2

No papillary bleeding was found in the 66% of subjects of group 1 at T_0 (PBI score equal to 0), just a mild papillary bleeding was instead observed only in the 34% of subjects (PBI score equal to 1). On the other hand, many subjects of group 2 showed no papillary bleeding (PBI score equal to 0), only in the 35% of the subjects a sever papillary bleeding (PBI score of 2 and 3) was still observed (Table 1).

Absence of papillary bleeding was reported in the 84% of subjects of group 1 (PBI score equal to 0) at T_1, nonetheless, a slight papillary bleeding persisted in the 16% of the subjects (PBI score of 1). In group 2, we observed a similar trend with an equally conspicuous percentage (76%) of subjects who showed no papillary bleeding (PBI score of 1).

This improvement was confirmed by the analysis of the variation of PBI mean values. From the analysis of the mean values it emerged that in group 1 PBI reduced from 0.4 ± 0.49 at T_0 to 0 at T_2 (Fig. 2), while in group 2 PBI switched from 1.25 ± 1.34 at T_0 to 0 at T_2 (Fig. 2), showing a marked positive effect in this group.

3.5. Self-assessment questionnaire

At the end of this observational clinical study, we analyzed the answers given by all the subjects to the self-assessment questionnaire. Subjects were asked to indicate on a rating scale (Fig. 3), the improvements they thought to have achieved about their general health status, about their smell and taste perception, about the frequency of respiratory diseases, and finally, about the need to turn back to smoke combustible cigarettes.

Almost 71% of the subjects felt an amelioration of their general health status (55 out of 110 marked "better" on the rating scale, while 23 out of 110 marked "quite better") at the end of the observational study. Less than 1/3 of all subjects (30 out of 110) did not felt any clear change, neither positive nor negative, of their general health status, while only 2 subjects indicated a worsening of the general health status (Fig. 3A).

Unanimous positive response was reported for the self-perception of smell and taste variations: none of the subjects reported a worsening. More in detail, over 80% of subjects clearly indicated a positive variation in both smell and taste perception (Fig. 3B and C); the other subjects did not feel substantial changes to disclose (Fig. 3B and C).

Similarly, a large percentage (78%) of subjects interestingly reported a reduction of the frequency of respiratory diseases (Fig. 3D). The final entry of the questionnaire, about the perceived need to smoke, revealed that 96 out of 110 subjects felt only a moderate or absent need to smoke; the other 14 patients revealed to perceive the need to turn back to combustible cigarettes (Fig. 3E).

No patient reported to have occasionally smoked the combustible cigarettes, during the study: at the end of the study, the recruited subjects signed a declaration, where they ensured the complete agreement to the recommendations of the clinicians. As proof of this, the 22 subjects selected for the Smoke Check-meter assay showed satisfactory values (Fig. 4).

4. Discussion

The clinical observations highlighted in this research work were aimed to assess the improvements of periodontal health in smokers that switched to e-cigarettes. A clinical approach was used for the evaluation of general health status and, more in detail, of oral health status.

Systemic diseases induced by tobacco smoking are well known and widely documented in the scientific literature.[27–31] Furthermore, several studies assess that tobacco smoking entails an overall increase of the risk to develop severe periodontal diseases.[32]

Our observations revealed an interesting growing trend, relating to PI, BI, and PBI in the 110 subjects considered in this study. To our knowledge, there are no data in literature related to the variations of such periodontal indexes in subjects that dropped the tobacco cigarette, and started to use the e-cigarette instead.

We observed a constant reduction of bacterial plaque on teeth surfaces, from baseline at T_0 to the end of the observational period at T_2. More precisely, subjects of group 1 showed a homogeneous presence of a thin film of plaque at T_0, which visibly decreased toward T_1 until it completely disappeared in all

Subject	T_0	T_1	T_2	Reliability
1				Reliable
2				Reliable
3				Reliable
4				Reliable
5				Reliable
6				Reliable
7				Reliable
8				Reliable
9				Reliable
10				Reliable
11				Reliable
12				Reliable
13				Reliable
14				Reliable
15				Reliable
16				Reliable
17				Reliable
18				Reliable
19				Reliable
20				Reliable
21				Reliable
22				Reliable

Color-code	CO (Carbon Monoxide parts per milion)	Type of Smokers	Reliability related to this study
Green	0-6	Very Light Smokers (VLS) or not	High Reliability (RELIABLE)
Yellow	7-10	Light Smokers (LS)	Good Reliability (RELIABLE)
Red	11-20	Heavy Smokers (HS)	Bad Reliability (NOT RELIABLE)

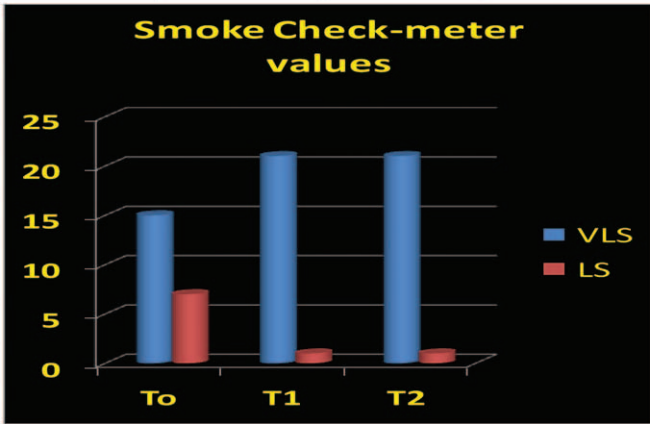

Figure 4. Composite figure. On the left is represented the table reporting the "Smoke Check-meter" values, related to 22 out of 110 randomly selected patients: values are indicated with a color according to the colorimetric scale, briefly reported on the right part of the figure in a separate table. The colorimetric scale is aimed to assess the estimated smoke consumption; in this light, it should represent an index of the reliability of the study. Starting from the null hypothesis each patient has stopped his smoke consumption at the start of this study, it is useful to understand that the green and yellow colors are the desiderable values because they are indicative of absence/limited presence of CO in the patient's breathing. The histogram describes the numerosity of patients classified as VLS and LS, according to the amount of CO detected by "Smoke Check-meter." CO = carbon monoxide, LS = light smokers, VLS = very light smokers.

subjects of group 1 at T_2. Interestingly, this result was more marked in subjects of group 2 characterized by a huge presence of plaque at T_0.

Epidemiological studies have clearly demonstrated that tobacco smokers have a worse oral hygiene than nonsmokers[33]. There are some evidences that smoking habit increases the mineralizing potential of saliva.[34] Moreover, recent studies have demonstrated that the plaque quantity, the plaque architecture, and its bacterial composition are rather similar between smokers and nonsmokers patients; instead, smokers show a nicotine-related vasoconstriction of the gingival tissue,[33] leading to a slight decrease of the crevicular fluid flow: such flow reduction is able to impair the immunological reply to bacterial growth on dental tissues; moreover, the gingival vasoconstriction inhibits the early signs of gingivitis. In conclusion, since PI is mainly related to plaque control and to a proper flow of crevicular fluid, and since heavy smokers were found to have worse oral hygiene and worse crevicular fluid flow than nonsmokers: the PI variation, reported in this study, could be related to the difference in the crevicular fluid flow and to the different ability of e-smokers to manage their oral hygiene.

Appreciable improvements were likewise observed for gingival bleeding. Although there might be some controversy regarding the effect of tobacco consumption on the gingival vasculature, there is a clear clinical evidence that nicotine induces vasoconstriction of peripheral blood vessels, thus reducing bleeding.[33]

On the other hand, as shown in literature, nicotine represents a contributing cause to periodontal degradation by affecting the fibroblasts attachment ability,[35,36] collagen production, and integrin production.[37,38] Moreover, nicotine increases the amount of proinflammatory cytokines in cultured gingival keratinocytes and fibroblasts.[39,40]

The results observed in our study could be explained by the fact that the combined harmful effects of tobacco and nicotine on periodontal health[41] are now limited only to the amount of nicotine in the e-cigarettes thus contributing to the reduction of the typical side effects of smoking habit, and of the severity of smoke-related oral diseases.

In our study, we analyzed for the first time the changes of the status of periodontal health in individuals who have dropped the common cigarette and started to use e-cigarette.

A first relevant take-home message deriving from our observational/clinical study is that many subjects showed a reduction of the need to smoke combustible cigarettes, even if this only a limited pilot study that must be enlarged and confirmed by other more numerous RCTs. This major result has a high relevance as it implies the reduction of the addiction to the chemical component of the combustible cigarettes, and to the psycho-social aspect that characterizes the typical smoker.

Nevertheless, although e-cigarette represents a valuable alternative to traditional cigarettes, thus a concrete aid for all the smokers needing to quit smoking; however, many respectable studies suggested that the main components of e-cigarette liquids could be potentially harmful, because of the still poorly known effects of such substances on the human organism.[42]

In our role of highly experienced physicians in the field of oral medicine, we want to highlight how the switching from combustible to e-cigarette can represent a valid support toward a clear improvement in some specific oral health parameters, leading also to overall benefits toward patients' wellbeing.

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