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Adress: Cappadocia University, Urgup Campus, Faculty of Dentistry
Urgup / Nevsehir
Phone: +90 (384) 353 5009 Fax: +90 (384) 353 5125

Adress: Cappadocia University, Urgup Campus, Faculty of Dentistry
Urgup / Nevsehir
Phone: +90 (384) 353 5009 Fax: +90 (384) 353 5125

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Adress: Cappadocia University, Urgup Campus, Faculty of Dentistry
Urgup / Nevsehir
Phone: +90 (384) 353 5009 Fax: +90 (384) 353 5125

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Research Article

Predicting Treatment Success Of The Functional Therapy in Class II Division 1 Patients

Fatih Celebi[1*], Ali Altug Bicakci[2], Yildirim Ozdemir[3]

[1]Private Practice, Sivas, Turkey.
[2]Tokat Gaziosmanpasa University, Faculty of Dentistry, Department of Orthodontics, Tokat, Turkey.
[3]Private Practice, Istanbul, Turkey.

*Corresponding author: fatihcelebi5860@gmail.com

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Predicting Treatment Success Of The Functional Therapy in Class II Division 1 Patients

Fatih Celebi, Ali Altug Bicakci, Yildirim Ozdemir

Abstract

Objective: The aim of this study was to determine the cephalometric variables that may predict treatment success of the Twin Block appliance in patients with skeletal class II divison 1 malocclusion.

Materials and Methods: Patients treated with the Twin Block appliance were recruited from the archive of the clinic. They were divided into 2 groups as success and failure according to the change in ANB angle. By the 6th month after treatment, patients with a change in ANB angle of 3º or more were included in the success group (14 patients; 7 females, 7 males). Patients with a change of 1º or less were included in the failure group (14 patients; 5 females, 9 males). Seventy-five variables were measured on the pre-treatment lateral cephalograms and the groups were compared. For each variable that showed a statistically significant difference between the two groups, the percentage of correct classifications was calculated.

Results: Of the seventy-five variables, fifteen showed a statistically significant difference between the two groups ($p < 0.05$). The percentages of correct classification ability of the variables varied between 82% and 57%. The variables with the highest classification success were as follows: Pg-NB (mm) (82.1%), U1NA (°) (78.6%), and L1-NB (mm) (75%).

Conclusions: The variables with the highest predictive ability showed that patients with a prominent chin tip, protrusive upper incisors and retrusive lower incisors were more likely to be successfully treated with the Twin Block appliance.

Key Words: Prediction, treatment success; twin block appliance.

Introduction

Class II division 1 is a common type of malocclusion in society, which is not only aesthetically disturbing but also causes functional problems due to the increased possibility of trauma to the upper incisors. Trehan et al. and Al Jadidi et al. reported a prevalence of 5.5% and 11%, respectively, in the populations they studied (1,2). Although the amount varies from study to study, it is one of the main reasons why patients consult orthodontists. In their study, Willems et al. found that 52% of patients undergoing orthodontic treatment had Class II Division 1 malocclusion (3)

Functional appliances are valuable therapeutic tools for skeletal correction in Class II subjects characterised by mandibular retrognathia in the pubertal or prepubertal period (4,5). Despite minor differences in configuration, these devices share a common mechanism of action.

The Twin-Block appliance was designed and introduced by Clark in 1982 and has since become one of the most widely used functional appliances (4,6). Because it consists of two separate parts, it has advantages over other removable functional appliances such as more comfortable speech and partial movement of the lower jaw, increasing patient comfort and cooperation (4,5).

Although some researchers have suggested early treatment to reduce the possibility of upper incisor trauma (7), it has been shown that the pubertal growth spurt is the optimal time for maximum skeletal correction in the minimum amount of time (8,9). In clinical practice, functional appliances usually do excellent work if treatment is performed at the optimal time. They correct Class II molar and canine relationships, eliminate increased overjet-overbite, and improve the soft tissue characterized by a retracted mandible, resulting in a better profile.

However, we have observed that sometimes, even when we follow the same treatment procedure and do not have problems with patient co-operation, successful results are short-term. In these patients, during the fixed orthodontic treatment, which was the second phase of treatment, the overjet increased and the corrected canine and molar relationships were disrupted. We had to modify our treatment plan to eliminate the overjet by using the fixed functional appliance, class II intermaxillary elastics, or by extracting the upper first premolars.

There are many conflicting results in the literature about the success of the skeletal effects of functional appliances (10-13). The aim of this study was to investigate whether there

are any cephalometric predictors that can be used to predict the success of the Twin Block appliance.

Materials And Methods

This study was approved by the Clinical Research Ethics Committee of Tokat Gaziosmanpaşa University and informed consent forms were obtained from the parents of the patients. The clinical archive of the Orthodontic Department of Tokat Gaziosmanpaşa University was searched retrospectively. A total of 323 Class 2 Division I patient records were detected and patients treated with the Twin Block appliance between 2013 and 2020 and were identified. As a routine procedure in our clinic, Twin Block treatment were used for 6-8 months, wearing it for 18 hours daily, followed by an additional 3-4 months of night-time wear. The patients' final records were obtained 6 months later after the treatment.

The inclusion and exclusion criteria were listed in Table 1. In cases that met the inclusion criteria, ANB angles were measured before the treatment and at the end of the retention period. Cases with a decrease in ANB angle of more than 3° due to functional treatment were classified as successful, and those with a decrease of less than 1° were classified as unsuccessful. Cases with a decrease between 1° and 3° were considered borderline and excluded from the study. As a result of the measurements, 14 patients (5 females, 9 males) and 14 patients (7 females, 7 males) were allocated into the failure and success groups, respectively.

Table 1. Inclusion and exclusion criteria

Inclusion Criteria
Having Class II division 1 malocclusion with an ANB angle more than 6°
Being at the CVMS 3 or CVMS 4 maturational stage at the beginning of the treatment
Not having a history of cooperation problem during treatment
Having complete pre-post treatment and post retention cephalometric records
Exclusion Criteria
Receiving rapid maxillary expansion (RME) or headgear therapies as a part of the treatment
Having craniofacial anomaly
Having poor image quality in cephalometric records

A total of seventy-five measurements were carried out using thirty-three cephalometric landmarks on pre-treatment lateral cephalometric radiographs. Tracings and measurements were made by using Dolphin Imaging software (Dolphin Imaging & Management Solutions,

Chatsworth, CA, USA). The landmarks, angular measurements, and linear measurements used in the study were shown in Figure 1, 2, and 3, respectively.

To determine the measurement error, twelve radiographs were randomly selected, and the cephalometric tracings and measurements were repeated after two weeks. The method error between the first and second measurements was calculated using the Dahlberg formula $\sqrt{(\Sigma d^2/2n)}$. The angular measurements showed errors ranging from 0.24º (ANB º) to 1.89º (Articuler angle), while the linear measurements showed errors ranging from 0.22 mm (Po-NB) to 1.68 mm (Co-Gn).

Statistical analysis

The data were analysed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, version 22.0; Armonk, NY: IBM Corp.). Statistical significance was defined as p-values less than 0.05.

To compare variables between the success and failure groups, an independent samples t-test was used for variables with a normal distribution, and the Mann-Whitney U test was used for variables with a non-normal distribution. In order to determine the classification success of the variables that showed statistical significance, the variables analysed with the Independent Samples t-test were subjected to a discriminant analysis, while the variables analysed with the Mann-Whitney U test were subjected to a logistic regression analysis.

The Independent Samples t-test was used to assess whether there was a statistically significant difference between the groups in terms of treatment times. The effect of gender on treatment success was assessed using the chi-squared test.

Results

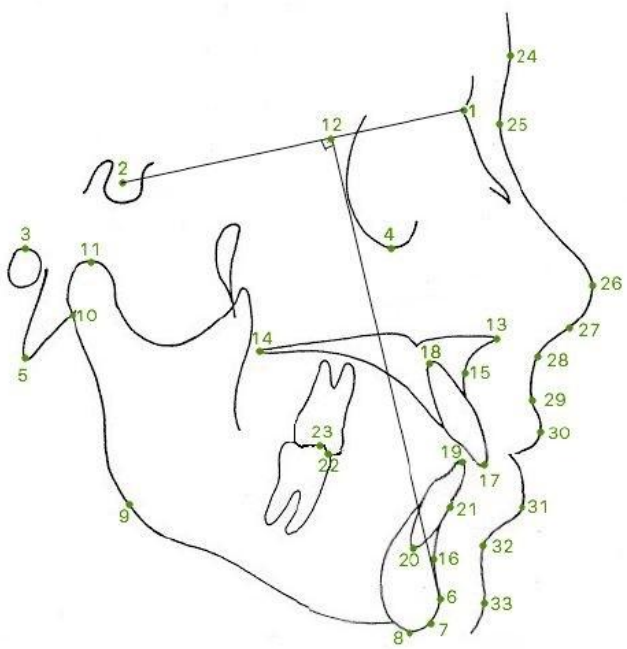
No significant difference was observed between the success and failure groups in terms of treatment duration. (p=0.286; mean duration (success):10.17±2.00 months, mean duration (failure): 9.32±2.16 months) There was no significant associationbetween the success status and the gender of the participants. (x^2= 0.583, p= 0.445)

The comparison results of the variables with normal distribution, evaluated by independent samples t-test, were presented in Table 2. As a result of the analysis, statistically significant differences (p<0.05) were found between the success and failure groups in fourteen variables:1-) U1-SN (°), 2-) U1-PP (°), 3-) U1-NA (°), 4-) FMIA (°), 5-) OP-FH (°), 6-)Li-B'-Pg' (°),

7-) N-Me (mm), 8-) L1-NB (mm), 9-) Pg-NB (mm), 10-) Li-E (mm), 11-) Li-H (mm), 12-) Overjet (mm), 13-) L6-MP (mm), 14-) L1-MP (mm).

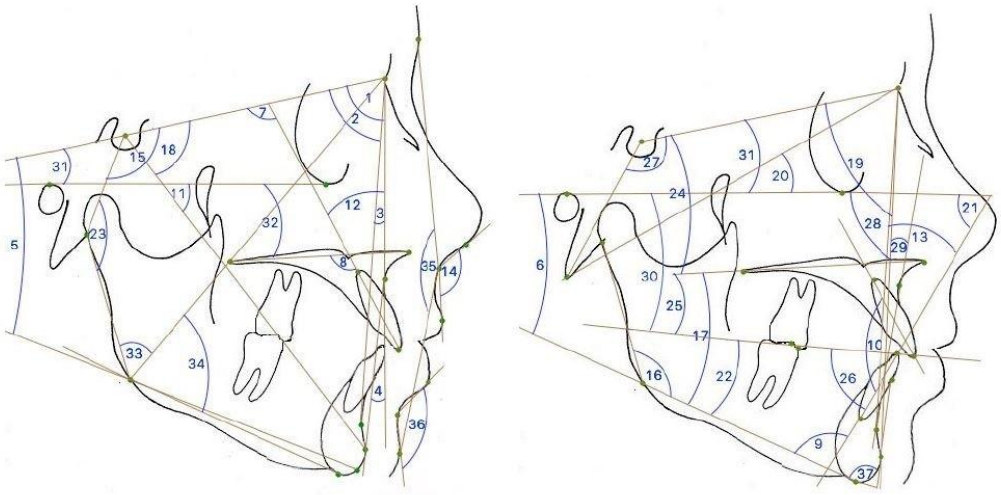
The variables that did not show a normal distribution were evaluated using the Mann-Whitney U test and the results are presented in Table 3. Except for the L1-NB/Pg-NB, no significant difference was observed between the groups in other variables.

The 14 variables that showed significant differences between the groups as a result of the t test were analysed separately by discriminant analysis and the data related to the classification success of the variables are presented in Table 4. The highest percentage of correct classification (82.1%) was found for the variable Pg-NB (mm). A logistic regression analysis was performed for the variable L1-NB/Pg-NB, which showed a significant difference between the groups as a result of the Mann-Whitney U test. According to the results, if the value of L1-NB/Pg-NB increases by 1 unit, the odds of failure increased 1.6-fold. L1-NB/Pg-NB correctly classified the groups by 75%.



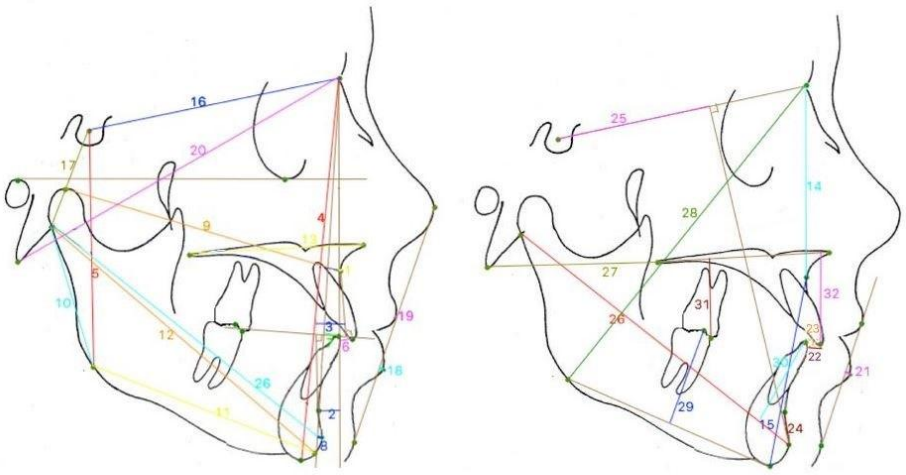
1-) Nasion (N), 2-) Sella (S), 3-) Porion (Po), 4-) Orbitale (Or), 5-) Basion (Ba), 6-) Pogonion (Pg), 7-) Gnathion (Gn), 8-) Gonion (Go), 9-) Menton (Me), 10-) Articulare (Ar), 11-) Condylion (Co), 12-) L point, 13-) Anterior Nasal Spine (ANS), 14-) Posterior Nasal Spine (PNS), 15-) A point, 16-) B point, 17-) U1i, 18-) L1i, 19-) L1a, 20-) U1a, 21-) Infradentale (Id), 22-) U6, 23-) L6, 24-) Soft tissue Glabella (G'), 25-) Soft tissue Nasion (N'), 26-) Pronasale (Prn), 27-) Columella (Col), 28-) Subnasale (Sn), 29-) Soft tissue A point (A'), 30-) Labrale süperior (Ls), 31-) Labrale inferior (Li), 32-) Soft tissue B point (B'), 33-) Soft tissue Pogonion (Pg')

Figure 1: Landmarks used in the study.



1-) SNA (°), 2-) SNB (°), 3-) ANB (°), 4-) (NA-APog) (°), 5-) SN-GoGn (°), 6-) FMA (°), 7-) U1-SN (°), 8-) U1-PP (°), 9-) IMPA (°), 10-) Interincisal angle (°), 11-) SGn-FH (°), 12-) U1-NA (°), 13-) L1-NB (°), 14-) Nasolabial angle (°), 15-) Saddle angle (°), 16-) Gonial angle (°), 17-) PP-MP (°), 18-) SGn-SN (°), 19-) SN-NPog (°), 20-) Cranial deflection angle (°), 21-) FMIA (°), 22-) OP-MP (°), 23-) Articuler angle (°), 24-) SN-PP (°), 25-) OP-PP (°), 26-) L1-OP (°), 27-) SN-Ba (°), 28-) Facial angle (°), 29-) NPg-AB (°), 30-) OP-FH (°), 31-) FH-SN (°), 32-) FH-PP (°), 33-) Ar-Go-N (°), 34-) N-Go-M (°), 35-) Facial convexity angle (°), 36-) Labiomental angle (°), 37-) IdPg-MP (°)

Figure 2: Angular measurements used in the study.



1-) A-Nperp (mm), 2-) Pg-Nperp (mm), 3-) Wits appraisal (mm), 4-) N-Me (mm), 5-) S-Go (mm), 6-) U1-NA (mm), 7-) L1-NB (mm), 8-) Pg-NB (mm), 9-) Co-A (mm), 10-) Ar-Go (mm), 11-) Go-Gn (mm), 12-) Co-Gn (mm), 13-) ANS-PNS (mm), 14-) N-ANS (mm), 15-) ANS-Me (mm), 16-) S-N (mm), 17-) S-Ar (mm), 18-) Lower lip-E-plane (mm), 19-) Upper lip-E-plane (mm), 20-) N-Ba (mm), 21-) Lower lip-H line (mm), 22-) Overjet (mm), 23-) Overbite (mm), 24-) B-Pg (mm), 25-) S-L (mm), 26-) Ar-Pog (mm), 27-) PNS-Ba (mm), 28-) N-Go (mm), 29-) L6-MP (mm), 30-) Lli-MP (mm), 31-) U6-PP (mm), 32-) Uli-PP (mm), 33-) Co-Gn (mm), 34-) N-ANS/ANS-M (mm), 35-) L1-NB/Pg-NB (ratio), 36-) S-Go/N-Me (ratio), 37-) S-Ar/Ar-Go (ratio), 38-) S-N/Go-Gn (ratio)

Figure 3: Linear and rational measurements used in the study.

Table 2. Comparison of variables with normal distribution

Variable	Group	Mean	Standard	t	P[a]
SNA (°)	Success group	80.57	4.07	-0.005	0.996
	Failure group	80.58	2.85		
SNB (°)	Success group	73.91	3.77	-0.119	0.906
	Failure group	74.06	3.22		
ANB (°)	Success group	6.68	1.81	0.328	0.746
	Failure group	6.48	1.39		
NA-APo (°)	Success group	11.56	4.31	-0.485	0.631
	Failure group	12.24	2.97		
SN-GoGn (°)	Success group	32.91	5.64	-1.081	0.289
	Failure group	35.07	4.93		
U1-SN (°)	Success group	109.90	7.33	2.280	**0.033***
	Failure group	104.76	4.19		
U1-PP (°)	Success group	119.27	5.61	2.604	**0.015***
	Failure group	114.26	4.50		
IMPA (°)	Success group	98.58	7.37	-0.658	0.516
	Failure group	100.31	6.56		
SGn-FH (°)	Success group	62.92	4.22	-0.807	0.427
	Failure group	64.09	3.41		
U1-NA (°)	Success group	29.31	5.66	2.837	**0.009***
	Failure group	24.20	3.69		
Nasola-bial angle	Success group	115.76	7.16	0.169	0.867
	Failure group	115.22	9.467		
Saddle angle	Success group	127.71	7.39	1.162	0.256
	Failure group	124.94	4.96		
Gonial angle	Success group	129.21	3.67	-1.687	0.107
	Failure group	132.54	6.38		
PP-MP (°)	Success group	25.90	5.75	-1.194	0.243
	Failure group	28.20	4.34		
SGn-SN (°)	Success group	69.92	4.22	-0.807	0.427
	Failure group	71.09	3.41		
SN-NPog (°)	Success group	75.54	3.78	0.487	0.630
	Failure group	74.89	3.35		

NBa-FH (°)	Success group	29.59	2.84	-0.132	0.896
	Failure group	29.71	2.27		
FMIA (°)	Success group	58.17	6.72	2.351	**0.027***
	Failure group	52.66	5.65		
OD-MD (°)	Success group	20.21	2.09	-0.469	0.644
	Failure group	20.78	4.06		
Articuler angle	Success group	138.37	7.76	-0.742	0.465
	Failure group	140.20	4.98		
SN-PP (°)	Success group	9.38	4.09	-0.077	0.940
	Failure group	9.49	3.27		
OD-PP (°)	Success group	5.70	4.78	-1.084	0.288
	Failure group	7.41	3.45		
L1-OD (°)	Success group	61.23	6.61	1.055	0.301
	Failure group	58.92	4.82		
SN-Ba (°)	Success group	134.77	6.59	1.905	0.068
	Failure group	130.57	4.97		
FH-NPo (°)	Success group	87.57	2.67	1.931	0.064
	Failure group	85.53	2.92		
OP-FH(°)	Success group	3.06	3.28	-2.318	**0.029***
	Failure group	6.26	3.99		
FH-SN (°)	Success group	12.03	2.33	1.555	0.132
	Failure group	10.64	2.38		
FH-PP (°)	Success group	-2.64	3.38	-1.167	0.254
	Failure group	-1.16	3.36		
Ar-Go-N (°)	Success group	54.88	3.16	-0.213	0.833
	Failure group	55.18	4.22		
N-Go-Me (°)	Success group	74.32	4.63	-1.852	0.075
	Failure group	77.36	4.02		
G′-Sn-Po′ (°)	Success group	155.71	4.63	1.231	0.229
	Failure group	153.54	4.67		
(Li-B′-Pg′) (°)	Success group	110.56	11.15	-2.782	**0.010***
	Failure group	122.49	11.54		
İdPg-MP (°)	Success group	70.64	5.51	-2.050	0.051
	Failure group	74.85	5.36		
	Success group	2.56	3.41	1.248	0.223

A-Nperp	Failure group	1.17	2.37		
Pg-Nperp (mm)	Success group	-4.37	4.64	2.039	0.052
	Failure group	-8.36	5.67		
Wits (mm)	Success group	7.12	3.17	1.074	0.293
	Failure group	5.91	2.79		
N-Me (mm)	Success group	107.16	6.08	-2.356	**0.026***
	Failure group	113.01	7.04		
S-Go (mm)	Success group	68.85	4.13	-1.509	0.143
	Failure group	71.46	4.97		
U1-NA (mm)	Success group	5.53	1.77	0.048	0.962
	Failure group	5.50	1.32		
L1-NB (mm)	Success group	5.05	2.30	-3.098	**0.005***
	Failure group	7.38	1.62		
Pg-NB (mm)	Success group	2.8	1.02	3.986	**0.000***
	Failure group	1.51	0.77		
Co-A (mm)	Success group	83.66	5.96	-0.620	0.540
	Failure group	84.97	5.16		
Ar-Go (mm)	Success group	43.45	3.85	0.141	0.889
	Failure group	43.26	3.38		
Co-Gn (mm)	Success group	107.07	5.84	-1.054	0.302
	Failure group	109.43	6.00		
ANS-PNS (mm)	Success group	53.84	3.93	-0.027	0.979
	Failure group	53.87	2.96		
N-ANS (mm)	Success group	50.74	3.25	-1.468	0.154
	Failure group	52.56	3.32		
ANS-Me (mm)	Success group	59.87	5.24	-2.036	0.052
	Failure group	63.92	5.28		
S-N (mm)	Success group	65.98	3.02	-1.527	0.139
	Failure group	68.11	4.26		
S-Ar (mm)	Success group	31.84	3.30	-1.722	0.097
	Failure group	33.90	3.02		
Lİ-E (mm)	Success group	-0.19	2.17	-2.266	**0.032***
	Failure group	2.10	3.09		
Ls-E (mm)	Success group	-0.24	1.46	-1.689	0.103
	Failure group	1.00	2.33		

N-Ba (mm)	Success group	100.68	6.10	-0.698	0.491
	Failure group	102.24	5.70		
Li-H (mm)	Success group	-0.036	1.85	-2.180	**0.038***
	Failure group	1.60	2.11		
Overjet (mm)	Success group	9.21	2.45	2.675	**0.013***
	Failure group	7.13	1.56		
B-PG (mm)	Success group	6.18	1.33	1.799	0.084
	Failure group	5.39	0.98		
S-L (mm)	Success group	40.56	8.16	0.161	0.873
	Failure group	40.11	6.27		
Ar-Pg (mm)	Success group	94.59	5.64	-0.777	0.444
	Failure group	96.14	4.88		
PNS-Ba (mm)	Success group	42.81	3.30	0.293	0.772
	Failure group	42.42	3.66		
L6-MP (mm)	Success group	25.89	2.19	-2.633	**0.014***
	Failure group	28.31	2.64		
L1-MP (mm)	Success group	37.29	2.68	-2.585	**0.016***
	Failure group	39.86	2.60		
U6-PP (mm)	Success group	20.11	1.42	-1.549	0.134
	Failure group	21.24	2.31		
U1-PP (mm)	Success group	26.13	2.8	-1.457	0.157
	Failure group	27.64	2.7		
Co-Gn – Co-A (mm)	Success group	19.7	3.29	-0.669	0.509
	Failure group	20.49	2.97		
S-Go/N-Me (ratio)	Success group	64.33	3.52	0.738	0.467
	Failure group	63.31	3.75		
S-Ar/Ar-Go (ratio)	Success group	76.41	9.39	-1.376	0.181
	Failure group	80.8	7.39		
S-N/Go-Gn (ratio)	Success group	98.02	6.1	-0.838	0.41
	Failure group	100.35	8.43		

[a] Independent samples t-test, * Statistically significant

Table 3. Comparison of variables with non-normal distribution

Variable	Group	Mean	Standard deviation	z	P[a]
FMA (°)	Success group	23.25	4.04	-1.930	0.054
	Failure group	27.03	4.32		
Interincisal angle	Success group	116.26	8.17	-0.873	0.382
	Failure group	117.25	6.83		
L1-NB (°)	Success group	27.76	7.85	-1.288	0.198
	Failure group	32.08	4.63		
FP-AB (°)	Success group	-13.26	3.61	-1.632	0.103
	Failure group	-10.76	2.21		
GO-GN (mm)	Success group	67.56	5.37	-0.253	0.800
	Failure group	68.16	5.36		
N-GO (mm)	Success group	106.57	5.42	-1.057	0.291
	Failure group	109.57	7.16		
N-ANS/ANS-Me (ratio)	Success group	0.84	0.076	-6.56	0.512
	Failure group	0.82	0.07		
Overbite (mm)	Success group	5.23	2.23	-1.890	0.059
	Failure group	4.14	1.93		
L1-NB/Pg-NB (ratio)	Success group	2.48	2.39	-3.355	**0.001***
	Failure group	8.82	13.31		

[a]Mann-Whitney U test, * Statistically significant

Table 4. Discriminant values and classification success percentages in discriminant analysis

	Discriminant value	Categorisation ability of the success group (%)	Categorisation ability of the failure group (%)	Average categorisation ability for both groups (%)
U1SN (°)	107 (+)	57.1	64.3	60.7
U1PP (°)	116.5 (+)	50	64.3	57.1
U1NA (°)	26.7 (+)	71.4	85.7	78.6
FMIA (°)	55.5 (+)	64.3	64.3	64.3
ODFH (°)	4.7 (-)	71.4	57.1	64.3
Ls-B'-Pg' (°)	116.7 (-)	71.4	64.3	67.9
N-ME (mm)	110.1 (-)	78.6	64.3	71.45
L1-NB (mm)	6.2 (-)	78.6	71.4	75
Pg-NB (mm)	2.2 (+)	78.6	85.7	82.1
Li-H (mm)	0.82 (-)	78.6	57.1	67.9
Li-E (mm)	1 (-)	78.6	57.1	67.9
Overjet (mm)	8.2 (+)	64.3	71.4	67.9
L6-MP (mm)	27.1 (-)	64.3	64.3	64.3
L1-MP (mm)	38.56 (-)	71.4	64.3	67.9

Discussion

In this study, the ANB angle was used to classify treatment outcomes as successful or unsuccessful. A reduction of 3º or more in the angle was considered a success of functional therapy, and a reduction of 1º or less was considered unsuccessful. Cases with a reduction between 1° and 3° were not included in the study, as it would be difficult to determine whether this was a growth-related reduction or a success of functional treatment.

Just as there are studies using the ANB angle as a success criterion (14,15), there are also studies using different criteria (16,17). Patel et al have investigated the cephalometric determinants of successful functional appliance therapy and they have used ANB as a success criterion (14). Caldwell and Cook have investigated on predicting the outcome of twin block functional appliance treatment and they have used changes in overjet as a success criterion (17). In the present study, as overjet is a data that can change easily depending on the inclination of the incisors, we preferred to use the ANB angle, which is a more skeletal indicator.

In this study, both groups were created by patients who were at the pubertal peak period. The stage of growth and development was measured using the cervical vertebral maturation method (CVM). This method has been shown to be a reliable and reproducible method for determining the maturation level (18). Franchi and Baccetti have also used the same method in their studies, and included patients who were in the Stage 316. Although the growth-development period is a crucial factor in the success of the functional appliances, some studies have either ignored this issue or used chronological age, which is unreliable (15,19-21). We think that this situation makes these results contradictory.

Out of the seventy-five cephalometric variables analysed, the Independent Samples t-test revealed statistically significant differences in fourteen variables between the success and failure groups. Additionally, the Mann-Whitney U test showed statistically significant differences in one variable between the success and failure groups. Three of the variables that differed significantly (U1-SN(º), U1-PP(º) and U1-NA(º)) were the angles related to the upper incision inclination and were found to be higher in the success group. Consistent with these data, the amount of initial overjet was also statistically higher in the success group (Table 2).

In some patients with Class II Division 1 malocclusion, the lower lip is posturally positioned on the palatal surface of the upper lip. In such cases, the lower lip pressure causes the upper incisors to protrude, the lower incisors to retrude, and the amount of overjet increases. Although the malposition of the lower lip is initially a consequence of the Class II Division 1 malocclusion, it worsens the situation over time and becomes the cause of the malocclusion. In these patients, the treatment is successful because the functional appliance also acts as a habit breaker and removes the obstacle to the forward growth of the mandible. It was also found that Li-E and Li-H distances were statistically lower in the success group. We think that these findings are also related to the habitual positioning of the lower lip behind the upper incisors in some patients and that it proves the accuracy of the hypothesis described above. In such patients, while the sagittal development of the mandible continues normally, the lower lip is positioned farther back than it should be because it is blocked by the upper incisors.

N-Me, L6-MP, and L1-MP distances and OP-FH were found to be statistically lower in the success group. All these measurements are related to the vertical growth pattern of the mandible. Functional treatment was found to be more successful in patients with a low angle

growth pattern and counter clockwise mandibular rotation. In a similar study which also aimed to investigate cephalometric determinants about successful functional appliance therapy by Patel et al., they reported that both the lower and upper anterior face pretreatment heights were lower in the successful group (14). The data obtained from the present study revealed that there was no difference between the two groups in terms of the sagittal size of the mandible, but there was a difference in the measurements related to the direction of growth. This suggests that the direction of growth, rather than the size of the lower jaw, is a factor in the success of the treatment. Interestingly, the classical cephalometric measurements used to evaluate the vertical growth pattern; Go-GN-SN and FMA angles, did not show any difference between the two groups. Wide variations in the location of sella and porion in the cranium may be the cause of this situation.

Although the sagittal size of the mandible was similar in both groups, the measurements of Pg-NB distance and Li-B'-Pg' angle revealed differences in the morphology of the symphysis between the two groups. It was found that the success group had a more pronounced chin prominence. According to the results of the present study, a prominent symphysis formation is a serious sign that the functional treatment will be successful.

Our study may be considered similar to the study by Patel et al. in some aspects. In their study, the researchers used three different functional appliances; medium opening activator, Twin Block and Frankel II. 28 patients were divided into two groups as successful and less successful. However, there is no data on how many of the 13 patients in the study were treated with which appliance. In addition, the medium opening activator, one of the three appliances used, is an appliance designed to allow the lower molars to elongate and is mainly used in skeletal class II patients with a deep bite. Although the Frankel II is a functional appliance, it has a different working principle. It reorganises the muscle activity that determines the position and function of the mandible. This creates pressure from the muscles and surrounding soft tissues onto the hard tissues, and the redirection of the forces created by the appliance reshapes the form and function of the retruded mandible. In the present study, both the success and failure groups were treated with the same appliance, allowing a much more consistent interpretation of the results obtained.

Conclusions

This study was carried out in order to determine the cephalometric variables that can be used to predict the treatment success in patients treated with the Twin Block appliance. Of the seventy-five cephalometric measurements investigated, fifteen measurements showed significant differences between the groups. The correct classification rates of these variables were calculated for each variable, and it was observed to be in the range of 82.1% (Pg-NB) to 57.1% (U1-PP°).

The highest correct classification success belonged to Pg-NB (mm) (82.1%). It showed that the tip of chin was more pronounced in the success group.

The success group had a higher value of U1NA (°) and a lower value of L1-NB (mm) than the failure group. Prediction success percentages were 78.6% and 75%, respectively.

The value of the N-Me (mm) was lower in the success group.

This study showed that patients with a prominent chin tip, protrusive upper incisors, retrusive lower incisors, and lower anterior face height were more likely to be successfully treated with the Twin Block appliance.

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Research Article

Onkolojik Tedavi Gören Çocuk Hastaların Ağız İçi Bulgularının Değerlendirilmesi: Kesitsel Bir Çalışma

Didem Odabaşı[1*], Sibel Arslan Kayaaltı[2], Nihal Beldüz Kara[1]

[1]Ordu Üniversitesi, Diş Hekimliği Fakültesi, Pedodonti Anabilim Dalı, Ordu, Türkiye.
[2]Özel Poliklinik, Kayseri, Türkiye

*Corresponding author: dt_odabasi@hotmail.com

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Onkolojik Tedavi Gören Çocuk Hastaların Ağız İçi Bulgularının Değerlendirilmesi: Kesitsel Bir Çalışma

Didem Odabaşı, Sibel Arslan Kayaaltı, Nihal Beldüz Kara

Özet

Amaç: Kanser vücuttaki bazı hücrelerin kontrolsüz olarak çoğalması nedeniyle oluşan ve her yıl yüksek oranda ölüm ile sonuçlanan hastalıkların başında gelmektedir. Kanser tedavilerinde yüksek sitotoksisite nedeniyle birçok yan etki görülmektedir. Mukozitis, diş etlerinde kanama, ağız kuruluğu, ağrı, tat kaybı ve değişikliği oral komplikasyonlardan başlıcalarıdırBu çalışmanın amacı Tıp Fakültesi Hematoloji Onkoloji Servisinde tedavi gören 3-18 yaş arası çocuk hastaların ağız içi bulgularının ve oral hijyen alışkanlıklarının değerlendirilmesidir.

Malzeme ve Yöntemler: Hematoloji Onkoloji Servisinde tedavi gören 3 ile 18 yaş arasında 50 çocuk hasta ebeveynlerinin eşliğinde muayene edildi. Hastaların ebeveynlerinden bilgilendirilmiş onam formu alındı. Hastaların ebeveyn eşliğinde hastalığı, kemoterapi/radyoterapi durumu, tedavi süresi, beslenme şekli, diyet ve ağız bakım alışkanlıkları sorgulandı. Hastaların DMFT indeksleri ölçüldü. Çocuklarda ağız kuruluğu, tat kaybı ve oral mukozit varlığı kayıt altına alındı.

Bulgular: Çalışmamıza katılan hastaların sosyo-demografik verileri incelendiğinde yaş ortalamaları 9,6 ± 4,45 (min 3- max 18)'tir ve %70'i (n=35) erkek, %30'u (n=15) kız çocuktur. DMFT indekslerinin ortalaması 4,1 ± 3,46 (min 0- max 13)'dır. Hastaların aldıkları tanılar değerlendirildiğinde en sık akut lenfoblastik lösemi (ALL) (n=25) tümörü nedeniyle hastanede tedavi altında oldukları belirlenmiştir. Tedaviye bağlı oral yan etkiler incelendiğinde %24'ünün (n=12) tat kaybı yaşadığını, %34'ünün (n=17) oral mukozit olduğu, %42'sinin (n=21) de ağız kuruluğu şikayetleri olduğu belirlenmiştir. Yapılan analiz sonuçlarına göre tedavi şekli ile ağız kuruluğu arasında (p=,009) ve tedavi şekli ile tat kaybı arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur (p=,027).

Sonuç: Kanser ve kanser tedavisinde uygulanan antineoplastik protokoller hastanın ağız sağlığı üzerinde olumsuz etkilere sebep olmakta ve bu da hastanın yaşamını oldukça zorlaştırmaktadır. Bir çocuk diş hekiminin tedavi öncesi ve tedavi sırasındaki müdahalesi ile etkili bir ağız bakımı sağlanabilir ve palyatif bakımda önemli bir fark yaratılabilir. Tedavi süresince ağız sağlığının korunmasında çocuk doktoru, çocuk diş hekimi ve onkolog iş birliği ile multidisipliner çalışma oldukça büyük önem taşımaktadır.

Anahtar kelimeler: Çocuk diş hekimliği, kemoterapi, mukozitis, oral komplikasyon, radyoterapi.

Abstract

Objective: Cancer is one of the leading causes of disease-related deaths worldwide, primarily resulting from the uncontrolled proliferation of certain cells in the body. Cancer treatments are often associated with significant side effects due to high cytotoxicity. Among the most common oral complications are mucositis, gingival bleeding, xerostomia, pain, and loss or alteration of taste. This study aims to evaluate the intraoral findings and oral hygiene habits of pediatric patients aged 3 to 18 years who are receiving treatment in the Hematology-Oncology Department of a Faculty of Medicine.

Materials and Methods: Fifty pediatric patients aged between 3 and 18 years, undergoing treatment in the Hematology-Oncology Department, were examined in the presence of their parents. Informed consent was obtained from the parents of all participants. Data were collected regarding the patients' medical diagnoses, chemotherapy/radiotherapy status, duration of treatment, nutritional patterns, dietary habits, and oral hygiene routines. The DMFT (Decayed, Missing, and Filled Teeth) index was recorded. Additionally, the presence of xerostomia, taste alterations, and oral mucositis was noted. Analysis results revealed a statistically significant relationship between treatment type and dry mouth ($p=0.009$) and between treatment type and loss of taste ($p=0.027$).

Results: Sociodemographic analysis revealed that the mean age of the participants was 9.6 ± 4.45 years (range: 3–18 years), with 70% (n=35) being male and 30% (n=15) female. The mean DMFT index was 4.1 ± 3.46 (range: 0–13). The most common diagnosis among the patients was acute lymphoblastic leukemia (ALL), observed in 50% (n=25) of cases. Evaluation of treatment-related oral side effects showed that 24% (n=12) of patients experienced taste loss, 34% had oral mucositis, and 48% reported symptoms of xerostomia.

Conclusion: Cancer and the antineoplastic protocols employed in its treatment can adversely affect patients' oral health, significantly impacting their quality of life. The involvement of a pediatric dentist before and during treatment can help ensure effective oral care, making a meaningful contribution to palliative care. A multidisciplinary approach involving pediatricians, pediatric dentists, and oncologists is of paramount importance in maintaining oral health throughout the treatment process.

Keywords: Chemotherapy, mucositis, oral complications, pediatric dentistry, radiotherapy.

Giriş

Kanser vücuttaki bazı hücrelerin kontrolsüz olarak çoğalması nedeniyle oluşan ve her yıl yüksek oranda ölüm ile sonuçlanan hastalıkların başında gelmektedir (1). Kanser popülasyonunun önemli bir bölümünü pediatrik hasta grubu oluşturmaktadır (2). Türkiye'de her yıl yaklaşık 2500-3000 yeni pediatrik kanser vakası bildirilmektir (3). Lösemi, lenfoma, beyin-spinal kord tümörleri, retinoblatom ve kemik tümörleri gibi kanserler en sık görülen çocukluk çağı kanserleri olmakla birlikte %30 oranında ALL ilk sırada yer almaktadır (2, 4).

Kanser tedavisinde birçok farklı yöntem kullanılmakta ve sağlık alanında yaşanan gelişmelerle beraber yeni tedavi yöntemleri de eklenmektedir. En sık başvurulan tedavi yöntemleri ise kemoterapi, radyoterapi ve cerrahi tedavidir (5). Lokal problemlerin ortadan kaldırılmasında cerrahi tedavi ve radyoterapi beraber uygulanırken, kemoterapi sistemik durumları kontrol altına almak ve tedavi etmek amacıyla uygulanmaktadır. Radyoterapide amaç kanserli hücrelerin öldürülmesi ve hedef bölgenin küçültülmesidir. Kemoterapi tedavisinde ise amaç kemoterapötik ajanlar kullanarak hücre bölünmesini durdurmak ya da apopitozu indükleyerek hücre ölümüne yol açmaktır (6). Bu tedavi protokollerinin sitotoksitesinin yüksek olmasından dolayı hem kemoterapi hem de radyoterapinin hastalarda birçok yan etkisi bulunmaktadır. Radyoterapi ve kemoterapi alan hastaların immün sisteminin baskılanmasıyla vücutta fiziksel ve sistemik değişimler meydana gelmekte, enfeksiyon riskinde artış görülmektedir (6, 7).

Kemoterapi ve radyoterapi sonrası oral komplikasyon gelişme riski pediatrik hastalarda yetişkin hastaların üç katı kadardır. Bu yüzden kemoterapi ve radyoterapi alan pediatrik kanser hastalarının ağız sağlığının korunması oldukça büyük öneme sahiptir (8, 9).

Kanser tedavilerinde yüksek sitotoksisite nedeniyle birçok yan etki görülmektedir (10). Tedaviye bağlı oral komplikasyonlar tedavi sırasında veya tedavinin hemen sonrasında gelişebilmektedir. Mukozitis, diş etlerinde kanama, ağız kuruluğu, ağrı, tat kaybı ve değişikliği oral komplikasyonlardan başlıcalarıdır. Kanser tedavisi aynı zamanda uzun yıllar devam eden problemlere de neden olabilmektedir. Ağız kuruluğu, kemik nekrozu, diş demineralizasyonu ve diş çürükleri, TME rahatsızlığı, trismus, oral ülserasyonlar, tat kaybı kanser tedavisinin geç/kronik komplikasyonları arasında sayılabilmektedir (11, 12). Yoğun doz radyoterapi veya kemoterapi gören hastalarda yaşam kalitesini olumsuz etkileyen aguzi ve disguzi

sıklıkla görülmektedir. Radyoterapi gören hastalarda direk tat reseptörlerinde oluşan değişiklikler ve sekonder enfeksiyonlarla sonuçlanan tükürük miktarındaki azalma nedeniyle tat duyusu bozuklukları oldukça sık görülmektedir. Kemoterapi tedavisinde özellikle sülfidril grubu kemoterapötik ilaç kullanan hastalarda; sülfidril grubu çinko gibi ağır metalleri bağladığı için çinko eksikliğine bağlı olarak tat bozuklukları oluşmaktadır (13, 14, 15).

Mukozit, radyasyon tedavisinin başlamasından sonraki ikinci haftada ortaya çıkabilir, daha sonra kademeli olarak yoğunlaşabilir ve tedavinin tamamlanmasından sonra iki ila üç hafta sürebilir. Başlangıçta, etkilenen mukoza hiperemi sonucu kırmızı ve ödemli görünür. Mukoza daha sonra soyulur, ülsere olur (16). Tüm bu komplikasyonların şiddeti; bireysel faktörlere, uygulanan tedavinin türüne, süresine ve dozuna göre değişiklik gösterebilir (17, 18).

Bu çalışmanın amacı 19 Mayıs Üniversitesi Tıp Fakültesi Hematoloji Onkoloji Servisinde tedavi gören 3-18 yaş arası çocuk hastaların ağız içi bulgularının ve oral hijyen alışkanlıklarının değerlendirilmesidir.

Malzeme ve Yöntemler

Kesitsel bir araştırma olan çalışmamız Ondokuz Mayıs Üniversitesi Sağlık Uygulama ve Araştırma Merkezi ile Ordu Üniversitesi Klinik Araştırmalar Etik Kurulu Başkanlığından 2022/300 numarası ile yazılı izin alındıktan sonra, 1 Ocak 2023 – 1 Şubat 2023 tarihleri arasında Tıp Fakültesi Hematoloji Onkoloji Servisinde tedavi amacıyla yatan hastalar üzerinde yapıldı. Sistemik hastalığı sebebi ile ağız bulgusu görülen ve özel sağlık bakımı gerektiren, izolasyon önlemleri dahilinde muayene edilemeyen hastalar çalışma dışı bırakıldı. Hematoloji Onkoloji Servisinde tedavi gören 3 ile 18 yaş arasında 50 çocuk hasta ebeveynlerinin eşliğinde muayene edildi. Hastaların ebeveynlerinden bilgilendirilmiş onam formu alındı. Hastaların ebeveyn eşliğinde hastalığı, kemoterapi/radyoterapi durumu, tedavi süresi, beslenme şekli, diyet ve ağız bakım alışkanlıkları sorgulandı. Hastaların DMFT indeksleri ölçüldü. Çocuklarda ağız kuruluğu, tat kaybı ve oral mukozit varlığı sorgulandı. Tüm veriler kaydedildi.

İstatiksel Analiz

Toplanan verilerin istatiksel analizinde SPSS (V22.0) kullanıldı. Tanımlayıcı istatistikler, ortalama (±) standart sapma, frekans dağılımı ve yüzde olarak sunuldu. Kategorik değişkenlerin karşılaştırılmasında Ki-Kare testi uygulandı. Verilerin normalite testleri Kolmogorov-Smirnov testi ile bakılarak normal dağılım gösterenler için varyans analizi (One way Anova)

testi, normal dağılım göstermeyen veriler için ise Mann-Whitney U testi yapılmasına karar verildi.

Bulgular

Çalışmamız onkolojik tedavi gören 50 çocuk hasta ile gerçekleştirilmiştir. Çalışmamızda radyoterapi, kemoterapi veya radyoterapi ile kemoterapinin kombinasyonu tedavi olan hastaların ağız içi bulgulara etkisi incelenmeye çalışıldı.

Çalışmamıza katılan hastaların sosyo-demografik verileri incelendiğinde yaş ortalamaları 9,6 ± 4,45 (min 3- max 18)'tir ve %70'i (n=35) erkek, %30'u (n=15) kız çocuktan oluşmaktadır. DMFT indekslerinin ortalaması 4,1 ± 3,46 (min 0- max 13) olarak tespit edildi.

Hastaların aldıkları tanılar değerlendirildiğinde en sık ALL (n=25) gözlenirken, sonrasında değişen sıklıklarda (n=4 - n=1) akut myoloblastik lösemi, burkit, epandinom, ewing sarkomu, glioblastom, lenfoma, hodgkin lenfoma, hepatoblastom, nöroblastom, osteosarkom, piliosilik, rabdomiyosarkom vespinal kord tümörü nedeniyle hastanede tedavi altında oldukları belirlendi.

Hastaların tedavilerine ilişkin verilerin dağılımları incelendiğinde hastaların %82'sinin (n=41) kemoterapi, %18'inin ise kemoterapiye ek olarak radyoterapi ile tedavi edilmeye çalışıldıkları görüldü.

Tedavi görme sürelerinin ortalaması 6,74 ay ± 13,96 (min 1- max 84)'dır. Tedaviye bağlı oral yan etkiler incelendiğinde %24'ünün (n=12) tat kaybı yaşadığı, %34'ünün (n=17) oral mukozit olduğu, %42'sinin (n=21) de ağız kuruluğu şikayetleri olduğu bilgisi alındı.

Çalışmaya katılan 50 hastanın 12'sinde tat kaybı saptanmıştır. Tat kaybı yaşayan 7 hasta sadece kemoterapi alırken, 5 hasta hem kemoterapi hem de radyoterapi ile tedavi edilmiştir (Tablo 1). Tedavi şekli ile tat kaybı arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur (p=,027) (Tablo 2).

Tablo 1. Tedavi şekli ile tat kaybı arasındaki ilişki

Tedavi Şekli	**Tat Kaybı Var**	**Tat Kaybı Yok**	**Toplam**
Kemoterapi	7	34	41
Kemoterapi ve Radyoterapi	5	4	9
Toplam	**12**	**38**	**50**

Tablo 2. Tedavi şeklinin tat kaybına etkisi

Test Adı	(χ^2 / p)	df	p*
Pearson Ki-Kare	5,992[a]	1	,014
Continuity Correction Ki-Kare	4,068	1	,044
Likelihood Ratio	5,265	1	,022
Fisher's Exact Test (2 yönlü)	-	-	**,027**
Linear-by-Linear	5,872	1	,015

Çalışmaya katılan 50 hastanın 17'sinde (%34) oral mukozit gelişmiştir. Mukozit gelişen hastalardan 13'ü yalnızca kemoterapi alırken, 4'ü hem kemoterapi hem de radyoterapi ile tedavi edilmiştir (Tablo 3). Tedavi şekli ile oral mukozit gelişimi arasındaki ilişkiyi değerlendirmek amacıyla yapılan istatistiksel analizler sonucunda anlamlı bir ilişki saptanmamıştır (p=,467)(Tablo 4).

Tablo 3. Tedavi şekli ile mukozit arasındaki ilişki

Tedavi Şekli	Mukozit Var	Mukozit Yok	Toplam
Kemoterapi	13	28	41
Kemoterapi ve Radyoterapi	4	5	9
Toplam	**17**	**33**	**50**

Tablo 4. Tedavi şeklinin oral mukozit oluşumuna etkisi

Test Adı	(χ^2 / p)	df	p*
Pearson Ki-Kare	,534[a]	1	,465
Continuity Correction Ki-Kare	,117	1	,732
Likelihood Ratio	,517	1	,472
Fisher's Exact Test (2 yönlü)	-	-	**,467**
Linear-by-Linear	,523	1	,470

Tedavi şekli ile ağız kuruluğu arasındaki ilişkiyi değerlendirmek amacıyla yapılan çapraz tablo analizinde, sadece kemoterapi alan hastaların %39,0'ında (16/41), hem kemoterapi hem radyoterapi alan hastaların ise %88,9'unda (8/9) ağız kuruluğu görüldüğü tespit edilmiştir (Tablo 5). Tedavileri sırasında ağız kuruluğu yaşayan hastaların 16'sının sadece kemoterapi ile tedavi edildiği, 8'inin ise hem kemoterapi hem radyoterapi ile tedavi edildiği belirlenmiştir. Yapılan analiz sonuçlarına göre tedavi şekli ile ağız kuruluğu arasında istatistiksel olarak anlamlı bir ilişki olduğu belirlenmiştir (p=,009) (Tablo 6).

Tablo 5. Tedavi şekli ile ağız kuruluğu arasındaki ilişki

Tedavi Şekli	Ağız Kuruluğu Var	Ağız Kuruluğu Yok	Toplam
Kemoterapi	16	25	41
Kemoterapi ve Radyoterapi	8	1	9
Toplam	24	26	50

Tablo 6. Tedavi şeklinin ağız kuruluğu oluşumuna etkisi

Test Adı	(χ^2 / p)	df	p*
Pearson Ki-Kare	7,352	1	**0,465**
Continuity Correction Ki-Kare	5,490	1	0,007
Likelihood Ratio	8,109	1	0,019
Fisher's Exact Test (2 yönlü)	-	-	**0,009**
Fisher's Exact Test (1 yönlü)	-	-	0,008
Linear-by-Linear	7,205	1	0,007

Tartışma

Çocuklukta en sık görülen kanser türü lösemilerdir. Yılmaz ve arkadaşları yaptıkları tez çalışmasında löseminin çocukluk çağı kanserlerinin en sık (%97) karşılaşılan formu olduğunu belirtmişlerdir. Lösemiler arasında ALL %75 oranla ilk sırada yer almaktadır (19). Çalışmamızda da kemoterapi ve radyoterapi tedavisi gören 50 pediatrik hastanın %50'sinin (n=25) ALL sebebi ile tedavi gördüğü tespit edilmiştir.

Çocukluk çağı kanserlerinin tedavisinde kemoterapi, radyoterapi ve cerrahi yöntemler en sık kullanılan tedavi yöntemleridir (20). Çalışmamıza dahil edilen 50 pediatrik hastanın %82'sinin (n=41) kemoterapi, %18'inin (n=9) kemoterapi ve radyoterapi tedavisini beraber aldığı görülmüştür. Çalışmamız dahilindeki hastalar içerisinde yalnız radyoterapi alan hasta mevcut değildir.

Onkolojik tedavi alan hastalarda kansere veya uygulanan tedaviye bağlı tat ve koku duyusunda değişiklikler ortaya çıkar. Yoğun dozda radyasyon ve/veya kemoterapi tedavisi alan birçok hasta tat almada azalma veya tat almada değişiklik yaşar (21). Hem kemoterapinin hem de radyoterapinin tat kaybı üzerinde etkisinin olması, aynı zamanda ağız kuruluğunun tat alma üzerindeki etkisinden dolayı her iki tedaviyi beraber alan hasta grubunda anlamlı

fark bulunması olasıdır (22). Çalışmamızda da 50 hastanın 12'sinde (%24) tat kaybı saptanmıştır. Tat kaybı yaşayan 7 hasta sadece kemoterapi alırken, 5 hasta hem kemoterapi hem de radyoterapi ile tedavi edilmiştir Tedavi şekli ile tat kaybı arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur (p=,027). Bu bulgular, radyoterapinin kemoterapiye ek olarak tat alma duyusu üzerinde daha fazla olumsuz etkisi olabileceğini düşündürmektedir.

Kemoterapi ve radyoterapinin ağız kuruluğuna etkisi karşılaştırıldığında ağız kuruluğunun radyoterapi alan hastalarda daha çok görüldüğü belirtilmiştir (8). Tedavi süresi arttıkça ağız kuruluğu ve tat kaybının arttığını bildiren çalışmalar olmuştur (22). Çalışmamızda yalnızca radyoterapi tedavisi alan hasta grubu bulunmamakla beraber, tedavi süresi ile ağız kuruluğu arasında anlamlı bir ilişki bulanamamıştır. Bunun nedeni; örneklem büyüklüğümüz ve takip süremiz ile ilişkilendirilebilir.

Kemoterapi ve radyoterapi tedavisi alan hastalarda azalan tükürük akışı, düşük ph ve tamponlama kapasitesi ağız içinin asiditesinin artışına, bu artış da çürük oluşma riskinin artmasına neden olmaktadır (22). Delikan ve arkadaşlarının 2020 yılınca kanser tedavisi bitmiş çocuk hastalar üzerinde yaptıkları bir araştırmada; vaka grubu hastalarının DMFT skoru ortalaması 3,2±3,33, kontrol grubunun DMFT skoru ortalaması 1,98±2,72 olarak bulunmuştur. Her iki grup arasında istatistiksel olarak anlamlı farklılık olduğu belirlenmiştir (23). Çalışmamızda 50 pediatrik onkoloji hastasının mevcut DMFT skoru ortalaması 4,1 ± 3,46 olarak bulunmuştur. Çalışmamızda bir kontrol grubu olmadığından istatiksel olarak bir karşılaştırma yapılamamıştır.

Sonuç

Birincil kanser odağı ağız dışında bulunsa dahi, uygulanan kanser tedavilerinin sistemik yan etkileri orofasiyal bölgede çeşitli komplikasyonlara yol açarak pediatrik hastalarda yaşam kalitesini olumsuz yönde etkileyebilecek önemli sağlık sorunlarına neden olabilmektedir. Kanser ve kanser tedavisinde uygulanan antineoplastik protokoller hastanın ağız sağlığı üzerinde olumsuz etkilere sebep olmakta ve bu da hastanın yaşamını oldukça zorlaştırmaktadır. Kanser tedavisi gören hastalarda, oral mukozit, ağız kuruluğu, tat alma bozukluğu, diş çürüğü gibi yan etkiler oldukça sık ortaya çıkmaktadır. Bir çocuk diş hekiminin, tedavi öncesi ve tedavi sırasındaki müdahalesi ile etkili bir ağız bakımı sağlanabilir ve palyatif bakımda önemli bir fark yaratılarak tedavinin kesintiye uğraması/sürecin uzaması kontrol altına alına-

bilir. Hastalara, ebeveynlerine ve çocuğun bakımından sorumlu kişiye iyi bir oral hijyen eğitimi verilmelidir. Tedavi süresince ağız sağlığının korunmasında multidisipliner çalışma oldukça büyük önem taşımaktadır.

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Research Article

Ex-vivo Evaluation of the Torque Force on Periodontal Tissues During Endodontic Treatment

Ahmet Aydoğdu[1]

[1]Galata University, Faculty of Dentistry, Department of Periodontology, İstanbul, Turkey.

*Corresponding author: ahm0067@hotmail.com

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Ex-vivo Evaluation of the Torque Force on Periodontal Tissues During Endodontic Treatment

Ahmet Aydoğdu

Abstract

Objective: To examine the torque force generated on periodontal tissues by three different Ni-Ti endodontic file systems during root canal preparation in freshly extracted teeth.

Methods: Sixty single root teeth with an apical diameter corresponding to the size 15K-file were included to this study. Three experimental groups (n=20) were arranged. After establishing the working length teeth were placed on a digital torque-meter via self-curring polymethylmetacrylate adaptor. Thereafter, the following Ni-Ti file systems were tested: WaveOne Primary File (WO), WaveOne Gold Primary file (WOG) and size 25 OneShape (OS). In all groups, canals were prepared with the manufacturers' recommendations. The values measured with the torque meter were recorded.

Results: There was no statistical difference at WO-WOG groups comparisons ($p>0.05$). However, there were statistical differences at WO–OS and WOG–OS groups comparisons ($p<0.016$). The minimum torque value was at OS Group (2.0 Ncm) while maximum torque value was at WO Group (5 Ncm).

Conclusion: The results of this study showed that torque forces generated with reciproc files were significantly higher than that of Ni-Ti rotary file. Further we can speculate that eliminating inflammation-related tooth mobility through phase I periodontal therapy before endodontic treatment can reduce the risk of damage caused by rotational forces during endodontic treatment.

Key words: Endodontics, periodontium, root canal preparation, trauma, torque.

Özet

Amaç: Yeni çekilmiş dişlerde kök kanal hazırlığı sırasında üç farklı Ni-Ti endodontik eğe sistemi tarafından periodontal dokularda oluşan tork kuvvetinin incelenmesidir.

Yöntem: #15 K-tipi eğeye karşılık gelen apikal çapa sahip altmış tek köklü diş üç ayrı deney grubuna (n = 20) ayrılmıştır. Çalışma uzunluğu oluşturulduktan sonra dişler, polimetilmetakrilat adaptör ile dijital bir torkmetre üzerine yerleştirildi. Daha sonra dişler WaveOne Primary File (WO), WaveOne Gold Primary file (WOG) ve size #25 OneShape (OS) olmak üzere üç farklı Ni-Ti eğe sistemi ile şekillendirildi. Tüm gruplarda kanallar üreticilerin önerilerine göre şekillendirildi. Torkmetre ile ölçülen değerler kaydedildi.

Bulgular: WO-WOG grup ile karşılaştırıldığında istatistiksel olarak anlamlı fark bulunmadı ($p > 0.05$). Bununla birlikte, WO – OS ve WOG – OS grup karşılaştırmasında istatistiksel anlamlı fark bulundu ($p < 0,016$). Minimum tork değeri OS grubunda (2.0 Ncm) iken, maksimum tork değeri WO grubunda (5 Ncm) görüldü.

Sonuç: Bu çalışmanın sonuçları, reciproc eğeler ile üretilen tork kuvvetlerinin, döner aletlere göre daha yüksek olduğunu göstermiştir. Ayrıca, endodontik tedaviden önce periodontal inflamasyon kaynaklı diş hareketliliğinin faz I periodontal tedavi ile ortadan kaldırılmasının endodontik tedavi sırasında rotasyonel kuvvetlerin neden olduğu hasar riskini azaltabileceği düşüncesindeyiz.

Anahtar kelimeler: Endodonti, kök kanal preparasyonu, periodonsiyum, travma tork

Introduction

The periodontium supports teeth during function and maintains its structural integrity via stimulation by external forces. There is a homeostatic and constant equilibrium between functional forces and periodontal structures. The periodontal ligament is one of those structures that transmit external forces to the bone and resist occlusal forces. In patients with severe or untreated periodontitis, periodontal tissue destruction makes periodontium vulnerable to external forces (1).

During function; an approximate force of 1N applied at the crown is enough for the movement of a tooth in the dentoalveolar socket and this movement ranges from 0.05 to 0.10 mm at central incisors (2). In case of higher force, (5N) the tooth moves by 0.10 to 0.20mm and this results in reversible damage. Forces higher than 5N may lead to irreversible damage to healthy periodontium. However, if the periodontium has already been reduced, even a force of 5N may cause irreversible damage (2, 3).

Periodontal ligament fibers have been anatomically arranged to meet occlusal forces best along the long-axis of the tooth (4). The risk of damage to the periodontium is greater with lateral and torque forces. Studies showed that rotational torque forces cause two times more apical stress at central incisors (5, 6). Para-functional habits, bite anomalies orthodontic/endodontic therapy, tooth extractions are some of these conditions which cause torque forces on teeth and supporting tissues.

In modern endodontics, rotary Ni-Ti endodontic file systems are widely used for the advantage of reducing chair-side time, minimizing iatrogenic damage and risk of complication, and providing improved root canal shaping (7-9). Torque forces in these systems preserves rotation speed of the file against resistance that occurs during the preparation of root canal surface and provides efficient shaping. Recent reviews have emphasized that torque generation in Ni-Ti instruments is multifactorial, influenced by alloy type, taper, cross-sectional geometry, and motion kinematics (10). Abnormal torque values increase the risk of fracture and deformation of the file (11). Rotary instruments have different cutting tips and this variability may have effects on the torque force produced.

In recent years, Ni-Ti file systems which complete root canal preparation with only 1 instrument has been introduced. WaveOne (Dentsply Maillefer, Ballaigues, Switzerland) (WO) and recently introduced WaveOne Gold (Dentsply Maillefer, Ballaigues, Switzerland) (WOG) are single-file systems working in reciprocating motion while OneShape (Micro-Mega, Besancon Cedex, France) (OS) files are the ones working in a continuous rotation motion (12). To the best of our knowledge, no study has examined the effects of rotary endodontic file system-induced torque force on the periodontal tissues. Considering the lack of research on this issue, we aimed to investigate the torque force generated on periodontal tissues by three different rotary endodontic file systems during root canal preparation in freshly extracted teeth.

Materials And Methods

This study was carried out, between November 2018 - May 2019 at Galata University, Faculty of Dentistry, Department of Periodontology, and Department of Endodontics. (Ethical Approval Number: 5402245-0.50.05.04). Also the study was conducted in accordance with the Helsinki Declaration as revised in 2013. The teeth used in this study were maxillary central, lateral, and canine teeth which were scheduled for extraction due to severe periodontal destruction. Extracted teeth were placed in sterile saline solutions and measurements were performed on the prefabricated experimental setup in 2 hours following extraction. The inclusion criteria comprised maxillary incisors and canine teeth having root canal diameters that correspond to a #15 K-type file (M-Access, Dentsply Maillefer, Ballaigues, Switzerland) which stopped at the apical foramen and root canal working length of less than 25 mm. Periapical radiographs were taken in the bucco-lingual and mesio-distal directions to ensure that the tooth has single root canal. Teeth with internal or external resorption, caries, and calcified canals and root canal curvature of more than 10° were excluded from the study.(13) The working length (WL) was established by using a #15 K-type file ® that was inserted into the canal until the file tip became visible at the apical foramen. Teeth that had the root canals with an initial apical size equivalent to size #10 K-file and working length less than 25 mm were used in the study. Based on the criteria above, 60 teeth were selected and divided into three experimental groups with 20 teeth each: WO; WOG and OS files. Teeth were randomly assigned to one of the three groups consisting of 7 central incisors, 7 lateral incisors and 6 canines by drawing from a pool of lots. The group which completed the designated tooth number was excluded from randomization. The teeth were placed on a previously calibrated torque meter giving a torque value in newton per centimeter (Ncm) with the aid of an adapter constructed of self-polymerizing polymethylmethacrylate. (Figure 1).

Figure 1. Digital Torque Meter

Root canal preparation protocol

All the root canal preparations were done by using a single file in each tooth at the three groups. The highest torque value reached during the preparation procedure was also recorded.

WO and WOG files: The root canals were instrumented with the setting "WaveOne All" mode of the X-Smart Plus endomotor (Dentsply Maillefer, Ballaigues, Switzerland). The preparation was performed with in-and-out pecking motion at an amplitude of 3 mm until the WL was reached. The canal was then irrigated with 5% sodium hypchlorite (NaOCl) solution and the patency was checked with a #10 K-file.

OS file: #25 One Shape file with a taper of 0.06 was used in continuous rotation until the WL was reached taking into consideration the instructions of the manufacturer. The endomotor operated at rotation speed- 350 rpm and torque 2.5N cm. The canal was then irrigated with 5% NaOCl and patency were checked with a #10 K-file. Each instrument was used for one canal.

Statistical Analysis

Statistical tests were performed using statistical software (IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA)). The median 25-75 percentiles were calculated for canal length and torque values, and the tooth was taken as the unit of analysis. $p < 0.05$ was considered to be statistically significant.

The primary outcome variable-torque value could not be used to determine the sample size and the power of the study since, no precise information was available on torque value. Therefore, the current estimates were based on a pilot study which included 10 teeth in each experimental group. It was determined that a sample size of 16 teeth in each group would allow for a type II error level of $b = 0.20$ (80% power) and a type I error level of $a = 0.05$ (5% probability). Taken into consideration the possible dropouts, 20 teeth were included in each group. Since no sample size calculation could be performed a priori, a retrospective power analysis was calculated.

The Shapiro–Wilk test was used to test for normality of data. Intergroup comparisons in terms of root canal length and torque values were performed using the Kruskal–Wallis nonparametric test. Bonferroni adjusted Mann Whitney-U test was used to find out which of the

two groups showed a significant difference. For the Bonferroni correction, a=0.05/3 = 0.016 was considered to be statistically significant.

Results

The mean root canal length and torque values for each file are presented in Table 1. There was no statistically significant difference between the groups in terms of root canal length values (p>0.05) but a statistically significant difference existed between the groups in relation to the torque values (p<0.05). Post hoc pair sample test revealed that there was no significant difference between resiprocal files (p>0.016). However, a significant difference was observed between OS file and WO/WOG file groups (p<0.016) (Figure 2). The minimum and maximum torque values for the study groups are given in Table 2. While the maximum torque value was observed in the WO file group; OS file group had the minimum torque value. No correlation was found between root canal length and torque values (p>0.05).

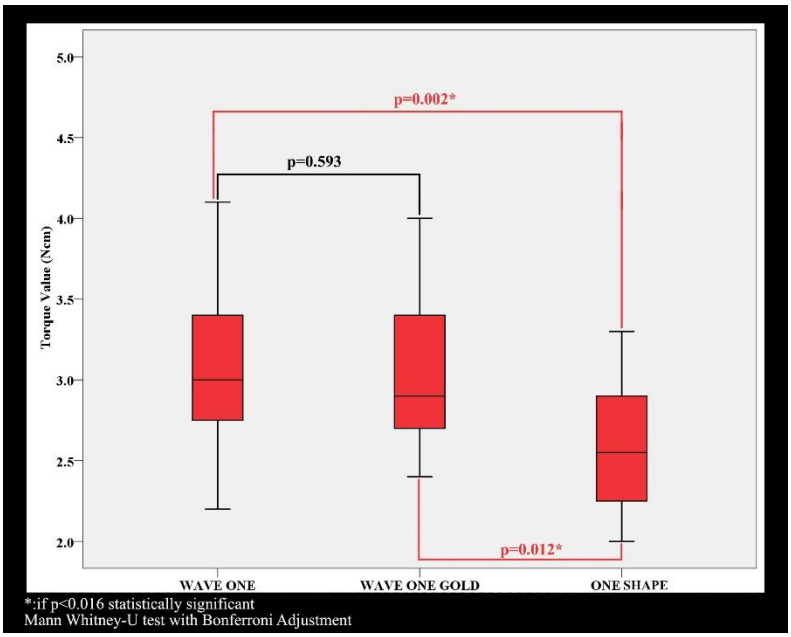

Figure 2. Intergroup comparison in terms of torque values

* Statistically significant difference between groups (Bonferroni-adjusted Mann–Whitney U test).

Data are presented as box and whisker plots. The median value is indicated by the line within the box plot. The box extends from the 25th to the 75th percentiles. Whiskers extend to show the highest and lowest values.

Table 1. Distribution of root canal length and Torque values among the groups

	Groups			
	WO	WOG	OS	p value
Root Canal Length (mm)	23 (21.6-23)	22.5 (21.4-23)	22 (21-23)	0.410
Torque Value (Ncm)	3.00 (2.73-3.4)	2.90 (2.65-3.43)	2.55 (2.25-2.90)	0.006*

Kruskall-Wallis H test
Values given as median (%25-%75) percentiles
* Statistical significance with a confidence of 95 % (p value <0.05)

Table 2. Minimum and maximum torque values (Ncm) during root canal preparation

	Minimum	Maximum
WO	2.2	5.0
WOG	2.4	4.5
OS	2.0	3.3

Discussion

The principal fibers of the periodontal ligament are arranged so that they best tolerate occlusal forces along the long axis of the tooth. The change in the direction of the occlusal forces causes a change in the distribution of the stress and occlusal load on periodontium and this may have different outcomes (i.e., lateral (horizontal) and torque (rotational) forces have the potential to injure the periodontium). Studies have shown that rotational torque forces generate 2 times more stress on the periodontal tissues compared to forces from different directions (5, 6).

With the introduction of rotary instruments to endodontics, torque forces generated by the cutting edges of the rotary files gained increasing importance. There are numerous studies on the effects of these torque forces both on the deformation of the rotary file itself and on the occurrence of stress-related adversities such as cracks and fractures generated in the root canal (14). There is no study that has yet examined the effects of these rotational forces on the supporting tissues of the tooth. Therefore, we aimed to investigate the force exerted on periodontal tissues by 3 different rotary Ni-Ti endodontic file system during root canal instrumentation in a specially developed experimental set-up. The results of our study showed that torque forces induced with both types of reciproc files were significantly higher than that of rotary file.

In our study, we used freshly extracted teeth instead of simulated canals in resin blocks because we think that it best represents the real conditions from the point of the structure of the instrumented material. Since one must not forget that great differences exist between the

two structures regarding physical properties. Heat generated during instrumentation could soften the resin material in resin blocks (15).

Recently, Jamleh et al. evaluated the amount of vertical force in the apical and coronal directions induced with WO and WOG systems during the canal shaping of extracted teeth. The authors concluded that WOG system had significantly lower apically and coronally directed peak force values compared with the WO system (11). The findings of our study are inconsistent with the findings of this study.

The cross-section, taper, NiTi alloy properties and motion kinematics may affect the amount of vertical force(i.e. torque values) (16). Although both WO and WOG file systems work with reciprocating motion, they differ from each other in terms of taper and cross-section design. Moreover, recent studies demonstrate that rotational speed settings can significantly alter torque values and fracture resistance during instrumentation, underscoring the clinical relevance of motor parameters (17). WO file has a modified convex triangular cross-section with 8% taper while WOG file has a parallelogram-shaped off-centered cross-section with %7 taper.(18) On the other hand, OS file system works with continuous rotary motion and has variable cross-section design with 6% taper (19). The lower taper design of the OS files may have been responsible for the lower torque values in this study. In the endodontic treatment of a tooth with reduced periodontium which is more vulnerable against external forces, the latter may serve as an option.

One plausible explanation for the observed differences in torque values between file systems lies in their taper designs. Instruments with larger tapers inherently possess greater stiffness and cross-sectional mass, which increases their contact area with dentin and thus elevates frictional resistance, requiring higher torque to maintain rotation. This concept is supported by Faus-Llácer et al. (20), who demonstrated that increased taper and apical diameter lead to decreased cyclic fatigue resistance, implicitly indicating greater internal stresses at higher taper levels. Moreover, in retreatment settings, Kim et al. (21) found that NiTi systems with greater taper may generate higher torque and are more susceptible to buckling, suggesting that taper not only influences cutting mechanics but also structural stability under load. In the context of our results, the file systems with steeper tapers likely encountered more resistance in dentin walls, contributing to their higher torque readings. Conversely, lower taper instruments would engage less frictional surface area, reducing the load required to rotate, which

could explain why in our study the system with smaller taper consistently showed lower torque values. Clinically, this implies that when shaping teeth with compromised periodontium, selecting instruments with reduced taper may mitigate excessive torque-induced stress on root surfaces

Additionally, operator-dependent variables such as the amplitude of reciprocating pecking motions have been shown to influence torque and stress distribution, suggesting that clinical technique is also a determinant of mechanical load on the periodontium (22).

Limitations of the Study

Our study has some limitations that should be considered. First, an existing periodontal ligament could not be simulated in the body of the experimental set-up. In other words, rigid fixation of the tooth to the adapter just resembling an ankylosed tooth was accomplished by using self-polymerized acrylic resin. Second, the presence of external forces from gingival fibers (dento-gingival, circular, transseptal, intra-papillary), root surface area–related differences between teeth due to their rigid attachment on the experimental set-up and variations in apico-coronal orientation of periodontal ligament fibers could not be modeled. Along with the listed factors above, the rigid model is far from distinguishing adversities such as the reduction of resistance to strength caused by reduced periodontium.

Despite all the shortcomings of, this model is important in terms of giving a general idea about the resultant rotational forces generated on the external root surface by endodontic Ni-Ti files during root canal therapy of single rooted teeth. However, a more advanced engineering model is needed that highlights the effects of these forces on periodontium.

Conclusion

The results of this study showed that torque forces generated with reciproc files were significantly higher than that of rotary file. However, a definite conclusion cannot be drawn such that files which work in reciprocating motion should be preferred over those working in continuous rotation motion in clinical practice. Since, there is a need for a more advanced engineering model incorporating components mimicking periodontal structures that meet torque forces in order to examine the behavior of periodontal tissues against such forces.

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Research Article

Uzman Tıp Hekimlerinin Periodontal Hastalıklar Bakımının Farkındalıklarının ve Bilgi Düzeylerinin Değerlendirilmesi

Sena Balkız[1*], Varol Çanakçı[2], Yunus Emre Güner[2]

[1]Motto Ağız ve Diş Sağlığı Polikliniği, Ordu, Türkiye.
[2]Ordu Üniversitesi, Diş Hekimliği Fakültesi, Periodontoloji Anabilim Dalı, Ordu, Türkiye.

*Corresponding author: senabalkiz@gmail.com

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Sena Balkız, Varol Çanakçı, Yunus Emre Güner

Özet

Sorunun Açıklanması: Periodontitis, yalnızca lokal bir olasılık değil; Diyabet, taşıyıcı nakil, fetus kompartmanları ve solunum yolu hastalıklarıyla birlikte kullanılabilirliği sistemik etkiler göstermektedir. Ancak farklı branşlardaki tıp hekimlerinin periodontal tedavi açısından bilgi ve düzeyde düzeyde kalması, bu da erken tanı ve yönlendirmede önemli bir biçimde bir araya gelmesinden oluşmaktadır.

Amaç: Periodontitis; Kronik ve multifaktöriyel bir enflamatuvar problem. Bu sağlama amacı, farklı branşlardaki uzman hekimlerin periodontal hastalık ve bunların sistemik etkilerinin bilgilerini ve kalıcılıklarını sürdürmektir.

Malzeme ve ücretlendirme: Kesitsel tipteki bu anket çalışması, Ordu Üniversitesi Klinik Araştırmalar Etik Kurulunun ayrılması (2021/01) ile Mart–Eylül 2021 tarihleri arasında yürütülmektedir. Daha önceki çalışmaların temel raporu 32 sorudan oluşan orijinal bir anket hazırlanmış ve Google Forms üzerinden İç Hastalıkları (İ.HU), Kadın Hastalıkları ve Doğum (KHDU), Kalp ve Damar Cerrahisi (KDCU) ve Kulak Burun Boğaz (KBBHU) standartna göre hazırlanmıştır. NCSS 2007 paket programından elde edilen 330 verinin toplam programı analiz edilmiştir. Tanımlayıcı istatistikler, ki-kare testi ve tek yönlü varyans analizi (Tukey post-hoc testi) ile değerlendirilmiş, anlamlılık düzeyi $p<0,05$ olarak kabul edilmiştir.

Bulgular: Katılımcıların %59,7'si kadın, yaşları 32,94±7,44 yıldır. Katılımcıların %71,5'i periodontitis tanımını doğru bilmiş, %68,2'si ilk bulgunun dişeti kanaması olduğunu ifade etmiştir. KBBHU ülkeleri arasında en yüksek seviyedeydi (%71,3 eğitim görmüş; p=0,0001), KHDU bileşenleri ise gebelik birimleri ile periodontitis arasındaki ilişki büyük oranda (erken doğum %72,3; düşük doğum ağırlığı %56,6). İ.HU'nun %69,1'i periodontal lezyonların prognozunu olumlu yönde güçlendireceğini göstermiştir. KDCU'nun %78,8'i periodontitisin taşıyıcısı için risk faktörü olduğunu doğru bilmiştir. Genel olarak zayıflamanın %90,3'ü sigaranın risk faktörü olduğunu, %73'ü periodontitisin semptomsuz ilerleyebileceğini belirtti. Ancak yalnızca %37,9'u hastalarını düzenli olarak diş hekimine yönlendirmekte, %19,1'i rutin ağız muayenesi yapmaktadır.

Sonuç: Bu çalışma, uzman hekimler arasında periodontal sağlık bilgisinin branşlara göre değişkenlik gösterdiğini ancak genel olarak yetersiz olduğunu ortaya çıkardı. KBBHU ve KHDU grupları daha yüksek bilgiye sahipken, İ.HU ve KDCU gruplarında bilgi düzeyi görece düşüktür. Bulgular, tıp eğitiminde periodontal sağlık konularının daha fazla vurgulanması, multidisipliner iş birliğinin uygulanması ve klinik uygulamalarda ağız-sistemik sağlık ilişkilerine yönelik daha fazla artırıcı programların geliştirilmesi gösterilmektedir.

Anahtar kelimeler: Farkındalık, periodontitis, sistemik hastalıklar, uzman hekimler,

Giriş

Periodontitis, disbiyotik dental plak biyofilmleri ile ilişkili, diş destek dokularının ilerleyici yıkımı, klinik ataçman kaybı ve inflamasyonla karakterize kronik, multifaktöriyel bir hastalıktır (1). Hastalığın gelişiminde bakteriyel etkenlerin yanı sıra konak yanıtı, genetik yatkınlık, diyabet, sigara kullanımı ve stres gibi çevresel ve edinilmiş faktörler de önemli rol oynamaktadır (2,3).

Kardiyovasküler hastalıklar (KVH), dünya genelinde yaygın görülen sistemik hastalıklar arasında yer almakta ve ciddi bir halk sağlığı sorunu oluşturmaktadır (4). Periodontitisin, geleneksel risk faktörlerinden bağımsız olarak KVH için potansiyel bir risk faktörü olduğu bildirilmektedir. Dental enfeksiyonların koroner aterosklerozun şiddeti ile ilişkili olabileceği, %50'den fazla dişte 4 mm'yi aşan kemik kaybının KVH riskini artırdığı saptanmıştır (5). Ayrıca, periodontal bakterilerin kalp kapakçıkları ve aortta da izlenmesi bu ilişkiyi desteklemektedir (6). Bakteriyel endotoksinler ve proinflamatuar mediyatörlerin dolaşıma geçmesiyle sistemik inflamasyonun tetiklenmesi, periodontitis ile KVH arasındaki bağlantıyı açıklamaktadır (7).

Diyabet, genetik yatkınlık ve çevresel faktörlerin etkisiyle gelişen, hiperglisemi ile karakterize kronik metabolik bir hastalıktır (8). Diyabetin hem gingivitis hem de periodontitis için önemli bir risk faktörü olduğu ve periodontitisin diyabetin "altıncı komplikasyonu" olarak tanımlandığı belirtilmektedir (9). Diyabetik bireylerde nötrofil fonksiyonlarının bozulması periodontal enfeksiyonlara karşı savunmayı zayıflatmakta ve dokularda yıkımı artırmaktadır (10). Aynı zamanda bağ doku metabolizmasındaki bozulmalar, alveoler kemik kaybı ve ataşman kaybı ile ilişkilidir (11, 12). Glisemik kontrolün sağlanması periodontitisin ilerlemesini

yavaşlatabilir; ancak bu etkinin sağlanabilmesi için iyi bir oral hijyen ve periodontal tedavi gereklidir (13).

Cinsiyet hormonları da periodontal hastalıkların patogenezinde etkili modifiye edici faktörler arasında yer almaktadır (14). Özellikle gebelik döneminde hormonal değişikliklere bağlı olarak dişetinde inflamasyon ve hiperplazi görülebilmektedir (15,16). Gingival indeks değerlerinde özellikle ikinci ve üçüncü trimesterlerde artış gözlenmekte, doğum sonrası ise bu değerler azalmaktadır. Ayrıca, bu dönemde görülen "hamilelik tümörü" (pyogenic granuloma), lokal irritanlara karşı abartılı inflamatuar yanıt sonucu oluşmaktadır (15). Periodontitisin, erken doğum ve düşük doğum ağırlığı gibi olumsuz gebelik sonuçlarıyla ilişkili olabileceği bildirilmiştir (17,18).

Son yıllarda yapılan çalışmalar, periodontal inflamasyonun yalnızca lokal etkilerle sınırlı kalmayıp sistemik inflamatuar yanıtı tetikleyerek kronik sistemik hastalıkların gelişme riskini artırabileceğini göstermektedir (19,20). Özellikle kronik obstrüktif akciğer hastalığı (KOAH) ile periodontitis arasında pozitif bir ilişki bulunmuş olup, her iki hastalık benzer risk faktörleri ve inflamatuar süreçleri paylaşmaktadır (21,23). Ağız hijyeninin bozuk olması, solunum patojenlerinin diş plağında kolonizasyonuna neden olarak sistemik inflamasyonu artırabilir (24,25). Periodontal tedavinin uygulanması, KOAH hastalarında hastane yatışlarını azaltmakta ve yaşam kalitesini artırmaktadır (26).

Araştırmanın amacı, uzman tıp hekimlerinin periodontal hastalıklar konusundaki bilgi düzeylerini ve farkındalıklarını değerlendirmektir.

Malzeme ve Yöntemler

Bu çalışma, Ordu Üniversitesi Klinik Araştırmalar Etik Kurulu'nun 22.02.2021 tarihli ve 2021/01 karar numaralı onayı ile gerçekleştirilmiş olup, Ordu Üniversitesi Diş Hekimliği Fakültesi Periodontoloji Anabilim Dalı bünyesinde planlanmıştır.

Çalışmada veri toplama aracı olarak, 28'i ortak ve 4'ü farklı olmak üzere toplam 32 sorudan oluşan özgün bir anket formu geliştirilmiştir. Anket, daha önce çeşitli dergilerde yayınlanan benzer çalışmalardan uyarlanarak ve Türkiye koşullarına göre modifiye edilerek hazırlanmıştır. Öncelikle bir pilot uygulama ile test edilen anket, içerik geçerliliği sağlandıktan sonra nihai hale getirilmiştir. Hedef katılımcı grubu; İç Hastalıkları, Kadın Hastalıkları ve Doğum, Kalp ve Damar Cerrahisi ile Kulak-Burun ve Boğaz Hastalıkları uzmanları olarak belirlenmiştir.

Anket formu Google Formlar uygulaması aracılığıyla dijital ortama aktarılmış ve Mart 2021 itibariyle altı ay süreyle erişime açılmıştır. Katılımcılara e-posta ve sosyal medya platformları (WhatsApp, Facebook, Instagram) üzerinden ulaştırılan bağlantı aracılığıyla veri toplanmıştır. Ankete katılanlardan isim veya kişisel bilgi talep edilmemiş, anketin başlangıcında bilgilendirilmiş onam metni sunulmuştur.

Anket, katılımcıların demografik bilgileri (cinsiyet, yaş, mesleki branş, mesleki deneyim yılı, çalışılan kurum) ile; periodontal hastalıkların tanımı, etiyolojisi, belirtileri, sistemik hastalıklarla ilişkisi ve hasta yönlendirme davranışları hakkındaki bilgi ve farkındalık düzeylerini ölçmeye yönelik soruları içermektedir. Ayrıca katılımcıların kişisel ağız sağlığı alışkanlıkları ve hastalarına yönelik periodontal danışmanlık uygulamaları da sorgulanmıştır.

Araştırmanın örneklemini, Türkiye'de aktif görev yapan ilgili uzmanlık alanlarındaki uzman hekimler ve araştırma görevlileri oluşturmaktadır. Örneklem büyüklüğü, daha önce yapılmış benzer çalışmalardan (27,28) faydalanılarak %5 hata payı ve %90 güç düzeyiyle, her bir grupta en az 80 kişi olacak şekilde toplamda minimum 320 kişi olarak hesaplanmıştır.

Toplanan veriler Google Forms üzerinden Excel formatına aktarılmış ve analizler NCSS (Number Cruncher Statistical System) 2007 programı kullanılarak yapılmıştır. Tanımlayıcı istatistiksel analizlerin yanı sıra, değişkenlerin dağılımı Shapiro–Wilk testi ile değerlendirilmiş; parametrik veriler için tek yönlü varyans analizi, alt grup karşılaştırmaları için Tukey testi ve nitel veriler için ki-kare testi kullanılmıştır. Tüm analizlerde anlamlılık düzeyi $p<0,05$ olarak kabul edilmiştir.

Bulgular

Bu çalışmaya toplam 330 uzman tıp hekimi katılmıştır. Katılımcıların %24,85'i (n=82) İç Hastalıkları Uzmanı (İ.H.U.), %25,15'i (n=83) Kadın Hastalıkları ve Doğum Uzmanı (K.H.D.U.), %25,76'sı (n=85) Kalp ve Damar Cerrahisi Uzmanı (K.D.C.U.) ve %24,24'ü (n=80) Kulak Burun Boğaz Hastalıkları Uzmanı (K.B.B.H.U.)'ndan oluşmaktadır. Katılımcıların yaş ortalaması 32,94±7,44 olup, %59,7'si (n=197) kadın, %40,3'ü (n=133) erkektir. Katılımcıların %38,48'i (n=127) devlet/şehir hastanelerinde, %21,52'si (n=71) özel hastane/kliniklerde, %40'ı (n=132) ise üniversite hastanelerinde görev yapmaktadır (Tablo 1).

Tablo 1. Demografik Veriler

				Kadın Hastalıkları ve Doğum Uzmanı n:83		İç Hastalıkları Uzmanı n:82		Kalp ve Damar Cerrahisi Uzmanı n:85	KBB Hastalıkları Uzmanı n:80		p+
Yaş		32,94±7,44		34,49±7,63		33,04±6,56		34,6±6,51	32,94±7,44		0,257
Cinsiyetiniz?	Erkek	133	40,30%	25	30,12%	32	39,02%	37	43,53%	39	48,75%	
	Kadın	197	59,70%	58	69,88%	50	60,98%	48	56,47%	41	51,25%	0,095
Hangi kurumda çalışıyorsunuz?	Devlet\Şehir hastanesi	127	38,48%	25	30,12%	39	47,56%	39	45,88%	24	30,00%	
	Özel hastane\Üniversite\Klinik	71	21,52%	25	30,12%	10	12,20%	20	23,53%	16	20,00%	
	Üniversite hastanesi	132	40,00%	33	39,76%	33	40,24%	26	30,59%	40	50,00%	0,072
Uzmanlığınızda çalışma süreniz nedir?	Uzmanlık Öğrencisi	139	42,12%	35	42,17%	42	51,22%	24	28,24%	38	47,50%	
	<5 Yıl	88	26,67%	16	19,28%	19	23,17%	33	38,82%	20	25,00%	
	5-10 Yıl	49	14,85%	13	15,66%	11	13,41%	14	16,47%	11	13,75%	
	>10 Yıl	54	16,36%	19	22,89%	10	12,20%	14	16,47%	11	13,75%	0,064
Dişlerinizi günde kaç kere fırçalarsınız?	Düzenli fırçalamıyorum	10	3,03%	2	2,41%	2	2,44%	3	3,53%	3	3,75%	
	Günde 1 kez	88	26,67%	19	22,89%	28	34,15%	25	29,41%	16	20,00%	
	Günde 2 kez	197	59,70%	52	62,65%	42	51,22%	52	61,18%	51	63,75%	
	Günde 2'den fazla	35	10,61%	10	12,05%	10	12,20%	5	5,88%	10	12,50%	0,542
Ne sıklıkla diş hekimine gidiyorsunuz?	Hiç Gitmiyorum	7	2,13%	2	2,41%	5	6,10%	0	0,00%	0	0,00%	
	Yılda 1 Kez	57	17,33%	13	15,66%	14	17,07%	13	15,29%	17	21,52%	
	Rutin Kontrol Amacıyla 6 ayda bir	40	12,16%	13	15,66%	10	12,20%	6	7,06%	11	13,92%	
	Şikayetim Olduğu zaman	225	68,39%	55	66,27%	53	64,63%	66	77,65%	51	64,56%	0,090

Katılımcıların %71,52'si periodontitisin tanımını doğru olarak belirtirken, %68,18'i periodontal hastalığın ilk belirtisinin dişeti kanaması olduğunu ifade etmiştir. Katılımcıların %57,27'si periodontal hastalıkların en önemli etiyolojik faktörünün mikrobiyal dental plak olduğunu doğru bilmiştir (p=0,078). Katılımcıların %51,81'i günde en az iki kez dişlerini fırçaladığını, %17,57'si düzenli olarak diş ipi kullandığını ifade etmiştir. Bununla birlikte, %52,42'lik bir oran kendi ağız ve diş sağlığı sorunlarında bir diş hekimine başvurmadığını belirtmiştir. Kendi ağız hijyen alışkanlıkları ile hasta yönlendirme davranışları arasında anlamlı bir ilişki saptanmıştır (p<0,01).

Katılımcıların %44,38'i eğitim sürecinde ağız sağlığı ve dental problemler hakkında eğitim aldığını bildirmiştir. En yüksek oran K.B.B.H.U. grubunda (%71,25) saptanmıştır (p=0,0001). Katılımcıların periodontal sağlık bilgilerini değerlendirme puanları arasında anlamlı farklılık gözlenmiştir (p=0,014). K.B.B.H.U. grubunun puan ortalaması diğer gruplardan daha yüksek bulunmuştur (Tablo 2).

Tablo 2. Uzman tıp hekimlerinin periodontal/dental konusunda eğitim durumları

	Total n:330		**Kadın Hastalıkları ve Doğum Uzmanı n:83**		**İç Hastalıkları Uzmanı n:82**		**Kalp ve Damar Cerrahisi Uzmanı n:85**		**KBB Hastalıkları Uzmanı n:80**		**p**
Eğitim süreciniz boyunca ağız sağlığı ve dental problemler hakkında eğitim aldınız mı?	146	44,38%	32	39,02%	32	39,02%	25	29,41%	57	71,25%	0,0001+
Anketimize başlamadan önce, periodontal sağlık ve hastalıklarla alakalı bilgilerinizi nasıl değerlendirirsiniz?	2,35±1,15		1,96±1,23		1,8±1,09		1,95±0,94		2,35±1,15		0,014*

Periodontal hastalığa sahip her hasta antibiyotik kullanmalıdır" sorusuna verilen doğru yanıt oranı oldukça düşüktür; K.H.D.U. (%4,82) ve İ.H.U. (%6,10) gruplarında daha yüksek oranda doğru yanıt verilmiştir (p=0,0001). Katılımcıların %73,03'ü "Periodontitis semptomsuz ilerleyebilir" ifadesini doğru yanıtlamıştır; en düşük oran K.H.D.U.'da bulunmuştur (p=0,049). Katılımcıların %90,3'ü sigaranın periodontal hastalıkların semptomlarını artırdığını doğru bilmektedir (p=0,235). Stresin periodontal hastalıklar üzerindeki etkisi konusunda %69,09 "yanlış" seçeneğini işaretlemiş, K.B.B.H.U. grubu diğerlerine göre anlamlı olarak daha fazla "doğru" cevabı vermiştir (p=0,007). Katılımcıların %94,85'i bazı sistemik hastalık ilaçlarının periodontal probleme yol açabileceğini doğru olarak belirtmiştir (p=0,360).

Katılımcıların %32,42'si hastalarına oral sağlığın önemini anlattığını, %36,36'sı bazen anlattığını, %31,21'i ise hiç anlatmadığını belirtmiştir. Branşlar arasında anlamlı farklılık bulunmuştur; K.D.C.U. grubunda öneride bulunan oran daha düşüktür (p=0,002). Katılımcıların %37,88'i hastalarını diş hekimine sevk ettiğini, %56,67'si gerektiğinde sevk ettiğini, %5,45'i ise hiç sevk etmediğini bildirmiştir. K.H.D.U. (%53,01) ve K.B.B.H.U. (%50) gruplarında sevk oranı daha yüksek bulunmuştur (p=0,0001). Klinik muayenede oral değerlendirme yapan katılımcıların oranı %19,09, gerektiğinde yapanların oranı %42,42 iken, %38,48'i hiç yapmadığını belirtmiştir. K.H.D.U. ve K.D.C.U. gruplarında oral muayene oranı anlamlı olarak daha düşük bulunmuştur (p=0,0001) (Tablo 3).

Tablo 3. Uzman tıp hekimlerin periodontal sağlık açısından hastalarına yaklaşımı

			Kadın Hastalıkları ve Doğum Uzmanı		**İç Hastalıkları Uzmanı**		**Kalp ve Damar Cerrahisi Uzmanı**		**KBB Hastalıkları Uzmanı**		**p+**
			n:83		**n:82**		**n:85**		**n:80**		
Hastalarınıza oral sağlığın önemini anlatıp, düzenli diş fırçalamayı tavsiye ediyor musunuz?	Hayır	103 31,21%	21	25,30%	20	24,39%	41	48,24%	21	26,25%	
	Evet	107 32,42%	29	34,94%	27	32,93%	16	18,82%	35	43,75%	
	Bazen	120 36,36%	33	39,76%	35	42,68%	28	32,94%	24	30,00%	0,002
Oral\Dental problemlerden dolayı hastalarınızı diş hekimine sevk ediyor musunuz?	Hayır	18 5,45%	6	7,23%	9	10,98%	2	2,35%	1	1,25%	
	Evet	125 37,88%	44	53,01%	24	29,27%	17	20,00%	40	50,00%	
	Gerektiği zaman	187 56,67%	33	39,76%	49	59,76%	66	77,65%	39	48,75%	0,0001
Hastalarınıza kendi klinik teşhisinizi belirlerken oral muayene yapıyor musunuz?	Hayır	127 38,48%	42	50,60%	10	12,20%	65	76,47%	10	12,50%	
	Evet	63 19,09%	9	10,84%	20	24,39%	4	4,71%	30	37,50%	
	Gerektiği zaman	140 42,42%	32	38,55%	52	63,41%	16	18,82%	40	50,00%	0,0001

Branşlara göre yapılan değerlendirmelere baktığımız zaman;

•**K.B.B.H.U.:** Ağız solunumu şikayetinde %62,5 oranında oral muayene yaptığı, %62,5 oranında kulak/boğaz ağrısı şikayetinde hastayı diş hekimine yönlendirdiği, ağız kokusunu en çok kötü ağız hijyeni (%97,5), sistemik hastalıklar (%95) ve bademcik iltihapları (%90) ile ilişkilendirdiği görülmüştür. Ayrıca %97,5'i "diş enfeksiyonu sinüsleri, sinüs enfeksiyonu dişleri etkileyebilir" ifadesini doğru bulmuştur.

•**K.D.C.U.:** Katılımcıların %78,82'si periodontitisin kardiyovasküler hastalıklar için risk faktörü olduğunu doğru bilmiştir. Ancak aterom plağı–periodontal bakteri ilişkisi hakkında %60 "bilmiyorum" cevabı verilmiştir. Katılımcıların %51,76'sı kan sulandırıcı kullanan hastalarda dental işlemler için gerekli uyarıları yaptığını bildirmiştir.

•**K.H.D.U.:** Hamileliğin oral semptomları en çok diş eti büyümeleri (%81,93) ve diş eti kanaması (%80,72) olarak belirtilmiştir. Katılımcıların %85,54'ü gebelikte periodontal prob-

lemler daha sık görülür demiştir. Ayrıca %72,29'u erken doğum, %56,63'ü düşük doğum ağırlığı, %28,92'si preeklampsi ve %42,17'si koryoamniyonit ile periodontal hastalık ilişkisi olduğunu ifade etmiştir.

• **İ.H.U.:** Diyabetus mellitus hastalarında %45,12 oranında ağız bulguları konusunda bilgilendirme yapıldığı, en sık belirtilen bulguların tükürük akışında azalma (%81,48), değişmiş tat duyusu (%81,48), C. albicans artışı (%77,78) ve ağız yanması (%60,49) olduğu bildirilmiştir. Katılımcıların %69,14'ü periodontal tedavinin diyabet prognozunu etkilediğini, %71,60'ı periodontitisin glisemik kontrolü bozduğunu belirtmiştir.

Tartışma

Bu çalışmada, farklı tıp branşlarından uzman hekimlerin periodontal hastalıklarla ilgili bilgi düzeyleri, tutumları ve farkındalıkları değerlendirilmiştir. Bulgular, multidisipliner klinik pratikte sıklıkla karşılaşılan ancak hekimlerin bilgi düzeylerine göre yönetimi değişebilen periodontal hastalıklar konusunda önemli veriler sunmaktadır. Özellikle sistemik hastalıklarla olan ilişkiler, yönlendirme davranışları, tanısal bilgi düzeyi ve eğitim sürecindeki yeterlilik gibi çeşitli parametrelerde elde edilen sonuçlar, ülkemizdeki hekim farkındalığını ve eğitim ihtiyacını değerlendirmek açısından kıymetlidir.

"Periodontitis nedir?" sorusuna %71,52 oranında doğru yanıt verilmesi olumlu bir bulgu olarak değerlendirilmiştir. Mosley ve ark. (29), benzer bir oran (%70) bildirirken; Fransa'da Cohen ve ark. (30) bu oranı %85,8 olarak tespit etmiştir. Bu fark, ülkeler arasındaki müfredat farklılıklarıyla ilişkili olabilir. Yine de %28,48'lik eksik bilgi oranı, tanı süreçlerinde önemli bir boşluğa işaret etmektedir. Aynı şekilde, "Gingivitiste kemik kaybı görülür" gibi yanlış bir ifade karşısında %11,82'lik bir "yanlış" cevabın olması da periodontal hastalıkların sınıflandırılması konusunda eksiklikleri ortaya koymaktadır.

Katılımcıların %59,7'sinin günde iki kez diş fırçaladığı belirtilmiştir. Bu oran, Fatima ve ark. (31)'in çalışmasında %69 olarak bildirildiğinden daha düşüktür. Aynı çalışmada diş ipi ve gargara kullanım oranları da düşüktür; bu durum, hekimlerin kişisel ağız sağlığı alışkanlıklarıyla hasta eğitimi arasında paralellik olmayabileceğini göstermektedir. Katılımcıların yalnızca %44,38'i eğitim sürecinde ağız sağlığı hakkında bilgi aldığını belirtmiştir. Cohen ve ark. (30) çalışmasında bu oran %19,7, Quijano ve ark. (32)'da ise %10 olarak raporlanmıştır. Bu sonuç, ülkemizde kısmi bir gelişmeye işaret etse de ağız sağlığı eğitim müfredatının hâlâ yetersiz olduğunu göstermektedir.

Çalışmamızda katılımcıların %56,67'si hastalarını gerektiğinde diş hekimine yönlendirdiğini belirtmiştir. Bu oran, Hindistan'da Jaiswal ve ark. (33) (%39,33), Suudi Arabistan'da Asaad ve ark. (34) (%67) ve Ürdün'de Al-Habashneh ve ark. (35) (%50) gibi çalışmalarda bildirilen oranlarla uyumludur. Ayrıca İ.H.U. grubunun %10,98'i yönlendirme yapmadığını belirtmiştir. Bu farklar, branşlar arası farkındalık düzeyinin değişken olduğunu göstermektedir.

Periodontitis, lokal inflamasyonun ötesinde sistemik inflamatuar yanıtla karakterize edilen bir hastalık olup diyabet, kardiyovasküler hastalıklar, gebelik komplikasyonları ve solunum yolu hastalıkları gibi birçok sistemik durumla ilişkilidir (36). Çalışmamızda yer alan K.D.C.U.'nın %78,82'si periodontitisin kardiyovasküler hastalıklar için bir risk faktörü olduğunu belirtmiştir. Bu oran, Mosley ve ark. (29)'nın Kuzey Karolina'da yaptığı çalışmadaki %72 oranı ve Ustaoğlu ve ark. (37)'nın Türkiye'deki çalışmasındaki %56,56'lık oranla karşılaştırıldığında anlamlı şekilde yüksektir. Bu durum, Türkiye'de bu konuya ilişkin klinik farkındalığın arttığını göstermektedir.

Çalışmamızda ayrıca İ.H.U.'nın %69,14'ü periodontal tedavinin diyabetin prognozunu olumlu etkileyebileceğini belirtmiştir. Bu oran, Owens ve ark. (38)'nın İ.H.U. grubuyla gerçekleştirdiği çalışmadaki %49 oranının oldukça üzerindedir. Periodontal hastalıkların glisemik kontrolle olan ilişkisi çok sayıda randomize kontrollü çalışmada ve meta-analizde ortaya konmuştur (39,40). Ancak %23,46'lık "bilmiyorum" cevabı bu konudaki eğitim düzeyinin daha da geliştirilmesi gerektiğini ortaya koymaktadır.

Gebelikte periodontal hastalıkların; preterm doğum, düşük doğum ağırlığı ve preeklampsi gibi komplikasyonlarla ilişkili olabileceği gösterilmiştir (41,42). Çalışmamızda K.H.D.U. grubunun %85,54'ü bu ilişkiyi doğru tanımlamıştır. Bu oran, Fransa'da Cohen ve ark. (30)'in %83,2'lik, Hindistan'da Satyanarayana ve ark. (43)'nın %77,6'lık sonuçlarından daha yüksektir. Bu sonuç, ülkemizde gebelik-oral sağlık ilişkisinin kadın doğum uzmanları tarafından klinik pratiğe daha çok yansıdığını düşündürmektedir. Bununla birlikte, yönlendirme sıklığına dair verilen yanıtlarda yalnızca %16,87'lik bir "her zaman" oranı olması, farkındalıkla pratik uygulama arasındaki boşluğa işaret etmektedir. Ayrıca K.H.D.U.'ların %72,29'u periodontitisin erken doğumla ilişkili olduğunu bildirmiştir. Benzer şekilde Brezilya'da Rocha ve ark. (44) ve Morgan ve ark. (45) periodontal hastalıkların gebelik komplikasyonları ile ilişkili olduğunu ortaya koymuştur. Bu sonuçlar, ülkemizdeki K.H.D.U.'ların

gebelik ve periodontal sağlık arasındaki ilişkiye dair farkındalıklarının yüksek olduğunu göstermektedir.

K.B.B.H.U. katılımcılarının ağız kokusu, ağız solunumu ve oral muayene konularında farkındalıkları diğer branşlara göre belirgin derecede yüksektir. Katılımcıların %97,5'i ağız kokusunu kötü ağız hijyeni ve periodontal nedenlere bağlamıştır. Ayrıca %62,5'i ağız solunumu olan hastalara rutin oral muayene yaptığını belirtmiştir. Bu bulgular, Yarbasi ve ark. (46)'nın KBB uzmanlarının ağız mukozası muayenesi konusundaki yüksek farkındalık oranlarıyla uyumludur.K.B.B.H.U.'ların branşlarının doğrudan oral bölge ile ilişkili olması, bu yüksek farkındalığı açıklamaktadır. Literatürde bu konudaki çalışma sayısı sınırlı olup daha fazla araştırmaya ihtiyaç vardır (47,48).

Sonuç

Bu çalışmanın sonuçları, multidisipliner yaklaşımla hastaya bütüncül sağlık hizmeti sunmanın, yalnızca periodontal sağlığı değil aynı zamanda sistemik hastalıkların yönetimini de iyileştirebileceğini göstermektedir. Eğitim müfredatlarında diş hekimliği ve tıp fakülteleri arasında ortak modüller oluşturulması, erken yönlendirme alışkanlıklarının kazandırılması ve uzmanlık eğitimlerinde multidisipliner vaka tartışmalarına ağız sağlığı konularının dahil edilmesi önerilmektedir. Ayrıca, tıp kongrelerinde ve sempozyumlarında periodontal hastalıkların sistemik etkilerine dair farkındalık oturumlarının artırılması faydalı olacaktır.

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Review Article

Nanotechnology in Oral And Maxillofacıal Surgery

Elif Ceyda Kayasöken[1], Selime Ecem Sinanoğlu[1], Mehdi Babaei[1], Mesture Ayfer Kaynar[1*]

[1]Istanbul Yeni Yuzyıl Unıversıty, Faculty of Dentistry, Oral and Maxillofacial Surgery, Istanbul,Turkey

*Corresponding author: ayferkaynar@gmail.com

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Nanotechnology in Oral And Maxillofacıal Surgery

Elif Ceyda Kayasöken, Selime Ecem Sinanoğlu, Mehdi Babaei,

Mesture Ayfer Kaynar

Abstract

Nanotechnology has rapidly advanced in the fields of science and medicine over the past few decades. Thanks to developments in medicine, it has gained increasing popularity in oral, dental, and maxillofacial surgery. This review article discusses recent advancements in nanotechnology, particularly in bone regeneration, diagnosis and treatment of oral cancer, drug delivery systems, and dental implants.

Keywords: Dental implant, drug delivery system, nanoskeleton, nanoparticle, nanotechnology, oral cancer, oral surgery.

Özet

Nanoteknoloji geçtiğimiz birkaç on senede bilim ve tıp alanında hızlı bir gelişim göstermektedir. Özellikle tıp alanındaki gelişmeler sayesinde ağız, diş ve çene cerrahisinde de popülerliğini artırmıştır. Bu derleme makalesinde, nanoteknolojinin özellikle kemik rejenerasyonu, oral kanser tanı ve tedavisinde, ilaç taşıma sisteminde ve dental implantlarda yapılan son gelişmeler konu alınmıştır.

Anahtar kelimeler: Ağız kanseri, ağız cerrahisi, diş implantı, ilaç verme sistemi, nanoiskelet, nanopartikül, nanoteknoloji.

Introduction

The word "nano" originates from the Greek word meaning "dwarf." The concept of nanotechnology was first introduced in detail by Nobel laureate physicist Richard Feynman in his 1959 lecture titled "There's Plenty of Room at the Bottom." At the end of his lecture, he concluded the topic by stating, "This is a development that I think is inevitable." (1,2)

The accepted definition of nanotechnology is the research and development of technology at the atomic, molecular, or macromolecular level; at a scale of approximately 1 to 100 nanometers, to understand the phenomena and materials in nanostructures at a fundamental level and to create and use structures, devices, and systems with new properties and functions due to their small and/or intermediate sizes (3,4).

Nanotechnology has emerged as a research field emerging with various applications in science and technology (5). Due to its unique properties, such as high surface-to-volume ratios and high compressive and bending strengths, scientists have explored different application methods and industries that could benefit from the use of these materials (6,7).

Today, it is observed that nanotechnology shows dynamic development in all fields of medicine:

- Medical diagnosis
- Cancer treatment
- Gene therapy
- Treatment of infections
- Tissue or organ regeneration
- Medical imaging (6)

Literature Review

1. Types of Nanomaterials

The regeneration of oral tissues is very challenging, and accordingly, nanomaterials have great potential for future applications in craniofacial and oral defect-based tissue engineering and regenerative medicine (TE/RM). Nanomaterials are materials that have components smaller than 100 nm in at least one dimension. These may include atomic clusters, grains, fi-

bers, films, nanopores, and composites made of their combinations. One-dimensional nanomaterials are referred to as "sheets," two-dimensional ones as "nanowires" and "nanotubes," and three-dimensional ones are called "quantum dots" (1,8).

1. Fullerenes are carbon allotropes that can adopt different shapes, one of which is carbon nanotubes. The cylindrical shape is derived from the hexagonal lattice structure of carbon atoms, and this structure can fold into a sheet. This molecular arrangement provides significant hardness and tensile strength (50 times that of steel). When an antithrombotic surface is added, carbon nanotubes become suitable for vascular microcatheters, stents, and implants (3,9).

2. Nanoparticles, such as quantum dots (QD), can serve as drug carriers or labels for tracking cells. QDs are particularly suitable for imaging because they emit fluorescence at different wavelengths depending on the particle size (3,9).

3. Nanocomposites are multiphase solid materials in which one of the phases has dimensions smaller than 100 nanometers. In tissue engineering, scaffolds are enhanced with nanoparticle fillers. These fillers are either placed between layers or evenly distributed to increase the surface area (3,9).

The most commonly studied nanomaterials for oral tissues include nanofibers, nanoparticles, nanosheets, nanotubes, and nanospheres. These nanomaterials can be composed of inorganic and organic materials (Figure 1) (10).

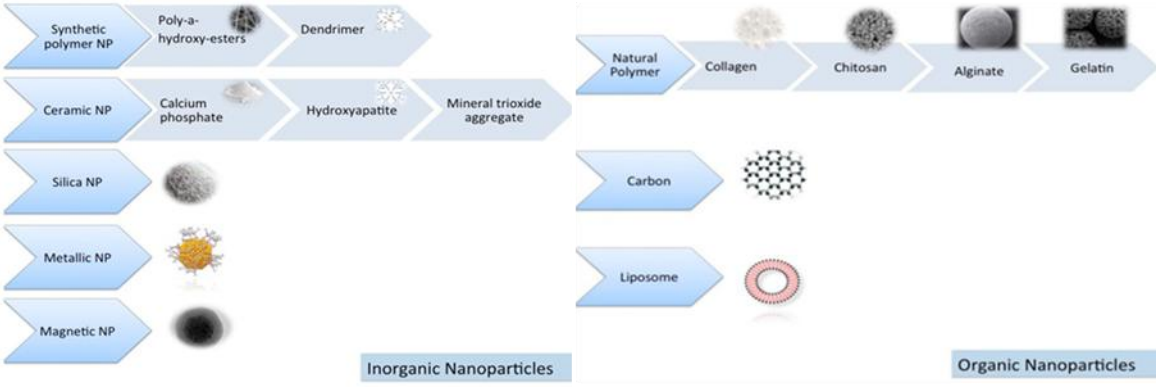


Figure 1: Inorganic and organic nanoparticles (10)

Generally, nanomaterials have excellent physicochemical properties and biomimetic characteristics to enhance cell growth and tissue regeneration. Due to their similarity to extracellular matrices and high porosity, nanomaterials create an ideal environment for cell migration. Additionally, nanotubes and nanoparticles can enhance the chemical and mechanical properties of the scaffold, increase cell migration and proliferation, and promote tissue regeneration. Nano-scaffolds stabilize bioactive agents through encapsulation or surface attachment, encourage molecular internalization, target their distribution within cells, and allow control of biological factor release at the intended site. They can also be used to label cells for continuous tracking and monitoring. Furthermore, nanoparticles can provide improved osseointegration, osteoconduction, and osteoinduction (10).

In oral and maxillofacial surgical applications, nanotechnology has enabled the development of tissue engineering, imaging, drug delivery systems, and contributed to the improvement of implants (Figure 2) (3). These innovations have allowed for better outcomes in surgical treatments and significant progress in the use of biomaterials.

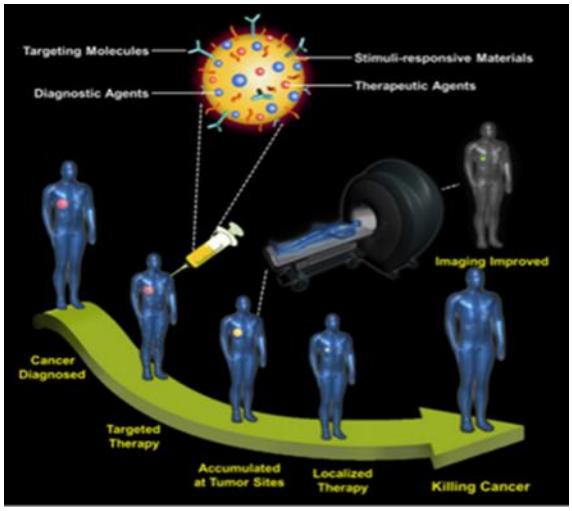


Figure 2: Contribution of Nanotechnology in Summary (3).

2. Nano-Scaffolds for Tissue Engineering

Applications of nanotechnology in oral surgery have primarily focused on enhancement procedures for bone tissue regeneration and improving the osseointegration of oral implants. Nanomaterials aim to overcome the fundamental issues encountered with current scaffolds used for bone regeneration, such as insufficient mechanical strength, instability of released growth factors, and impaired cellular differentiation (10).

Nanostructures for tissue engineering (nano-scaffolds) are biocompatible nanomaterials that mimic the architecture of natural bone. These structures resemble the bone composition made up of collagen fibrils, hydroxyapatite, and proteoglycans, and they promote tissue regeneration by supporting cell adhesion, proliferation, and differentiation. Polylactic acid

(PLA) from polydihydroxy acid derivatives, poly-L-lactic acid (PLLA), polyglycolide (PGA), polycaprolactone (PCL), and nanophase hydroxyapatite (HA) have been widely studied (3,11).

PLLA has been approved by the FDA for use in bone reconstruction surgery. To improve its biological properties, PLLA nanofibers are often combined with hydroxyapatite, activated with arginylglycylaspartic acid (RGD) peptide, or supported with proteins such as bone morphogenetic protein 2 (BMP-2). Studies have shown that PLLA nanofibers facilitate colonization in bone defects and increase bone formation when used with BMP-2.3,12,13 Additionally, it has been shown that the osteointegrative properties of nanophase hydroxyapatite (HA) are enhanced. When bone marrow is added to three-dimensional porous nano-HA scaffolds, their adhesion, proliferation, and differentiation abilities have been observed. Nano-HA, which more closely mimics the nanostructure of natural bones, can be used to produce better implants. These features promise better osseointegration, more natural mechanical properties, reduced immune responses, and better control of cellular responses (3,14).

It has been demonstrated that nanotube structures have great potential for bone regeneration. Rosette nanotubes (RNT) are biomimetic and self-assembling new nanomaterials. Materials coated with RNTs have significantly increased cell regeneration because these structures create a suitable environment for cells (3,15). Carbon nanotubes (CNT) are other suitable scaffold materials that support the proliferation of osteoblasts. CNTs have excellent mechanical properties, which allow them to be used as reinforcement materials when combined with other biomaterials, supporting bone growth (3,16).

3. Effects of Nanotechnology on Imaging

Quantum dots (QD) are nanomaterials with narrow and size-tunable emission spectra that extend from ultraviolet to near-infrared light. They have long-lasting photostability, good photoluminescence, and a high signal-to-noise ratio. Due to these properties, they are particularly suitable for labelling and tracking specific cells and tissues, especially in non-invasive imaging, and can

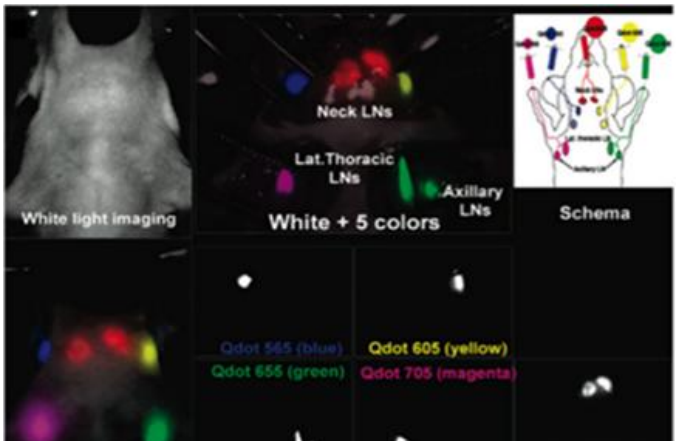


Figure 3: Quantum dots can be used as new imaging agents for lymph node imaging in head and neck cancer (3).

be used for the in vivo diagnosis of diseases and long-term monitoring (Figure 3)[3]. They provide better contrast and sensitivity in imaging. Quantum dots, when combined with paramagnetic ions, can enhance the quality of MRI images. This combination offers high sensitivity and high resolution, helping to identify tumor cells (3,17).

4. Oral Cancer Treatment and Nanotechnology in Drug Delivery Systems

Due to the very small size of nanoparticles, they are capable of overcoming certain barriers that larger microparticles normally cannot pass, thus reducing systemic toxicity (3,18). Among nanostructured drug delivery systems, liposomes and drug-conjugated nanoparticles (figure 4) (3) are of particular interest, especially in cancer therapy.

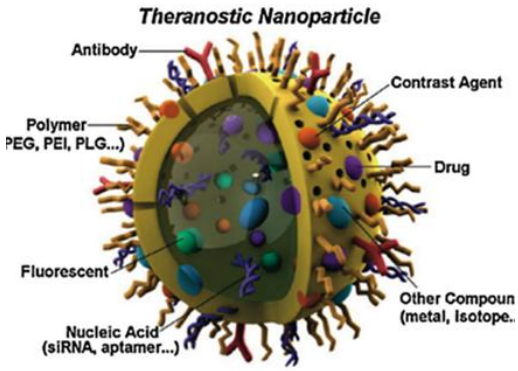


Figure 4: Therapeutic nanoparticle example (3)

4.1. Oral Cancer Diagnosis and Treatment

Oral cancer (oral cavity and oropharynx) is a common and aggressive form of cancer that can invade local tissues, metastasize, and has a high mortality rate. The 5-year mortality rate for oral cancer worldwide is approximately 50% (19,20). This indicates a poor prognosis, particularly for developing countries (21). Recurrence rates for Oral Squamous Cell Carcinoma (OSCC), which constitutes the majority of oral cancers, range from 18% to 76% in patients undergoing standard treatment. The primary factor limiting significant survival improvements is the delay in initiating treatment (22). To confirm the diagnosis of oral cancers, biopsy and histopathological examination are essential before treatment, and if possible, prior cytological findings can also be used as supporting evidence. These lengthy and costly diagnostic tests only delay the initiation of treatment. Delays in the diagnosis of oral cancer lead to extended treatment initiation times and, consequently, a decrease in patient survival rates (21,23,24,25). Although traditional treatment methods, such as surgery and chemoradiotherapy, have advanced in recent decades, they have not yet reached the ideal level. Cancer research, particularly in oral cavity and oropharyngeal cancers, is currently focused on improving diagnostic and therapeutic methods. Nanotechnology plays a crucial role in overcoming all these limitations. It involves the design, production, characterization, and application of nanoscale drug

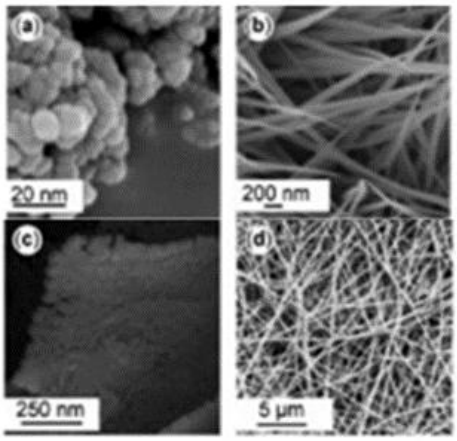
delivery systems, playing an important role in this field (26). Nanotechnology-based drug delivery systems, including polymeric nanoparticles (PNPs), solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), gold nanoparticles, hydrogels, cyclodextrin complexes, and liquid crystals (LCs), are emerging as promising options to enhance oral cancer treatment and minimize therapy side effects.

4.2. Nanotechnology-Based Drug Delivery Systems

Nanoparticles can be defined as ultra-dispersed solid supermolecular structures with submicrometer sizes ranging from 10 to 1,000 μm. Drugs can be solubilized, entrapped, encapsulated, or bound to the nanoparticulate matrix, which serves as a critical reservoir in drug delivery systems, especially in oncology (27-30).

Nanomaterials used in drug delivery systems can be classified based on their geometry, morphology, chemical composition, uniformity, and aggregation properties: (31)

A) According to geometric classification, nanomaterials are categorized into four groups: zero-dimensional, one-dimensional, two-dimensional, and three-dimensional (Figure 5) (31).



a. 0D: SiO_2 nanoparticles;

b.1D: CoO nanowires;

c. 2D: ZnO-NiO nanosheets;

d. 3D: PA6 nonwoven structure

Figure 5: Examples of nanomaterials types (31)

B) Nanomaterials classified according to chemical composition: (31)

1. Metal-Based Nanomaterials. Examples include: Silver nanoparticles, copper nanoparticles, gold nanoparticles.

2. Metal Oxide Nanomaterials. These materials are composed of a combination of oxygen and metal atoms. Examples include: Silica, titanium dioxide (titania).

3. Carbon-Based Nanomaterials. Examples include: Carbon nanotubes, fullerenes.
4. Dendrimers are highly branched, tree-like macromolecules.
5. Nanocomposites.

C) Another Category are Dendrimers: These are highly branched, monodisperse macromolecules composed of three distinct regions: the central core, branching units, and a densely packed surface. The branched structures located on the dendrimer's surface are referred to as dendrons. Dendrons can be chemically modified by attaching or substituting functional groups. These modifications alter the chemical and physical properties of the entire dendrimer.32 Dendrimers are formed through the iterative addition of polymeric layers around a central core. Drug molecules can be transported via covalent bonds or electrostatic interactions with the dendrimer surface, or by encapsulation within the dendrimer's core region (32).

D) Quantum Dots are of significant importance in the medical field and are particularly utilized in cancer imaging and cellular tracking applications. These are semiconductor nanocrystals exhibiting autofluorescent properties. Examples include binary metal complexes such as CdSe, CdS, and CdZn (32-33).

In addition to those mentioned, lipid-based nanomaterials, including solid-lipid nanoparticles, liposomes, and micelles, also hold significant relevance in medicine. Solid-lipid nanoparticles are submicron-sized lipid emulsions in which liquid lipids are replaced by solid lipids. Liposomes, typically 50–200 nm in size, are biocompatible structures that are used as novel drug carriers, particularly for the delivery of biological molecules like genes, peptides, and proteins. Liposomes also provide high drug encapsulation efficiency. Liposomes and bilayer structures are amphiphilic materials with both hydrophilic and hydrophobic properties. These properties coexist within the same structure. Liposomes can encapsulate hydrophilic drugs and maintain an aqueous core, making them capable of binding to cell membranes during endocytosis and continuously releasing drugs. Research has shown that liposomal formulations improve the pharmacokinetics and pharmacodynamics of related products (34-35).

Similarly, micelles are nanomaterials exhibiting amphiphilic properties; in aqueous environments, the hydrophilic parts of the molecules are located on the outer surface, while the hydrophobic components reside in the inner core. These structures can encapsulate hydrophobic drugs within their inner core and protect them from the external environment, while simultaneously being able to absorb polar drugs with their outer surface (Figure 6) (32).

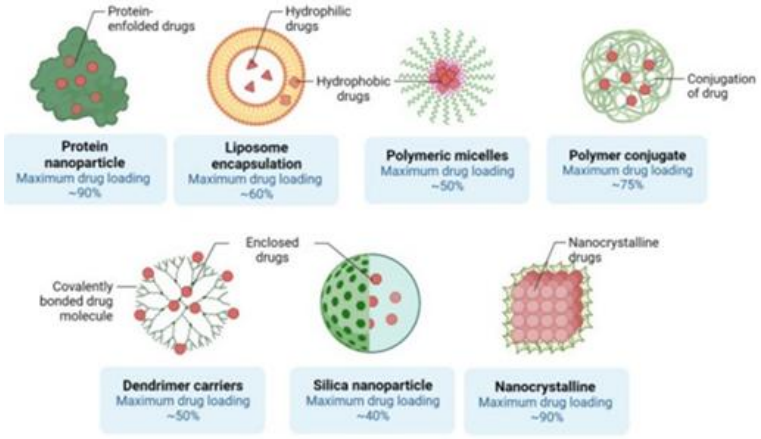


Figure 6: Types of Nanomaterials Used in Drug Delivery Systems (35)

4.3. Durability of Nanomaterials in the Body

The durability of the nanomaterial-drug complex is influenced by renal clearance or the activity level of the reticuloendothelial system (RES), which affects blood circulation through the kidneys. Relatively small nanomaterials are easily cleared by the kidneys, whereas larger nanostructures are removed by the RES. The capture of nanomaterials by RES cells reduces their systemic bioavailability. However, surface functionalization of nanomaterials with water-soluble polyethylene glycol (PEG) chains imparts "stealth-like" properties to these nanostructures, thereby reducing immune responses against them. This modification prevents their detection and phagocytosis by the mononuclear phagocytic system, allowing them to persist in the bloodstream (36-37). Additionally, PEGylation makes the nanomaterials appear as "empty" entities, enabling them to adsorb proteins, which prevents accumulation in biological systems. This property helps to avoid nanoparticle aggregation in solution and the formation of clusters as they enter the vascular system (38-39).

PEGylation, which extends the half-life of nanoparticles, is schematically illustrated in Figure 7.

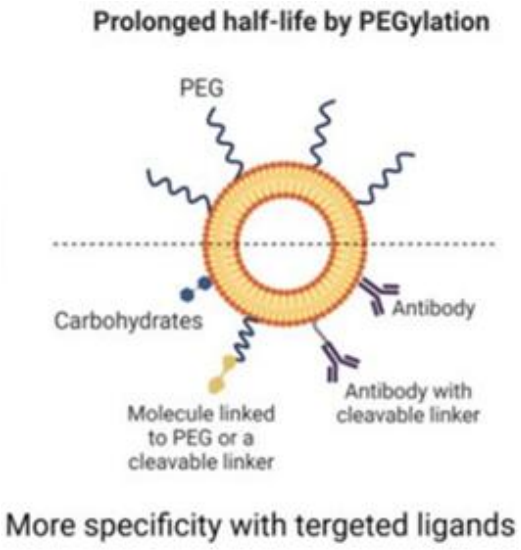


Figure 7: Illustration of nanoparticles with half-life extended through PEGylation (35)

4.4. Advantages and Disadvantages of Nanotechnology in Cancer Diagnosis and Treatment

Advantages:

The unique characteristics of nanoparticles, such as their diminutive size, large surface area-to-mass ratio, and functionalized structures, confer several significant advantages, which include:

- Prolonged circulation time
- Targeted drug delivery to the site of interest
- Enhanced bioavailability
- Reduced systemic toxicity

While advancements in drug delivery using nanotechnological devices have been remarkable, there remain several unresolved challenges that need to be addressed.

Disadvantages:

1. A more comprehensive understanding of the intracellular uptake mechanisms and the biodistribution and clearance of nanodevices in biological tissues is essential.

2. The potential for adverse or off-target effects resulting from the interactions between nanodevices and biological systems, such as free radical generation and damage to adjacent tissues.

3. Scaling up from preclinical trials to large-scale production, the cost of raw materials, and ensuring rigorous quality control for nanodevice fabrication.

4. Difficulties in securing financial support for startup companies that aim to commercialize nanopharmaceuticals.

The challenges faced by targeted drug delivery systems utilizing nanoparticles can be mitigated through an in-depth investigation of the limitations of nanoparticle-based strategies, as well as optimizing the current potential of nanoparticle formulations and devices (40).

4.5. New Approaches

The ultimate goal of cancer therapy is to eradicate as many cancer cells as possible without damaging healthy cells. However, the ability of a drug to target specific regions within the body to achieve desired therapeutic effects remains an area requiring further development.

In this context, nanotechnology-based drug delivery systems are emerging as a potential alternative to overcome some of the barriers previously encountered. These systems exhibit promising features, including superior anti-tumor effects against oral cancers, which conventional chemotherapy cannot achieve. As a result, the U.S. Food and Drug Administration (FDA) recently approved a clinical trial for a nanoparticle-based system for the treatment of solid tumors in humans (26).

Additionally, the submucosal injection of Cuburbitacin BE poly-lactic acid nanoparticles (CuBE-PLA-NPs) for the targeted delivery to cervical lymph nodes and the evaluation of clinical therapeutic efficacy has been assessed. The results showed significantly higher drug concentrations in the cervical lymph nodes following CuBE-PLA-NP injection compared to the control group. Moreover, the drug concentrations in the bloodstream of the CuBE-PLA-NP group were found to be significantly lower than those in the control group (41-42).

Thus, in the near future, oncologists and patients will be able to benefit from suitable nanotechnology-based drug delivery systems, improving therapeutic outcomes while reducing costs. Although clinical studies on oral cancer using nanotechnology are limited, nanotechnology is expected to transform healthcare in dentistry, redefine cancer with novel methodologies, and personalize patient treatment profiles (43). However, further research is needed to translate the concepts of nanotechnology into practical applications and to achieve the correct drug doses and ideal release profiles from these systems. Moreover, studies should continue to better understand the efficacy of these systems for various cancers treated by different molecular and cellular mechanisms (26).

5. Nanotechnology in Implantology

Implants are widely used in dentistry. In fact, titanium is the clinically most suitable material in dentistry. Titanium implants have many advantages, including good biocompatibility, mechanical properties, and generally adequate corrosion resistance. Additionally, titanium is a material with a very low likelihood of causing immunological reactions (6,44).

Although the acidic and saline conditions in the oral cavity can lead to electrochemical reactions between the implant and tissues, the corrosion resistance of titanium implants is not absolute. Under such conditions, implants are still prone to releasing wear particles and ions, which can lead to local immune responses, material degradation, and ultimately implant failure. Another factor influencing corrosion is the effect of microorganisms. The impact of their

enzyme-dependent activities can cause the loss of the surface passivation, thereby increasing the rate of corrosion (6,45).

Implants designed with the addition of nanoarchitecture aim to be resistant to infection, reduce the body's immune response, have higher integration, and release degradable drugs over time.46

Surface properties of nanocomposite implants can be modified to alter the immune response developed against the implant or the ability of bacteria to colonize it; there is a theory that the reduction in immune response is more dependent on the surface properties rather than the chemistry of the nanometric materials (3,47).

Uncoated implants generally exhibit lower osseointegration, which leads to impaired long-term healing. The surface roughness increases protein and tissue adsorption and proliferation on the implant. One of the advantages of coating implants is the increase in stress transfer; a thicker coating can provide better stress reduction, and the nanoporous structure can lead to a more homogeneous stress distribution (6).

Among the surface treatments of clinically used implants are mechanical processing, sandblasting, acid etching, sandblasting and acid etching, anodization, and plasma treatment (46,48).

Mechanical processing is considered a pioneering modification strategy applied to dental implants, supported by the significant work of P.I. Brånemark and his group (46,49). This process involves shaping the base material using harder metals at high rotational speeds, and this process reveals properties ranging from macro to micro scale; these properties have evolved from manual processing to digitally controlled processing methods.46

The combination of sandblasting and acid etching (SLA or sandblasted large-grit acid-etched) is a popular option in clinical practice. Studies have reported that accelerated osseointegration occurs within 1-2 months on micro/nano SLA implant surfaces. This bidirectional physical and chemical process is considered the most effective dental implant surface modification strategy, showing long-term success in pre-clinical and clinical research (46,50,51).

Controlled titanium (TiO2) nanostructures, such as nanotubes and nanopores, can be produced on titanium-based implants using electrochemical anodization (EA). This process allows the formation of regular nanotube and nanopore structures on Ti implants. This process results in titanium oxidation (TiO2) driven by the electric field, and fluoride-induced TiO2

dissolution in a fluoride-containing organic electrolyte, leading to the self-organization of titanium nanotubes/nanopores upon reaching electrochemical equilibrium. By adjusting EA parameters like electrolyte composition (water/fluoride content), voltage, current, and duration, various nanostructures, including nanotubes, nanopores, nanograss, and nanotemplates, can be produced. Optimum EA ensures controlled nanostructures are produced on these surfaces (Figure 8) (46). Anodization parameters, electrolyte age, composition (water/fluoride content), anodization voltage, current, or duration can be adjusted to produce complex nanostructures on the implant surfaces. Titanium nanotubes (TNTs) are hollow, test tube-like structures with open tops and closed bottoms, and their modification has been widely researched to enhance cell biological activity. Most of the research suggests that TNTs are recommended as an implant modification to enhance osseointegration (bone integration) (46,52).

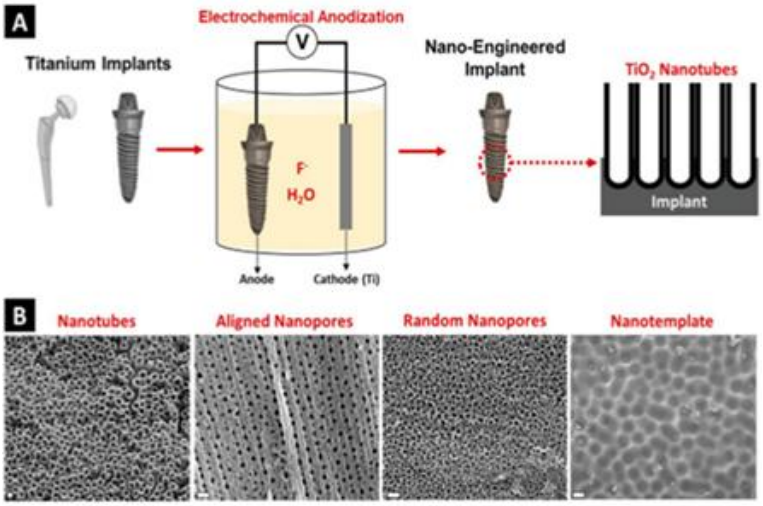


Figure 8: Various titanium nanotubes obtained as a result of electrochemical anodization[46]

Plasma treatment, on the other hand, involves coating the implant with the desired material through melting and sintering in a vacuum or low-pressure environment. As a result, the implant surface is coated with micro/nano-scale layers; however, these adhesive layers may peel off or separate; therefore, careful surgical handling may be required during implant placement (46).

The anodization and production of titanium nanotubes (TNT) on Ti implants is considered an ideal nano-engineering strategy based on key reasons such as easy and cost-effective

production, anodizing complex shapes and geometries, ease of arranging nanostructures, enhanced biological activity, preservation of micro-roughness, and broad in vitro and in vivo support.

Nanomaterials are typically used as surface coatings, playing a special role by allowing changes in topology (increased surface area of the coating with bone) and biological activity (enhancement of healing and cell adhesion). The use of nanomaterials offers the possibility of optimizing the topography of the implanted region by adding hierarchical micro/nanostructures to the surface; this not only significantly increases the surface area but also strengthens osseointegration (3).

For example, a commonly used implant alloy, Ti-6Al-4V, has been coated with hierarchical topography by plasma spraying HT or Sr-HT micron-sized powders onto commercially available Ti alloy plates. As a result of this process, a micron-rough ceramic was coated with surface nanoparticles of strontium-substituted hardystonite (Sr-HT). Another implant was coated with classical hydroxyapatite (HAp), while the Sr-HT-coated implant showed improved cell adhesion, remineralization, and new bone tissue formation, with a synergistic effect between the hierarchical topography and dissolution products (6,53).

Calcium silicate (CS)-based nanocoatings are also used to enhance osseointegration. The combination of atmospheric plasma spraying (APS) and hydrothermal technology (HT) imparts desirable characteristics, including high crystallinity to the coating, and enhances its degradation rate, crucial for the storage and transport of potential implants (6,54).

Compared to traditional CS coatings, nanostructured CS coatings offer improved hydroxyapatite mineralization, enhanced cell adhesion, increased cell proliferation, better osteogenic differentiation, and higher angiogenic factor levels (6,54).

The advantages brought by these titanium nanotubes created on the implant surface are summarized in figure 9.

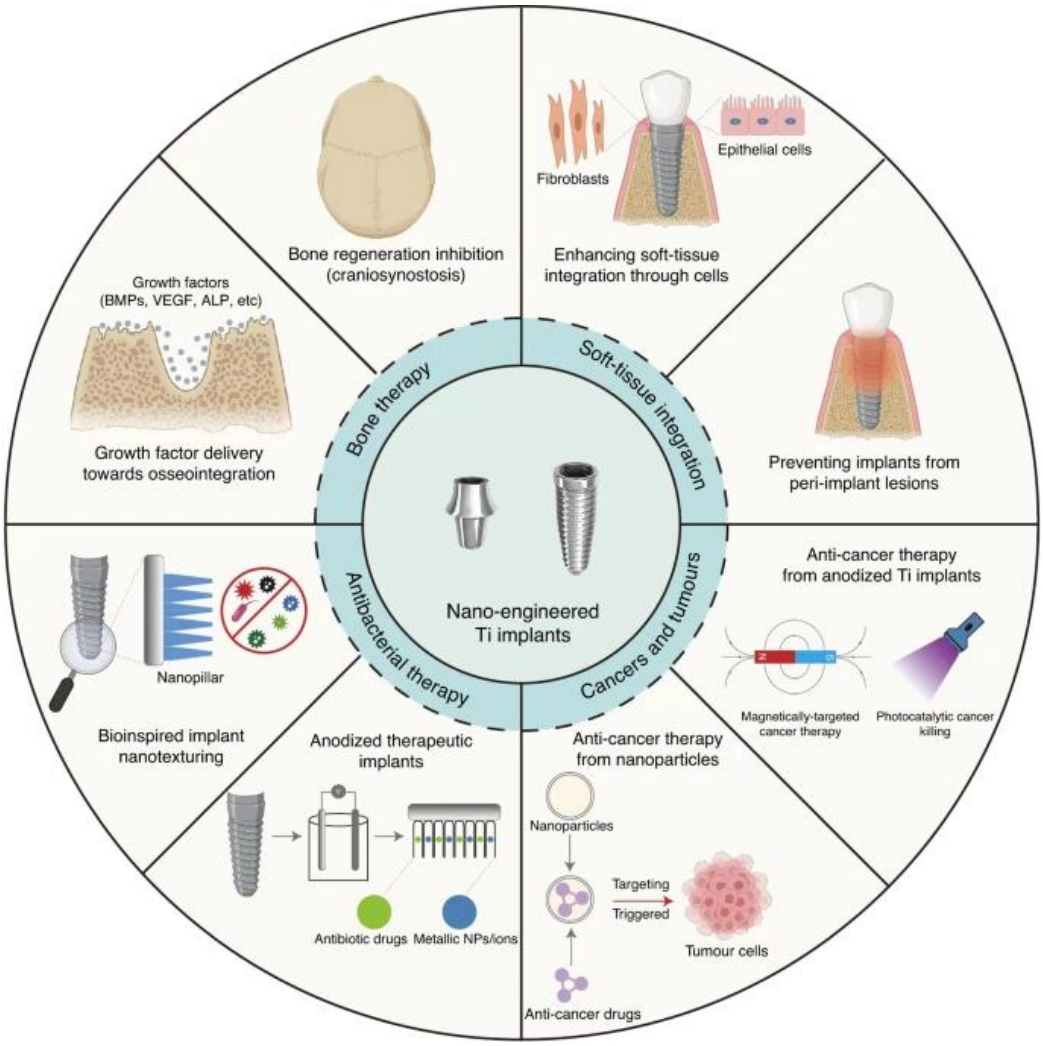


Figure 9: The advantages brought by these titanium nanotubes created on the implant surface[3]

The success of the implant is largely dependent on the quality of surface modifications, which are related to osteointegration, immune system response, and infection control. The ideal scenario is to maximize the therapeutic release and safely direct it to the implant's microenvironment, especially to the trauma site. These therapeutic agents can be bound to the surface of titanium (Ti) implants by modifying them with polymers, hydrogels, or nanoparticles. This way, the healing process can be accelerated, biocompatibility improved, and the long-term success of the implant can be ensured (46,55,56,57).

Some compounds added to TNTs to enhance osteointegration are as follows:

• **Bone Morphogenetic Protein-2 (BMP-2):** This is the most commonly used orthopedic biological substance for modifying titanium (Ti) implants with TNTs to enhance implant osteogenesis (46).

• **Strontium ranelate:** This anti-osteoporotic drug is used to guide research on the integration of strontium (Sr) into titanium (Ti) implants (46,58).

• **Pamidronic acid (PDA):** It enhances osseointegration and reduces bone resorption. It also demonstrates biocompatibility with osteoblasts and hematopoietic stem cells, while inducing apoptosis in osteoclasts derived from hematopoietic stem cells (46,59).

• Studies conducted with **parathyroid hormone (PTH)** and **fetal bovine serum (FBS)** have also shown an increase in osteogenic activity (46,60,61).

Ideal titanium nanostructures with antibacterial modifications should prevent adhesion, inhibit colonization, prevent biofilm formation, and stop proliferation. In the past decade, research for the design of next-generation bacteriostatic and bactericidal implants has focused on micro and nanoscale topographic modifications to prevent biofilm formation (46,62). With the rise of implant-associated infections, research has shifted toward providing local treatment through implant coatings and the loading and release of potent antibiotic agents (63,64). The high surface area of nanotopography and reduced shear forces enhance the adhesion of bacteria and osteoblasts. Ti implants anodized with TNTs have been found to have great potential for providing controlled local therapy to combat infections (46,53).

Biomimetic nanotexturing applied to implant surfaces (such as the creation of nanopillars, nanodroplets, or nanohairs, which mimic dragonfly wings or lizard skin) has exhibited antibacterial activity through a 'spiked bed' mechanism. Although static nanoscale implant topography can initially prevent adhesion, it may also protect attached and dead bacteria, as well as other microbes, from the underlying surface. Therefore, the development of 'dynamic' modifications, which trigger bactericidal activity in response to electrical or magnetic fields, has become increasingly important (63,64).

The goal is to address the drawbacks of systemic treatments by enhancing surface conditions, enabling local drug release, maximizing therapeutic efficacy, and ensuring safe delivery to the trauma site within the implant’s microenvironment. These therapeutic substances can be attached to the surface of titanium (Ti) implants through modification with polymers, hydrogels, or nanoparticles (55,56,57).

Studies have shown positive developments in infection control through the loading of gentamicin and vancomycin onto nanotubes that release antibiotics (46,65-67). These loadings are possible due to the coating of the implant surface with biopolymers.

The placement of drug-releasing implants can result in high drug concentrations that may cause local cytotoxicity and potentially trigger bacterial adhesion again. Therapeutic release can be controlled by adjusting TNT size or coating drug-loaded TNTs with degradable biopolymers like polydopamine (PDA), PLGA [poly(lactic-co-glycolic acid)], and chitosan to achieve sustained long-term release (46,68).

Another method involves integrating strong metallic/semimetallic ions or nanoparticles onto or into TNT-based titanium (Ti) implants to provide potent bactericidal functions. Examples of added ions and nanoparticles include silver (Ag), gold (Au), copper (Cu), boron (B), phosphorus (P), calcium (Ca), gallium (Ga), selenium (Se), magnesium (Mg), fluorine (F), and zinc (Zn) (46).

Additionally, studies have been conducted with ibuprofen to reduce the anti-inflammatory response.6 Modification of titanium nanotubes illustrated in figure 10 (46), advantages and disadvantages of modifications added to TNTs illustrated in figure 11 (69,70).

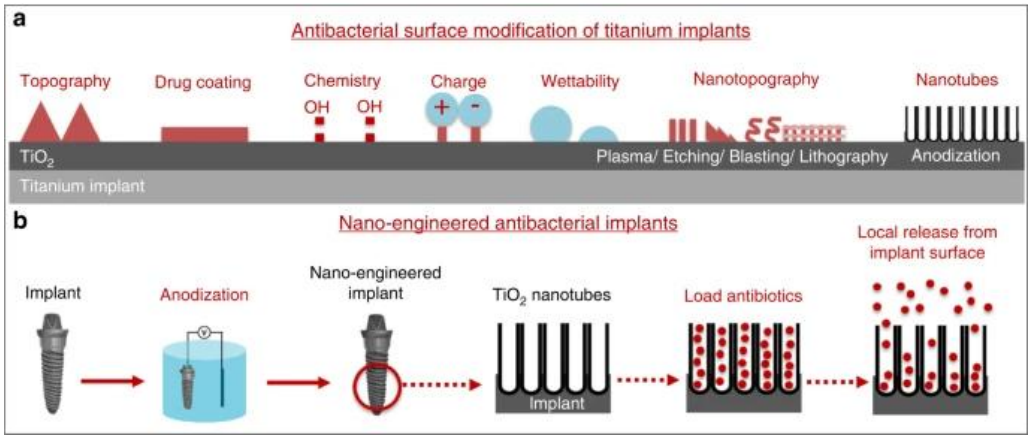


Figure 10: Antibacterial modification of Ti implant surfaces: a. different physical and chemical surface modification techniques; and b. electrochemically anodized Ti implants featuring TiO_2 nanotubes for localized antibiotic release (46).

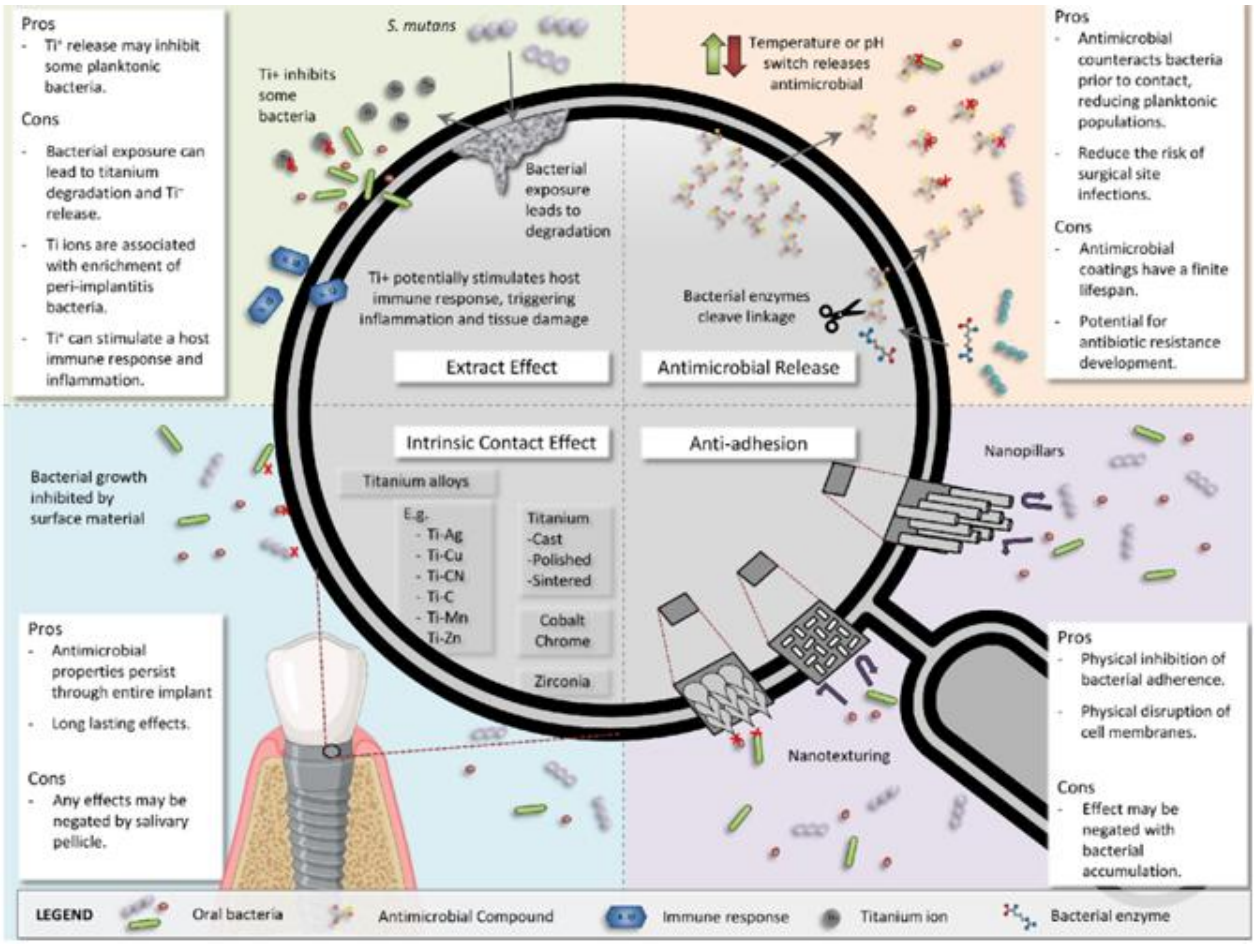


Figure 11: Illustration of the advantages and disadvantages of modifications added to TNTs (69,70)

6. Nanoanesthesia

Anesthetic nanorobots are still at the conceptual level. This idea involves the use of a suspension containing nanobots that can reach the dentin and move toward the dental pulp. The navigation factor could be, for example, a temperature gradient, chemical agents, or a computer used externally by the dentist. Once reaching the site of action, the nanobots would alter neurotransmission and maintain this state until the medical procedure is completed. Despite the growing opportunities for developing such technological structures since the discovery of scanning tunneling microscopy and atomic force microscopy, there has been no significant further development (1,6).

7.Potential Side Effects and Limitations

In order to fully utilize nanotechnology and minimize potential toxic effects, the long-term health impacts of nanoparticles must be thoroughly researched. The reduced size of nanomaterials can cause some potential issues. As they move through the body, nanoparticles may accumulate in target organs (liver, lungs, kidneys, heart, and spleen), penetrate cell membranes and mitochondria, and trigger a series of negative events. For example, manganese oxide, titanium dioxide, aluminum oxide, zinc oxide, and silver can accumulate and cause harmful reactions, or a nanoparticle may be small enough to cross the blood-brain barrier (3,71). High surface area ratios make nanoparticles biologically active, which can lead to outcomes such as infection and oxidative stress. For successful tissue engineering, scaffolds must be developed in a way that provides necessary oxygen and nutrients to dense cellular clusters in all organs (10,46,72).

The release of Ti particles and ions (including nanoparticles) results from (tribo-)corrosion. The presence of unintended or released nanoparticles (NPs) due to surface corrosion of the implant can also lead to specific toxicity. NPs loaded onto the implant surface (e.g., metals and drugs) can be unexpectedly released. These released NPs may interact chemically or physically with biological fluids, regardless of their composition.

Uncontrolled and high drug/protein concentrations, along with the contact between Ti (particles or ions) and tissues at the implant site, can lead to toxic effects on the surrounding tissues or newly regenerating bone. Ti particles cause an increase in osteoclast differentiation and resorption activity, continuously triggering the release of RANK-L and pro-inflammatory cytokines (such as IL-1 and TNF-β) (46,73). This can create a vicious cycle that enhances osteoclastogenesis, contributing to the corrosion of Ti dental implants and causing the accumulation of metal ions/particles in the cytoplasm of precursor cells. All of these events trigger a pro-inflammatory response from immune cells, negatively impacting tissue integration and wound healing (46).

Due to their small size, metal types (NPs or ions) and ROS can diffuse through nuclear pores and enter the nucleus. AgNPs, Au, and metal oxides such as TiO_2 or ZnO can act as DNA intercalators, causing severe oxidative DNA damage (46,74).

As previously mentioned, Ti implants designed with nano-engineering have extraordinary potential in terms of biological activity and therapeutic applications. However, important questions arise regarding the transition from the laboratory to clinical applications. The clinical translation of nano-engineered Ti dental implants faces the following challenges (Figure 12): (23)

- Optimization of production
- Achieving local sustained drug release
- Enhancement of biological activity
- Adaptation of in vivo models
- Achieving corrosion resistance and electrochemical stability
- Selection of sterilization process (23)

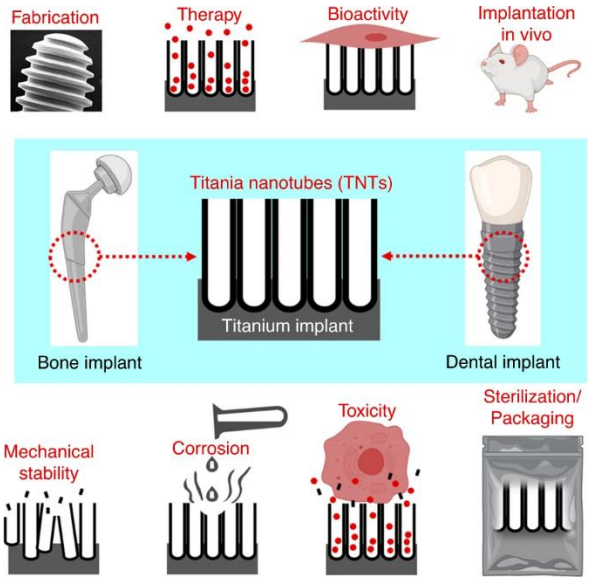


Figure 12: Clinical transition challenges (46)

It is anticipated that advanced engineering and design approaches will increase the effectiveness and safety of these implants, thereby expanding their applications in the field of dentistry (46).

Conclusion

The integration of regenerative nanotechnology into oral and maxillofacial surgery is advancing at an accelerated pace, with recent breakthroughs highlighting its transformative potential. Nanomaterials exhibit exceptional physical, chemical, and biomimetic properties that facilitate cellular proliferation and tissue regeneration, positioning them as promising candidates for future therapeutic interventions. Although the use of biomaterials for bone regeneration is well-established, the application of nanoscience and nanotechnology in oral and maxillofacial surgery remains an emerging and rapidly evolving field, offering novel avenues for clinical advancement.

Although some nanostructures have not yet proven effective for clinical use, certain innovative nanostructures offer promising new therapeutic benefits for cancer treatment in the near future. Both in cultured cells and in vivo experimental animals, long-term and short-

term toxicity evaluations must be conducted for these nanomaterials until they receive FDA approval for clinical application. However, nanotechnology has successfully developed innovative methods for cancer diagnosis, management, and monitoring throughout the 21st century, and continues to support our commitment to early intervention by identifying the molecular pathways of cancer.

The integration of nanotechnology into the development of titanium dental implants presents both exciting opportunities and significant challenges. While the potential of nano-engineered implants for improving biological activity, therapeutic outcomes, and long-term stability is evident, several obstacles remain in terms of production optimization, achieving sustained drug release, enhancing biological interactions, and ensuring corrosion resistance. Additionally, the safe clinical application of these implants requires careful consideration of potential toxicity, as nanoparticle accumulation in vital organs, the release of metal ions, and oxidative stress could lead to adverse effects. The clinical translation of nano-engineered titanium dental implants requires further research, especially in optimizing the balance between efficacy and safety. Addressing these challenges through advanced engineering methods and in vivo model adaptation is crucial for enhancing implant performance and expanding their application in the field of dentistry. The "set and forget" concept-based implants are expected to be the future of dental applications, ensuring early stability and long-term success. This will minimize the need for treatment or corrections, reducing clinical visits and patient complaints. It will make it possible to achieve a high success rate in both healthy and at-risk patient conditions. Achieving this will pave the way for a broader implant market, including orthopedic implants, joint replacements, and craniofacial implants.

Regenerative nanotechnology in oral and maxillofacial surgery offers significant potential for improving tissue regeneration and therapeutic outcomes, particularly in dental implants and cancer treatments. However, challenges remain in optimizing production, achieving sustained drug release, ensuring corrosion resistance, and assessing the potential toxicity of nanoparticles, necessitating further research for safe clinical application.

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