SYSTEMATIC REVIEW
Sistematik Derleme

Cadmium Toxicity in Dental Materials: Could it Play a Role in Oral Cancer? A Systematic Review

Diş Materyallerde Kadmiyum Toksisitesi: Ağız Kanserinde Rol Oynayabilir mi? Sistematik Bir Derleme

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ABSTRACT
Cadmium, one of the carcinogenic/toxic trace elements, is an important sub-title in tobacco-related oral cancer (OC) research. The toxicity of cadmium in dental materials and its role in OC formation were investigated using articles in PubMed. Thus, a total of 13 studies from these databases were included in the review. It has been revealed that cadmium in dental materials is generally at a level that cannot cause toxic effects. In addition, it can be said that dental materials cannot be among the etiological factors in the formation of cadmium-induced OC today, where there are major sources for cadmium such as tobacco products, foods, air pollution and drinking water.

Key Words:
Cadmium, Dental material, Oral cancer, Cadmium toxicity

ÖZ
Kanserojen/toksik eser elementlerden biri olan kadmiyum, tütüne bağlı oral kanser (OK) araştırmalarında önemli bir alt başlıktır. Kadmiyumun dental materyallerdeki toksisitesi ve OK oluşumundaki rolü PubMed'deki makaleler kullanılarak araştırıldı. Böylece, bu veri tabanından toplam 13 çalışma incelemeye dahil edilmiştir. Dental materyallerdeki kadmiyumun genel olarak toksik etkilere neden olmayacak düzeyde olduğu ortaya konmuştur. Ayrıca tütün ürünleri, gıdalar, hava kirliliği ve içme suyu gibi kadmiyumun önemli kaynaklarının bulunduğu günümüzde kadmiyum kaynaklı OK oluşumunda dental materyallerin etyolojik faktörler arasında olamayacağı söylenebilir.

Anahtar Sözcükler:
Kadmiyum, Dental materyal, Oral kanser, Kadmiyum toksisitesi

INTRODUCTION

Oral cancer (OC) is one of the head and neck cancers, which has an increasing incidence in individuals under 40 years and whose most important etiological factors are considered to be tobacco and alcohol use (1). There are many studies (2-4) examining the mechanism of action of tobacco products in the formation of OC. Cadmium (Cd), one of the carcinogenic/toxic trace elements, is an important sub-title in tobacco-related OC research (5).

Although tobacco products are considered to be the most important source, exposure to Cd is also caused by food, drinking water and air pollution (6-9). European Food Safety Authority (EFSA) and The World Health Organization (WHO) accept a one-week Cd intake is safe to be below 2.5 µg/kg and 5.8 µg/kg, respectively (5,10,11). It has been shown by many studies (12-14) that Cd has a toxic effect with its accumulation in various tissues.

It is thought that direct contact of Cd with dental tissues, especially the oral mucosa, may be effective in the formation of oral neoplasm. It is shown with cell line studies that Cd increases the formation of reactive oxygen species and influences autophagic reactions via cause imbalanced apoptosis mechanisms and thus on neoplastic formation (2,3,5). Today, many dental materials used for various purposes are in short-term or continuous direct contact with the oral mucosa, and the Cd in its content may be a potential etiological factor in the cytotoxic effect and formation of OC (15,16).

The aim of this study is to evaluate the studies examining the toxic effect of Cd in dental materials and its effect on OC formation.

MATERIALS and METHODS

Search strategy

A literature search was conducted using the terms *"cadmium oral"* or *"cadmium dental"* or *"cadmium dental material"* or *"cadmium dentistry"* in PubMed and Web of Science Library between November 28 and December 7, 2021.

Study Selection

The study excluded reviews, case reports, letters to the editor, and articles that were not open access, were not written in English, or contained the term cadmium only in their references.

RESULTS

Thirteen articles (15-27) were included in the review (Fig. 1). Based on the fields of dentistry, the most articles were written in Endodontics. While one study (16) has mentioned the toxic effect of Cd, there is no statement in any study about the relationship of Cd with OC. In one study (18), the potential of Cd to cause an allergic reaction was emphasized. The most used method for the determination of Cd is the concentration determination by ICP-MS/ICP-OES devices (Tab. 1).

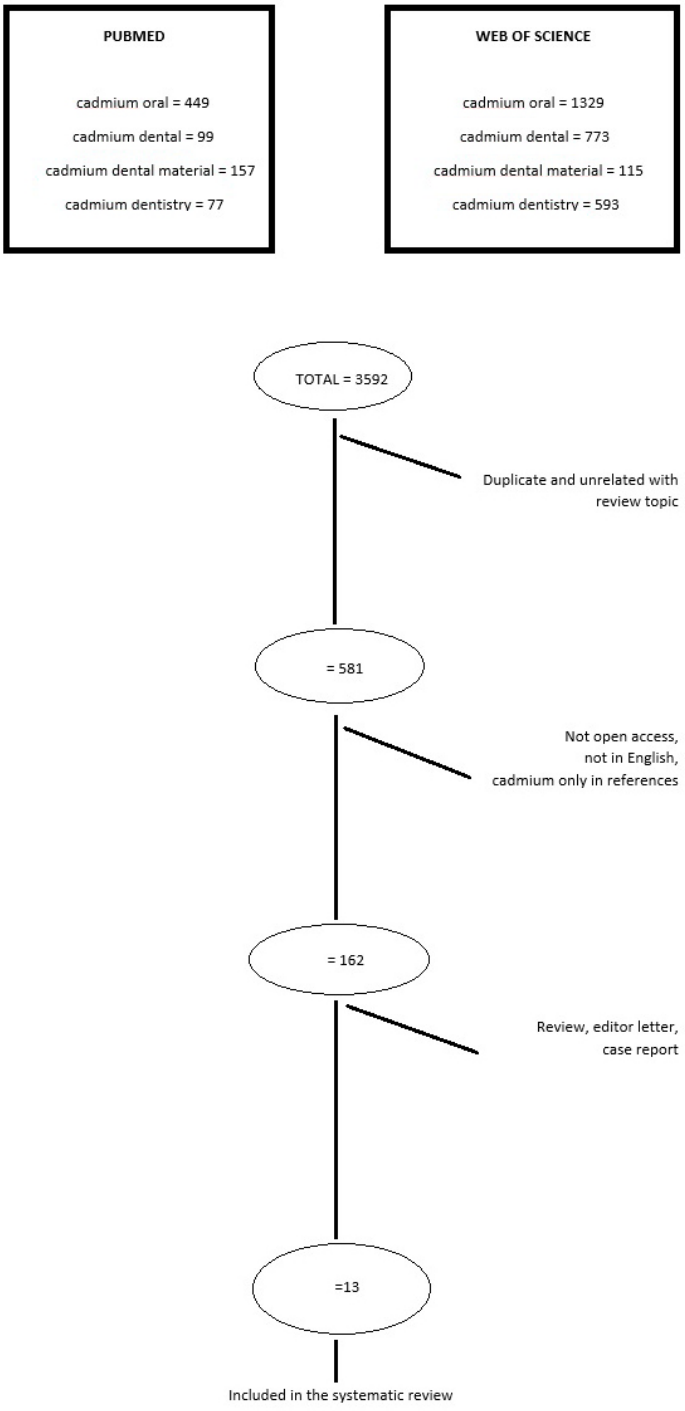

Figure 1. Flow chart of selected articles

Table 1. Study characteristics.

	Field of Dentistry	Topic related Cd	Technique used	Information on Cd toxicity	Cd in oral cancer
Nikolic et al (2004) (15)	Prosthetic Dentistry	Cd in dental materials & teeth	PSA	Cd not found in dental materials, no information	No information
Kiat-Amnuay et al (2006) (17)	Prosthetic Dentistry	Technical study examining color pigments containing Cd	SPM	No information	No information
Marino et al (2009) (18)	Oral Diseases	Relationship between BMS & Cd	Allergy patch test	Cadmium sulfate in prosthetic materials is considered a high allergen, however, a significant relationship with BMS is not clear	No information
Alves et al (2010) (19)	Restorative Dentistry	Optical properties of dental resins	SPM	It has been stated that composites with added cadmium selenide/zinc sulfide are bactericidal and nontoxic	No information
Chang et al (2010) (20)	Endodontics	Cd in MTA & Portland cement	ICP-OES	The amount of Cd detected is equal to that in the diet, a larger amount is required to be toxic	No information
Stejskal et al (2013) (21)	Prosthetic/ Restorative Dentistry	Cd in the etiology of FM	MELISA	It has been stated that Cd cause lymphocyte response, no information about the allergen/ toxic effect of Cd	No information
Kum et al (2013) (22)	Endodontics	Cd in MTA	ICP-OES	Proroot MTA contained more heavy metals than Ortho MTA. But the Cd level is very low. Even a little bit of Cd detection is tied to the method (ICP-OES protocol?). However, both MTAs are considered safe	No information
Dorileo et al (2014) (23)	Endodontics	Cd in MTA	AAS	Cd could not be detected in any materials as it remained below the detection limits	No information
Gonçalves et al (2014) (24)	Orthodontics	Cytotoxic effect of Cd in orthodontic bands	YPD agar	It has been mentioned that Cd in the bands can be replaced by Zn. The bands were found to be cytotoxic. No information on Cd toxicity	No information
Kum et al (2014) (25)	Endodontics	Cd in MTA & tricalcium silicate	ICP-OES	Small amounts of Cd were found in MTA Angulus and MicroMega MTA, while only Al was detected in Bioaggregate. It was stated that the detected Cd level is not toxic. It is mentioned that the use of ICP-OES makes the results of the study more reliable	No information
Jang et al (2014) (26)	Endodontics	Cd in MTA & tricalcium silicate	ICP-MS	It is stated that BioDentine (BD) contains more heavy metals than Bioaggregate and MTA but BD contains not significantly high Cd. High levels of different heavy metals were detected. For this reason, it was said that BD may be the most toxic material among three	No information
Mikulewicz et al (2014) (27)	Orthodontics	Cd amount in pig tissues after bracket	ICP-OES	Compared to the control group, a significant difference was found only in the aorta and in the hair sample taken 3 months after the contamination. They concluded that metal ions did not reach toxic levels and that hair was a good marker as a noninvasive biomarker	No information
Borges de Olival et al (2018) (16)	Prosthetic Dentistry	Cd in hydrocolloids	ICP-MS	Cd was detected in all 8 different hydrocolloids. It has been said that it can have a toxic effect. It was stated that the CD was detected above the acceptable level. It has been mentioned that during the use of hydrocolloids, it is in close contact with the oral mucosa for about 2 minutes	No information

Cd: Cadmium, PSA: Potentiometric stipping analysis, SPM: Spectrophotometry, BMS: Burning Mouth Syndrome, MTA: Mineral trioxide aggregate, ICP-OES: Inductively coupled plasma optical emission spectrometry, FM: Fibromyalgia, MELISA: Lymphocyte transformation test, AAS: Atomic absorption spectrometry, YPD: Yeast extract peptone dextrose, ICP-MS: Inductively coupled plasma-mass spectrometry

It was emphasized that although Cd was detected in some studies (20,22,23,25,27), especially in tricalcium silicate materials such as mineral trioxide aggregate (MTA), it would not be considered toxic.

The amount of Cd in fixed prosthetic dental materials is at a trace level and the toxic/allergenic effect is ignored (15,18,20). It has been claimed that a Cd-containing product used to improve the structure of composite resins is bactericidal and tissue-friendly (19). Hydrocolloids have been shown as the most suspicious product in terms of Cd toxicity among prosthetic dentistry materials (16).

DISCUSSION

In studies (20,22,25-27) to determine the amount of Cd, it has been revealed that Cd in dental materials is generally at a level that cannot cause toxic effects. Since none of the studies in the review included any information about Cd causing OC formation, it can be said that it is not possible or clear for Cd in dental materials to play a role in the etiology of OC.

The fact that the amount of Cd in tricalcium silicate materials used in endodontic treatment is determined far below toxic levels and that it is trapped in the pulp chamber as a result of their use does not suggest that it may be involved in the etiology of OC with a direct effect. The probability of a scenario where tricalcium silicate contacts the oral mucosa iatrogenically during endodontic treatment and the magnitude of the neoplastic effect it may create with its Cd content is negligible.

There are animal experiments (28,29) showing toxic effects when cadmium is added to the structure of hormones or forms compounds with different elements. Conversely, because of the study conducted with cadmium selenide/zinc sulfide material added to the structure of composite resins in order to improve the aesthetic properties of restorative dental materials, it has been reported (19) that this particle has a bactericidal effect. This suggests that the biological behavior of differ-

ent forms of Cd differ. The biological safety of cadmium can be understood more clearly with new studies examining the form and biological effects of Cd in the structure of dental materials.

The toxic level of Cd in the structure of hydrocolloid, which is a widely used dental impression material, and the fact that it is in contact with the oral mucosa for a few minutes during the procedure makes this material the most suspicious product among all dental materials in terms of its involvement in the etiology of OC. However, considering the short time that prosthetic treatment patients are exposed to hydrocolloid throughout their lives and the weak effect of the cytotoxic/neoplastic performance of Cd during the procedure, it shows that all dental materials, including hydrocolloid, are innocent in the formation of Cd-induced OC. In addition, hydrocolloid, which is the most suspicious material in terms of its involvement in the etiology of Cd-induced OC, has begun to leave its place to digital intraoral scanners in recent years (30). It can be said that dental materials cannot be among the etiological factors in the formation of Cd-induced OC today, where there are major sources for Cd such as tobacco products, foods, air pollution and drinking water.

CONCLUSION

The lack of sufficient studies demonstrating that Cd in the structure of dental materials has a toxic effect and the absence of any studies showing that it may play a role in the etiology of OC makes the role of Cd in dental materials in the etiology of oral cancer unclear. Today, due to the large literature on Cd from tobacco products, foods, air pollution and drinking water, these factors can be considered as potential suspects in the etiology of OC. New studies are needed to clearly reveal the role of Cd in the structure of dental materials in the etiology of OC.

Ethics Committee Approval:
No need.

Author contribution statement:
Planning of design and study process – S.Ş., T.Ç., M.N.K., H.N.B., T.D.Ç., and K.E.; literature review – S.Ş., M.N.K., H.N.B., T.D.Ç.; critical language revision – K.E. and writing – S.Ş. and K.E.

Conflict of Interest:
The authors declare that they have no conflict of interest.

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