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Review

Multiple Sclerosis and Dentistry: A Contemporary Evaluation

Multipl Skleroz ve Diş Hekimliği: Güncel Bir Değerlendirme

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Summary

Multiple sclerosis (MS) is an inflammatory, demyelinating condition affecting the central nervous system. MS exhibits characteristics of an auto-immune disease. Etiology of this condition remains unknown but environmental and genetic factors are often thought to be responsible. A possible relationship between dentistry and MS has often been mentioned in the literature. Special attention and interdisciplinary cooperation are required in the diagnosis of MS and the application of dental treatments in order to optimize general and dental health status of patients with MS. In this review, MS-dental related studies and recommendations for dental treatment approaches for individuals with MS are discussed. (Turkish Journal of Neurology 2015; 21:1-6)

Key Words: Multiple sclerosis, dentistry, dental care, periodontal diseases

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Özet

Multipl skleroz (MS) santral sinir sistemini etkileyen kronik, enflamatuvar, demiyalizan bir hastalıktır. Hastalık otoimmün özellikler sergilemektedir. Etiyolojisi tam olarak bilinmemesine rağmen çevresel ve genetik faktörler suçlanmaktadır. MS ile diş hekimliği uygulama ve klinik tablolarının arasındaki ilişki literatürde sıklıkla tartışılmıştır. Gerek MS teşhisi, gerekse de dental tedavinin gerçekleştirilmesinde özel dikkat gerektiren süreçlerin bulunması MS hastalarının genel ve dental sağlık durumlarının optimize edilmesi için disiplinler arası işbirliğini zorunlu kılmaktadır. Bu derlemede, MS ile diş hekimliği alanında yapılan çalışmalar, MS'i bulunan bireylerde dental tedavi sürecindeki öneriler irdelenmiş ve tartışılmıştır. (Türk Nöroloji Dergisi 2015; 21:1-6)

Anahtar Kelimeler: Multipl skleroz, diş hekimliği, ağız bakımı, periodontal hastalıklar

Çıkar Çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemiştir.

Introduction

Multiple sclerosis (MS) is a demyelinating autoimmune, neurodegenerative and inflammatory disease of central nervous system (1). In this disease, brain, spinal cord and optic nerves can be involved to varying degrees, changing the symptoms of the disease. According to the course of the disease, MS can be of relapsing-remitting, primary-progressive, secondary-progressive and progressive-relapsing types (2). The etiology of the disease is not fully known. However, environmental and genetic factors are thought to play important roles (3,4,5,6,7). The main findings of the disease include fatigue, loss of sensation and orientation, vision, bladder and bowel dysfunction, gait coordination problems, emotional changes, depression, spasticity, and less often difficulty in swallowing or speaking and tremor (8). The first

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symptoms in MS usually appear at the ages of 20-30 years. At its global maximum, the prevalence of MS is around 30/100.000. Epidemiologically, MS shows geographical variation and it is less frequently seen in the Equatorial belt. Multiple sclerosis is seen more commonly in females (11,12,13,14). Genetic studies have shown clear familial transmission patterns for MS (15). The fact that it is seen in heterogeneous patterns in most countries underlines the importance of environmental factors and genetic risk factors (14,16).

In a study using Turkish population, the average age onset for MS was 30, and the prevalence of familial MS was found to be 11.5%. In the epidemiological studies in Turkey, MS prevalence was found to be between 41-101.4/100.000 (18,19,20). In the diagnosis of MS, all other inflammatory, infectious, multiple metabolic, genetic, neoplastic and spinal conditions should be ruled out (9,21). McDonald criteria are used in the diagnosis of MS. Published in 2001, these benchmarks were revised again in 2005 and 2010, and some changes have been made. Diagnosis is mainly based on clinical signs and symptoms. The supporting laboratory findings are magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) and Visual evoked potentials (VEP) (22,23,24).

Today, there is no definitive treatment of MS. The treatment of MS is conducted using a variety of approaches based on the present complaints of each patient (9,25,26).

Dentistry and MS

Cavities and Fillings

Published studies on MS and dentistry frequently discussed cavities and the use of amalgam (27,28,29). Talking about MS and cavity epidemiology in his 1978 paper (10), Craelius discussed certain etiological factors (e.g. excess in certain nutritional fats and vitamin D deficiency) that these two conditions share. McGrother et al. (27) documented an increased incidence of cavities in MS patients. The same study examined the amount of mercury located in the bodies of individuals with MS as compared to the control group, and no statistical difference was found. However, both in the control group and MS group there was a linear correlation between amalgam fillings and the amount of mercury in the body (27). Kovac et al. (29) found that the number of cavities and missing teeth was higher in the MS group compared to controls, but MS group had a smaller number of fillings. In a study that investigated the protein changes in the CSF after the removal of the dental amalgam from the oral cavity, it was found that all proteins in the CSF except for the albumin bands had changes at the 24-48 hours following the dental procedure compared to before, as shown by gel electrophoresis (28). Numerous studies, literature reviews and scientific institutes report a lack of support between dental amalgam and MS (30,31,32,33,34,35). Bangsi et al. (30) suggested that long-term amalgam fillings in large numbers may constitute a risk factor for MS but they failed to find any difference between control and patient groups in their study in terms of the variables of interest. In a study in Spain that looked at Decay-missing-filled teeth index (DMFT) and gum health for different age groups, it was seen that people with MS had DMFT index values similar to the general population (36). In a review paper on Italian population, there was no relationship found between MS group and controls in terms of existing amalgam fillings and mercury-amalgam exposure (37). For the moment, there is no standing evidence for replacing amalgam fillings with other types, although the topic itself is still a matter of current debate (38).

Periodontal Status

Periodontal disease can be defined as a group of inflammatory illnesses of bacterial etiology that affect the gum and tooth supporting tissues (39). In the recent years, a close attention is given to the relationship between periodontal diseases and certain systemic diseases. The focus of these discussions and studies are periodontal diseases, and systemic diseases and conditions such as diabetes mellitus, metabolic syndrome, cardiovascular diseases, abnormal pregnancy conditions (low birth-weight), pulmonary infections, rheumatoid arthritis and Alzheimer's disease (40,41). Periodontopathogens or their side products can get in the bloodstream through different mechanisms and travel onto target organs or tissues. The inflammatory mediators in the gingival tissue (proinflammatory cytokines, e.g. tumor necrosis factor alpha (TNF-α), interleukin [IL] etc.) can incur an additional burden on the inflammatory load of the body (39,40). In a review paper, periodontal pathogen bacterias like P. gingivalis may also play a role in central nervous system infections much like MS (42). Certain studies suggested that C-reactive protein (CRP) levels, is are an acute phase protein, may be associated with the periodontal status (39,43,44). It was shown that periodontal treatment may lead to favorable systemic CRP levels (43,45). The possible relationships with Alzheimer's disease (AD), which is a neurodegenerative disease, and periodontal diseases, have also been investigated (46,47,48). When compared to the healthy individuals, people with AD had elevated plasma Ig G and TNF-α levels against periodontal bacteria (P. gingivalis, T. forsythia ve A. actinomycetemcomitans), There were no differences found in IL–1β and IL–6 levels (46). In a similar study, levels of F. nucleatum and P. intermedia antibodies seen in periodontal diseases were found to be elevated in people with AD compared to controls (47). The fact that periodontal diseases can be treated or managed suggested that they may pose a changeable risk factor for AD (48). There is a relatively smaller number of studies on MS and clinical periodontal status. Symons et al. (49) failed to find an increased tendency for cavities and periodontal diseases in a small number of people with MS. The ratio of MS patients with healthy gums were 30% which led to the conclusion that these individuals may need to pay an increased attention to their gum health (36). Similarly, more than 30% of people with MS reported difficulties continuing their oral hygiene practices (50). Ali et al. (51) drew attention to an important relationship between periodontitis and autoimmunity, and discussed certain findings suggesting plaque bacteria activating the complement system and causing immune reactions. This finding should be studied with caution since MS is hypothesized as having an autoimmune pathogenesis. Sheu and Lin (52) showed that a relationship between chronic periodontitis and MS was observed in female patients. Under the light of existing literature findings, we think that the study of the relationship and interplay between MS and periodontal diseases may produce new lines of research.

Pain/Trigeminal Neuralgia-Temporomandibular Joint

There have been reports of temporomandibular joint (TMJ) problems in the maxillofacial area and pain in the face area of MS patients (29,53,54). It was shown that jaw clenching and

bruxism seen in MS patients may affect temporal bones, causing enlargement of cranial cavity (55). A study using 50 MS patients showed that MS may play an etiological role in TMJ disorders (29). A case study in the literature also emphasized that condylar hypermobility and pain may be included in the clinical symptoms of individuals with MS (56). Pain findings akin to trigeminal neuralgia (TN) around the facial region of MS patients have commonly been reported (57,58,59). It is reported that facial paralysis and trigeminal sensory neuropathies may accompany MS symptoms and may present as early symptoms (57). Cruccu et al. (59), held pontine-located demyelinating plaque damage responsible for the involvement of primary afferents in TN seen in MS (59). In terms of preventing unnecessary dental interventions in the individuals followed with TN, it is important to study the diseases that may cause or relate to the etiology of TN (such as MS) (58). It is normal for certain findings to be present in the maxillofacial area preceding the systemic findings of MS. Facial numbness, loss of sensation, tingling, dysesthesia may be the early indicators of MS (60).

Considering the clinical properties and symptoms reviewed above, it is clear that dentists may also play a role in the diagnosis of MS within an interdisciplinary framework. The necessity to refer individuals to relevant medical units in the event of pain or sensations that are not incompatible with dental or oral status is evident (57,60).

Multiple Sclerosis Drugs and Oral Cavity

During the attacks of the disease, steroids (prednisone, methylprednisolone, etc.) are the most frequent pharmacological agents. Aside from their systemic side-effects, corticosteroids may also cause certain conditions that are important for dental care, such as adrenocortical deficiency, delayed wound healing, increased risk for postoperative infections and, in the long-term use, osteoporosis (25). The role of long-term corticosteroid use in the development of periodontal diseases has been discussed. Safkan and Knuuttila (61), reported that corticosteroids used for neurological purposes over the course of 1-4 years did not cause a significant changes in clinical parameters that are indicative of periodontal disease. Regardless of the reason, it should be kept in mind that the use of corticosteroids may produce the outlook of a healthy periodontium through the suppression of main inflammatory reactions (62). On the other hand, it was shown that dexamethasone application led to more severe bone destruction in rats with experimentally induced periodontal diseases (63). In order to manage the progression of the disease and control its activity, Interferon-β (IFNβ) derivatives (IFNβ-1a, IFNβ-1b), glatiramer acetate, monoclonal antibody (natalizumab) and immunosuppressive drugs (mitoxantrone, azathioprine, methotrexate, cyclophosphamide) are being used (25,26). In a large portion of these drugs, side effects concerning the oral cavity, in addition to systemic side-effects, are also seen. These include increased risk of infection, mucositis, and ulcerative stomatitis. Side effects concerning the oral area such as dry mouth (xerostomia) and taste changes In IFNβ derivative medications, and taste changes, swallowing difficulty and salivary gland swelling in glatiramer acetate are seen (25,64). In a study published in 1994, it was found that gum swelling can be more frequently seen in MS patients who use cyclosporine A, depending on the dose (>400 ng/ml) (65). In the presence of clinical symptoms such as spasticity, atonical and spastic bladder, fatigue and neuralia, the primary symptomatic medicines are the muscle relaxants (baclofen, tizanidine), tricyclic antidepressants, anticonvulsants (carbamazepine, gabapentin) and anticholinergic drugs. Xerostomia in the oral cavity is a possible outcome for all these drugs (25).

Points of Consideration in the Dental Care for MS Patients

Preliminary approaches to dental care should be employed prior to the treatment in these individuals. In this context, the patient's current systemic status and drug use should be examined thoroughly. Those who are on steroids have tendency for developing infection (25,57). Therefore, prior to any dental intervention (especially surgical ones), steroid dosage should be adjusted and the use of a prophylactic antibiotic should be kept in mind (57). In order to control the postoperative bleeding and minimize the postoperative complications, it is necessary to investigate the possible side effects of the MS drugs related to liver involvement (especially for those who use IFNβ derivatives and immunosuppressants) (57) prior to any surgical attempt. It is also necessary to consider the possibility of the liver involvement and peptic ulcer risk, as well as interaction effects of the drugs commonly prescribed following dental procedures, such as analgesics, non-steroidal anti-inflammatory drugs, as well as MS drugs. Special attention must be paid to the antibiotics used for dental purposes and their interaction with MS drugs (e.g. carbamazepine-clarithromycin) (66). It is necessary to remember the possibility of opportunistic infections (candidiasis etc.) and secondary malign conditions in people using immunosuppressive drugs in the long-term, and include these in the dental evaluation of the oral cavity and treatment (57). Mouth moisturizers (in mouth rinse and gel forms), and cavity protection (commonly in gel form) and salivary stimulants should be considered for the treatment of dry mouth in individuals who use medications for MS (67). In daily application, sugar-free lemon drops or a few drops of lemon juice can be effective for the stimulation of parotid gland in order to alleviate mouth dryness. Maintaining good hydration and decreasing alcohol, caffeine use and smoking are also effective in managing mouth dryness. As the discussion above suggested, dental treatment can be modified according to the MS treatment. It is important to acknowledge the individual variations in these conditions and that additional disorders may accompany the clinical status. Therefore, prior to dentists and dental treatment, the consultation mechanism between neurologist and the dentists must be in place. The duration of dental treatment must be kept short in consideration of the patient's physical condition (68). In order to prevent unwanted pulmonary aspiration, dental intervention in a supine position in people with MS would be a correct approach (25,68).

In order to minimize the muscle spasms and fatigue in physically affected MS patients, dental equipment to reduce unwanted mouth movement (opening and closing of the mouth, biting the doctor's fingers etc.), mouth openers, tongue depressors, finger protectors and retractors should be used. If the patient is confined to wheelchair, and if the head position and the surrounding space allow it, the dental procedure may be conducted while the patient is in the wheelchair or alternatively in a reclining wheelchair specifically designed for dental procedures

(38). Moving dental applications (e.g. moving apparatus used for orthodontic treatment etc.) in individuals with severe cases of MS must be planned carefully (69). During the planning of dental treatment, the presence of MS-related conditions should guide the use of sedation and general anesthesia (25,38,68).

Daily care and habits of individuals with MS should be modified according to their physical status. For example, it can be recommended that the person brushes their teeth while sitting down, in order to prevent fatigue (34). There could be additional obstacles to perform proper dental care, such as difficulty in grasping the toothbrush. It is possible, however, to overcome such grasping difficulties. A custom-made toothbrush handle to enable easier grasping (such as with a tennis ball) can be fashioned (Figure 1). Attaching the brush to the palm with a rubber band or tape is also another measure that has been seen to work in order to prevent dropping it (70). Electrical toothbrushes and mouth douches can also provide beneficial outcomes for oral hygiene (34,70). In individuals with increased disability levels, a parent or a caretaker can maintain the oral hygiene. For this purpose, it is important for the doctor or the assisting clinical personnel to train the caregiver. Example: The caregiver puts the patient in a sitting position and perform the brushing action while either sitting down or standing (70,71) (Figure 2). Being a very effective methods of cleaning the side surfaces of the teeth, flossing can be performed either with separately sold holders or with flosses that come with their own disposable holders. Flossing before bedtime can provide quite effective in preventing bacteria from reproducing (34). Fluoride applications (tablet, gel, mouthwash or varnish) are quite useful in terms of preventing cavities (71). Again, according to the status of the individual, a doctor-recommended mouthwash can be useful to perform daily oral hygiene requirements. Multiple sclerosis can manifest as a clinical condition that affects multiple parts of the body. A multidisciplinary approach is important in the treatment of MS. Recent scientific evidence indicating the relationship between oral health and systemic diseases suggested an increased need for causal explanations by dentistry for the systemic clinical findings of unknown etiologies. On the other hand, it is possible that dentists should play a role during the diagnosis of MS, identify the effects of MS drugs on the oral cavity and take additional precautions during the dental treatment of people with MS. In this respect, it is possible to see that dentists play an important role in the general treatment approach for MS.

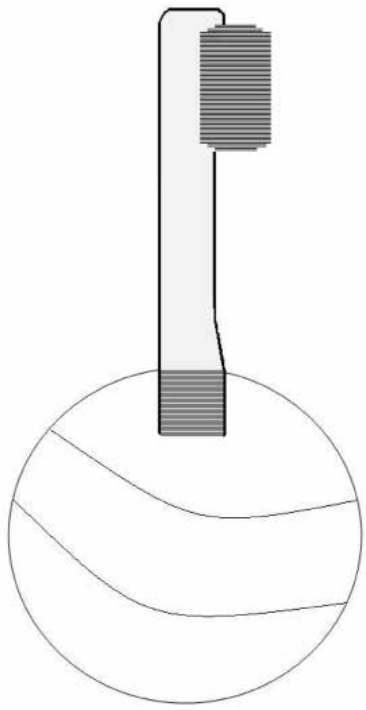

Figure 1. HaBased on their ability to use their hands, certain facilitative modifications can be made to ensure a better grip for oral hygiene tools such as a toothbrush. The tennis ball handle for the toothbrush is an example of such modifications

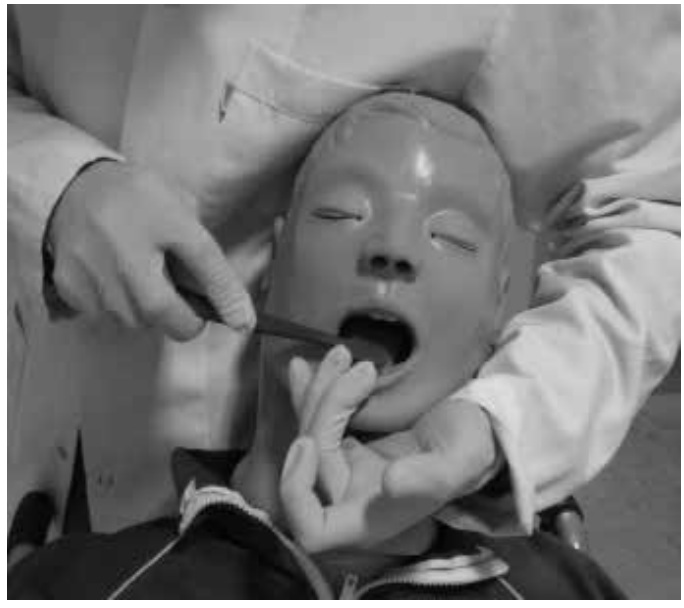

Figure 2. In the case of advanced physical disability, the oral hygiene needs of a patient can be performed by a parent or a caregiver. For example the caregiver can be standing or sitting down and approach the patient in the illustrated position. Oral care applications can be modified according to the physical state of the person. A dentist should be consulted about the most proper approach

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