EC Dental Science Editor's Column - 2016

Angiogenesis in Dental and Oral Conditions: Too Important to Ignore

Constantinos M Mikelis
Texas Tech University Health Sciences Center
USA

Md Sanaullah Sajib and Constantinos M Mikelis*

Department of Biomedical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX, USA

COLUMN ARTICLE

Angiogenesis is the formation of new vessels from pre-existing ones. The oral cavity, like the rest of the human body, is formed by highly vascularized tissues which maintain tissue and cellular homeostasis. This is achieved through intense angiogenesis during development. Although angiogenesis is not considered a regular event in the adult life, angiogenesis imbalance mediates many pathological oral and dental conditions. In the present editorial article, we highlight clinical and biological processes mediated by angiogenesis, where pro- and anti-angiogenic treatments can significantly affect clinical practice.

Dental pulp is the connective tissue filling the center of the tooth. Under physiological conditions, it is characterized by abundant expression of growth factors [1], where they regulate multiple cellular functions [2]. Under wound healing conditions, like regenerative endodontics, revascularization through angiogenesis is a prerequisite for successful dental pulp regeneration. Highly angiogenic dental pulp stem cells are easily obtained from teeth after extraction and can efficiently applied, providing new vessel formation and thus nutrient and oxygen supply for pulp regeneration [3]. Alternatively, growth factor application after stem cell re-transplantation in the root canal space has been shown to increase the survival rate of re-transplanted tissues and is becoming standard care in clinical practice [4].

Increased formation of new vessels is one of the characteristics of periodontal disease. Angiogenesis in periodontitis seems to be triggered from overproduction of pro-angiogenic factors in the inflamed gingiva. VEGF and HIF-1α levels are increased in periodontal tissue, demonstrating angiogenic processes in periodontitis [5,6]. Furthermore, salivary levels of VEGF are also indicative of the periodontal status [5]. The expression of pro-angiogenic factors present in periodontal disease can be regulated also from other factors apart from hypoxia, like bacterial endotoxins and inflammatory cytokines [6].

According to the American Association of Orthodontists, the need for orthodontic treatment is rapidly increasing worldwide. Orthodontic forces facilitate orthodontic tooth movement through bone remodeling. Existing periodontal ligament vessels are occluded on the pressure side of the dental root, decreasing blood perfusion and generating hypoxia. Hypoxia is one of the main inducers of angiogenesis, which in turn leads to the formation of a new vascular plexus, contributing to bone remodeling [7].

Development of anti-angiogenic therapies consists one of the most active fields for anti-cancer research and head and neck cancer could not be an exception. With more than half a million new cases every year, head and neck cancer represents the sixth most common cancer in the world. Multiple genetic and epigenetic events, including the expression and function of growth factors and cytokines

Citation: Md Sanaullah Sajib and Constantinos M Mikelis. "Angiogenesis in Dental and Oral Conditions: Too Important to Ignore". EC Dental Science ECO.01 (2016): 43-44.

and the hypoxic conditions actively increase angiogenesis, providing a malignant phenotype, correlated with primary tumor growth and metastatic dissemination [8]. VEGF consists the main target growth factor for anti-angiogenic therapies, although several other growth factors, chemokines, like CCL2, CCL5 and CXCL8/IL-8, and prostaglandins have been shown to actively participate in tumor-induced angiogenesis, consisting targets for intense scientific efforts [9].

One of the side-effects of bisphosphonate-related cancer treatment can be considered the bisphosphonate-related osteonecrosis of the jaw. This disease, which has been described about a decade ago, is getting more common among bisphosphonate-treated cancer patients but lacks therapeutic intervention due to its unknown pathogenesis and the lack of clinical and basic science data. Bisphosphonates have been shown to have anti-angiogenic effects both *in vitro* and *in vivo*, which eventually leads to suppression of bone remodeling. Tooth extraction is usually the initiating event for bisphosphonate-related osteonecrosis of the jaw. Normally, tooth extraction is followed by a series of healing steps, like clot formation, conversion of clot to crenulation tissue, then to connective tissue and finally bone. Angiogenesis is an important component for bone remodeling, thus insufficient angiogenesis and eventually reduced blood flow could compromise tissue viability. Pro-angiogenesis efforts could potentially provide effective therapeutic intervention of this debilitating condition [10].

Overall, the rapid growth of scientific knowledge has revealed the importance of angiogenesis imbalance in the formation of various oral and dental related pathological conditions and has provided some novel, promising therapeutic interventions. Intense ongoing scientific efforts provide potential for effective new treatments and hope to patients suffering from the aforementioned conditions.

BIBLIOGRAPHY

1. Grando Mattuella L., *et al*. "Vascular endothelial growth factor and its relationship with the dental pulp". *Journal of Endodontics* 33.5 (2007): 524-530.

2. Kim SG., *et al*. "Effects of growth factors on dental sem/progenitor cells". *Dental Clinics of North America* 56.3 (2012): 563-575.

3. Nakashima M., *et al*. "Human dental pulp stem cells with highly angiogenic and neurogenic potential for possible use in pulp regeneration". *Cytokine and Growth Factor Reviews* 20.5-6 (2009): 435-440.

4. Saghiri MA., *et al*. "Role of angiogenesis in endodontics: contributions of stem cells and proangiogenic and antiangiogenic factors to dental pulp regeneration". *Journal of Endodontics* 41.6 (2015): 797-803.

5. Booth V., *et al*. "Vascular endothelial growth factor in human periodontal disease". *Journal of Periodontal Research* 33.8 (1998): 491-499.

6. Vasconcelos RC., *et al*. "Immunoexpression of HIF-1α and VEGF in Periodontal Disease and Healthy Gingival Tissues". *Brazilian Dental Journal* 27.2 (2016): 117-122.

7. Niklas A., *et al*. "The role of hypoxia in orthodontic tooth movement". *International Journal of Dentistry* (2013).

8. Molinolo AA., *et al*. "Dysregulated molecular networks in head and neck carcinogenesis". *Oral Oncology* 45.4-5 (2009): 324-334.

9. O'Hayre M., *et al*. "Novel insights into G protein and G protein-coupled receptor signaling in cancer". *Current Opinion on Cell Biology* 27 (2014): 126-135.

10. Allen MR and Burr DB. "The pathogenesis of bisphosphonate-related osteonecrosis of the jaw: so many hypotheses, so few data". *Journal of Oral and Maxillofacial Surgery* 67.5 (2009): 61-70.