

Anuvinda SS¹, H.Soniya²

¹Department of Prosthodontics, KLE Dental College, Bangalore.

²Thai Moogambigai Dental College, Chennai

ABSTRACT

Dental implants made of titanium are placed directly into the bone tissue, which is a complex and dynamic tissue. This bone tissue not only helps maintain calcium homeostasis and serves as a hematopoietic organ, but it also acts as an immune regulator. The presence of a titanium implant during bone healing has recently been demonstrated to stimulate the immune system and cause type 2 inflammation, which appears to guide the connection between the host and the implant. This tends to show that osseointegration is a dynamic process involving a complicated series of reactions involving numerous host systems and pathways. Foreign Body Equilibrium (FBE) is a continuous equilibrium that occurs when osseointegration is not disrupted. To sustain the FBEs long-term integrity, the implant-host interaction must be improved further, notably when the mechanisms implicated in osseointegration breakdown start to function. The immune system may be stimulated as a result, disrupting the delicate balance between the osteoblast and the osteoclast, resulting in bone resorption. The immunomodulatory function of the Mesenchymal stem cell (MSC) has also been investigated, and in this vein, the notion of osseointegration immunomodulation through therapeutic mechanotransduction, particularly by extracorporeal shock waves therapy (ESWT), has recently been postulated. Mechanobiology has allowed us to investigate the impact of mechanical forces on cellular processes, revealing the intricate cellular control involved in mechanical signal transduction. Not only bone cells, but also MSC, can be stimulated by mechanical stimulation. Mechanical stimulation can also alter the cellular shape of immune cells, affecting their phenotypic and function.

KEYWORDS

Mechanotransduction, Osteogenesis, BIC, Osteocytes, ESWT

How To Cite This Article: Anuvinda SS, H.Soniya: Mechanotransduction In Dental Implants -. Int J Prosth Rehabil 2020 1: 2:18-20

Received: 26-08-20; Accepted: 28-09-20; Web Published: 13-12-2020

Introduction

Mechanotransduction

We now know that osteogenesis is not solely dependent on the skeletal system's bone cells; rather, there is a multicellular collaboration. The complexity grows even more when we consider a fourth factor, mechanical stimuli, which can play a role in maintaining the material-host relationship's balance. Physical forces play a role in embryonic development, tissue homeostasis, and pathogenesis, among other things. The role of mechanical signals in controlling cellular activities, on the other hand, has just recently been acknowledged. As a result, novel study models to examine the influence of mechanical stresses on cells and tissues are being developed as interest in the topic of mechanobiology rises^[1-9]. Shear, tension, and compression forces all affect the cells. Tissues respond to mechanical signals in a variety of ways, including the creation of ECM components^[10]. Through the mechanotransduction signal, a mechanical change can influence gene expression and cellular activity^[11]. The cytoskeleton filaments, such as actin and microtubules, would convey these mechanical impulses, which would then be converted into biochemical signals,

Address of correspondence

Dr. Anuvinda SS

Department of Prosthodontics, KLE Dental College, Bangalore.

Email Id: anunagr@gmail.com

with cell surface integrins crucial for mechanotransduction^[12]. In fact, good clinical outcomes acquired by progressive loading protocol and instantaneous loading protocol^[13] suggest that physiological mechanical stimuli can be advantageous to accompany the osseointegration of a dental implant and allow for successful osseointegration^[14]. In this regard, Duyck et al. demonstrated that mechanical stimulation can increase bone-implant contact (BIC) in an animal model using a bone chamber model^[15]. However, because mechanical stimuli are important for bone remodelling, further damage can result in implant failure^[16]. ESWT are commonly used in the area of therapeutic mechanotransduction at the moment. ESWT are supersonic waves that are created by a variety of technologies, including electrohydraulic, piezoelectric, electromechanical, and pneumatic devices,

and cause transient pressure changes in the tissues they are applied to^[17]. The mechanical shocks created by ESWT are thought to increase the permeability of the cell membrane, triggering the release of cytoplasmic ribonucleic acid (RNA) via an active process involving exosomes. This cellular event is the one that causes the effects seen in tissue repair to speed up. However, more research is needed to fully understand the underlying mechanism. The bone appears to be programmed to seal any portion that compromises its integrity, sealing and safeguarding the marrow content by restoring a cortical bone barrier. As a result, we might suppose that the "raw ingredients" (phosphate, calcium, and so on) are more readily available from a cortical bone source. In this regard, oral implants placed in low-density bone tissue (bone type IV) have been shown to have a greater failure rate^[18]. On the other hand, there is an increase in peri-implant bone loss in patients with osteoporosis, despite the fact that there has been no difference observed yet in the survival rate of oral implants implanted in patients with and without osteoporosis^[19]. In rats, Koolen et al. revealed at the histology level that after ESWT, de novo bone production occurs in bone defects restored with a titanium scaffold as a bone substitute. In a similar vein, Koolen et al. predicted that perioperative shock wave treatment could improve screw fixation and osseointegration of cortical and cancellous orthopedic screws, particularly in patients with osteoporosis. They were able to show that an ESWT performed immediately after the implantation of titanium screws (Ti6Al4V grade 5) increased screw attachment of the cortical screw, as measured by better mechanical strength and osseointegration, in a healthy rodent bone model. Shock waves have been suggested to cause the conversion of progenitor cells into osteogenic precursor cells, resulting in anabolic effects in the bone. Another theory is that ESWT causes osteocytic cell death via a process known as cavitation. This osteocyte death could stimulate local bone remodelling, prompting the osteoblast to make additional osteoid, and eventually leading to the formation of a neocortex^[20]. Osteocytes are mechanosensors and essential regulators of cellular homeostasis. The presence of HBMMSC and immune cells in the peri-implant milieu led us to believe that the ESWT may have an immunomodulatory effect favouring osseointegration. HBMMSCs can be identified not only in the peri-implant environment, but also on the titanium surface. In monocytes, macrophages, and dendritic cells, mechanical signals play a significant role in the regulation of immunological and cellular processes^[20]. Immune cells that infiltrate the wound play a vital part in determining the wound's varying fate. The systemic depletion of macrophages, for example, has been shown to cause a

persistent failure in the axolotl's regeneration potential, as well as significant fibrosis. However, after the macrophage population is restored, the axolotl's regeneration potential is restored^[21]. While the use of immunomodulatory implants in and of themselves (clean implants) results in appropriate osseointegration, the FBE can be affected by clinical circumstances such as overload. ESWT is a promising therapeutic alternative to increase clinical success in oral implants and sustain FBE long-term due to the possibility of guiding the transition between the M1 inflammatory phase and the M2 anti-inflammatory phase by mechanotransduction. Because the capacity for tactile perception of osseointegrated implants, known as "osseoperception," grows over time^[22], this could potentially improve the feedback loop to the sensory brain. Furthermore, it has been suggested that adding nerve growth factor (NGF) to oral implants on a topical basis could aid to increase tactile sensitivity and reduce occlusal overload, and ESWT has been shown to be beneficial in enhancing NGF expression^[23].

Conclusion

Mechanotransduction can help to strengthen the interaction between the implant and the host. However, research at the cellular and molecular level are required in order to determine the medical device as well as the most effective treatment range. All of this is being done in order to improve, maintain, and restore the balance of this trio of elements, namely bone cells, immune cells, and implants, which ultimately determines FBE's fate.

Authors contribution

Anuvinda SS: Manuscript editing, Literature search, data collection

H Soniya: Data Analysis, manuscript drafting

Acknowledgement

The authors would thank all the participants for their valuable support and thank the dental institutions for the support

Conflict of interest- None

Source of funding- Agarwal and Co.

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