The Effect of Static Magnetic Field in Enhancing the Level of BMP-2 and FGF-2 during Early Phase of Osseointegration

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Abstract

Growth factors have been reported play a significant role in accelerating osseointegration and to increase implant stability, especially bone morphogenetic protein-2 (BMP-2) and fibroblast growth factor-2 (FGF-2) that can stimulate bone formation and remodelling. Static magnetic field (SMF) is known to able to support osseointegration in several studies by advancing bone regeneration.

The aim of this study was to evaluate the effects of SMF as healing abutment in accelerating osseointegration and enhancing implant stability, illustrated in the level of BMP-2 and FGF-2. An experimental analytic study with randomized control trial design, single blind, on patients. There were 40 implants installed at mandibular D2 bone and were divided into control group (n=20) and intervention group (n=20). Control group was installed titanium healing abutment, and intervention group used SMF healing abutment. Patients were advised to come on day 3, 10, 30, and 60 for control and sample collecting purposes. Gingival sulcus fluid was taken from peri-implant sulcus using Periopaper and analyzed it with ELISA to get BMP-2 and FGF-2. Statistic used was software R, 4.1 version.

The use of SMF healing abutment is able to significantly increase FGF-2 level at day 3 and 10 post implant placement, compared to control group. The level of BMP-2 also increases significantly throughout the monitoring period in intervention group. This may suggest a faster osseointegration process. SMF as a promising healing abutment can increase the level of FGF-2 and BMP-2 in early phase of osseointegration; hence it can reduce the marginal crestal alveolar bone loss after dental implant placement.

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Introduction

Ossointegration is a direct, light-microscopic attachment between an endosseous implant and the living bone, which is important for long-term success and stability. There is no standardisation in terms of osseointegration and prosthetic loading timing. This procedure can take anything from 0 to 6 months. Several approaches are being investigated in order to shorten this interval. Changes in implant surface characteristics and design have improved primer stability and the health of the peri-implant tissue. These modifications intended to improve bone-implant surface connection and speed healing. Another approach of speeding osseointegration is to modulate healing after an implant is placed. In return, bioactive molecules that promote osteoblastic differentiation and accelerate bone regeneration in the vicinity of the implant can accomplish this modulation.[1,2,3]

Growth factors are proteins that regulate wound healing. Many growth factors are present in platelet-containing preparations derived from human blood, including bone morphogenetic protein-2 (BMP-2), platelet-derived growth factor

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(PDGF), insulin-like growth factor (IGF), fibroblast growth factor-2 (FGF-2), vascular endothelial growth factor (VEGF), and transforming growth factor-β (TGF-β) are also in bone healing. These growth factors attract undifferentiated mesenchymal cells to the wound site, allowing angiogenesis, inflammation, and cell proliferation to occur.[4,5]

This study aims to assess the impact of SMF to BMP-2 and FGF-2 level on implant stability. The study's findings suggest that it will be feasible to decrease the duration needed for osseointegration and increase implant stability.

Materials and methods

The study was conducted in accordance to the approval of the ethics committee from the Ethical Committee Universitas Airlangga, Surabaya, Indonesia (Number 553/HRECC.FODM/IX/2021). This is an experimental analytic study with randomized control trial design, single blind, design. Forty implants were placed in patients' mandibular D2 bone at Indo Dental Center. They were then divided into two groups: the control group, of twenty implants, and the intervention group, which also consisted of twenty implants. While the titanium healing abutment was implanted in the control group, the SMF healing abutment was placed in the intervention group. BMP-2 and FGF-2 were collected from gingival sulcus fluid peri-implant sulcus using periopaper and then analyzed with an enzyme-linked immunosorbent assay (ELISA). Patients were advised to return on day 3, 10, 30, and 60 post implant placements for control and sample collecting purposes. Statistic was analyzed with software R, 4.1 version, 2021.

Results

Statistical investigation showed that BMP-2 levels began to rise on day 3 and continued to rise until day 30, when they began to plateau. When compared to the control group, this increase was greater in the intervention group (Figure 1).

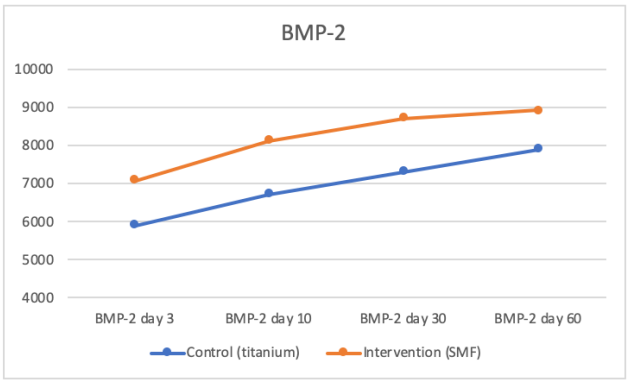

Figure 1. Mean plot of BMP-2 level during study ($p<0.05$).

Statistical investigation showed that FGF-2 levels began to rise on day 3 and continued to rise until day 10, when they began to slope down. When compared to the control group, this increase was greater in the intervention group (Figure 2).

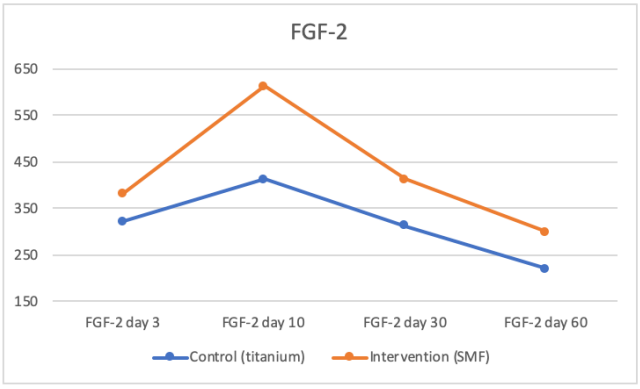

Figure 2. Mean plot of FGF-2 level during study ($p<0.05$).

Discussion

Primary or mechanical stability is considered a necessary condition for successful osseointegration in implant dentistry. The success of anchored endosseous implants is determined by the alveolar bone architecture at the implant drilling site. The implant placement is generally more successful with D1 and D2 bones, since they possess higher mechanical strength and density compared to other bone types, which can present more difficulties. Following immediately and persisting for several months, a sequence of cellular and molecular processes occurs.[6,7] Michels, *et al*[8] exhibited that static magnetic field (SMF) may improve bone regeneration by exerting an osteogenic action.

Furthermore, it has been demonstrated that SMF promotes osteogenic development in mesenchymal stem cells.[9]

Bone morphogenetic protein-2 (BMP-2) is a highly significant factor that stimulates the differentiation of progenitor cells into osteoblasts and facilitates the formation of bone.[10] It promotes the proliferation and differentiation of mesenchymal cells into active osteoblast cells, thus increasing alveolar bone quality.[11] Bone repair is a dynamic and complex process administrated by a number of growth factors and cytokines. Vasculature development and subsequent angiogenesis are required for the improved function of regenerated bone tissues during the late stage of bone regeneration. BMP-2 is a key regulator of osteogenesis, whereas VEGF is a key regulator of vascularization and angiogenesis. In general, early VEGF release promotes waste clearance and nutrient supply during bone repair, which is aided by BMP-2.[4,11] From our result, the level of BMP-2 is higher in the intervention group. This suggests that the use of SMF as healing abutment may propose to a better osteogenesis, as the level of BMP-2 keeps increasing from day 0 to day 30, BMP-2 acts as late-acting growth factor. It is supported by good implant stability.[12,13]

Fibroblast growth factor-2 (FGF-2) is known to have strong bone-forming ability. It is a potent stimulator of cell proliferation and migration, including fibroblasts and endothelial cells. This is important for the recruitment of cells to the implantation site and the subsequent formation of new tissue. FGF-2 level increases significantly in early phase of osseointegration, as shown in the results of our study, because at the beginning of osseointegration, there is immune response and angiogenesis where FGF-2 crucially involved in. It may suggest better enhance osseointegration using SMF healing abutment compared to control group. FGF-2 has been shown to increase osteogenic differentiation and bone formation which is important for integrating the implant into the surrounding bone tissue as part of implant healing.[14]

FGF-2 is also involved in angiogenesis. This promotes the growth of blood vessels, which is important for providing nutrients and oxygen to regenerating tissue. This is why, increasing FGF-2 level in the early osseointegration will contribute to angiogenesis at wound healing, together with VEGF. Additionally, FGF-2 has anti-apoptotic effects that may aid cell survival and tissue regeneration at the implantation site.[14] A study by Nagayasu-Tanaka, *et al*[15] showed that FGF-2 can expedite bone formation and improve implant stability. As a result, high level of FGF-2 could potentially decrease the treatment duration and minimise the risk of implant failure in cases where there is low primary stability.

Conclusions

From the study we may conclude that SMF healing abutment could significantly increase the level of BMP-2 and FGF-2 in osseointegration, which improves the process.

Declaration of Interest

The authors report no conflict of interest.

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