http://dx.doi.org/10.1590/1981-86372020000452021010 6

| REVIEW

The possible impact of COVID-19 pandemic on dental implant therapy: narrative review

O possível impacto da pandemia de covid-19 na terapia com implantes dentários: revisão narrativa

Maria Cristina **PEDRAZINI**[1,2] 0000-0002-7649-6626

Larissa **PAVANELLO**[1] 0000-0003-3469-4226

André Antonio **PELEGRINE**[2] 0000-0001-7935-1062

ABSTRACT

The COVID-19 has challenged the professions and Implantology also has its challenges in the pandemic. Several factors can interfere with the osseointegration process and more associated factors, greater the interference risks. Risk assessment in the therapy indication is the main decision to define the best technique, the best biomaterial, the best surgical access and the best moment to intervene. The purpose of this review was to investigate and synthesize the scientific evidence on the factors that may interfere with dental implant therapy in the midst of pandemic. The literature was reviewed in databases such as PubMed, Web of Science, Sciello and Google Scholar using the keywords "COVID-19", "pandemic", "risk factors", "impact factor", "dental implants", "dentistry", "oral health", "osseointegration", "bone metabolism", "drug risk factors", "chronic stress", "antidepressants", "zinc", "hydroxychloroquine", "ivermectin", "vitamins", "corticosteroids", "surgical risks" and "disinfection". The present review showed that chronic stress and depression caused by the pandemic, the consequent use of antidepressants, the use of prophylactic and therapeutic drugs such zinc, vitamin D, hydroxychloroquine and corticosteroids, can interfere with bone metabolism and consequently in osseointegration establishment and/or maintenance. Any osseointegrable biomaterial can be influenced by systemic factors and drugs' actions that can affect the homeostasis of the inflammatory process, cell proliferation and bone remodeling. These factors' influence on dental implant therapy should be investigated through new reviews, observational studies and randomized clinical trial.

Indexing terms: COVID-19. Dental implants. Risks factors.

RESUMO

A COVID-19 desafiou as profissões e a Implantodontia também tem seus desafios na pandemia. Vários fatores podem interferir no processo de osseointegração e quanto mais fatores associados, maiores os riscos de interferência. A avaliação do risco na indicação da terapia é a principal decisão para definir a melhor técnica, o melhor biomaterial, o melhor acesso cirúrgico e o melhor momento para intervenção. O objetivo desta revisão foi investigar e sintetizar as evidências científicas sobre os fatores que podem interferir na terapia com implantes bucais em meio a uma pandemia. A literatura foi revisada em bancos de dados como PubMed, Web of Science, Sciello

[1] Universidade Estadual de Campinas - UNICAMP, Faculdade de Odontologia de Piracicaba, Departamento de Biociência. Av. Limeira, 901, 13414-903, Areião, Piracicaba, SP, Brasil. Correspondence to: MC Pedrazini. E-mail: <m860702@dac.unicamp.br>.

[2] Faculdade São Leopoldo Mandic, Instituto de Pesquisas São Leopoldo Mandic, Curso de Odontologia, Departamento de Implantodontia. Campinas, SP, Brasil.

How to cite this article

Pedrazini MC, Pavanello L, Pelegrine AA. The possible impact of covid-19 pandemic on dental implant therapy: narrative review. RGO, Rev Gaúch Odontol. 2022;70:e20220045. http://dx.doi.org/10.1590/1981-86372020000452021010 6

e Google Scholar usando as palavras-chave "COVID-19", "pandemia", "fatores de risco", "fator de impacto", "implantes dentários", "odontologia", "saúde bucal", "osseointegração", "metabolismo ósseo", "fatores de risco medicamentosos", "estresse crônico", "antidepressivos", "zinco", "hidroxicloroquina", "ivermectina", "vitaminas", "corticosteróides", "riscos cirúrgicos" e "desinfecção". A presente revisão mostrou que o estresse crônico e a depressão causados pela pandemia, o consequente uso de antidepressivos, o uso de drogas profiláticas e terapêuticas como zinco, vitamina D, hidroxicloroquina e corticosteroides, podem interferir no metabolismo ósseo e consequentemente no estabelecimento da osseointegração e/ou sua manutenção. Qualquer biomaterial osseointegrável pode ser influenciado por fatores sistêmicos e ações de drogas que podem afetar a homeostase do processo inflamatório, proliferação celular e remodelação óssea. A influência desses fatores na terapia com implantes dentários deve ser investigada por meio de novas revisões, estudos observacionais e ensaios clínicos randomizados.
Termos de indexação: *COVID-19. Implantes dentários. Fatores de risco.*

INTRODUCTION

The Implantology has proved to be of great relevance for the oral rehabilitation area due to the ability of an implant to replace, satisfactorily, a dental element lost due to caries or trauma, as well as to rehabilitate cases of agenesis and impacted elements where traction is not possible [1,2]. It is one of the Dentistry areas that has made the most progress over the years in order to prioritize forms of rehabilitation that meet the patient's expectations, restoring the stability of the stomatognathic system, aesthetics, phonetics and psychological balance [3].

Several factors can interfere with the success of implant therapy [4-6] and when talking about the success, the factors that can interfere in osseointegration establishment or its maintenance are considered, as well as the factors that compromise the surgical procedure for the installation of any biomaterial [5,7,8].

In 2020, new factors may have emerged with the COVID-19 pandemic. The unknown about what are the consequences of so many medication protocols and / or emotional factors leads to the need for more detailed studies on the possible interference of these factors in the osseointegration process, in implant maintenance, in the surgery act or in the healing of hard and soft tissues.

The COVID-19 disease is transmitted through direct contact with oral and nasal respiratory droplets [9]. On March 11th, 2020, the "COVID-19 pandemic" was declared [10] and the dissemination by asymptomatic patients has been documented, being one of the main reasons for fear of many dental professionals due to direct contact with oral fluids and aerosols [11]. In addition, the fact that this virus often has a long incubation period, exposes dental surgeons to a high risk of both contracting the disease and spreading it [12].

At the beginning of the pandemic, only emergency and urgency procedures should be performed with an extreme focus on personal protective equipment and disinfection protocols [13], but with a better understanding of the risks, the Brazilian Ministry of Health developed guidelines for the resumption of elective care in an orderly and gradual way, divided into essential and expanded, giving priority to groups and clinical conditions that should not be postponed. In this way, it avoids the accumulation of pent-up demand and promotes the resumption of treatments that were in progress, as well as the provision of care that avoids the harm to oral health with repercussions on general health [14].

The COVID-19 pandemic also altered significantly the oral rehabilitation course that encompasses a wide range of procedures, from single prostheses to major surgeries with oral implants, with aerosol present in almost all procedures [15]. Thereby, is important to consider the devastating psychological consequences for patients who are not receiving their rehabilitation treatments, either due to the fear of being contaminated or due to the protocols stipulated in some dental centers, that still limit the procedures to urgency and emergency following the first guidelines [13]. At this time, the Dentistry should rely on efforts to review the existing literature and guidelines from different national and international sources, in order to suggest the implementation of a systematic workflow by professionals to also ensure the safe practice of elective procedures, whether they are curative, aesthetics and / or rehabilitators [16]. It is worth mentioning that the patient with suspicion or confirmation for COVID-19, should not undergo elective treatment and dentists should use their professional judgment to determine the need for urgent or emergency care [17].

With a focus on patients who need to be rehabilitated during the COVID-19 pandemic, there are some that are not contaminated, and between them, the ones who are candidates for oral implant therapy. The challenge for dental implant specialists is to know how these patients will return to their offices, analyzing the possible consequences of treatment with implants in people who are depressed, extremely anxious or stressed, or who are using antidepressants, pre-exposure prophylactic medications or who have gone through the sad phase of this disease treatment, the "post COVID patients".

Thus, the aim of this study was to review the relevant literature and discuss the risks involved patients" treatment in the midst of the COVID-19 pandemic and about possible factors that may interfere with the success of osseointegrable implants therapy.

METHODS

This narrative review included searches in the PubMed, Web of Science, Sciello and Google Scholar databases using the keywords "COVID-19", "pandemic", "risk factors", "impact factor", "dental implants ", dentistry", "oral health", "osseointegration", "bone metabolism", "medication risk factors", "chronic stress", "antidepressants", "zinc", "hydroxychloroquine", "ivermectin", "vitamins", "corticosteroids ", "surgical risks" and "disinfection". The search was complemented by the manual search of the references cited in the chosen articles and updated until July 2021.

DISCUSSION

Osseointegration

Osseointegration was originally defined as a direct structural and functional connection between ordered living bone and the surface of an implant [18]. Although the osseointegration term was initially used in reference to titanium metal implants, the concept is currently applied to all biomaterials that have the ability of osseointegration [19]. The success rates of oral implants depend on factors related to operator, biomaterial, prosthetic load and mainly to factors related to patient's local and systemic conditions [4,5,20].

In relation to systemic factors and which may interfere with bone metabolism, there is stress [21], which is very present during the COVID-19 pandemic and which may be due to fears of contamination or the fact that a "prophylactic quarantine" has been instituted [22,23].

First preventive treatment against COVID-19 - the prophylactic quarantine

"Prophylactic quarantine" was defined as extremely necessary to stop the virus transmission and was based on the positive results of other quarantines in small groups of a few hundred people, due to the SARS-CoV-1, MERS-CoV, H1N1 and Ebola viruses. Even though these quarantines were relatively short, from 10 to 21 days, an increase in risks to mental health could be seen as a consequence [22,23], but the COVID-19 quarantine was different and this fact gave a negative character to the resilience of mental health. If isolation is partly important for the protection of physical health by controlling the contagion and virus transmission, on the other hand, the longer the isolation time, the greater the risks of the psychic diseases' emergence [23], an increase in alcohol abuse, symptoms of post-traumatic stress and deep depression [24].

The low adherence to quarantine requirements, raises concerns about its effectiveness as a public health measure [25].

Stress, anxiety and cortisol

COVID-19 is an exclusive threat that contributes to panic and mass stress, causing obsessive-compulsive disorders, chronic stress and anxiety with worrying systemic results [26].

During the stress, the hypothalamus-pituitary-adrenal pathway activation occurs. The hypothalamic paraventricular nucleus secretes a greater amount of corticotrophin-releasing hormone, stimulating the release of adrenal corticosteroids such as cortisol, through the secretion of adrenocorticotropin by the anterior pituitary gland [27]. The chronic elevation of cortisol can alter its own negative regulation with multiple long-term consequences for physical and psychological health [28].

Studies showed that chronic social stress, presented greater bone loss when compared to the ones who did not undergo psychosocial stress [21]. During the stress, the elevated plasma cortisol peak was associated with accelerated mineral density loss provide evidence that circulating endogenous glucocorticoids influence bone loss rate in healthy individuals [29].

Little is known about the stress effects and high cortisol levels on mineral density around implants with randomized clinical studies however, in animal models, osseointegration was affected due to chronic stress and the consequent cortisol elevation showing a delay in soft tissue healing as well as an interference in bone-implant connections [30] in the initial fase of osseointegration, but not in the final process [31].

Since the increase in cortisol levels can interfere with bone metabolism [29] and once it is affected, the osseointegration process or its maintenance can also be compromised [32], randomized clinical studies are necessary in this regard to confirm this mechanism.

During the COVID-19 pandemic, stress levels are high, and anxiety or depression arise with it. The causes are diverse and among them, are the fear of illness and social isolation. Treatment, especially of post-traumatic depression, is carried out with psychotherapies and drug therapies [33].

Drug therapy for post-traumatic anxiety and depression - antidepressants

Depression is a mood disorder that provokes a persistent sadness feeling, loss of interest associated with changes in behavioral and neuroendocrine systems, may also cause irritability, difficulty concentrating, anhedonia (reduced ability and willingness to experience pleasure), appetite and sleep disorders (neurovegetative symptoms) as well as anxiety disorders [34]. It is strongly associated with decreased bone mineral density, being considered a risk factor for osteoporosis because it can influence bone metabolism by decreasing levels of osteocalcin (protein with bone metabolism agonist activity) [35]. The both, depression alone and the use of antidepressants, have been identified as secondary causes of osteoporosis [36].

Antidepressants are the gold standard treatment option for depression symptoms and among the drugs prescribed, are selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), antidepressants atypical (AAs) and monoamine oxidase inhibitors (MAOIs). Antidepressant users taking SSRIs or TCAs are exposed to a greater risk of implant failure than non-users. The effects of TCAs are based on a limited number of cases, however, as SSRIs are the most frequently prescribed for its effectiveness and low risk of adverse effects, they are also the most investigated in relation to osseointegration failures [34].

Serotonin receptors have been shown to be present in peripheral tissues, including the digestive tract, blood platelets, as well as in osteoblasts and osteoclasts [37]. In bone metabolism, blocking the reuptake of serotonin causes increased of osteoclasts differentiation and decreased of osteoblasts proliferation, which eventually results in decreased bone mass and bone mineral density. Due to the negative effects of SSRIs on bone metabolism, it is possible that there is interference with osseointegration by the same mechanism [32].

The relationship between the use of SSRIs and the increased risk of failure in implants osseointegration is still unclear due to the lack of data, but the systemic administration of SSRIs has been associated with an increased risk of implant failure in two retrospective cohort studies, one of them showed significant results [38,39]. Another study with 931 dental implants in 300 patients showed a failure rate of 3.3% in non-users and 12.5% in users of SSRIs [37]. The results of these studies may suggest the need of a different surgical treatment plan for patients treated with SSRIs.

An investigation was conducted involving a unicortical defect regeneration and a titanium implant osseointegration with a group treated with sertraline and the control with saline. After two weeks, through micro-CT and histology, bone formation was observed. Regeneration in bone defects was significantly less ($p < 0.05$) in rats treated with sertraline and the percentage of osseointegration was significantly lower ($p < 0.05$) concluding that sertraline (SSRIs) hindered bone healing and implant osseointegration [40].

According to other research, not only SSRI antidepressants can have negative effects on bone metabolism and osseointegration. Were evaluated 1,820 implants placed in 771 patients whom 89.6% did not use antidepressants, whereas 10.4% used at least one class of these drugs. The frequency of implant failure was significantly higher in antidepressants users (13.9%) than in non-users (3.9%), presenting a risk 4.3 times greater. The antidepressants influence on dental implants survival may be related to its negative impact on osseointegration establishment and/or maintenance [34].

Pre-exposure prophylaxis and initial therapy against the severe form of COVID-19

The National Institutes of Health (NIH) does not recommend the use of any drugs for SARS-CoV-2 pre-exposure prophylaxis but recommends that healthcare professionals follow the Centers for Disease Control and Prevention (CDC) recommendations, regarding the use of vaccines against SARS-CoV-2 and that continue the appropriate use of personal protective equipment (PPE). However, this same committee supports some studies where drugs are being tested prophylactically, pre-exposure [41].

Several other observational studies with prophylactic therapies have offered evidence that serum concentration of some vitamins is inversely correlated with the incidence or severity of COVID-19. To date, the evidence generally meets the criteria for consistency, strength of association, biological gradient, temporality, plausibility and coherence. Thus, these criteria appear to be sufficient for patients and physicians to use or recommend vitamins or supplements to prevent or treat COVID-19 in view of its safety and wide therapeutic window. New results from large-scale randomized clinical trials with vitamins are in progress [42].

Drugs, vitamins, supplements and vaccines are constantly being evaluated in efforts to contain the terrible COVID-19 consequences, with varying success degrees. As another example, we also have various action mechanisms with the use of mineral supplementation as an adjuvant to vaccines, as a prophylaxis or as a component of the therapeutic regimen in the current treatment of COVID-19, it is strongly recommended [43].

Some prophylactic therapeutic protocols in attempt to avoid the severe form of the disease, are being used by health professionals in some countries in several patients, until a safe and effective vaccine is available to everyone [44,45]. Human clinical trials are currently underway to assess drugs therapeutic indexes already approved for other diseases, i.e., the reuse of drugs [46].

There is no scientific evidence that some medications available in Brazil, alone or in combination, or vitamins and minerals, are able to prevent the disease onset in uninfected people [47] however, it can be seen in clinical practice that many health professionals at high risk of exposure, are using some drugs and vitamins [46] in the hope of avoiding a severe clinical condition in case of contagion.

Zinc

Zinc is a mineral that has positive immunomodulatory activity showing a decrease in synthesis of viral genetic material in the host cell, reducing the viral load of SARS-CoV-2. This mineral has potential health benefits against current

pandemic, improving the immune response, minimizing infection and inflammation, preventing lung injury, inhibiting viral replication through interference in transcription of virus genome, in proteins translation and in host infectivity [43].

Despite the lack of clinical data, it has been suggested that zinc supplementation may be beneficial against COVID-19 because in vitro experiments demonstrate that Zn2 + has antiviral activity through the inhibition of SARS-CoV-2 RNA polymerase. This effect may explain the chloroquine therapeutic efficiency, known to act as a zinc ionophore. This mineral also has an anti-inflammatory activity and modulates the regulatory functions of T cells that can limit the COVID-19 cytokine storm [48].

The zinc low level in patients' blood with COVID-19, has been associated with the severe form of disease and since zinc supplementation for a short period is not harmful to health, a combination of zinc with HCQ has been proposed in patients infected with COVID- 19, with promising results [49].

Bone homeostasis is regulated by osteoclasts and osteoblasts [50] and zinc has been shown to have a stimulating effect on osteoblastic bone formation and an inhibitory effect on osteoclastic bone resorption, thereby increasing bone mass. Supplemental intake of zinc combined with genistein (phytoestrogen) has been shown to have a preventive effect on osteoporosis in humans, suggesting a role in preventing bone loss [51] and zinc with vitamin D, in vivo, showed statistically significant differences in the counter-torque values for removal of the implant, in bone volume and in the BIC [50]. Given this information, a patient being supplemented with zinc could have an improvement in osseointegration.

Vitamin D

Infection with the new coronavirus SARS-CoV-2 produces a change in the pathophysiological mechanism of pulmonary infection and is the main cause of mortality. Several researchers have focused their studies to demonstrate that vitamin D and its metabolites would be able to promote an increase in immunity. However, it was observed that low doses in daily or weekly regimens, would have greater protective effects than monthly regimens, warning that high doses would cause adverse effects [52].

Several clinical trials have revealed a strong association between the high risk of developing respiratory diseases and hypovitaminosis, concluding that vitamin replacement would reduce infectious events in the respiratory tract. Changes in vitamin D levels interfere not only in the response to coronavirus but also to other viruses such as influenza, dengue, hepatitis, herpesvirus and human immunodeficiency virus (HIV) [53].

Implant specialists are also increasingly interested in the effects of vitamin D on bone metabolism. The deficiency of this vitamin is widespread all over the world, which is worrying because it has an important role in the regulation of phosphocalcic metabolism, as well as in a large number of biological and metabolic processes. According to some studies, vitamin D deficiency can be a risk for bone healing and for dental implants osseointegration [54].

The correct concentration of this vitamin is potentially correlated with success in all stages of osseointegration of endosseous implants. An adequate level of cholecalciferol is crucial from the day of surgery as it has a positive effect on regeneration metabolism as well as on continuous bone remodeling around the implant after loading. Maintaining an adequate level of these ions in bone tissue and extracellular fluid is necessary for proper bone tissue mineralization [55].

Since osseointegration depends on homeostasis of bone metabolism and mineralization, low levels of vitamin D in blood can affect negatively bone repair and maintenance around oral implants. Until 2018, few studies had investigated the possible connection between serum vitamin D levels and early implant failure, i.e., a failure that occurs within 4 months after installation, before the connection of the prosthetic abutment [56] however, recent studies have suggested that there is indeed a link between this vitamin deficiency and early implant failures, requiring adequate supplementation [20,50].

Some authors have verified, through a systematic review, that vitamin D levels in patients with peri-implantitis are lower than in healthy patients however, literature reviews suggest that more longitudinal clinical investigations are needed to elucidate its mechanism of action both in osseointegration and in the peri-implantitis prevention [57,58].

In post-COVID-19 patients, it would be prudent to check for vitamin D deficiency. Supplementation may be useful to positively influence the immune system and bone metabolism. In the near future, every effort should be made to investigate the risks involved in bone metabolism in patients who have recovered from SARS-CoV-2 infection [59].

Hydroxychloroquine

Hydroxychloroquine (HCQ) is a chloroquine analog with immunomodulatory properties, commonly used in the treatment of malaria, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) [60]. Although it has been presented as a promising therapeutic option for the control of COVID-19, of low cost and easy availability, few studies have evaluated its effectiveness against this virus [61].

Several studies with HCQ have been examined for efficacy, time of administration and safety, and it was found that this drug would be consistently effective against COVID-19 when supplied at the beginning, in the event of a contagion, thus preventing the development of a serious form of the disease [62].

The HCQ is widely prescribed by rheumatologists in patients with RA, demonstrating to prevent bone resorption after 3 to 6 months of treatment. The improvement in bone mineral density was verified by measuring serum levels of β-CTx [59] and to understand its influence on bone metabolism, researchers conducted studies on its action on osteoclasts and osteoblasts [63,64].

When its interference with bone resorption was evaluated, an inhibition in osteoclast activity was found concluding that HCQ, in vitro, interfered in bone remodeling due to its interference in osteoclasts. As for in vivo analysis, there was a decrease in the bone resorption marker β-CTx [63].

Another hypothesis would be that HCQ "attacks" the lysosomal membrane of mesenchymal cells by removing cholesterol, which would lead to decreased differentiation into osteoblasts. In addition, it could affect extracellular matrix composition causing a cell adhesion decrease [64]. This possible HCQ mechanism, may suggest that for osseointegration and its maintenance, this drug could have a negative action since bone turnover is necessary in implants therapy however, randomized clinical studies with this objective are necessary to validate its influence on osseointegration process.

Ivermectin

Ivermectin is an anthelmintic drug used to treat some parasites such as strongyloidiasis, onchocerciasis, filariasis, ascariasis, scabies and pediculosis. In relation to SARS-CoV-2, an in vitro analysis proved its effectiveness. The explanation would be that ivermectin could have the ability to reduce viral RNA replication by binding to cell transport proteins, preventing the virus from entering the cell nucleus [65].

Countries with mass administration of prophylactic drugs, including ivermectin, have a significantly lower incidence of COVID-19 [45]. Medical records of 280 patients hospitalized at four Broward Health hospitals in Florida with COVID-19, between March 15 and May 11, 2020, were revised. Evaluating the therapeutic protocols, 173 were treated with ivermectin and 107 did not use this drug. The analysis showed lower mortality in the ivermectin group (15.0% vs 25.2%; $P = 0.03$) however, the authors inferred that more randomized clinical trials are still needed to confirm these findings [65].

Some risks of adverse effects are reported in patients that are using ivermectin and among them, the related to the central nervous system (CNS) such as dizziness, drowsiness, vertigo and tremor. This drug is believed to act as an agonist for the neurotransmitter gamma-aminobutyric acid (GABA), interrupting GABA-mediated neurosynaptic transmission [66]. This agonist effect of ivermectin sends a warning to implantodontists in their clinical practice regarding

the use of pre-surgical benzodiazepines in anxious patients [67], as there may be a potentialization of effects on CNS with the interaction of two drugs. Regarding the positive or negative effects of ivermectin on bone metabolism, studies with this scope were not found in the researched databases.

Other drugs prescribed for the COVID-19 treatment

There are several therapies being proposed for the COVID-19 treatment [44,45] with different protocols for each type of disease form (mild, moderate and severe), and should be appropriately evaluated for its effectiveness and safety. As there is still no specific treatment for SARS-CoV-2 infection, several clinical studies are underway to find a gold standard therapeutic regimen with high efficacy and low side effect. Several drugs, such as those mentioned so far, continue to be investigated, as well as antivirals, monoclonal antibodies, immunomodulators, immunodepressants and glucocorticoids [68].

Existing protocols and recommendations are being continuously reviewed to show new evidence. The recommendation of antimicrobials will be assertive in COVID-19 patients with suspected bacterial co-infection and not prophylactically. Glucocorticoids are strongly investigated and indicated for inflammatory storm treatment and its routine use is contraindicated, but on a case-by-case basis. For thromboembolism prophylaxis, the routine use of venous anticoagulants has been recommended for inpatients [69].

In relation to glucocorticoids, patients in moderate or severe condition, use this drug for long periods to control secundary inflammation to viral invasion [70] and it is known that steroidal anti-inflammatory drugs in chronic use can interfere with bone metabolism [71], as well as endogenous glucocorticoids released during stress [29].

Resorption and reduction in bone formation is one of the most common and debilitating side effects associated with prolonged therapy with glucocorticoid high doses which can negatively affect osseointegration. However, there is evidence to demonstrate that once osseointegration has occurred, the long-term prognosis for the implant would be favorable despite its chronic use. The deleterious effects of this group of drugs on bone remodeling and renewal, can be explained by the apoptosis of osteoblasts and favoring the differentiation of bone marrow cells into adipocytes. Together, these changes lead to decreased osteogenesis, thus shifting the balance to bone loss [72], which can harm the early stages of osseointegration.

Management of candidate patients for osseointegrable implants therapy in the midst of pandemic

The dental environment, due to its characteristic, promotes an increased risk of cross infection between patients and dentists. The fact of working in the oral cavity with sprays causing aerosol "clouds", makes dental offices a potential area of COVID-19 dissemination and rigorous and effective protection protocols are mandatory to reduce viral transmission [73].

Rigorous and effective protection protocols, allow patients with elective procedures to also be assisted. In addition, to indications for personal protective equipment and air filtration systems, pre-service rinses would be another measure of adjuvant protection. The provisional ADA guidelines suggested pre-oral procedure rinsing with hydrogen peroxide 1,5% or PVP-I 0,2% but other authors also suggested rinsing with antimicrobials such as chlorhexidine gluconate [15]. Before the pandemic, it was the mouthwash of choice in concentrations of 0.12% or 0.2%, to reduce the number of microorganisms disseminated through aerosol generated in dental procedures [74] however, the SARS-Cov-2 was not sensitive to chlorhexidine and was only completely inactivated by oral antiseptic rinse of PVP-I, in vitro, at a concentration of 0.5% for 15 seconds. Hydrogen peroxide was also tested at concentrations of 1.5% and 3.0%, but it was minimally effective as a viricidal agent, even with 30 seconds of application. Therefore, the pre-procedure rinse with PVP-I diluted in the range of 0.5% to 1.5%, may be preferable to hydrogen peroxide during the COVID-19 pandemic [75].

PVP-I is safe for use in oral cavity at concentrations of up to 5% and in the nasal cavity is safe up to 1.25%. In the absence of suitable commercially available preparations for routine use, a 1:20 dilution of 10% commercially available povidone iodine was recommended. A solution of 0.5 cc of 10% povidone iodine and 9.5 cc of sterile saline or sterile water could be used clinically. At these concentrations, iodine absorption is minimal and is below the safe total daily intake (150 µg) for a healthy adult. Contraindications include anaphylactic allergy to iodine, pregnancy, active thyroid disease and those undergoing radioactive iodine therapy [15].

Regarding the ones who are using or have used drugs therapies, whether preventive against the severe form of the disease or curative [44,45], it is important to remember that clinical performance of osseointegrated implants can be affected by these drugs and the effects, positive or negative, must be investigated beforehand [38].

In addition, patients' management during COVID-19, it is necessary to consider the risk factors that involve the surgical act for the implants' installation [7,8]. The best time for an elective surgery leaves an alert to oral surgeons. While everyone is not vaccinated, there is also a risk of a post-operative SARS-CoV-2 infection. This occurrence can increase the risk of death because they are weakened by the surgery. The outcomes in surgical patients who were infected with SARS-CoV-2 before surgery were compared to those without previous infection. The primary end point was postoperative mortality at 30 days. In patients with a pre-operative diagnosis of SARS-CoV-2, mortality increased when submitted to surgery within 0-2, 3-4 and 5-6 weeks after diagnosis (4.1 %, 3.9% and 3.6% respectively). Surgery performed 7 weeks or more after the diagnosis of SARS-CoV-2 was associated with a risk of mortality similar to those without previous infection. In patients operated 7 weeks or more of diagnosis but who still had an ongoing symptom, the mortality rate was higher than in the ones whose symptoms were resolved or who were asymptomatic. The conclusion was, whenever possible, elective surgery should be postponed for at least 7 weeks after infection by SARS-CoV-2 in patients without symptoms, but in the ones who are still symptomatic, the risks will be less if this time is extended beyond 7 weeks, when asymptomatic [76].

Other care in surgeries in the middle of the pandemic is also being considered. A pre-test of RT-PCR is mandatory in hospitals for all elective surgery patients. It is known that diagnostic accuracy remains challenging with an estimated false negative rate of 2 to 29%. The probability of registering a false negative result is highest in the four days prior to the onset of symptoms, being lower at the onset of symptoms. Another preventive measure to be considered would be a 14-day quarantine prior to surgery in asymptomatic patients with a history of potential exposure to the virus [77]. Dental surgeon must consider all preventive measures in his consultations, whether hospital or outpatient.

It is also important to be attentive to the constant publications on risk factors in the success of the implants, whether they are risk factors for osseointegration, for its maintenance or factors associated with surgical risks to installation [7,8]. The final results of the current pandemic are not yet fully known. In this new period in which humanity lives, many doubts arise, and long periods of evaluations and studies will be necessary to understand the true impact of the COVID-19 pandemic on mental and systemic health [22].

CONCLUSION

The COVID-19 pandemic can interfere in osseointegrable implants therapy, either due to the postponement or interruption of treatments, or due to psychological changes in patients who may consequently have been using antidepressants or by possible interference from prophylactic or therapeutic drugs, which may affect the homeostasis of the inflammatory process, cell proliferation and remodeling bone.

The impact of the pandemic on dental implant therapy, whether in establishing or maintaining osseointegration, or in increasing surgical risk, should be investigated through new reviews, observational studies and randomized clinical trials.

Collaborators

MC Pedrazini, lead-author - researcher responsible for the conceptualization, bibliographic review, writing and article submission. L Pavanello, co-author - researcher responsible for support in the bibliographic survey and final article review. AA Pelegrine. Co-author - researcher responsible for support in final article review. All authors read and approved the final draft.

REFERENCES

1. Maahs MA, Berthold TB. Etiologia, diagnóstico e tratamento de caninos superiores permanentes impactados/ Etiology, diagnosis and treatment of impacted permanent upper canines. Rev Ciênc Méd Biol. 2004;3(1):130. http://dx.doi.org/10.9771/cmbio.v3i1.4418
2. Felice P, Barausse C, Stefanini M, Pistilli R, Zucchelli G. A minimally invasive approach using a 4-mm implant without extraction of impacted maxillary canine: four-year postloading results. Int J Periodontics Restorative Dent. 2017;37(6):819-824. http://dx.doi.org/10.11607/prd.3334
3. Pedrazini MC, Oliveira RAF, Fabiano S, Montagner AM, Wassall T. Evaluation of the laboratorial processes' quality applied to titanium prostheses: plasma casting and laser welding - metallographic analysis. RGO, Rev Gaúcha Odontol. 2013;61(2):221-226.
4. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants (I): success criteria and epidemiology. Eur J Oral Sci. 1998;106(1):527-51. http://dx.doi.org/10.1046/j.0909-8836..t01-2-.x
5. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants (II): etiopathogenesis. Eur J Oral Sci. 1998;106(3):721-64. http://dx.doi.org/10.1046/j.0909-8836..t01-6-.x
6. Oliveira RAF, Pedrazini MC, Wassall T. Relative area measurement of maxillary sinus by computed tomography. RGO, Rev Gaúch Odontol. 2014;62(2):7-12. http://dx.doi.org/10.1590/1981-86372014000200012556
7. Pedrazini MC, Montagner AM, Shimaoka CA, Held AB, Alves ALC. O significado de uma diferença elevada na pressão arterial entre os dois braços e antes dos implantes dentários: um alerta preocupante, reflexões e tratamento. INPerio. 2016;1(8):1561-9.
8. Pedrazini MC, Groppo FC. Crise hipertensiva: considerações e condutas no transcirúrgico em Implantodontia. INPerio. 2020;5(2):260-7.
9. Bhanushali P, Katge F, Deshpande S, Chimata VK, Shetty S, Pradhan D. COVID-19: changing trends and its impact on future of dentistry. Int J Dent. 2020;2020:8817424. http://dx.doi.org/10.1155/2020/8817424
10. Balkhair AA. COVID-19 pandemic. A new chapter in the history of infectious diseases. Oman Med J. 2020;35:e123. http://dx.doi.org/10.5001/omj.2020.41
11. Yu X, Yang R. COVID-19 transmission through asymptomatic carriers is a challenge to containment. Influenza Other Respir Viruses. 2020;14(4):474-475. http://dx.doi.org/10.1111/irv.12743
12. Ge ZY, Yang LM, Xia JJ, Fu XH, Zhang YZ. Possible aerosol transmission of COVID-19 and special precautions in dentistry. J Zhejiang Univ Sci B. 2020;21(5):361-368. http://dx.doi.org/10.1631/jzus. B2010010
13. Ministry of Health and Familu Welfare. Guidelines for Dental Professionals in COVID-19 pandemic situation [internet]. Government of India, New Delhi: Ministry of Health and Familu Welfare. 2020 [cited 2021 May 12]. Available from: <https://www.mohfw.gov.in/pdf/DentalAdvisoryF.pdf>.
14. Brasil. Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Departamento de Saúde da Família. Guia de orientações para atenção odontológica no contexto da Covid-19 [internet]. Brasília: Ministério da Saúde; 2021 [cited 2021 May 12]. Available from: <http://bvsms.saude.gov.br/bvs/publicacoes/guia_orientacoes_odontologica_covid19.pdf>.
15. Tessema B, Frank S, Bidra A. SARS-CoV-2 viral inactivation using low dose povidone-iodine oral rinse-immediate application for the prosthodontic practice. J Prosthodont. 2020;29(6):459. http://dx.doi.org/10.1111/jopr.13207
16. Pruthi G, Parkash H, Bharathi P V, Jain R, Gupta A, Rai S. Comprehensive review of guidelines to practice prosthodontic and implant procedures during COVID-19 pandemic. J Oral Biol Craniofac Res. 2020;10(4):768-775. http://dx.doi.org/10.1016/j.jobcr.2020.10.010
17. American Dental Association (ADA). What constitutes a dental emergency? [internet]. Government of United State of America, 2021 [cited 2021 May 18]. Available from: <https://success.ada.org/~/media/CPS/Files/Open%20Files/ADA_COVID19_Dental_Emergency_DDS.pdf>.
18. Brånemark PI, Hansson BO, Adell R, Breine U, Lindström J, Hallén O, et al. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Scand J Plast Reconstr Surg.1977;16(10):1-132.
19. Guglielmotti MB, Olmedo DG, Cabrini RL. Research on implants and osseointegration. Periodontol 2000. 2019;79(1):178-189. http://dx.doi.org/10.1111/prd.12254
20. Pourshahidi S, Yousefain M. The relationship between serum level of vitamin D3 and osseointegration around the dental implant. J Oral Implantol. 2021;47(1):88-90. http://dx.doi.org/10.1563/aaid-joi-D-19-00341
21. Follis SL, Bea J, Klimentidis Y, Hu C, Crandall CJ, Garcia DO, et al. Psychosocial stress and bone loss among postmenopausal women: results from the Women's Health Initiative. J Epidemiol Community Health. 2019;73(9):888-892. http://dx.doi.org/10.1136/jech-2019-212516

22. Afonso P. O Impacto da pandemia COVID-19 na saúde mental. Acta Med Port. 2020;33(5):356-357. http://dx.doi.org/10.20344/amp.13877
23. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. Lancet. 2020;395(10227):912-920. http://dx.doi.org/10.1016/S0140-6736(20)30460-8
24. Wu P, Liu X, Fang Y, Fan B, Fuller CJ, Guan Z, et al. Alcohol abuse/dependence symptoms among hospital employees exposed to a SARS outbreak. Alcohol Alcohol. 200;43(6):706-12. http://dx.doi.org/10.1093/alcalc/agn073
25. Reynolds DL, Garay JR, Deamond SL, Moran MK, Gold W, Styra R. Understanding, compliance and psychological impact of the SARS quarantine experience. Epidemiol Infect. 2008;136(7):997-1007. http://dx.doi.org/10.1017/S0950268807009156
26. Shuja KH, Aqeel M, Jaffar A, Ahmed A. COVID-19 pandemic and impending global mental health implications. Psychiatr Danub. 2020;32(1):32-35. http://dx.doi.org/10.24869/psyd.2020.32
27. Semenoff-Segundo A, Porto AN, Semenoff TA, Cortelli JR, Costa FO, Cortelli SC, et al. Effects of two chronic stress models on ligature-induced periodontitis in Wistar rats. Arch Oral Biol. 2012;57(1):66-72. http://dx.doi.org/10.1016/j.archoralbio.2011.07.014
28. Borráz-León JI, Cerda-Molina AL, Mayagoitia-Novales L. Stress and cortisol responses in men: differences according to facial symmetry. Stress. 2017;20(6):573-579. http://dx.doi.org/10.1080/10253890.2017.1378341
29. Reynolds RM, Dennison EM, Walker BR, Syddall HE, Wood PJ, Andrew R, et al. Cortisol secretion and rate of bone loss in a population-based cohort of elderly men and women. Calcif Tissue Int. 2005;77(3):134-8. http://dx.doi.org/10.1007/s00223-004-0270-2
30. Bozoglan A, Dundar S, Yildirim TT, Bulmus O, Ertugrul AS, Bozoglan MY. et al. Effects of different levels of restraint stress on bone-implant contact. J Craniofac Surg. 2019;30(4):1294-1297. http://dx.doi.org/10.1097/SCS.0000000000005104
31. Siqueira CR, Semenoff TA, Palma VC, Borges ÁH, Silva NF, Segundo AS. Effect of chronic stress on implant osseointegration into rat's mandible. Acta Cir Bras. 2015;30(9):598-603. http://dx.doi.org/10.1590/S0102-865020150090000003
32. Altay MA, Sindel A, Özalp Ö, Yildirimyan N, Kader D, Bilge U, et al. Does the intake of selective serotonin reuptake inhibitors negatively affect dental implant osseointegration? A retrospective study. J Oral Implantol. 2018;44(4):260-265. http://dx.doi.org/10.1563/aaid-joi-D-17-00240
33. Bhatia MS, Goyal S, Singh A, Daral A. COVID-19 pandemic-induced panic disorder. Prim Care Companion CNS Disord. 2020;22(3):20l02626. http://dx.doi.org/10.4088/PCC.20l02626
34. Hakam AE, Vila G, Duarte PM, Mbadu MP, Ai Angary DS, Shuwaikan H, et al. Effects of different antidepressant classes on dental implant failure: A retrospective clinical study. J Periodontol. 2021;92(2):196-204. http://dx.doi.org/10.1002/JPER.19-0714
35. Ak E, Bulut SD, Bulut S, Akdağ HA, Öter GB, Kaya H, et al. Evaluation of the effect of selective serotonin reuptake inhibitors on bone mineral density: an observational cross-sectional study. Osteoporos Int. 2015;26(1):273-9. http://dx.doi.org/10.1007/s00198-014-2859-2
36. Chau K, Atkinson SA, Taylor VH. Are selective serotonin reuptake inhibitors a secondary cause of low bone density? J Osteoporos. 2012;2012:323061. http://dx.doi.org/10.1155/2012/323061
37. Chrcanovic BR, Kisch J, Albrektsson T, Wennerberg A. Is the intake of selective serotonin reuptake inhibitors associated with an increased risk of dental implant failure? Int J Oral Maxillofac Surg. 2017;46(6):782-788. http://dx.doi.org/10.1016/j.ijom.2017.01.016
38. Mahri M, Shen N, Berrizbeitia F, Rodan R, Daer A, Faigan M, et al. Osseointegration pharmacology: a systematic mapping using artificial intelligence. Acta Biomater. 2021;119:284-302. http://dx.doi.org/10.1016/j.actbio.2020.11.011
39. Wu X, Al-Abedalla K, Rastikerdar E, Abi Nader S, Daniel NG, Nicolau B, et al. Selective serotonin reuptake inhibitors and the risk of osseointegrated implant failure: a cohort study. J Dent Res. 2014;93(11):1054-61. http://dx.doi.org/10.1177/0022034514549378
40. Abu Nada L, Al Subaie A, Mansour A, Wu X, Abdallah MN, Al-Waeli H, et al. The antidepressant drug, sertraline, hinders bone healing and osseointegration in rats' tibiae. J Clin Periodontol. 2018;45(12):1485-1497. http://dx.doi.org/10.1111/jcpe.13015
41. National Institutes of Health. COVID-19 treatment guidelines - prevention and prophylaxis of SARS-CoV-2 infection. 2021 [cited 2021 April 21]. Available from: <https://www.covid19treatmentguidelines.nih.gov/overview/prevention-of-sars-cov-2/>.
42. Mercola J, Grant WB, Wagner CL. Evidence regarding Vitamin D and risk of COVID-19 and its severity. Nutrients. 2020;12(11):3361. http://dx.doi.org/10.3390/nu12113361
43. Oyagbemi AA, Ajibade TO, Aboua YG, Gbadamosi IT, Adedapo ADA, Aro AO, et al. Potential health benefits of zinc supplementation for the management of COVID-19 pandemic. J Food Biochem. 2021;45(2): e13604. http://dx.doi.org/10.1111/jfbc.13604
44. Shah S, Das S, Jain A, Misra DP, Negi VS. A systematic review of the prophylactic role of chloroquine and hydroxychloroquine in coronavirus disease-19 (COVID-19). Int J Rheum Dis. 2020;23(5):613-619. http://dx.doi.org/10.1111/1756-185X.13842
45. Hellwig MD, Maia A. A COVID-19 prophylaxis? Lower incidence associated with prophylactic administration of ivermectin. Int J Antimicrob Agents. 2021;57(1):106248. http://dx.doi.org/10.1016/j.ijantimicag.2020.106248
46. Pal A, Squitti R, Picozza M, Pawar A, Rongioletti M, Dutta AK, et al. Zinc and COVID-19: basis of current clinical trials. Biol Trace Elem Res. 2020;22(1):1-11. http://dx.doi.org/10.1007/s12011-020-02437-9

47. Brazilian Society of Pulmonology and Phthisology (SBPT). SBPT's position on the prophylaxis and treatment of COVID-19. 2020 [cited 2021 May 20]. Available from: <http://www.sopterj.com.br/wp-content/uploads/2020/06/Profilaxia-e-tratamento-COVID-19.pdf>.

48. Skalny AV, Rink L, Ajsuvakova OP, Aschner M, Gritsenko VA, Alekseenko SI, et al. Zinc and respiratory tract infections: perspectives for COVID 19 (Review). Int J Mol Med. 2020;46(1):17-26. http://dx.doi.org/10.3892/ijmm.2020.4575

49. Gautret P, Million M, Jarrot PA, Camoin-Jau L, Colson P, Fenollar F, et al. Natural history of COVID-19 and therapeutic options. Expert Rev Clin Immunol. 2020;16(12):1159-1184. http://dx.doi.org/10.1080/1744666X.2021.1847640

50. Nastri L, Moretti A, Migliaccio S, Paoletta M, Annunziata M, Liguori S, et al. Do dietary supplements and nutraceuticals have effects on dental implant osseointegration? A scoping review. Nutrients. 2020;12(1):268. http://dx.doi.org/10.3390/nu12010268

51. Yamaguchi M. Nutritional factors and bone homeostasis: synergistic effect with zinc and genistein in osteogenesis. Mol Cell Biochem. 2012;366(1-2):201-21. http://dx.doi.org/10.1007/s11010-012-1298-7

52. Fernandes CCBS, Rodrigues CCN, Cruz GNAP, Costa JCA, Melo MGR, Pessôa TR. The role of vitamin d in the sars-cov-2 Coronavirus infection: literature review. Braz. J Hea Rev. 2020;3(4): 9092-9106. http://dx.doi.org/10.34119/bjhrv3n4-150

53. Martín Giménez VM, Inserra F, Tajer CD, Mariani J, Ferder L, Reiter RJ, et al. Lungs as target of COVID-19 infection: Protective common molecular mechanisms of vitamin D and melatonin as a new potential synergistic treatment. Life Sci. 2020;254:117808. http://dx.doi.org/10.1016/j.lfs.2020.117808

54. Waskiewicz K, Oth O, Kochan N, Evrard L. Des facteurs de risque généralement négligés en chirurgie orale et en implantologie: le taux élevé de LDL-cholestérol et le taux insuffisant de la vitamine D [Risk factors generally neglected in oral surgery and implantology: the high LDL-cholesterol and the insufficient level of vitamin D]. Rev Med Brux. 2018;39(2):70-77. http://dx.doi.org/10.30637/2018.17-075

55. Trybek G, Aniko-Wlodarczyk M, Kwiatek J, Preuss O, Brodkiewicz A, Sinicyn A, et al. The effect of vitamin D3 on the osteointegration of dental implant. DOAJ. 2018;10(4):25-33. http://dx.doi.org/10.29359/BJHPA.10.4.02

56. Guido Mangano F, Ghertasi Oskouei S, Paz A, Mangano N, Mangano C. Low serum vitamin D and early dental implant failure: Is there a connection? A retrospective clinical study on 1740 implants placed in 885 patients. J Dent Res Dent Clin Dent Prospects. 2018;12(3):174-182. http://dx.doi.org/10.15171/joddd.2018.027

57. Machado V, Lobo S, Proença L, Mendes JJ, Botelho J. Vitamin D and periodontitis: a systematic review and meta-analysis. Nutrients. 2020;12(8):2177. http://dx.doi.org/10.3390/nu12082177

58. Costa LC, Fonseca MAD, Pinheiro ADR, Aguiar TRDS, Machado AN, Quinelato V, et al. Chronic periodontitis and RANKL/OPG ratio in peri-implant mucosae inflammation. Braz Dent J. 2018;29(1):14-22. http://dx.doi.org/10.1590/0103-6440201801241

59. Salvio G, Gianfelice C, Firmani F, Lunetti S, Balercia G, Giacchetti G. Bone Metabolism in SARS-CoV-2 Disease: Possible Osteoimmunology and Gender Implications. Clin Rev Bone Miner Metab. 2020;18(4):51-57. http://dx.doi.org/10.1007/s12018-020-09274-3

60. Singh H, Chauhan P, Kakkar AK. Hydroxychloroquine for the treatment and prophylaxis of COVID-19: The journey so far and the road ahead. Eur J Pharmacol. 2021;890:173717. http://dx.doi.org/10.1016/j.ejphar.2020.173717

61. Mégarbane B. Chloroquine and hydroxychloroquine to treat COVID-19: between hope and caution. Clin Toxicol (Phila). 2021; 59(1):70-71. http://dx.doi.org/10.1080/15563650.2020.1748194

62. Prodromos C, Rumschlag T. Hydroxychloroquine is effective, and consistently so when provided early, for COVID-19: a systematic review. New Microbes New Infect. 2020;38:100776. http://dx.doi.org/10.1016/j.nmni.2020.100776

63. Both T, Zillikens MC, Schreuders-Koedam M, Vis M, Lam WK, Weel AEAM, et al. Hydroxychloroquine affects bone resorption both in vitro and in vivo. J Cell Physiol. 2018;233(2):1424-1433. http://dx.doi.org/10.1002/jcp.26028

64. Both T, van de Peppel HJ, Zillikens MC, Koedam M, van Leeuwen JPTM, van Hagen PM, et al. Hydroxychloroquine decreases human MSC-derived osteoblast differentiation and mineralization in vitro. J Cell Mol Med. 2018;22(2):873-882. http://dx.doi.org/10.1111/jcmm.13373

65. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter JJ. Use of ivermectin is associated with lower mortality in hospitalized patients with coronavirus disease 2019: the Ivermectin in COVID nineteen study. Chest. 2021;159(1):85-92. http://dx.doi.org/10.1016/j.chest.2020.10.009

66. Drug Bank. Ivermectin. 2021 [cited 2021 May 18]. Available from: <https://go.drugbank.com/drugs/DB00602>.

67. Bovaira M, Herrero Babiloni A, Jovaní M, Peñarrocha-Diago M, González-Lemonnier S, Peñarrocha-Oltra D. Preoperative anxiety and its influence on patient and surgeon satisfaction in patients receiving dental implant surgeries performed under intravenous conscious sedation. Int J Oral Maxillofac Implants. 2017;32(4):912-918. http://dx.doi.org/10.11607/jomi.5712

68. Sahebnasagh A, Avan R, Saghafi F, Mojtahedzadeh M, Sadremomtaz A, Arasteh O, et al. Pharmacological treatments of COVID-19. Pharmacol Rep. 2020;72(6):1446-1478. http://dx.doi.org/10.1007/s43440-020-00152-9

69. Falavigna M, Colpani V, Stein C, Azevedo LCP, Bagattini AM, Brito GV, et al. Guidelines for the pharmacological treatment of COVID-19. The taskforce/consensus guideline of the Brazilian Association of Intensive Care Medicine, the Brazilian Society of Infectious Diseases and the Brazilian Society of Pulmonology and Tisiology. Rev Bras Ter Intensiva. 2020;32(2):166-196. http://dx.doi.org/10.5935/0103-507x.20200039

70. Keyt H. WHO recommends corticosteroids for patients with severe or critical COVID-19. Ann Intern Med. 2021;174(1):JC2. http://dx.doi.org/10.7326/ACPJ202101190-002

71. Chiodini I, Merlotti D, Falchetti A, Gennari L. Treatment options for glucocorticoid-induced osteoporosis. Expert Opin Pharmacother. 2020;21(6):721-732. http://dx.doi.org/10.1080/14656566.2020.1721467

72. Ouanounou A, Hassanpour S, Glogauer M. The influence os systemic medication on osseointegration of dental implants. J Can Dent Assoc. 2016;82:g7.

73. Meng L, Hua F, Bian Z. Coronavirus Disease 2019 (COVID-19): emerging and future challenges for dental and oral medicine. J Dent Res. 2020;99(5):481-487. http://dx.doi.org/10.1177/0022034520914246

74. Marui VC, Souto MLS, Rovai ES, Romito GA, Chambrone L, Pannuti CM. Efficacy of preprocedural mouthrinses in the reduction of microorganisms in aerosol: A systematic review. J Am Dent Assoc. 2019;150(12):1015-1026.e1. http://dx.doi.org/10.1016/j.adaj.2019.06.024

75. Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B. Comparison of in vitro inactivation of sars cov-2 with hydrogen peroxide and povidone-iodine oral antiseptic rinses. J Prosthodont. 2020;29(7):599-603. http://dx.doi.org/10.1111/jopr.13220

76. COVIDSurg Collaborative; GlobalSurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. Anaesthesia. 2021;76(6):748-758. http://dx.doi.org/10.1111/anae.15458

77. Kovoor JG, Tivey DR, Williamson P, Tan L, Kopunic HS, Babidge WJ, et al. Screening and testing for COVID-19 before surgery. ANZ J Surg. 2020;90(10):1845-1856. http://dx.doi.org/10.1111/ans.16260

Received on: 31/8/2021
Final version resubmitted on: 31/3/2022
Approved on: 20/5/2022

Assistant editor: Luciana Butini Oliveira