

Systematic Review Dental Implants

Does local delivery of bisphosphonates influence the osseointegration of titanium implants? A systematic review

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Abstract. The aim of this study was to systematically review the influence of the local delivery of bisphosphonates on the osseointegration of titanium implants in humans. A search of health sciences databases was performed (The Cochrane Library, Embase, PubMed MEDLINE, ISI Web of Knowledge, Scopus, and SIGLE OpenGrey), including articles published until October 2016. A total of 679 articles were identified. Following the removal of duplicates, 278 were screened by title and abstract. The complete texts of seven studies were read, and of these, three met the inclusion criteria. Each article included in the analysis was submitted to a quality and level of evidence evaluation, and relevant data were extracted and tabulated. Despite methodological differences, all articles presented positive results for osseointegration when a local bisphosphonate was used: the authors reported greater implant stability, better implant survival rates, and reduced peri-implant bone loss when compared with the control groups. On the basis of the results of this systematic review, it is concluded that the local use of a bisphosphonate appears to favour the osseointegration of titanium implants in humans. Nonetheless, a higher level of standardization and the control of methodological bias is required in future research so that stronger evidence might be produced.

Key words: bisphosphonates; osseointegration; dental implants.

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Scientific developments in areas such as orthopaedics, medical traumatology, and implant dentistry have facilitated and extended the use of osseointegrated metal implants as a therapeutic option in the endeavour to re-establish functions lost

due to trauma, amputation, physical disability¹, tooth loss and agenesis². In spite of the dissemination of preventive methods in medicine and dentistry and the advancements in rehabilitative specialties, sequelae arising from these problems con-

tinue to be a prevalent reality, particularly in the elderly³. Because older persons present pathologies such as osteoporosis and diabetes, and as these are factors that have a direct influence on osseointegration^{4,5}, these patients are expected to show

lower success rates in rehabilitative therapy. Moreover, due to the aging process, their physiological response to healing is reduced⁶. In this context, new technologies and materials to promote, facilitate, and/or accelerate osseointegration have been investigated, particularly with the objective of immediate dental prosthesis insertion^{7,8}.

The bisphosphonate class of drugs represents one such material that is under investigation. These are substances that biomodulate the bone response and act by inhibiting osteoclast activity, such that

they may have a positive influence on bone remodeling^{9,10}. In orthopaedics and traumatology, they appear to diminish bone resorption⁷. In implant dentistry, there are reports that they promote a positive effect on peri-implant bone formation¹¹, by improving the bone turnover rate¹², in addition to acting on improving the fixation of osseointegrated implants in humans^{9,10,13}.

With a view to diminishing the side effects caused by the systemic use of bisphosphonates¹⁴, such as oesophagitis¹⁵ and osteonecrosis of the jaw^{16–19}, recent

studies have sought alternative systems for local delivery of the drug^{7,9,10,13,20}, either by means of immobilizing the bisphosphonate on the implant surface^{13,20,21} or by applying the drug directly to the surgical site before implant insertion^{7,12,22,23}.

The present systematic review was focused on the following question: Does the local delivery of bisphosphonates influence the osseointegration of titanium implants? Thus, the aim of the present study was to conduct a systematic review of previous studies that have investigated the influence of the local delivery of

Table 1. Search strategy through key words, by database.

Database	Search strategy
Cochrane Library http://www.cochranelibrary.com/	("Prostheses and Implants" OR "Dental Implants" OR "Orthopedic Fixation Devices" OR "Bone Screws" OR implant OR "mini-implant" OR miniscrew OR screw OR titanium) AND (local* OR topic* OR coat* OR surface OR immobil* OR "Coated Materials, Biocompatible") AND (Diphosphonates OR bisphosphonates OR zoledron* OR pamidron* OR alendron* OR ibandron* OR risedron* OR etidron* OR clodron* OR tiludron*) AND ("Bone-Implant Interface" OR Osseointegration OR "Prosthesis Implantation" OR "Dental Implantation, Endosseous" OR fixation OR integration OR stability OR success OR "ISQ" OR "implant stability quotient" OR "RFA" OR "Osstell" OR "Periotest value" OR "PTV" OR "Periotest")
Embase https://www.embase.com/	("Prostheses and Implants" OR "Dental Implants" OR "Orthopedic Fixation Devices" OR "Bone Screws" OR implant OR "mini-implant" OR miniscrew OR screw OR titanium) AND (local* OR topic* OR coat* OR surface OR immobil* OR "Coated Materials, Biocompatible") AND (Diphosphonates OR bisphosphonates OR zoledron* OR pamidron* OR alendron* OR ibandron* OR risedron* OR etidron* OR clodron* OR tiludron*) AND ("Bone-Implant Interface" OR Osseointegration OR "Prosthesis Implantation" OR "Dental Implantation, Endosseous" OR fixation OR integration OR stability OR success OR "ISQ" OR "implant stability quotient" OR "RFA" OR "Osstell" OR "Periotest value" OR "PTV" OR "Periotest")
PubMed MEDLINE http://www.ncbi.nlm.nih.gov/pubmed	(Prostheses and Implants [MeSH Terms] OR Dental Implants [MeSH Terms] OR Orthopedic Fixation Devices [MeSH Terms] OR Bone Screws [MeSH Terms] OR implant OR "mini-implant" OR miniscrew OR screw OR titanium) AND (local* OR topic* OR coat* OR surface OR immobil* OR Coated Materials, Biocompatible [MeSH Terms]) AND (Diphosphonates [MeSH Terms] OR bisphosphonates OR zoledron* OR pamidron* OR alendron* OR ibandron* OR risedron* OR etidron* OR clodron* OR tiludron*) AND (Bone-Implant Interface [MeSH Terms] OR Osseointegration [MeSH Terms] OR Prosthesis Implantation [MeSH Terms] OR Dental Implantation, Endosseous [MeSH Terms] OR fixation OR integration OR stability OR success OR "ISQ" OR "implant stability quotient" OR "RFA" OR "Osstell" OR "Periotest value" OR "PTV" OR "Periotest")
Web of Knowledge http://apps.webofknowledge.com	((Prostheses and Implants) OR (Dental Implants) OR (Orthopedic Fixation Devices) OR (Bone Screws) OR implant OR (mini-implant) OR miniscrew OR screw OR titanium) AND (local* OR topic* OR coat* OR surface OR immobil* OR (Coated Materials, Biocompatible)) AND (Diphosphonates OR bisphosphonates OR zoledron* OR pamidron* OR alendron* OR ibandron* OR risedron* OR etidron* OR clodron* OR tiludron*) AND ((Bone-Implant Interface) OR Osseointegration OR (Prosthesis Implantation) OR (Dental Implantation, Endosseous) OR fixation OR integration OR stability OR success OR (ISQ) OR (implant stability quotient) OR (RFA) OR Osstell OR (Periotest value) OR (PTV) OR Periotest)
Scopus http://www.scopus.com	("Prostheses and Implants" OR "Dental Implants" OR "Orthopedic Fixation Devices" OR "Bone Screws" OR implant OR "mini-implant" OR miniscrew OR screw OR titanium) AND (local* OR topic* OR coat* OR surface OR immobil* OR "Coated Materials, Biocompatible") AND (Diphosphonates OR bisphosphonates OR zoledron* OR pamidron* OR alendron* OR ibandron* OR risedron* OR etidron* OR clodron* OR tiludron*) AND ("Bone-Implant Interface" OR Osseointegration OR "Prosthesis Implantation" OR "Dental Implantation, Endosseous" OR fixation OR integration OR stability OR success OR "ISQ" OR "implant stability quotient" OR "RFA" OR "Osstell" OR "Periotest value" OR "PTV" OR "Periotest")
Grey literature (SIGLE) http://www.opengrey.eu/	("Prostheses and Implants" OR "Dental Implants" OR "Orthopedic Fixation Devices" OR "Bone Screws" OR implant OR "mini-implant" OR miniscrew OR screw OR titanium) AND (local* OR topic* OR coat* OR surface OR immobil* OR "Coated Materials, Biocompatible") AND (Diphosphonates OR bisphosphonates OR zoledron* OR pamidron* OR alendron* OR ibandron* OR risedron* OR etidron* OR clodron* OR tiludron*) AND ("Bone-Implant Interface" OR Osseointegration OR "Prosthesis Implantation" OR "Dental Implantation, Endosseous" OR fixation OR integration OR stability OR success OR "ISQ" OR "implant stability quotient" OR "RFA" OR "Osstell" OR "Periotest value" OR "PTV" OR "Periotest")

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