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Original Article

Dentistry Section

Evaluation of Protein Adsorption and Osseointegration Potential of Polyetheretherketone versus Titanium Dental Implants: A Systematic Review

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ABSTRACT

Introduction: The success of implant therapy depends on a number of parameters, including bone volume implant shape, surface topography, the patient's overall health, and local factors. Despite the fact that Polyetheretherketone (PEEK) implants have undergone a lot of alterations, only a small number of studies have examined the bioactivity and osseointegration of PEEK implants with titanium.

Aim: To summarise and evaluate protein adsorption and osseointegration capacity of PEEK and titanium dental implants.

Materials and Methods: Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were used and PROSPERO (CRD42023415494) registration was done. Electronic databases were searched for studies assessing the outcome in terms of protein adsorption and osseointegration capacity of PEEK and titanium dental implants. Quality assessment of included studies was evaluated using the Newcastle-Ottawa Scale (NOS).

Results: Depending on inclusion and exclusion criteria, seven studies fulfilled the eligibility criteria and were included in qualitative synthesis. Risk of bias assessment revealed that all the included studies were largely comparable in methodological quality. All the included studies had moderate to low-risk of bias with all the respective domains. All the included studies revealed that PEEK with optimal surface roughness might hold great potential for protein adsorption and osseointegration capacity.

Conclusion: Within the limitations of the study, it was found that compared to titanium, PEEK is less osseoconductive and bioactive. PEEK is therefore unsuitable for use as a dental implant in its unmodified form. Implantitis and implant failure occurs from improper osseoconductivity and bioactivity of dental implants.

Keywords: Bioactive, Newcastle-ottawa scale, Osseoconductivity

INTRODUCTION

Losing a tooth has profound effects on the patient's overall health, in addition to compromising aesthetics [1,2]. The goal of contemporary dentistry is to restore patients' oral health in a predictable way [3]. The missing teeth are replaced with the optimum option based on a person's geographical, environmental, physiological, mental, and financial circumstances [4].

Surgically inserted into the alveolar bone, a dental subgingival implant is a fixture that serves as an artificial root to support and anchor a fixed or removable prosthesis [5]. The implant fails if fibrous tissue grows in the space between implant and the bone. However, if a close, direct bone-implant contact forms, the implant is said to have osseointegrated into the alveolar bone [6].

Branemark's theory of osseointegration expanded the range of restorative choices for patients who were either partially or fully missing all of their teeth [7]. The concept of osseointegration is based on the concept of biotechnology's clinical applications which is still continuing to benefit dental patients and practitioners in long-term [8,9]. The four stages of osseointegration include protein adsorption, inflammatory cell adhesion/inflammatory response, additional relevant cell adhesion, and angiogenesis/osteogenesis, which are categorised according to several crucial biological processes [4]. Each stage's biological activity is closely related to the implant surface [5].

Protein adsorption is a complicated process that involves several interactions between protein and substrate and is controlled by a wide range of variables depending on the surface properties and chemical or biological environment [5]. It is widely accepted that a variety of driving forces, including van der Waals forces and hydrophobic or electrostatic interactions, can facilitate protein adsorption [6]. Surface topography/roughness, surface chemistry, protein charge, hydrophobicity/hydrophilicity, molecular weight, structural stability, solution pH, ionic strength, and protein concentration are the main parameters influencing protein adsorption on surfaces [7-9].

A well-designed implant material with a high degree of hydrophilicity and with appropriate surface characteristics are required [10,11]. Osteoconductive coatings, such as calcium phosphate, have been shown to hasten osseointegration when applied to dental implants [12]. The material of choice for endosseous implants has been commercially pure grade 2 or 4 titanium and its alloys [13]. But a number of faults in titanium have been discovered. Due to their high elastic modulus, titanium alloy dental implants run the risk of stress shielding and periodontal bone loss [14-16].

The use of organic-inorganic biocomposites as implants has been thoroughly studied over the last few decades [17]. Polyetheretherketone (PEEK), which has several notable qualities for an implant use, is one of the promising organic materials [18]. It has properties like excellent biocompatibility, mechanical strength, and elastic modulus are comparable to human cortical bone [19]. It has strong chemical and biomechanical resistance. PEEK is similar to cortical bone in that it possesses a Young's modulus in its pure condition of roughly 3.6 gigapascals (GPa). PEEK would therefore be thought to have less stress shielding than titanium [20].

According to the available data, no study has, to date, offered a thorough, qualitative comparison of the capacities for protein adsorption and osseointegration between PEEK and titanium dental implants. Therefore, this systematic review was conducted with the aim to summarise, appraise, and evaluate the protein adsorption and osseointegration capacity of PEEK and titanium dental implants.

MATERIALS AND METHODS

The recommended PRISMA statement [21] was followed in the conduct of this review, which was also registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the CRD42023415494.

The review aimed to compare the protein adsorption capacity of PEEK and titanium dental implants, which serves as an indicator of osseointegration in the Participants (P), Intervention (I), Comparison (C) and Outcome (O). The difference in the protein adsorption and osseointegration capacity of the PEEK and titanium dental implants are shown below:

Participants (P): The implant samples

Intervention (I): The protein adsorption and osseointegration capacity of PEEK dental implants

Comparison (C): The protein adsorption and osseointegration capacity of titanium dental implants

Outcome (O): To assess and evaluate the protein adsorption capacity of PEEK and titanium dental implants

Study design (S): In-vitro studies, comparative study, randomised controlled trials

Inclusion criteria: 1) Articles in English language and having sufficient data on the protein adsorption and osseointegration capacity of PEEK and titanium dental implants; 2) Studies published between January 2000-December 2022; 3) Study design: in vitro studies, cross-sectional studies; 4) Articles from open access journals.

Exclusion criteria: 1) Studies conducted before 2000; 2) Articles in languages other than English; 3) Reviews, abstracts, letter to the editor, editorials, animal studies; 4) Studies on zirconia implants.

Search strategy: For research published over the last 22 years (from 2000 to 2022), a thorough electronic search was conducted through December 2022 using the following databases: Pubmed, Google scholar, and EBSCO host to retrieve English-language papers. A manual search of prosthodontics journals was also conducted, including the British Dental Journal of Prosthodontics, American Dental Association Journal, International Journal of Prosthodontics and Restorative Dentistry, International Journal of Prosthodontics, Journal of Prosthodontic Dentistry, The Journal of Indian Prosthodontic Society, International Journal of Prosthodontics. Appropriate keywords and Medical Subject Headings (MeSH) terms were selected and combined with Boolean operators like AND/NOT: "dental implants" (MeSH term) AND "osseointegration" (MeSH term); "protein adsorption" (MeSH term) AND "titanium implants" (MeSH term) AND osseointegration (MeSH term); "PEEK implant" (MeSH term) AND "protein adsorption" (MeSH term) AND osseointegration (MeSH term); "surface modifications" (MeSH term) AND "dental implants" (MeSH term) NOT "zirconia implant".

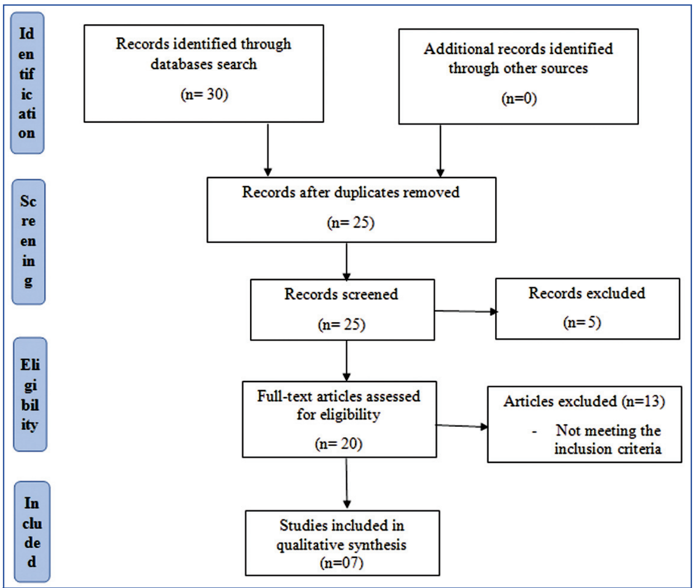
Data extraction: For included studies, following descriptive study details were extracted in Microsoft Excel sheet under the following headings: author(s), country of study, year of study, sample size, objective, time period, implant material placed, conclusion.

Screening process: Two authors carried out the search and screening. There was a two-phase process used to choose the articles. Two reviewers looked over all of the article titles and abstracts in phase one. Articles that didn't fit the requirements for inclusion were rejected. Phase two involved the independent screening and review of full papers by the same reviewers. Discussions were held to settle any disputes. A third reviewer was brought in to make the ultimate decision when two reviewers could not agree upon something. All three authors came to agreement on the choice in the end. When more information was needed, the study's corresponding authors were contacted by email.

Assessment of methodological quality: The quality of included studies was evaluated based on Newcastle-Ottawa Scale and accordingly a numeric score (NOS Score) was assigned [22]. The NOS uses a 9-star rating system with a maximum of 4 points available for selection, 2 for comparability and 3 for the assessment of the outcome or exposure. A study with a score from 7 to 9 was considered as high quality, 4 to 6 was considered as moderate quality and 0 to 3 was considered as low quality or very high-risk of bias [22].

RESULTS

Study selection: A total of (n=30) records were identified after database searching. After duplicates removal, reference list of included studies (n=25) was screened, of which five studies were excluded which could not be assessed for full text eligibility. After this, full text articles (n=20) were assessed for eligibility and articles that did not meet inclusion criteria (n=13) were excluded. Only seven studies were included in final review. A flowchart of identification, inclusion and exclusion of studies is shown in [Table/Fig-1] below.



[Table/Fig-1]: PRISMA 2009 flow diagram assessment.

Study characteristics: A summary of descriptive characteristics of included studies is provided in [Table/Fig-2] below. Seven studies [23-29] fulfilled the eligibility criteria and were included in qualitative analysis. Among the included studies, one study [23] was from UK,

S. No.	Authors and year	Country	Study design	Sample size	Objective	Time period	Implant material (control)	Implant material (test)	Outcome
1.	Sagomonyants KB et al., 2008 [23]	UK	Cross-sectional	12	Adhesion, proliferation and mineralisation assays of human osteoblasts	3 weeks	Ti (polished and rough)	PEEK (polished and rough), CFR-PEEK (polished and rough)	Biocompatibility of all samples comparable
2.	Olivares-Navarrete R et al., 2012 [26]	USA	Cross-sectional	12	Comparison of bone morphogenic proteins produced from human MG63 osteoblast-like and their phenotype	24 hours	Ti	PEEK (polished and rough)	More mature osteoblasts observed on Ti

3.	Zhao M et al., 2012 [25]	China	Cross-sectional	96	Proteomic analysis of human osteoblast-like MG-63 cells cultured on implant discs	2 weeks	Ti	PEEK	PEEK inhibited mRNA processing leading to lower MG-63 cells cultured on proliferation of cells
4.	Olivares-Navarrete R et al., 2013 [24]	USA	Cross-sectional	Not mentioned	Comparison of angiogenic factors produced from human MG-63 cells cultured on PEEK and Ti	Not mentioned	Ti	Polystyrene PEEK (rough and smooth)	Ti promoted production of angiogenic factors more than PEEK
5.	Olivares-Navarrete R et al., 2015 [27]	USA	Cross-sectional	6	Comparison of proinflammatory and osteogenic factors produced from human MG-63 cells cultured on PEEK and Ti	1 week	Ti	PEEK (rough and smooth)	PEEK promoted fibrotic changes and Ti promoted production of osteogenic factors
6.	Deng Y et al., 2015 [28]	China	Cross-sectional	12	Effect of surface roughness on osteogenesis in vitro and osseointegration in vivo of carbon fiber-reinforced PEEK–nanohydroxyapatite composite	Not mentioned	Ti	PEEK	The PEEK with optimal surface roughness might hold great potential as bioactive biomaterial for bone grafting and tissue engineering applications
7.	Sugimoto K et al., 2016 [29]	Japan	Cross-sectional	30	Proteomic analysis of bone proteins adsorbed onto the surface of titanium dioxide	Not mentioned	TiO_2	PEEK	Interface between bone and TiO_2 showed the presence of proteins, extracellular matrix, enzyme, and growth factor. TiO_2 incubated with proteins from guanidine-extracted proteins displayed increased calcium depositions. Proteome analysis using TiO_2 chromatography is a useful tool for investigating which bone proteins adhere to TiO_2

[Table/Fig-2]: Descriptive details of the included studies.
PEEK: Polyetheretherketone; Ti: Titanium

three studies [24,26,27] were from USA, two studies [25,28] from China, and one study [29] from Japan. Data was evaluated from an aggregate of 168 implant samples. All the studies evaluated a comparative evaluation between titanium and PEEK. With the outcome evaluated, it was concluded that with the PEEK with optimal surface roughness might hold great potential as bioactive biomaterial for bone grafting and tissue engineering applications.

Assessment of methodological quality: Among the included studies, only one study [24] reached the maximum score of the Newcastle-Ottawa scale. Only one study [24] gained the maximum score in the selection criteria and had highest level of quality with low-risk of bias; two studies [26,27] had the lowest score in the comparability outcome and had lowest level of quality with high-risk of bias; and all the studies had a partial score in the exposure outcome while only two studies [24,25] had the highest score for exposure outcome having the highest level of quality with low-risk of bias. Risk of bias of included studies is depicted in [Table/Fig-3] below.

Author and year	Selection (Max=4)	Comparability (Max=2)	Exposure (Max=3)	Overall quality score (Max=9)
Sagomonyants KB et al., 2008 [23]	**	**	**	6
Olivares-Navarrete R et al., 2012 [26]	***	*	**	6
Zhao M et al., 2012 [25]	**	**	***	7
Olivares-Navarrete R et al., 2013 [24]	****	**	***	9
Olivares-Navarrete R et al., 2015 [27]	**	*	**	5
Deng Y et al., 2015 [28]	**	**	**	6
Sugimoto K et al., 2016 [29]	***	**	**	7

[Table/Fig-3]: Risk of bias of included studies [23-29].

DISCUSSION

The success of implant therapy depends on a number of parameters, including bone volume, implant shape, surface topography, the patient's overall health, and local factors (such as dental cleanliness and smoking habits) [30]. After being inserted into the bone, implant surface properties are essential for establishing initial stability. Surface roughness at the micrometer and nanometer scales has been found to encourage cellular adhesion [4]. Additionally, covering the implant with substances like calcium phosphate and hydroxyapatite encourages the growth of osteoblasts [31]. It has been found that surface modification improves interfacial adhesion to the bone and bone-implant contact [32]. Despite the fact that PEEK implants have undergone a lot of alterations, only a small number of studies have examined the bioactivity and osseointegration of PEEK implants with titanium [33,34].

Osteoblasts, which were extracted from surgical patients, were grown on the surfaces of PEEK and titanium implants by Sagomonyants KB et al., who then evaluated cellular activity and proliferation on the two implant materials [23]. Similar to smooth and rough titanium, PEEK was found to enhance osteoblast proliferation, messenger Ribonucleic Acid (mRNA) synthesis, and collagen I turnover. This suggested that the degree to which titanium and Carbon Fibre Reinforced PEEK (CFR-PEEK) encouraged cellular differentiation and proliferation was equal. In vitro experiments, in contrast to the Sagomonyants KB et al., study, failed to find any parallels between the bioactivity of PEEK and titanium [23]. Results from a series of investigations by Olivares-Navarrete R et al., showed that while PEEK did drive cellular proliferation, the osteoconductive properties of the proliferating cells on PEEK were inferior to those on titanium [24]. Titanium promotes a more mature cell growth, as indicated by the enhanced Bone Morphogenetic Proteins (BMPs) generated by MG-63 cells. In fact, BMPs have been used in regenerative medicine for bone regeneration and have been thought to be suggestive of increased bone production. Angiogenesis, the growth of new blood vessels, is crucial for effective osseointegration and bone repair [35,36]. In addition, Olivares-Navarrete R et al., found that cells cultured on titanium expressed more endothelial growth factor A, angiopoietin-1, and fibroblast growth factor 2 than cells cultured on PEEK [26]. In addition, they found that PEEK induced a greater proliferation of inflammatory cells compared to titanium.

Cells cultivated on PEEK produced higher levels of proinflammatory interleukins and pro-apoptotic mRNA, which suggested a stronger fibrotic relationship between the polymer and bone. However, it was found that titanium seemed to encourage a biological response that was better suited to bone development. Zhao M et al., proteomic research revealed that PEEK favours less pro-osteoblast protein synthesis than titanium, supporting the idea that PEEK is less osseoconductive than titanium [25].

Furthermore, the study's design flaws may have resulted in biased findings [37]. Future research should concentrate on refining the study design to reduce bias sources. PEEK and PEEK-based composites' macroscopic properties, such as implant form and thread geometry, should be investigated further and contrasted with currently utilised titanium implants. More research should be done to analyse the PEEK apatite bonding even if coated PEEK may end up being a suitable titanium substitute. This is because dental implants are known to fail because the coating material delaminates [38]. Indeed, additional research is required to support the use of PEEK in dental implants. Published case reports describe the failure of uncoated PEEK implants as the result of severe peri-implantitis brought on by inadequate osseointegration. Despite being commercially accessible (PEEK-Optima and PEEK-Optima HA Enhanced, Invibio, Lancashire, UK), PEEK dental implants have been the subject of least clinical research to determine their clinical efficacy. Therefore, more human studies are essential before PEEK, in any form, is used clinically as a material for dental implants [39].

Limitation(s)

The study is limited by the fact that less studies were included in the final review. Also, conducting meta-analysis was not possible because of data heterogeneity due to which getting a pooled estimate or quantifying the study results statistically was not possible. Furthermore, more studies should be carried out to determine the safety of these implants in clinical situation.

CONCLUSION(S)

The review concluded that compared to titanium, PEEK is less osseoconductive and bioactive. PEEK is therefore unsuitable for use as a dental implant in its unmodified form. Dental implants with inadequate osseoconductivity and bioactivity may develop severe implantitis and fail. There should therefore be a lot more inclination towards research studies and extensive trials aimed at enhancing PEEK's bioactivity before it may be used as a dental implant. To determine whether PEEK has the potential to be a competitive alternative to titanium, more comparative animal and clinical research are required.

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