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The association between common NSAID use and early dental implant failure: A large-scale retrospective cohort study

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Abstract

Introduction

The impact of NSAIDs on osseointegration remains controversial, with conflicting evidence from animal models and human clinical trials. The aim of the study was to investigate the association between the use of common Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and the risk of early dental implant failure in a large, real-world patient cohort.

Methods

This retrospective cohort study utilized an EHR database of 12,943 patients receiving 49,997 implants. Patients were divided into an NSAID group ($n = 3133$) and a non-NSAID control group ($n = 9810$). The primary outcome was early implant failure, defined as implant removal within six months of placement. Multivariable logistic regression models were used to calculate Odds Ratios (ORs) for failure, adjusting for patient age, gender, history of diabetes, and history of osteoporosis. Analyses were conducted at both the implant and patient levels.

Results

Patients in the NSAID group were significantly older (62.8 vs. 58.7 years, $p < 0.0001$) and had a higher prevalence of diabetes (22.0% vs. 16.7 %, $p < 0.0001$) and osteoporosis (11.0 % vs. 7.0 %, $p < 0.0001$). After adjusting for confounders, implant-level analysis showed that Ibuprofen use (OR 2.29; 95 % CI 1.48–3.55; $p < 0.0001$) and Naproxen use (OR 2.65; 95 % CI 1.22–5.75; $p = 0.0137$) were significantly associated with increased odds of early failure. At the patient level, the association remained highly significant for Ibuprofen (OR 2.87; 95 % CI 1.83–4.51; $p < 0.0001$), but not for Naproxen ($p = 0.0689$).

Conclusion

The use of Ibuprofen and, to a lesser extent, Naproxen, is associated with a significantly increased risk of early dental implant failure, independent of other patient risk factors. Clinicians should consider these findings when formulating post-operative analgesic plans, particularly for patients with complex medical histories.

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are a cornerstone of post-operative pain management in dentistry, widely prescribed following procedures such as the surgical placement of dental implants. Their efficacy stems from their anti-inflammatory, analgesic, and anti-pyretic properties, which are achieved through the inhibition of the cyclooxygenase (COX) enzyme. This inhibition interferes with the synthesis of prostaglandins, which are key inflammatory mediators responsible for pain [1]. However, the very mechanism that makes NSAIDs effective for pain control raises important biological questions regarding their impact on bone healing, a process critical for the success of dental implants through osseointegration.

The process of osseointegration is biologically analogous to bone fracture healing, involving an initial inflammatory response that recruits osteoprogenitor cells and promotes their differentiation into bone-forming osteoblasts [2,3]. Prostaglandins, particularly those synthesized via the COX-1 and COX-2 pathways, are known to be upregulated during the initial stages of bone repair and play a complex role in bone metabolism [4,5]. Studies have shown that prostaglandins can stimulate bone formation and the differentiation of osteoblasts on titanium surfaces [6]. Consequently, the inhibition of prostaglandin synthesis by NSAIDs presents a plausible mechanism by which these drugs could negatively interfere with the bone healing cascade essential for successful osseointegration [7].

Despite this clear biological rationale, the existing body of evidence regarding the clinical impact of NSAIDs on implant outcomes is fraught with conflicting findings and a lack of consensus. A systematic review by Luo et al. (2018) highlighted this controversy, noting that while many animal studies suggest that both non-selective and selective COX-2 inhibitors can delay or impair bone healing, the available human clinical studies have not consistently supported this conclusion [8]. For

instance, clinical trials by Alissa et al. (2009) and Sakka et al. (2013) found that a short, 7-day post-operative course of ibuprofen did not significantly affect marginal bone levels around dental implants [9,10]. In stark contrast, a retrospective study by Winnett et al. (2016) reported a significant association between the perioperative use of NSAIDs and a higher incidence of failed osseointegration [11].

This discrepancy between animal models, in vitro data, and small-scale human clinical trials underscores a significant gap in the literature. Much of the concern has been extrapolated from orthopedic literature or animal studies, which may not accurately translate to the specific biological environment of the oral cavity and the pharmacokinetics in humans [8,12]. Furthermore, previous clinical studies have often been limited by small sample sizes and have not been able to adequately control for confounding patient-specific risk factors.

Therefore, the purpose of the present study is to address these uncertainties by analyzing a large, real-world patient cohort. By examining the association between the use of specific NSAIDs and early implant failure at both the implant and patient levels, and by statistically controlling for a wide range of demographic and systemic health variables, this study aims to provide a clearer, more definitive understanding of the clinical impact of NSAID administration on dental implant treatment outcomes.

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Section snippets

Study design and data source

This study was conducted as a retrospective cohort analysis utilizing a large, de-identified electronic health record (EHR) database from the Big Mouth Dental Repository. The dataset comprised patient demographics, medical histories, medication records, and detailed information on dental implant treatments provided between 2011 and 2022. The use of this de-identified dataset for research purposes was conducted in accordance with institutional guidelines and ethical principles for patient data ...

Results

This investigation began with a substantial cohort of 12,943 patients who had collectively received 49,997 dental implants. The primary objective was to determine if the use of Non-steroidal Anti-inflammatory Drugs (NSAIDs) influenced the likelihood of early implant failure, which was defined as failure within the first six months of healing. To isolate the study population, we identified all patients with a "current" prescription for an NSAID. This resulted in a specific cohort of 3133 ...

Discussion

This large-scale retrospective cohort study provides significant clinical evidence on the association between NSAID use and early dental implant failure. The primary finding was that, after controlling for significant patient-level confounders, the use of Ibuprofen and Naproxen was associated with a statistically significant increase in the odds of early implant failure at the implant level. At the more clinically focused patient level, this significant association remained robust for ...

Conclusions

In conclusion, this large-scale retrospective analysis of nearly 50,000 implants provides significant evidence that the use of certain common NSAIDs is associated with an increased risk of early dental implant failure. After statistically adjusting for confounding variables including patient age, gender, and a history of diabetes or osteoporosis, the use of Ibuprofen and Naproxen remained significant predictors of implant failure within the first six months. At the patient level, the ...

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CRedit authorship contribution statement

Georgios S. Chatzopoulos: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Larry F. Wolff:** Writing – review & editing, Validation, Supervision, Software, Methodology, Investigation, Conceptualization. ...

Declaration of competing interest

None. ...

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