



Relationship Between Corticosteroids and Immunosuppressants Causing Delayed Healing and Osteonecrosis in Extraction Socket

Dr. Kanimozhi¹, Sabhana. B², Suji Rajan³, Dr. Senthil Kumar⁴, Dr. Vandana Shenoy⁵

¹Senior lecturer, Department of oral and maxillofacial surgery, Thai moogambigai dental college and hospital, Chennai, India

²⁻³ Junior resident, Department of oral and maxillofacial surgery, Thai moogambigai dental college and hospital, Chennai, India

⁴Professor, Department of oral and maxillofacial surgery, Thai moogambigai dental college and hospital, Chennai, India

⁵Professor, Department of oral and maxillofacial surgery, Thai moogambigai dental college and hospital, Chennai, India

ABSTRACT

When tooth extraction is preferred on patients taking steroids, immunosuppressants, or bone modifying agents, delayed healing of the extraction socket is not unusual. Tooth extraction is one of the surgical procedure routinely performed by dentists. When extracting teeth from patients taking steroids, the most common precautions are delayed wound healing and wound infection in the extraction socket. Following tooth extraction, bone modifying or antiresorptive medications that target osteoclasts, such medications as bisphosphonates are known to contribute to osteonecrosis of the jaw (ONJ) and delayed wound healing. However, there is no information on whether such adverse events are brought on by medications, corticosteroids, immunosuppressants, biological substances, and disease-modifying antirheumatic drugs (DMARDs) are a few examples of substances that can impair immunity. This study sought to determine how frequently patients taking immunosuppressive drugs who had their teeth extracted experienced delayed post-extraction wound healing.

Keywords: Incidence of delayed wound healing, tooth extraction, corticosteroids, immunosuppressants.

INTRODUCTION

Corticosteroids exhibit strong anti-allergic and anti-inflammatory effects and are essential in the treatment of conditions such as autoimmune disease and severe inflammatory disease¹⁻⁴. Prednisolone is a typical example of such drugs a synthetic corticosteroid made from cortisol. Although steroids have potent pharmacological effects, prolonged use and high dosages also result in a number of side effects.⁵ Steroid osteoporosis and steroid diabetes are common examples⁵⁻⁶ other important side effects include delayed wound healing which should be considered specially in the perioperative period. Despite reports on the relationship between perioperative steroid use and delayed wound healing in various medical field, there is still no consensus.⁷ There have been some studies in dentistry that have shown a connection between tooth extraction and delayed healing of the extraction socket in patients who take steroids.⁸⁻⁹ Medication-related osteonecrosis of the jaw (MRONJ), also known as drug-related osteonecrosis of the jaw, is frequently reported in patients taking bone-modifying drugs (BMDs), such as bisphosphonates and the monoclonal antibody against receptor denosumab.¹⁰ After having teeth extracted, patients taking these medications may experience delayed wound healing or osteonecrosis of the jaw (ONJ).¹⁰ In 2014 (Ruggiero et al. 2014), the American Association of Oral and Maxillofacial Surgeons (AAOMS) released a revised position paper on MRONJ for its prevention, diagnosis, and treatment.¹⁰ The objective of this retrospective study was to examine the prevalence and pinpoint the causes of delayed post-extraction wound healing in dental extraction patients who were also taking immunosuppressive medications.

MATERIALS AND METHODS

A PubMed, science direct, Google scholar, ncbi and google search was undertaken of all controlled clinical trials on the terms of tooth extraction, incidence of delayed wound healing, corticosteroids and immunosuppressants. The review was limited to studies published in English over the last 27 yrs from the year of 1996 to 2022.

DISCUSSION

The wound healing process can be divided into three phases: (1) inflammatory phase (2) proliferative phase (3) remodeling phase.¹¹ The expression of cytokines and the migration of immune cells are regulated by corticosteroid (prednisolone) during each phase, leading to delayed wound healing.^{12,14} The preoperative dosage that causes delayed healing was determined to be 8.0 mg/day of prednisolone. While no specific relationship can be pointed out, this suggested that exceeding this dosage may increase the adverse effects described above and cause healing failure. The main dependent factors for delayed healing were the dosage of corticosteroids (prednisolone) and the extent of osteosclerotic changes around the tooth to be extracted.¹⁵ Numerous

factors have been reported to contribute to delayed or inadequate healing of extraction sockets.⁹ ¹⁶ When comparing BP linked osteomyelitis to other kinds of non-drug related osteomyelitis, Actinomyces proliferation at the surface of BP related necrotic bone of the jaw is frequently implicated (Kos et al. 2010, 2010). Due to the effects of BP on monocytes and macrophages, MRONJ is therefore not solely caused by osteoclast-mediated immune system suppression (Katsarelis et al. 2015). According to the study currently being conducted and the AAOMS position paper (Ruggiero et al. 2014), BMAs must be stopped at least three months prior to tooth extraction, and the effects of medications on wound healing were minimized.¹⁰ DM and the use of immunosuppressive drugs are typical examples.⁹ ¹⁷ Although no significant differences were found in this study, female sex, diabetes mellitus and bone modifying agents affected delayed healing compared with other factors. In women, menopause causes abnormal bone metabolism due to decrease in female hormones, such as estrogen.¹⁸ Delayed or inadequate recovery of extractive alveoli from the combined use of BMA and steroids was described and both were reported as risk factors for ARONJ.⁹ The results of the current investigation demonstrated a connection between delayed healing and the decline in lymphocytes and eosinophils. The number of neutrophils or monocytes that differentiate into macrophages and phagocytose encroaching bacteria, on the other hand, did not differ across the groups.¹⁹ Tacrolimus, mycophenolate mofetil, cyclosporine, and mizoribine are immunosuppressants that impede the activity of T and B lymphocytes, whereas azathioprine prevents the development of WBCs. Sirolimus, cyclosporine A, and tacrolimus have all been linked to a delayed rate of wound healing (Petri et al. 1998; Guilbeau 2002; Cavalli et al. 2014).¹⁹ Although the cause of ONJ by immunosuppressants has not been established, lymphocyte activity has frequently been suppressed. This was connected to recent discoveries about the possibility of delayed post-extraction wound healing. TNF-inhibitors, for instance, have been demonstrated to impair wound healing in animal experiments (Mooney et al. 1990; Salomon et al. 1991; Repala et al. 1996).¹⁹ After surgery in the oral cavity, wound healing can be suppressed and bacterial infection can occur. Moreover, surgical tooth extraction demands a large and extensive procedure, which increases the likelihood of microbial infection and decreased immunity during the healing process of the dental wound ¹⁹.

CONCLUSION

There is a risk of delayed wound healing and jaw osteonecrosis when teeth are extracted from individuals who are taking corticosteroids, immunosuppressants, biological medications, and disease-modifying antirheumatic medicines. In addition, surgical extraction, low eosinophil levels, and low lymphocyte counts are all major risk factors for osteonecrosis of the jaw and delayed wound healing. In these high-risk individuals, it is crucial to avoid surgical site infections and monitor wound healing for at least a few weeks after tooth extraction.

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