



A Clinical Evaluation of the Incidence of Peri-Implantitis by Post-Surgical Evaluation of Implant Healing Marker/C-Reactive Protein Levels Using Latex Enhanced Nephelometry (LEN) in Implant Surgeries Coupled with Platelet-Rich Plasma and Ozone Interventions: An In Vivo (Original Research) Study

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ABSTRACT:

Aim: This study aims to evaluate the incidence of peri-implantitis by post-surgical evaluation of implant healing marker (C-reactive protein) levels using latex-enhanced nephelometry (Len) in implant surgeries coupled with platelet-rich plasma and ozone interventions.

Materials and Methods: This study involved 50 patients with missing right mandibular posterior teeth seeking prosthetic replacement, who 30 preferred implant-supported prostheses. Eligible participants were aged 21-35 with adequate bone quality, while smokers, those with mental instability, pregnant individuals, and those with poor bone quality were excluded. Informed consent was obtained, and 6 ml of blood was collected for platelet-rich plasma (PRP) extraction. Ozone was generated and infused into water. Before implant placement, patients received a chlorhexidine rinse and local anesthesia. They were divided into two groups: Group 1 (n=15) received PRP therapy and Group 2 (n=15) received ozone therapy. C-reactive protein (CRP) levels were measured within 24 and 48 hours after implantation.

Statistical Analysis and Results: This study examined 30 patients aged 21 to 35 with missing mandibular posterior teeth. Platelet-rich plasma (PRP) was collected preoperatively, and patients were divided into two groups: Group 1 (15 patients) received PRP-enhanced implants, while Group 2 (15 patients) underwent ozone therapy. C-reactive protein (CRP) levels were measured within 24- and 48-hours post-surgery. Group 1 had CRP levels of 2.01 ± 0.14 mg/dl at 24 hours and 1.20 ± 0.12 mg/dl at 48 hours after implant placement. Group 2 showed lower levels of 1.05 ± 0.22 mg/dl at 24 hours, decreasing to 0.59 ± 0.09 mg/dl at 48 hours after implant placement, indicating ozone therapy's effectiveness in reducing inflammation. Statistical analysis was performed using one-way ANOVA.

Conclusion: This study concluded that there is an increased level of CRP within 24 hours post-surgery for both groups, with a decline after 48 hours. Notably, the ozone therapy group had lower CRP levels than the PRP group at both time points; suggesting ozone therapy may reduce CRP levels more effectively. Future long-term studies



are recommended to validate these findings for clinical practice.

Introduction

Over the next few decades, dental implants are poised to become even more popular and effective for replacing lost teeth. As research continues to evolve, we anticipate that over 85% of dental implants will still be lasting beyond 25 years.¹ However, there's growing awareness of potential complications associated with these procedures. We are likely to see an increase in discussions regarding diseases surrounding implants, such as peri-mucositis and peri-implantitis. These conditions, characterized by inflammation, may pose challenges that could lead to the loss of bone supporting implants, making it crucial for future advancements in dental care to address these concerns proactively.^{2,3} Detecting these problems early is important, but can be challenging. Scientists are looking at certain biological markers, which are indicators that may help identify issues around implants at an early stage. One such marker is C-reactive protein (CRP), which is a substance produced by the body in response to inflammation. It is very sensitive and can indicate various kinds of injuries, even when they are not directly related to dental health.^{4,5} CRP levels can be influenced by various factors, including smoking, obesity, and even chronic conditions like diabetes. Generally, CRP is mainly produced by the liver, but it can also be generated by other tissues in the body. Normal CRP levels can vary, but they usually fall between 1.0 to 3.0 mg/L. Advanced testing methods can detect even lower levels.^{6,7} There are different ways to measure CRP, including specific laboratory tests that use special techniques to get accurate readings. CRP levels can also change due to factors such as aging, alcohol consumption, lack of exercise, and other health conditions.^{8,9} Latex-enhanced immunoturbidimetric measurement is an advanced immunological technique that employs tiny latex spheres as markers. This method hinges on the specific interactions between antigens and antibodies, facilitating the detection and quantification of target substances in a sample. As the antigen-antibody complexes form, they cause turbidity changes in the solution, which can be accurately measured. This innovative approach allows for sensitive and precise analysis, making it valuable in various biomedical and

clinical applications.¹⁰ Platelet-rich plasma (PRP) is used to help heal after surgery, support bone growth, and improve results in dental implants and gum treatments. On the other hand, low doses of ozone (O₃) can be beneficial by creating a mild form of stress in the body. This kind of stress can encourage our cells to activate their protective mechanisms, helping them cope better without causing harm or inflammation.¹¹ This study aims to explore the incidence of peri-implantitis by examining CRP levels after dental implant surgeries, particularly focusing on cases that involve treatments like platelet-rich plasma and ozone therapy. By doing so, researchers hope to better understand implant healing and the associated risks.

Materials and Methods

This study involved 50 patients presenting with the chief complaint of missing right mandibular posterior teeth, all seeking prosthetic replacement. Among these, 30 patients expressed a preference for implant placement with an implant-supported prosthesis. Inclusion criteria encompassed individuals aged 21-35 years, both male and female, possessing adequate bone quality and quantity. Exclusion criteria included smoking, mental instability, pregnancy, and inadequate bone quality. Informed consent was meticulously obtained from all participants prior to the initiation of the procedure, ensuring that they fully understood the process and its implications. The extraction of platelet-rich plasma (PRP) was executed in strict adherence to aseptic protocols to maintain the highest standards of cleanliness and safety. A total of 6 ml of blood was drawn carefully from the antecubital fossa using a vacutainer needle, which was then specifically placed into vacutainers that contained no anticoagulant to prevent interference with the subsequent processing. Once collected, the blood samples were promptly subjected to centrifugation at a speed of 3,000 revolutions per minute for duration of 10 minutes. This critical step effectively separated the PRP from other blood components, allowing for the concentration of healing platelets. In a separate but equally important procedure, ozone was generated through a sophisticated corona discharge method. This technique enabled the production of ozone in high concentrations, reaching



levels of up to 140 micrograms per milliliter. The selection of this method was primarily due to its cost-effectiveness in yielding substantial quantities of ozone. Subsequently, the concentrated ozone was infused into water, preparing it for further use in the treatment process. Prior to implant placement, patients underwent a chlorhexidine mouth rinse. An inferior alveolar nerve block was administered for local anesthesia. An incision was made, and the implant was placed according to a standardized protocol utilizing a single operator and the same implant kit/system. The 30 patients were divided into two groups: Group 1 (n=15), where implants were placed using PRP therapy and Group 2 (n=15), where implants were facilitated with ozone therapy. Following implant placement, a cover screw was placed, and the flap was repositioned, followed by suturing. C-reactive protein (CRP) levels were measured using Latex Enhanced Nephelometry (LEN) in both groups. In Group 1, CRP was assessed within 24 hours post-procedure and again after 48 hours after implant placement. Similarly, in Group 2, CRP levels were detected before 24 hours and then again after 48 hours using LEN. This study aimed to evaluate and compare the levels of C-reactive proteins in both PRP and ozone therapy groups post-implantation.

Statistical Analysis and Results

In this study, we used SPSS software to help us with our statistical analysis. SPSS version 29.0 is a useful tool for working with data in the social sciences. To check if our findings were important, we used a method called the chi-square test. This test is good for looking at differences in percentages among different groups. By using this method, we were able to carefully compare categorical data, making sure our results truly show the patterns and connections in the data we studied.

Results

This study encompasses a total of 30 patients with missing mandibular posterior teeth who sought replacement through implant placement and implant-supported prostheses. The participants included both males and females aged between 21 and 35 years. Prior to commencing the study, platelet-rich plasma (PRP)

was collected from the patients through blood draws. Additionally, ozone therapy was administered using ozone generated via the corona discharge method. After completing the preoperative procedures, the patients were methodically divided into two distinct groups for the purpose of implant placement. Group 1 comprised 15 patients who received implants enhanced by the application of platelet-rich plasma (PRP), while Group 2 included another set of 15 patients who were treated with ozone therapy during their implant procedure. Following the meticulous placement of the implants and the careful repositioning of the surgical flaps, measurements of C-reactive protein (CRP) levels were taken. These measurements were carried out using the precise method of latex-enhanced nephelometry at two time points, within 24 hours post-surgery and again after 48 hours for both groups. In Table 1, a thorough statistical summary of the patient demographics is provided, which encompasses both age and gender distribution. Meanwhile, Graph 1 visually represents the demographic distribution, highlighting the specific details of the study population, which included a total of 16 males and 14 females. Table 2 focuses on the CRP assessments for Group 1 (n=15) at the 24-hour mark following the implant placement procedure, revealing a mean CRP value of 2.01 ± 0.14 mg/dl. Moving to Table 3, the CRP evaluation for Group 1 is further detailed at the 48-hour post-implant placement, showcasing a significant reduction in mean CRP levels to 1.20 ± 0.12 mg/dl. For Group 2, as presented in Table 4, the CRP results at 24 hours post-implant placement indicated a mean CRP level of 1.05 ± 0.22 mg/dl. Table 5 highlights their 48-hour evaluations, which revealed an even lower mean CRP level of 0.59 ± 0.09 mg/dl. Comparative analysis between the two groups indicated a notable trend: CRP levels were significantly lower in Group 2, which underwent ozone therapy, at the 48-hour mark. This difference underscores the efficacy of ozone therapy as an inflammation management strategy, as reflected by the CRP measurements. Finally, Table 6 summarizes the statistical findings across both groups, employing a one-way ANOVA to provide a clear estimation of the data collected throughout the study.



Table 1: Age & gender based statistical description of contributing patients

Age Group (Yrs)	Male	Female	Total	P value
21-23 years	2	3	5	0.06
24-26 years	3	4	7	0.20
27-29years	4	2	6	0.02*
30-32years	3	2	5	0.30
33-35years	4	3	7	0.07
Total	16	14	30	*Significant

*p<0.05 significant

Graph 1: Patients demographic distribution and associated details

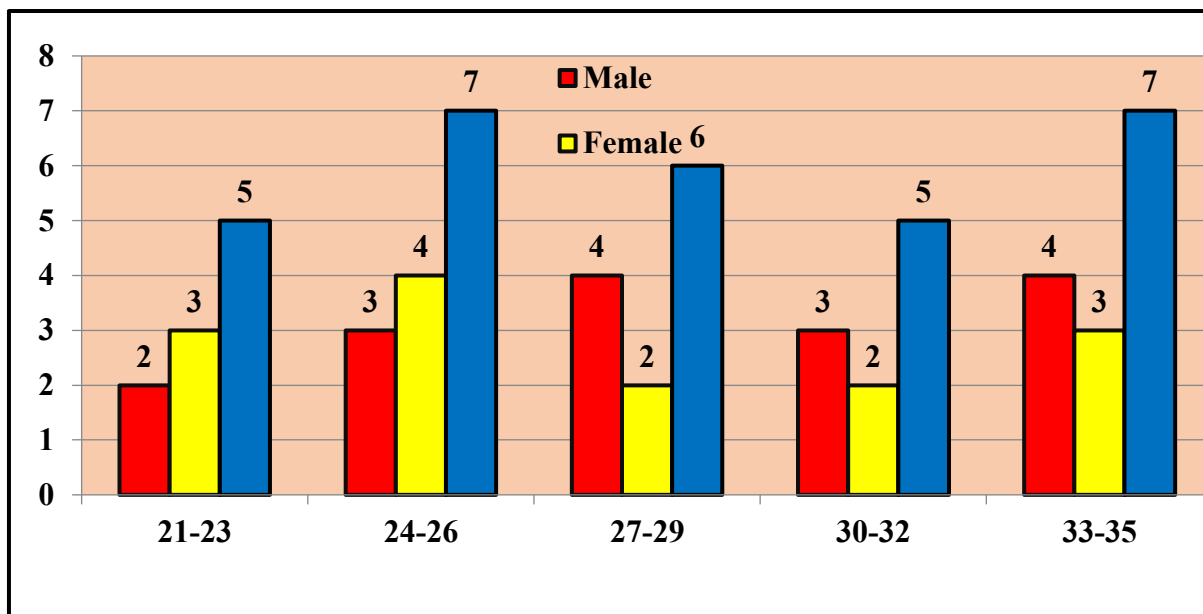


Table 2: Group 1 (n=15) Implant Surgeries Coupled with Platelet-Rich Plasma and C-reactive protein was evaluated in 24 hours after the implant placement by Latex Enhanced Nephelometry (LEN) and statistical assessment with the "Pearson Chi-Square" test at a specified level of significance

Age	duration	Mean	Std. Dev.	Std. Error	95% CI	Pearson Chi-Square Value	df	p value
21-35 years	24 hours	2.01±0.14	2.16	1.120	1.123	1.42	1.356	1.0*

*p<0.05 significant



Table 3: Group 1 (n=15) Implant Surgeries Coupled with Platelet-Rich Plasma and C reactive protein was evaluated in 48 hours after the implant placement by Latex Enhanced Nephelometry (LEN) and statistical assessment with the "Pearson Chi-Square" test at a specified level of significance

Age	duration	Mean	Std. Dev.	Std. Error	95% CI	Pearson Chi-Square Value	df	P value
21-35 years	48 hours	1.20±0.12	1.12	1.024	0.113	1.23	1.011	0.02*
*p<0.05 significant								

Table 4: Group 2 (n=15) Implant Surgeries Coupled with Ozone therapy and C reactive protein was evaluated in 24 hours after the implant placement by Latex Enhanced Nephelometry (LEN) and statistical assessment with the "Pearson Chi-Square" test at a specified level of significance

Age	duration	Mean	Std. Dev.	Std. Error	95% CI	Pearson Chi-Square Value	df	p value
21-35 years	24 hours	1.05±0.22	1.10	1.014	1.035	1.20	1.01	1.02*
*p<0.05 significant								

Table 5: Group 2 (n=15) Implant Surgeries Coupled with Ozone therapy and C-reactive protein was evaluated in 48 hours after the implant placement by Latex Enhanced Nephelometry (LEN) and statistical assessment with the "Pearson Chi-Square" test at a specified level of significance

Age	duration	Mean	Std. Dev.	Std. Error	95% CI	Pearson Chi-Square Value	df	P value
21-35 years	48 hours	0.59±0.09	0.12	0.094	1.005	0.23	0.231	1.0
*p<0.05 significant								

Table 6: Estimation amongst all studied groups using one-way ANOVA

Variables	Degree of Freedom	Sum of Squares Σ	Mean Sum of Squares $m\Sigma$	F	Level of Sig. (p)
Between Groups	2	2.230	1.333	1.4	0.001*
Within Groups	12	2.254	1.228		—
Cumulative	123.24	3.024	*p<0.05 significant		



Discussion

Urban IA et al reviewed in their study that inflammation is an important factor in the development of heart disease, and a protein called C-reactive protein (CRP) serves as a marker for low-level inflammation in the body. Research has shown that higher levels of CRP can predict heart problems, not just in people with existing heart issues but also in healthy individuals. Patients with gum disease, for instance, often have increased levels of inflammation markers like CRP.¹²⁻¹³ Kour P et al included in their study that one specific type of inflammation-causing molecule, known as interleukin-6 (IL-6), is elevated in these patients. Fortunately, these levels tend to drop when they receive appropriate treatment for their gum disease. IL-6 is particularly notable because it encourages the clotting process in the body and also triggers the production of CRP, which further promotes inflammation. Bezerra PL et al. showed in their study that in healthy individuals, C-reactive protein (CRP) is typically present in negligible quantities, averaging approximately 0.8 mg/L. Its primary function is to facilitate the immune response against infections. CRP can bind to phosphocholine residues found on the surface of certain pathogens, thereby enhancing the opsonization of these microorganisms and stimulating an effective immune response. Additionally, CRP plays a crucial role in modulating inflammation through various mechanisms, including the promotion of anti-inflammatory cytokine production.^{16,17} Fernandez-Cuadros M E et al. reviewed their study to explore the effects of ozone therapy on people with knee osteoarthritis (OA). This research looked at patients before and after they received treatment. The findings suggested that ozone therapy can help reduce pain and stiffness in the knees, as well as improve overall function and quality of life. Additionally, it was noted that ozone therapy might lower certain markers of inflammation in the body, which are often linked to pain and discomfort.¹⁸ Gough A et al reviewed in their study that for individuals with stable health, CRP levels exceeding 0.3 mg/dL are associated with an elevated risk of cardiovascular events. As such, precise assays are essential for the accurate quantification of low CRP levels. The nomenclature "C-reactive protein" is derived from its initial identification in patients exhibiting acute inflammatory responses, where it demonstrated

reactivity with the polysaccharides of pathogenic strains of *Streptococcus pneumoniae*.^{19,20} Pohanka M et al included in their studies that have shown that higher CRP levels can also be linked to bleeding around dental implants in overweight patients compared to those of a healthy weight. C-reactive protein (CRP) levels can be assessed using a variety of laboratory methods, each with its unique advantages. Among these, immunoturbidimetric tests and the more sophisticated enzyme-linked immunosorbent assay (ELISA) stand out. However, one of the most sensitive techniques for measuring CRP is nephelometry.^{21,22} Liu Y et al showed in their study that this method is well-regarded for its precision and reliability, making it a common choice in medical laboratories. Nephelometry works by illuminating the sample and measuring the scattered light, which correlates with the concentration of CRP and other proteins or antibodies present in the blood. Its widespread use reflects its importance in diagnosing and monitoring inflammatory conditions, highlighting the vital role CRP plays in medical assessments. Overall, monitoring CRP levels can provide valuable insights into a person's inflammation status, helping guide treatment and assess cardiovascular risks.^{23,24}

Conclusion

This study examines the incidence of peri-implantitis by assessing post-surgical levels of the inflammatory marker C-reactive protein (CRP) using latex-enhanced nephelometry (LEN). The research focuses on implant surgeries that are augmented with platelet-rich plasma (PRP) and ozone therapy. The study's findings concluded that C-reactive protein (CRP) levels were elevated within 24 hours following the placement of implants in both groups that received either platelet-rich plasma (PRP) or ozone therapy. However, after 48 hours, there was a noted decrease in CRP levels for both groups. Interestingly, the ozone therapy group exhibited moderately lower CRP levels compared to the PRP group at both the 24-hour and 48-hour intervals. This indicates that C-reactive protein, identified as an inflammation marker, demonstrates a superior reduction of C-reactive protein (CRP) through ozone therapy, facilitated by the use of latex-enhanced nephelometry (LEN). To further validate these findings and their implications for clinical practice, it is recommended that future long-term studies be conducted to enhance our understanding of these results.



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