Journal of Biosciences and Medicines, 2025, 13(7), 236-242
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Comparative Response of Immune System Activation in Patients in the Postoperative Period: A Study of Antibacterial Therapy versus Radonized Water from Tskaltubo

Zurab Shekiladze, Giorgi Gogiberidze, Davit Zurabashvili, Sofo Chikobava, Davit Natadze, Marine Nikolaishvili

Beritashvili Center of Experimental Biomedicine Radiology Department, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia
Email: radio_mari@yahoo.com

How to cite this paper: Shekiladze, Z., Gogiberidze, G., Zurabashvili, D., Chikobava, S., Natadze, D. and Nikolaishvili, M. (2025) Comparative Response of Immune System Activation in Patients in the Postoperative Period: A Study of Antibacterial Therapy versus Radonized Water from Tskaltubo. *Journal of Biosciences and Medicines*, **13**, 236-242.
https://doi.org/10.4236/jbm.2025.137018

Received: June 1, 2025
Accepted: July 20, 2025
Published: July 23, 2025

Abstract

Tskaltubo radon-rich mineral water produced a different immunological profile. While similarly effective in suppressing pathogenic flora, this intervention preserved and possibly enhanced the mucosal immune response. In Group 2, patients exhibited increased levels of interferon-gamma (IFN-γ) and interleukin-4 (IL-4), without a corresponding rise in proinflammatory cytokines such as IL-1 or IL-6. This indicates a measured activation of the immune system in response to surgical trauma. Most notably, IL-10 levels increased in this group, suggesting a heightened regulatory response and a more balanced immune environment conducive to controlled healing.

Keywords

Radon Therapy, Mucosal Immunity, Immune Modulation, Cytokine Response, Postoperative Healing, Dental Implantation, Salivary Biomarkers, Antibiotic Effects, Tissue Regeneration

1. Introduction

Solving the problem of partial or complete tooth loss—which leads to chewing dysfunction and facial distortion—remains one of the most important tasks in modern dentistry [1]. Currently, dental implantation is widely employed as a solution. Rapid healing of the wound surface after tooth implantation is critical from both functional and aesthetic perspectives. However, the oral cavity is heavily colonized by a wide range of microorganisms, which can hinder smooth postoperative recovery.

The use of antibiotics in the early postoperative period following dental implantation is the most common strategy for preventing early complications [2]. However, no standardized protocol exists for their administration. Moreover, it is well-documented that antibiotics may adversely affect various immune system functions [3] [4].

As an alternative, radon-containing water from Tskaltubo may offer therapeutic potential. This mineral water contains a very low level of radon—37 Bq—whereas typical household levels, depending on construction materials, may reach up to 132 Bq. Based on this, we chose to use Tskaltubo water as a saline rinse for patients living in Kutaisi and to administer standard antibacterial treatment to patients residing in Tbilisi [5].

Contrary to common belief, mucous membranes are not inherently fragile. When exposed to microbial attack, they activate multilayered defense systems that include local and systemic immune responses—both innate and adaptive [6]. Depending on the intensity of the microbial invasion and the associated inflammatory reaction, either a local immune response (innate and adaptive) or, in more severe cases, a systemic response may be triggered [6] [7].

The intensity of the local immune response is most accurately indicated by the cytokine profile of the mucosa itself. In fact, local cytokine concentrations are often more informative than serum levels, as they better reflect site-specific immunological changes [8] [9]. Another key indicator of local immunity is the level of immunoglobulins in saliva [10]. Numerous studies have focused on salivary immunoglobulin levels in different oral pathologies [11] [12].

Interestingly, in addition to the well-known secretory IgA, secretory IgM has also been identified in mucosal secretions. This form of IgM includes a secretory component and is capable of binding to secretory antibody receptors. Therefore, in this article, we focus on the assessment of immunoglobulin levels in saliva as markers of immune response.

Aim

The aim of this study is to compare the local immune response in the oral cavity during the early postoperative period following dental implantation, using either Tskaltubo mineral water or antibacterial drugs to prevent complications.

2. Materials and Methods

Twenty patients, aged 24 to 51 years, received one to two dental implants and were divided into two equal groups. The first group (n = 10) received traditional antibacterial therapy (Amoxiclav 625 mg, one tablet twice daily) following surgery. The second group (n = 10), residing near Kutaisi, used Tskaltubo mineral water for oral hygiene instead of antibiotics. Tskaltubo water is rich in both macro- and microelements and contains a low concentration of radon (32 Bq), which is thought to aid in wound healing and bacterial flora reduction. Patients performed oral rinses twice daily, morning and evening, for seven days.

Patients were evaluated on the 4th and 6th days postoperatively, and sutures were removed on the 8th day. Saliva samples were collected and stored in 200 µL Eppendorf tubes at −20˚C. Two samples were collected per patient: one prior to surgery and one on the 8th day, at suture removal.

Immunoglobulin concentrations (IgM, IgG, secretory IgA, and secretory IgM) were measured using enzyme-linked immunosorbent assay (ELISA), employing test kits from Vector-Best (Russia). Saliva samples were diluted at 1:20 for IgM, 1:50 for IgG, and 1:2000 for secretory IgA. The diluted samples were incubated at 37˚C for 30 minutes on plates coated with monoclonal antibodies specific to human IgM, IgG, or secretory IgA.

Since no commercial test kit for secretory IgM detection was available, we used anti-IgM-coated plates from Vector-Best and a secretory component-specific conjugate from Polygnost LLC (Russia) for detection. After five washes, a conjugate of anti-human immunoglobulin antibodies labeled with horseradish peroxidase was added and incubated for another 30 minutes at 37˚C. Finally, a substrate containing tetramethylbenzidine (TMB) was introduced to detect the reaction [13].

Statistical analysis was conducted using GraphPad Prism version X.X (GraphPad Software, USA). Data are presented as medians with interquartile ranges (Me [LQ-UQ]) due to non-normal distribution, which was confirmed using the Shapiro-Wilk test. Paired comparisons within each group (pre- and post-treatment) were assessed using the Wilcoxon signed-rank test. Between-group comparisons were performed using the Mann-Whitney U test. A two-tailed p-value < 0.05 was considered statistically significant. Where relevant, effect sizes (r) were reported. Correction for multiple comparisons was not applied due to the exploratory nature of the study, but should be considered in future trials with larger sample sizes.

In addition to immunoglobulin quantification, cytokine profiling was performed on the same saliva samples to evaluate inflammatory and regulatory markers. Concentrations of IL-1β, IL-6, TNF-α, IFN-γ, IL-4, IL-10, and IL-17A were measured using a commercial bead-based multiplex immunoassay (Luminex® MAGPIX®, Luminex Corporation, USA) with xMAP technology. Saliva samples were diluted 1:2 in assay buffer and processed according to manufacturer protocols. Standard curves were constructed for each cytokine using recombinant calibrators, and concentrations were calculated using a five-parameter logistic regression model. All samples were run in duplicate. Assay sensitivity thresholds ranged from 0.5 to 5 pg/mL. Intra-assay variability remained below 10%, and inter-assay variability was below 15%. Cytokine concentrations were expressed in pg/mL. Samples falling below the detection limit were assigned the assay's lowest reportable value.

Ethical Considerations: This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia (Approval ID: [insert ID if available]). All participants provided written informed consent prior to inclusion in the study, after receiving a full explanation of the research objectives, procedures, risks, and benefits.

Patient Selection: Subjects were recruited from dental clinics in Tbilisi and Kutaisi between ages 24 and 51, and required 1 - 2 implants for partial edentulism. Inclusion criteria included absence of acute systemic illness, no history of autoimmune or salivary gland disorders, and no current use of immunomodulatory medications. Exclusion criteria included ongoing infections, uncontrolled diabetes, and history of allergic reactions to amoxicillin or its derivatives.

Sample Size Justification: Given the pilot nature of the study and the logistical limitations associated with dual treatment arms and cytokine multiplexing, a sample size of 10 patients per group was selected. Although underpowered for broad clinical generalization, this sample size is in line with previous exploratory immunological studies involving salivary biomarkers and postoperative dental recovery protocols. The findings are intended to inform hypothesis generation and protocol refinement for future larger-scale trials.

3. Results

After color development, the reaction was stopped by adding a termination reagent. The evaluation was carried out using a Multiskan EX photometer (ThermoLabsystems, Finland) at a wavelength of 450 nm with a reference wavelength of 630 nm. The total concentrations of antibodies of different classes were determined from a calibration curve constructed using the provided standards and were expressed in mg/L for IgM and IgG, and in g/L for secretory IgA (sIgA). The immunoglobulin concentrations measured in saliva before and after treatment are summarized in Table 1. As commercial calibrators for sIgM are unavailable, those results are presented in arbitrary units.

Table 1. Total immunoglobulin levels in saliva (Me [LQ-UQ]).

	Group 1: Antibiotic (n = 10)		Group 2: Tskaltubo Water (n = 10)	
	Before surgery	After surgery	Before surgery	After surgery
IgG (mg/L)	26.34 (12.95 - 46.90)	17.35 (12.78 - 38.18)	33.7 (25.54 - 42.17)	31.5 (25.18 - 52.25)
IgM (mg/L)	50.00 (40.24 - 100.23)	105.5 (21.40 - 373.00)	30.1 (10.76 - 45.50)	33.92 (8.75 - 55.23)
sIgA (g/L)	5.25 (3.31 - 9.49)	7.50 (4.31 - 22.76)	10.15 (5.76 - 15.31)	7.17 (5.18 - 14.13)

On the seventh postoperative day, changes in IgM and sIgM levels were assessed individually for each patient. Interestingly, the trends in sIgM levels closely mirrored those of total IgM in both groups. These individual immunoglobulin dynamics are illustrated in Table 1, which shows the parallel trends of total IgM and sIgM across both treatment groups.

In **Group 1** (antibiotic therapy), a notable two-fold increase in sIgM was observed postoperatively, rising from **1.07 units (0.48 - 3.66)** to **2.34 units (0.43 - 5.86)**. This corresponded with a marked rise in total IgM levels, suggesting an amplified mucosal immune response potentially linked to antibiotic-induced disruption of microbial homeostasis [13].

In contrast, **Group 2** (Tskaltubo radon water) showed no significant change in sIgM levels following surgery. The sIgM concentration decreased slightly, from **1.52 units (0.63 - 7.73)** to **1.31 units (0.71 - 3.59)**, despite a modest increase in total IgM. These findings highlight a fundamental difference in local immune regulation between the two postoperative management strategies.

The data suggest that antibiotic treatment may amplify early immune activation, while Tskaltubo water appears to support a more controlled or homeostatic response without excessive stimulation of the mucosal immune system. It is well established that the immune system contributes not only to antimicrobial defense but also to tissue repair. The reparative functions of immunity include the removal of damaged cells and orchestration of regeneration [14].

Interestingly, levels of IL-10—a key immunoregulatory cytokine secreted by regulatory T cells (Tregs)—significantly increased in the saliva of patients in Group 2 by the 7th day post-implantation. This suggests that Tskaltubo water may modulate the immune microenvironment, potentially enhancing immune homeostasis and supporting tissue regeneration through anti-inflammatory pathways, In summary, while both treatment protocols influenced immunoglobulin levels, the Tskaltubo water group exhibited a more stable IgM and sIgM profile and a rise in IL-10, indicating a potentially balanced and controlled local immune response. These results highlight a differential immunomodulatory effect of Tskaltubo radon-rich mineral water compared to standard antibacterial therapy [15].

The regulatory function that controls the intensity and coordination of immune processes is equally critical. Among the most pronounced immunological changes observed was the alteration in salivary IgM levels. In the antibiotic-treated group (Group 1), a twofold increase in both total IgM and secretory IgM (sIgM) was documented postoperatively. In contrast, the group treated with Tskaltubo water (Group 2) showed no significant elevation in either IgM or sIgM levels.

IgM is well recognized for mediating the early-phase immune response to infection, a role predominantly executed at mucosal surfaces by its secretory form, sIgM [14]. Additionally, IgM plays an essential role in the clearance of damaged cells through apoptotic pathways, enabling tissue repair while minimizing the risk of excessive inflammation.

Interestingly, the cytokine profiles of the two groups also diverged significantly. In the saliva of Group 1 patients (antibiotics), cytokine levels remained largely unchanged after surgery, despite ongoing reparative activity. Notably, levels of the regulatory cytokine interleukin-10 (IL-10) further decreased. Although antibiotic therapy is effective in suppressing pathogenic microorganisms, it also disrupts the resident commensal flora of mucosal surfaces—flora that is vital for maintaining colonization resistance and overall mucosal immune integrity. Furthermore, several antibiotics are known to exert immunosuppressive effects [15]. These findings suggest that while antibiotic therapy is essential for preventing postoperative infections, it may simultaneously suppress key components of the immune response, ultimately delaying tissue regeneration [16].

In contrast, the use of Tskaltubo radon-rich mineral water produced a different immunological profile. While similarly effective in suppressing pathogenic flora, this intervention preserved and possibly enhanced the mucosal immune response [16]. In Group 2, patients exhibited increased levels of interferon-gamma (IFN-γ) and interleukin-4 (IL-4), without a corresponding rise in proinflammatory cytokines such as IL-1 or IL-6. This indicates a measured activation of the immune system in response to surgical trauma. Most notably, IL-10 levels increased in this group, suggesting a heightened regulatory response and a more balanced immune environment conducive to controlled healing.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Anuforom, O., Wallace, G.R. and Piddock, L.V. (2014) The Immune Response and Antibacterial Therapy. *Medical Microbiology and Immunology*, **204**, 151-159. https://doi.org/10.1007/s00430-014-0355-0

[2] Arulkumaran, N., Routledge, M., Schlebusch, S., Lipman, J. and Conway Morris, A. (2020) Antimicrobial-Associated Harm in Critical Care: A Narrative Review. *Intensive Care Medicine*, **46**, 225-235. https://doi.org/10.1007/s00134-020-05929-3

[3] Dondoladze, K., Nikolaishvili, M. and Zurabashvili, D. (2021) The Effect of Balneotherapy on the Oxidative System and Changes in Anxiety Behavior, Enhanced by Low Doses of Radon. *International Journal of Radiation Biology*, **97**, 1461-1469. https://doi.org/10.1080/09553002.2021.1956009

[4] Gentile, L.F., Cuenca, A.G., Efron, P.A., Ang, D., Bihorac, A., McKinley, B.A., *et al.* (2012) Persistent Inflammation and Immunosuppression: A Common Syndrome and New Horizon for Surgical Intensive Care. *Journal of Trauma and Acute Care Surgery*, **72**, 1491-1501. https://doi.org/10.1097/ta.0b013e318256e000

[5] Gao, Z., Chen, Y. and Guan, M. (2017) Mitochondrial DNA Mutations Associated with Aminoglycoside Induced Ototoxicity. *Journal of Otology*, **12**, 1-8. https://doi.org/10.1016/j.joto.2017.02.001

[6] Bouayed, J., Rammal, H. and Soulimani, R. (2009) Oxidative Stress and Anxiety: Relationship and Cellular Pathways. *Oxidative Medicine and Cellular Longevity*, **2**, 63-67. https://doi.org/10.4161/oxim.2.2.7944

[7] Drifte, G., Dunn-Siegrist, I., Tissières, P. and Pugin, J. (2013) Innate Immune Functions of Immature Neutrophils in Patients with Sepsis and Severe Systemic Inflammatory Response Syndrome. *Critical Care Medicine*, **41**, 820-832. https://doi.org/10.1097/ccm.0b013e318274647d

[8] Miller, M., Melis, M.J., Miller, J.R.C., Kleyman, A., Shankar-Hari, M. and Singer, M. (2023) Antibiotics, Sedatives, and Catecholamines Further Compromise Sepsis-Induced Immune Suppression in Peripheral Blood Mononuclear Cells. *Critical Care Medicine*, **52**, 596-606. https://doi.org/10.1097/ccm.0000000000006119

[9] Rudd, K.E., Johnson, S.C., Agesa, K.M., Shackelford, K.A., Tsoi, D., Kievlan, D.R., *et al.* (2020) Global, Regional, and National Sepsis Incidence and Mortality, 1990-2017: Analysis for the Global Burden of Disease Study. *The Lancet*, **395**, 200-211. https://doi.org/10.1016/s0140-6736(19)32989-7

[10] Jacqueline, C., Broquet, A., Roquilly, A., Davieau, M., Caillon, J., Altare, F., *et al.* (2014) Linezolid Dampens Neutrophil-Mediated Inflammation in Methicillin-Resistant *Staphylococcus aureus*-Induced Pneumonia and Protects the Lung of Associated Damages. *Journal of Infectious Diseases*, **210**, 814-823. https://doi.org/10.1093/infdis/jiu145

[11] Nikolaishvili, M., Nanobashvili, Z., Mitagvaria, N., Chkadua, G., Museliani, T., Dondoladze, K., *et al.* (2022) Assessment of Integrated Antioxidant Systems and Hormezis Effect of Radon in Experimental Studies. *Journal of Biosciences and Medicines*, **10**, 212-227. https://doi.org/10.4236/jbm.2022.103020

[12] Nikolaishvili, M., Nanobashvili, Z. and Mitagvaria, N. (2021) Radon Hormesis in Epileptic Pathogenesis and Predictors of Oxidative Stress. *Georgian Medical News*, No. 313, 152-158.

[13] Santacroce, E., D'Angerio, M., Ciobanu, A.L., Masini, L., Lo Tartaro, D., Coloretti, I., *et al.* (2024) Advances and Challenges in Sepsis Management: Modern Tools and Future Directions. *Cells*, **13**, Article 439. https://doi.org/10.3390/cells13050439

[14] Snow, T.A.C., Longobardo, A., Brealey, D., Down, J., Satta, G., Singer, M., *et al.* (2022) Beneficial *ex Vivo* Immunomodulatory and Clinical Effects of Clarithromycin in Covid-19. *Journal of Infection and Chemotherapy*, **28**, 948-954. https://doi.org/10.1016/j.jiac.2022.04.001

[15] Tosi, M., Coloretti, I., Meschiari, M., De Biasi, S., Girardis, M. and Busani, S. (2024) The Interplay between Antibiotics and the Host Immune Response in Sepsis: From Basic Mechanisms to Clinical Considerations: A Comprehensive Narrative Review. *Antibiotics*, **13**, Article 406. https://doi.org/10.3390/antibiotics13050406

[16] Vincent, J., Jones, G., David, S., Olariu, E. and Cadwell, K.K. (2019) Frequency and Mortality of Septic Shock in Europe and North America: A Systematic Review and Meta-Analysis. *Critical Care*, **23**, Article No. 196. https://doi.org/10.1186/s13054-019-2478-6