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Cold atmospheric plasma as an emerging adjunct in dental care: Mechanisms, efficacy, and clinical translation

Mohammad Ghanavati, Seyed Mahan Tabatabaei , Leila Tavanaei*

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ABSTRACT

Cold atmospheric plasma (CAP) has emerged as a novel adjunctive modality in dentistry, offering dual benefits of antimicrobial efficacy and tissue regeneration. Between 2020 and 2025, both international and Persian-language studies have demonstrated CAP's ability to disrupt resistant biofilms, reduce microbial load in root canals, enhance dentinal sealer penetration, and improve implant surface properties [6–14]. Safety assessments consistently report minimal thermal rise and negligible cytotoxicity, supporting its biocompatibility. Moreover, CAP has shown regenerative potential by stimulating angiogenesis and re epithelialization in oral tissues [10]. Despite these promising outcomes, heterogeneity in device types, working gases, and dosing parameters remains a barrier to standardized clinical adoption. Most clinical studies, including those conducted in Iran, are preliminary and limited in scale. Future research should prioritize multicenter randomized controlled trials, harmonized dose reporting, and long term safety evaluations. Collectively, CAP represents a transformative technology in dental care, bridging antimicrobial control with regenerative medicine, and holds promise for integration into endodontic, periodontal, and implant therapies

Introduction

Dental care increasingly contends with resilient polymicrobial biofilms, rising antimicrobial resistance, and the limitations of conventional chemotherapies, motivating interest in nonthermal physical modalities that can both inactivate pathogens and support tissue healing without collateral damage [1][2]. Cold atmospheric plasma (CAP)—a partially ionized gas at near-ambient temperature that delivers reactive oxygen and nitrogen species (ROS/RNS), transient electric fields, charged particles, and trace UV—has gained traction as a versatile adjunct across endodontics, periodontology/peri-implant care, oral surgery, and adhesive dentistry [1][3][4]. By generating short-lived and long-lived reactive species at clinically tolerable doses, CAP can disrupt extracellular polymeric substances, oxidize microbial membranes and DNA, and weaken biofilm cohesion, while simultaneously modulating host cell signaling relevant to re-epithelialization, angiogenesis, and extracellular matrix remodeling [2][3].

Recent systematic reviews and meta-analyses indicate that CAP enhances root canal disinfection beyond standard irrigants, achieving deeper dentinal tubule penetration and significant reductions in Enterococcus faecalis and mixed biofilms when used as an adjunct to sodium hypochlorite and EDTA [2]. In peri-implant and periodontal applications, CAP has shown efficacy against mature biofilms on titanium surfaces, increases in surface wettability and energy, and early clinical signals of improved soft-tissue healing and reduced inflammatory indices after decontamination [4][5]. Orthodontic bonding and restorative adhesion may also benefit from CAP-induced surface activation of enamel, dentin, composites, and titanium oxide, potentially improving bond strength and reducing early failure rates, although effects are parameter-dependent and require standardization [3][5].

Device heterogeneity remains a central challenge. Plasma jets (typically helium or argon) and dielectric barrier discharge (DBD) systems (often air) differ in species composition, energy delivery, plume dynamics, and treatment geometry, which translates into variable biological responses and outcome measures across studies [1][3]. Reported dosing commonly includes gas type, power/frequency, exposure time (10–120 s), electrode-to-surface distance (≈5–10 mm), and temperature rise, but unified metrics—such as energy density, ROS/RNS flux, and calibrated thermometry—are inconsistently captured, complicating cross-study comparisons and clinical protocol development [1][3]. Safety profiles are generally favorable at dental doses, with minimal thermal load, transient oxidative stress, and good patient tolerability; however, rigorous long-term evaluations and standardized adverse-event reporting are still limited [1][2].

Translationally, CAP is best positioned as an evidence-informed adjunct: supplementing chemical disinfection in endodontics, aiding peri-implant decontamination, and supporting oral wound care within established workflows and sterilization practices [2][4]. To progress toward routine clinical adoption, the field needs multicenter randomized controlled trials with clinically meaningful endpoints, harmonized device and dose reporting, and regulatory pathways tailored to dental indications. This review synthesizes contemporary evidence (2019–2025), contrasts device classes and parameters, and outlines practical considerations for integrating CAP into dental care while highlighting critical research gaps for safe, standardized, and effective translation [1–5].

Cold atmospheric plasma (CAP) has been increasingly investigated in dentistry over the past five years, with multiple studies highlighting its antimicrobial efficacy and biocompatibility. In 2021, **Rupf et al.** conducted one of the first systematic assessments of CAP in dental applications, demonstrating significant reductions in *Enterococcus faecalis* biofilms within root canals and enhanced penetration into dentinal tubules compared to conventional irrigants [8]. Their findings established CAP as a promising adjunct in endodontic disinfection.

Building on this, **Fricke and colleagues (2022)** performed a comprehensive safety evaluation of CAP in oral tissues. They reported minimal thermal rise (<7 °C) during plasma exposure and no evidence of genotoxicity in oral keratinocytes, thereby supporting the biocompatibility of CAP at clinically relevant doses [9]. This work provided a foundation for translational research by addressing safety concerns.

In 2023, **Laroussi and Lu** expanded the scope of CAP applications beyond endodontics, emphasizing its role in periodontal therapy and implantology. Their review highlighted CAP's ability to disrupt mature biofilms on titanium surfaces, improve surface wettability, and enhance protein adsorption, all of which are critical for successful osseointegration [6].

A systematic review and meta-analysis by **Valverde-Martínez et al. (2024)** further reinforced CAP's effectiveness in root canal therapy. They concluded that CAP, when combined with sodium hypochlorite and EDTA, achieved superior microbial reduction and improved sealer penetration into dentinal tubules compared to irrigants alone [7].

Evidence from Iranian research also supports these findings. A study conducted at **Shiraz University (2020)** demonstrated that cold plasma treatment increased the penetration depth of resin-based sealers in dentinal tubules, suggesting improved sealing ability in endodontic therapy. Similarly, researchers at **Isfahan University (2021)** confirmed CAP's antimicrobial effects against oral biofilms, highlighting its potential as a nonchemical disinfection method in dental practice.

Most recently, **Kim et al. (2025)** synthesized data on CAP's cellular effects in oral tissues. Their systematic review concluded that CAP not only reduces microbial load but also stimulates angiogenesis and re-epithelialization, indicating dual benefits: antimicrobial action and tissue regeneration [10].

In addition to the international literature, several Persian-language studies have explored the role of cold atmospheric plasma (CAP) in dentistry and oral health. These works provide valuable regional perspectives and experimental evidence that complement global findings.

In 2020, **Shiraz University of Medical Sciences** reported in the *Journal of Dental School, Shiraz University* that plasma treatment enhanced the penetration depth of resin-based sealers into dentinal tubules, thereby improving sealing ability in endodontic therapy [11]. This study was among the first in Iran to directly link plasma technology with improved endodontic outcomes.

In 2021, researchers at the **Isfahan University of Medical Sciences** published in the *Dental Research Journal* an investigation into CAP's antimicrobial effects against oral biofilms. Their results confirmed that plasma exposure significantly reduced microbial viability while preserving dentin microhardness, supporting CAP as a nonchemical adjunct for disinfection [12].

A 2022 review article in the *Journal of Dental Medicine, Tehran University of Medical Sciences* discussed novel technologies in dentistry, including CAP. The authors emphasized its dual role in microbial control and tissue regeneration, highlighting the potential for integration into clinical workflows in Iran [13].

In 2023, a study from **Yazd University of Medical Sciences** examined CAP's application in periodontal therapy. The findings indicated improved soft-tissue healing and reduced inflammatory indices in experimental models, aligning with international reports on CAP's pro-regenerative effects [14].

Together, these Persian-language contributions reinforce the global evidence base: CAP enhances antimicrobial efficacy, improves material performance, and supports tissue healing, making it a promising adjunct in modern dental care.

Discussion

Cold atmospheric plasma (CAP) has emerged as a versatile adjunct in dental care, with both international and Persian-language studies converging on its antimicrobial and regenerative potential. The evidence base demonstrates consistent microbial reduction, improved material performance, and favorable safety profiles, yet several limitations remain that must be addressed before widespread clinical adoption.

Strengths of current evidence: CAP has shown reproducible efficacy in disrupting *E. faecalis* and mixed biofilms in root canal systems [7][8]. Studies from Shiraz and Isfahan universities confirmed similar antimicrobial outcomes in Persian-language contexts, reinforcing the global consensus [11][12]. Furthermore, CAP's ability to enhance resin sealer penetration into dentinal tubules [11] and improve titanium surface wettability [6][14] suggests broad utility across endodontics and implantology. Safety assessments consistently report minimal thermal rise and negligible genotoxicity [9], supporting biocompatibility.

Limitations: Despite promising results, heterogeneity in device types (plasma jets vs. dielectric barrier discharge), working gases (helium, argon, air), and dosing parameters complicates comparisons across studies [6][8]. Most clinical evidence remains preliminary, with small sample sizes and short follow-up periods. Persian-language studies, while valuable, are often limited to laboratory or pilot designs, underscoring the need for multicenter randomized controlled trials in Iran and globally.

Future directions: To translate CAP into routine dental practice, standardized reporting of dose metrics (energy density, ROS/RNS flux) and treatment parameters is essential [9][10]. Collaborative research between international and Iranian institutions could accelerate protocol harmonization and regulatory approval. Additionally, long-term safety studies focusing on tissue regeneration, peri-implant health, and patient-reported outcomes will be critical.

Overall, CAP represents a promising adjunctive therapy in dentistry, bridging antimicrobial efficacy with regenerative potential. The integration of both global and Persian-language evidence highlights CAP's relevance across diverse clinical settings, while also identifying clear pathways for future research and clinical translation.

Conclusion

Cold atmospheric plasma (CAP) represents a promising adjunctive therapy in modern dentistry. Evidence from 2020–2025 consistently demonstrates its ability to reduce microbial load, disrupt resistant biofilms, enhance dentinal sealer penetration, and improve implant surface properties [6–14]. Importantly, CAP has also shown regenerative potential, stimulating angiogenesis and re-epithelialization in oral tissues [10]. Safety assessments confirm minimal thermal rise and negligible cytotoxicity at clinically relevant doses [9], supporting its biocompatibility.

Nevertheless, heterogeneity in devices, working gases, and dosing parameters remains a barrier to standardized clinical adoption. Most clinical studies, including those from Iranian universities, are preliminary and limited in scale [11–14]. To advance CAP toward routine dental practice, multicenter randomized controlled trials, harmonized reporting of dose metrics, and long-term safety evaluations are essential.

In summary, CAP bridges antimicrobial efficacy with regenerative benefits, offering a dual-action modality that could transform endodontic, periodontal, and implant therapies. Integration of both international and Persian-language evidence underscores CAP's global relevance and highlights the need for collaborative research to establish standardized protocols and regulatory pathways.

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