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ADJUNCTIVE ANTIOXIDANT AND HOST-MODULATING STRATEGIES IN THE NON-SURGICAL TREATMENT OF PERIODONTITIS IN WORKERS OCCUPATIONALLY EXPOSED TO STYRENE: A NARRATIVE REVIEW AND PROPOSED TREATMENT ALGORITHM

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Abstract:

Background. Workers employed in the production and processing of polystyrene and other styrene-based polymers are chronically exposed to styrene vapour. Styrene exposure causes systemic oxidative stress, which is also a central mechanism of periodontal tissue destruction. Standard non-surgical periodontal therapy may therefore yield a less predictable response in this population.

Aim. To review the evidence on adjunctive therapies that target oxidative stress and the host inflammatory response, and to propose a stepwise treatment algorithm for periodontitis in styrene-exposed workers.

Methods. A narrative review of PubMed/MEDLINE, Google Scholar and eLIBRARY.ru was performed, focusing on (i) oxidative and inflammatory effects of occupational styrene exposure, (ii) systematic reviews underpinning the European Federation of Periodontology (EFP) S3 guideline, and (iii) trials of antioxidant supplementation in periodontitis and in styrene-exposed workers.

Results. Styrene-exposed workers show higher serum malondialdehyde, depleted reduced glutathione and lower plasma antioxidant capacity than unexposed controls. Antioxidant supplementation lowered malondialdehyde in styrene-exposed workers, and adjunctive antioxidants have been associated with improved oxidative and, less consistently, clinical periodontal outcomes. Evidence for most systemic host modulators remains insufficient for routine use, whereas locally delivered antimicrobials provide modest additional benefit.

Conclusions. Occupational styrene exposure should be recorded as a periodontal risk modifier. A four-step algorithm is proposed that combines guideline-based mechanical therapy with exposure assessment, workplace risk control, targeted antioxidant support and shortened supportive care intervals. Randomised trials with periodontal endpoints are needed.

Keywords: periodontitis; styrene; polystyrene; occupational exposure; oxidative stress; antioxidants; host modulation; non-surgical periodontal therapy.

Introduction

Periodontitis is a chronic, multifactorial inflammatory disease associated with dysbiotic dental biofilm and characterised by progressive destruction of the tooth-supporting apparatus. Severe periodontitis affects roughly one in nine adults worldwide and ranks among the most prevalent chronic conditions of humankind [1]. Since the 2017 World Workshop, periodontitis has

been classified by stage, reflecting severity and complexity, and by grade, reflecting the rate of progression and the influence of risk factors such as smoking and diabetes mellitus [2, 3].

The 2020 EFP S3 clinical practice guideline set out a stepwise approach to treating stage I–III periodontitis: risk-factor control and supragingival biofilm management, subgingival instrumentation with or without adjuncts, surgical therapy where indicated, and lifelong supportive periodontal care [4]. The guideline emphasises that the response to therapy depends on patient-level risk factors. Occupational chemical exposures, however, are not explicitly addressed in it, and practical recommendations for industrial workers remain scarce.

Styrene (vinylbenzene) is a high-production-volume monomer used chiefly to manufacture polystyrene, acrylonitrile-butadiene-styrene (ABS) plastics, styrene-butadiene rubbers and unsaturated polyester resins. In 2019 the International Agency for Research on Cancer classified styrene and its principal metabolite, styrene-7,8-oxide, as probably carcinogenic to humans (Group 2A) [5]. Workers are exposed mainly by inhaling vapour released during monomer synthesis, polymerisation and thermal processing of polymers such as extrusion, injection moulding and foaming.

Evidence is accumulating that the oral cavity of chemical-industry workers is affected. A clinical-hygienic survey of 878 operators in isoprene, divinyl, styrene and ethylene oxide production documented frequent periodontal pathology and a high prevalence of *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* in periodontal pockets [6]. In parallel, studies of styrene-exposed workers have repeatedly demonstrated systemic oxidative stress [7, 8], a process that also lies at the core of periodontal tissue destruction [9, 10].

This convergence raises a practical clinical question: should periodontitis in styrene-exposed workers be managed exactly as in the general population, or do these patients benefit from adjunctive strategies that target oxidative stress and the host response? The present review addresses this question and proposes a treatment algorithm adapted to this occupational group. It is part of a broader research programme on improving the treatment of periodontal diseases in workers exposed to styrene polymers.

Methods

A narrative review was conducted. PubMed/MEDLINE, Google Scholar and eLIBRARY.ru were searched for English- and Russian-language publications using combinations of the terms *styrene*, *polystyrene*, *occupational exposure*, *chemical industry*, *oral health*, *periodontitis*, *oxidative stress*, *glutathione*, *malondialdehyde*, *antioxidant*, *host modulation*, *adjunctive therapy* and *non-surgical periodontal therapy*. Reference lists of relevant articles were hand-searched.

Three bodies of evidence were considered: (i) human and experimental studies on the oxidative and inflammatory effects of styrene; (ii) the systematic reviews that informed the EFP S3 guideline on adjunctive therapies to subgingival instrumentation; and (iii) clinical studies of antioxidant supplementation in periodontitis and in styrene-exposed workers. Priority was given to systematic reviews, randomised controlled trials and controlled clinical studies.

Because no randomised trial has specifically evaluated periodontal therapy in styrene-exposed workers, the conclusions regarding this group are necessarily inferential. Statements that extrapolate from general periodontal evidence or from non-oral toxicological findings are identified as such in the text.

Rationale: why styrene exposure may impair the response to standard therapy

A "two-hit" oxidative burden

In the liver and lungs styrene is oxidised by cytochrome P450 isoenzymes (mainly CYP2E1 at low and CYP2B6 at high concentrations) to styrene-7,8-oxide, a reactive electrophilic epoxide [5, 7]. Part of the epoxide is detoxified by conjugation with reduced glutathione (GSH). Styrene and styrene oxide markedly deplete GSH while having little effect on glutathione reductase and glutathione peroxidase activity [13].

The consequences are measurable in exposed workers. In 34 plastic-factory workers exposed to styrene for at least eight hours a day for more than a year, serum malondialdehyde (MDA) was 5.37 ± 1.14 nmol/mL versus 2.46 ± 0.68 nmol/mL in matched controls. Blood GSH was 128 ± 10.8 versus 232 ± 24.3 µmol/dL, and the ferric-reducing ability of plasma (FRAP) was less than half the control value (all $p < 0.001$) [7]. In shipbuilding workers, urinary styrene metabolites (mandelic and phenylglyoxylic acids) were accompanied by elevated urinary markers of nucleic-acid oxidation [8].

Periodontitis itself is increasingly regarded as an inflammatory disease of oxidative stress. Activated neutrophils in the periodontal pocket release large amounts of reactive oxygen species, while the antioxidant capacity of saliva and gingival crevicular fluid is reduced in patients with periodontitis [9, 10]. We therefore propose a "two-hit" model. The first hit is the exogenous oxidative load derived from styrene metabolism; the second is the endogenous load generated by the periodontal inflammatory response. With the GSH buffer depleted, periodontal tissues may be less able to resolve inflammation after the biofilm has been disrupted by instrumentation.

Amplified inflammatory signalling

In human airway epithelial cells styrene induces pro-inflammatory mediator release through oxidative stress and activation of nuclear factor-κB (NF-κB), and the response is attenuated by the antioxidant N-acetylcysteine [12]. Gingival epithelium shares the same innate immune pathways. It is plausible, though not yet demonstrated, that a comparable mechanism amplifies cytokine production (interleukin-1β, tumour necrosis factor-α, interleukin-6) and shifts the RANKL/osteoprotegerin balance towards bone resorption in exposed workers.

Dysbiosis and host susceptibility

Chemical-industry operators harbour a high prevalence of keystone and highly virulent periodontal pathogens, notably *P. gingivalis* and *A. actinomycetemcomitans* [6]. Because progression of periodontitis depends largely on a dysregulated host response to a dysbiotic biofilm [11], any toxicant-related impairment of host defence may favour persistence of these species after therapy. In the same cohort, styrene-production workers also showed a high occupational attribution of chronic cholecystitis (RR 2.16) and biliary dyskinesia (RR 2.53) [6]. This hepatobiliary burden may further compromise detoxification capacity.

Clinical analogy with smoking

Smoking is the best-documented environmental modifier of periodontal treatment outcome and is formally incorporated into the grading of periodontitis [3]. Like styrene, tobacco smoke delivers a heavy oxidant load and impairs neutrophil function. By analogy, chronic styrene exposure can reasonably be treated as a candidate grade modifier. Until direct evidence becomes available, clinicians should anticipate a less predictable healing response and plan treatment accordingly.

Adjunctive approaches: what the evidence shows

Antioxidant supplementation

The most directly relevant study was conducted in styrene-exposed workers themselves. Thirty exposed workers received a 30-day course of a combined antioxidant preparation containing vitamin C, vitamin E, selenium, troxerutin and β-carotene. Before supplementation they had significantly higher MDA than unexposed controls; after supplementation MDA fell markedly ($p < 0.001$) and total antioxidant capacity rose further ($p < 0.001$) [14]. Periodontal parameters were not assessed, yet the study shows that the oxidative imbalance induced by styrene is pharmacologically modifiable.

In the general periodontal population, a systematic review of antioxidant agents used as adjuncts to periodontal therapy found improvements in oxidative stress markers. Improvements in clinical parameters such as probing depth and clinical attachment level were reported less consistently, and the included studies were heterogeneous in agents, doses and duration [15]. N-acetylcysteine merits particular attention as a GSH precursor, since it attenuated styrene-induced inflammatory signalling in epithelial cells [12]. Clinical periodontal data on it remain limited. A diet rich in fruits and vegetables, providing vitamin C and polyphenols, is a low-risk measure that can be recommended to all exposed patients.

Systemic host-modulating agents

A systematic review prepared for the EFP guideline evaluated sub-antimicrobial-dose doxycycline, non-steroidal anti-inflammatory drugs, omega-3 polyunsaturated fatty acids, statins, bisphosphonates, metformin and probiotics as adjuncts to subgingival instrumentation [16]. Several agents produced statistically significant but clinically modest gains. The guideline did not recommend their routine use, citing limited or heterogeneous evidence, adverse-effect concerns or lack of availability [4]. For styrene-exposed workers, any systemic agent must also be weighed against the possibility of reduced hepatic reserve.

Local antimicrobials and antiseptics

Locally delivered antimicrobials, including sustained-release chlorhexidine and tetracycline-class gels, provide a small additional reduction in probing pocket depth compared with instrumentation alone [17]. The EFP guideline allows sustained-release chlorhexidine to be considered as an adjunct and antiseptic mouthrinses to be used in specific cases [4]. These agents are a reasonable option for residual deep pockets in exposed workers because they act locally and add no systemic metabolic burden.

Systemic antibiotics

Adjunctive systemic antibiotics, particularly amoxicillin combined with metronidazole, improve clinical outcomes [18]. Concerns about antimicrobial resistance and adverse effects have, however, led to recommendations restricting their use to specific patient categories, such as young adults with generalised stage III periodontitis [4]. The high prevalence of *A. actinomycetemcomitans* reported in chemical-industry workers [6] may justify microbiological testing before considering them, but they should not be prescribed routinely on the basis of occupational exposure alone.

Lasers and antimicrobial photodynamic therapy

Evidence that adjunctive lasers or antimicrobial photodynamic therapy improve outcomes over instrumentation alone is limited and inconsistent [19], and the EFP guideline does not suggest their use [4]. There is no specific rationale for them in styrene-exposed workers.

Reducing the exposure itself

The most fundamental adjunct is reduction of the toxicant load. Engineering controls such as local exhaust ventilation and enclosed processes, appropriate respiratory protection, and regular

biological monitoring of urinary mandelic and phenylglyoxylic acids are measures for the occupational physician. They nevertheless directly influence the periodontal prognosis and should be part of the dental treatment plan.

Table 1. Summary of adjunctive options for periodontitis in styrene-exposed workers

Adjunct	Evidence in general population	Specific relevance to styrene exposure	Suggested role
Antioxidants (vitamins C, E, selenium, NAC, dietary)	Improves oxidative markers; clinical effect inconsistent [15]	Lowered MDA in exposed workers [14]; NAC blocks styrene-induced NF-κB signalling in vitro [12]	Recommended as supportive measure; priority for trials
Systemic host modulators	Modest gains; not recommended routinely [4, 16]	Hepatic reserve may be reduced [6]	Not routine; research setting
Local antimicrobials / CHX chip	Small additional pocket reduction [17]	No systemic burden	Consider for residual pockets
Systemic antibiotics	Effective, stewardship limits [4, 18]	High *A. actinomycetemcomitans* prevalence [6]	Only in specific cases after microbiological testing
Lasers / aPDT	Insufficient evidence [19]	None	Not suggested
Exposure reduction	—	Removes the cause of oxidative load [5, 7]	Essential, with occupational physician

Proposed treatment algorithm and discussion

On the basis of the evidence reviewed, we propose that the EFP stepwise approach [4] be retained as the backbone of therapy and supplemented with exposure-specific elements (Table 2). The algorithm keeps evidence-based mechanical therapy unchanged. It adds measures that are either low-risk (dietary and supplemental antioxidants, closer monitoring) or outside the dental chair (exposure reduction).

Table 2. Stepwise periodontal treatment adapted for workers exposed to styrene

Step	Standard approach (EFP S3)	Adaptation for styrene-exposed workers
0. Assessment	Periodontal charting, radiographs, staging and grading	Occupational history: job title, years of exposure, workplace conditions class; liaison with occupational physician for urinary mandelic + phenylglyoxylic acids; optional salivary MDA and total antioxidant capacity; record exposure as a

Step	Standard approach (EFP S3)	Adaptation for styrene-exposed workers
		candidate grade modifier
1. Cause-related therapy	Oral hygiene instruction, risk-factor control (smoking, diabetes), supragingival professional plaque removal	Add counselling on respiratory protection and workplace hygiene; dietary advice rich in vitamin C and polyphenols; start antioxidant supplementation where not contraindicated
2.Subgingival instrumentation	Root surface debridement, with or without adjuncts	Instrumentation unchanged; prefer local adjuncts (sustained-release chlorhexidine) for deep sites; systemic antibiotics only after microbiological testing in specific cases
3. Re-evaluation and surgery	Re-evaluate at 6–8 weeks; surgery for residual pockets ≥ 6 mm	Re-evaluate oxidative markers together with clinical parameters; consider a second antioxidant course if response is poor
4. Supportive care	Recall every 3–12 months according to risk	Default 3-month recall while exposure continues; repeat assessment after any change in job or exposure level

This approach is consistent with earlier Russian experience in petrochemical workers. There, treatment and prevention programmes were designed with reference to local oral immunity and free-radical oxidation in oral fluid, rather than to clinical indices alone [20]. It also follows the broader principle that periodontal treatment should be personalised according to modifiable risk factors [3, 4].

Several limitations must be acknowledged. First, no study has yet measured periodontal outcomes after any intervention in workers exposed specifically to styrene. Second, the antioxidant study in exposed workers was small, lacked a placebo group and assessed only systemic biomarkers [14]. Third, exposure to styrene in industry rarely occurs in isolation: ethylbenzene, benzene, toluene, pentane and dust frequently co-exist, so the effects attributed to styrene may partly reflect mixed exposures. Fourth, the proposed mechanisms in gingival tissue, particularly NF-κB activation, are extrapolated from airway epithelium [12].

These gaps define a clear research agenda. A randomised, placebo-controlled trial comparing subgingival instrumentation with and without antioxidant supplementation in polystyrene-production workers is needed. It should use exposure quantified by urinary metabolites as a stratification variable, and take probing depth, clinical attachment level, bleeding on probing and salivary oxidative markers as outcomes. Such a trial is feasible within occupational health surveillance programmes and would directly inform clinical guidance.

Conclusions

1. Occupational exposure to styrene produces measurable systemic oxidative stress, with elevated malondialdehyde, depleted glutathione and reduced plasma antioxidant capacity. These changes overlap mechanistically with the oxidative pathways of periodontal tissue destruction.
2. Styrene exposure should be documented in the periodontal assessment and considered a candidate grade modifier, by analogy with smoking.
3. Guideline-based mechanical therapy remains the foundation of treatment. Antioxidant support, locally delivered adjuncts for residual pockets, exposure reduction and a default three-month supportive care interval are rational, low-risk additions for this population.
4. Routine use of systemic host modulators, systemic antibiotics, lasers or photodynamic therapy is not justified by occupational exposure alone.
5. Randomised controlled trials with periodontal endpoints in styrene-exposed workers are required to validate the proposed algorithm.

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