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Nasal Irrigation, Polyols, Nitrate Reducing Bacteria and Cardiovascular Disease

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Introduction

Nasal irrigation is a conventional but effective treatment modality against allergic rhinopathy. Its use started to expand during the early 1900s [1,2]. The technique involves rinsing the nasal cavity with saline solution (saltwater) delivered as liquid or spray. It can be performed with a squirt or spray bottle that creates low pressure saline flow or with a container that creates gravity-based pressure such as a device with a nasal spout (e.g., neti pot) [3]. Through removing contaminants, allergens (e.g., pollen) and excessive mucus that impedes ciliary function [4], nasal irrigation enhances mucociliary function [5,6] and improves coughing secondary to postnasal drip [7,8]. Reduced histamine and leukotriene C4 levels have also been observed in patients with allergic rhinitis who use sinus irrigation [4]. Regarding clinical outcomes, patients who were treated with sinus irrigation relied less on medication and made fewer doctor visits [4,7,9]. Studies performed by Chirico et al. [8] showed nasal irrigation improved symptoms, reduced the need for medications such as antihistamines, antibiotics, corticosteroids, and decongestants in pediatric patients suffering from acute sinusitis and allergic rhinitis. In patients with acute upper respiratory tract infection, a systematic review published in 2015 suggested that nasal saline irrigation has possible benefits for symptoms relief [10]. In terms of chronic rhinosinusitis (CRS), a systematic review published in Cochrane library included 2 randomized controlled trials (RCT) [11]. The article suggested there is some benefit in the use of daily large-volume (150 ml) saline irrigation with a hypertonic solution when compared with placebo, but the quality of the evidence is low for the three months as well as for the six months of treatment.

Nitrate reducing bacteria are now considered important commensals that are essential for host homeostasis. Indeed, nitrate reducing bacteria have a crucial role in reducing nitrates to nitrites, which are then further processed into nitric oxide after exposure to stomach acid. The absorbed nitric oxide is then concentrated by a factor of 10 in the host's saliva, and is considered instrumental in the host's oral defense [12]. Nitrate reducing commensals limit growth of cariogenic bacteria. Levels of salivary nitrate and the presence of nitrate reductase, associated with the commensals, have been correlated with caries resistance possibly due to the anti-microbial properties of nitric oxide [13]. Another important protective function of the nitrate reducing bacteria is the regulation of host blood pressure. Nitric oxide is a vasodilator and, according to a small number of studies, significantly moderates blood pressure in the host. Studies with anti-microbial mouthwashes have demonstrated that the loss of nitrate reducers significantly increase the host blood pressure [14,15]. Other benefits ascribed to the nitrate reducing bacteria include; protection against ischemia reperfusion damage, restoration of NO homeostasis with associated cardio protection, increased vascular regeneration after chronic ischemia, and a reversal of vascular dysfunction in the elderly [16]. Another role for the nitrate reducing bacteria would be the added benefit of increasing the host's capability for vasodilation, particularly important for the male of the species and possibly for the prevention of erectile dysfunction.

Nasal Membranes Respond to Increased Levels of NO

Of interest to microbiome researchers is the multiple roles that many commensal bacteria perform for the host, for example, *Rothia dentocariosa* is both a gluten metabolizer and a nitrate reducer [12]. *Rothia dentocariosa* is also maternally imprinted, present both in the placental and in the fetal microbiome. One would suspect that evolution tends to favor efficient mechanisms! *Rothia dentocariosa* is not particularly sensitive to polyols, such as xylitol and erythritol, making polyol solutions more desirable in nasal irrigation procedures.

Sinus Irrigation with Xylitol Saline Solution

Xylitol is a five-carbon sugar alcohol that when combined with saline solution, moisturizes the sinus cavity and boosts endogenous antibacterial activity [17]. It is proposed that xylitol acts upon the airway surface liquid (ASL), which is a thin layer of liquid that covers the airways and contains several antimicrobial agents such as secretory leukoproteinase inhibitor, lactoferrin, lysozyme, cathelicidin LL-37, secretory phospholipase A2, and human β defensins 1 and 2 [17]. Elevated levels of contaminants can disrupt ASL by increasing salt concentration, Xylitol has been shown to lower the ASL salt concentration therefore restores the activity of the endogenous antimicrobials on the airway surface [17]. Xylitol

solution is a nontoxic, hypertonic substance and has been safely administered in aerosolized, intravenous, and intranasal forms [17,18]. Intranasal administration xylitol significantly decreases the number of nasal coagulase-negative Staphylococcus and enhanced killing of *Pseudomonas aeruginosa* [17]. Furthermore, xylitol is poorly metabolized by bacteria and subsequently has anti-adhesive effects on bacteria [17,19]. Finally, the hypertonic nature of xylitol saline solution promotes the removal of moisture from swollen tissues, thereby reducing inflammation and congestion. Weisman [19] revealed significant reduction in symptoms (p=0.043), assessed by Sino-Nasal Outcome Test 20 scores, in the xylitol irrigation group compared to the saline irrigation group.

Conclusion

Sinus irrigation with saline removes contaminants and restores natural ciliary function. It reduces symptoms, improves patient satisfaction and can potentially decrease the need of pharmacologic therapy. Sinus irrigation with xylitol potentially offers additional benefit in modulating airway surface level, creating anti-adhesive environment and enhancing endogenous antimicrobial activity. In comparison to anti-histamine agents and intranasal corticosteroid, sinus irrigation is a safe approach with minimal adverse effect. Based on reported low quality RCTs, nasal irrigation likely provides symptoms relief in patients with acute sinusitis [8,10]. Further studies, preferably incorporating larger sample sizes and long-term follow up, are needed to compare different modality of nasal irrigation (low volume vs large volume, with or without xylitol) and establish their role in the setting of chronic rhinosinusitis and oronasal commensals.

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