Zinc lozenges and vitamin C for high-performance athletes

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In their International Olympic Committee consensus statement, Maughan et al. reviewed the evidence for dietary supplements for high-performance athletes [1].

They wrote in regard to zinc that “Cochrane review shows benefit of [using] zinc acetate lozenges (75 mg) to decrease duration of URS [upper respiratory symptoms]” [1, Table 4]. This statement was based on their reading of the Cochrane review (2013) by Singh and Das [2], which was withdrawn in 2015 because of plagiarism [3]. In addition, the same Cochrane review had a large number of other severe problems [4]. In the above statement, Maughan et al. imply that only zinc acetate lozenges are effective; however, a recent meta-analysis showed that, up until 2017 at least, there was no evidence that zinc gluconate lozenges are less effective than zinc acetate lozenges [5].

When discussing treatment effects, the size of the effect and its confidence interval should be considered [6]. Thereby a critically-minded reader can form his or her own opinion about whether the treatment effect is relevant. The data of 7 placebo-controlled double-blind RCTs showed that zinc acetate and zinc gluconate lozenges shortened common cold duration on average by 33% (95% CI 21% to 45%) [5]. Individual-patient data were available for 3 zinc acetate lozenge trials and on the basis of these findings, zinc lozenges shortened the duration of colds by 2.7 days (95% CI 1.8 to 3.3 days) [7], and increased the rate of recovery by RR = 3.1 (95% CI 2.1 to 4.7) [8]. So far, there is no published evidence to assume that the effects of zinc lozenges are less in athletes compared with the general population.

Maugham et al. wrote that many published studies had low quality, “specifically, small samples, poor controls and unclear procedures for randomization and blinding were commonplace” [1, p. 443]. To support this statement, they cited the above-mentioned Cochrane review [2] that was withdrawn in 2015 [3]. However, that Cochrane review [2] did not point out any relevant methodological problems in the 7 placebo-controlled double-blind zinc lozenge RCTs mentioned above in which colds were shortened by 33% [5].

Furthermore, Maugham et al. did not mention at all the effect of vitamin C on exercise-induced bronchoconstriction [EIB]. Three double-blind placebo-controlled cross-over RCTs found that vitamin C decreased exercise-induced FEV1 decline by 48% (95% CI 33% to 64%) [9,10]. Only some athletes
suffer from EIB, yet for them it may be worthwhile to test on an individual basis whether vitamin C has efficacy.

In our Cochrane review, we pooled 5 placebo-controlled double-blind RCTs on marathon runners, skiers and soldiers on subarctic exercises, and found that vitamin C reduced the risk of colds by 52% (95% CI 36% to 65%) [11]. Maugham et al. opined that there is only “moderate support for preventing URS”. Given that the 5 RCTs conducted by 4 different research groups over 3 different decades found highly consistent results with I-square = 0% [11], it is quite puzzling as to what kind of evidence Maugham et al. would require to conclude strong support over and above any moderate support. Evidently, more research is needed. However, vitamin C is a cheap and safe essential nutrient, thus those athletes who often have upper respiratory symptoms associated with exercise may test whether the vitamin might be beneficial for them personally.

Maugham et al. further wrote that for vitamin C, “immune measures [are] no different from placebo” [1, Table 4]. This statement is misleading for readers. A search of the PubMed for reviews on vitamin C and immunity identifies dozens of reports. Reviews have shown that there is a large number of studies indicating that vitamin C does have effects on the immune system, three of which I cite here [12-14]. The published effects on the immune system do not indicate whether vitamin C has practical relevance, but it is misleading to claim that the effects of vitamin C on immune measures are no different from placebo [1].

Finally, Maugham et al. wrote that “Cochrane reviews show no benefit of initiating vitamin C supplementation (>200 mg/day) after onset of URS” and they cited refs 100,101 in their review [1, Table 4]. First, Maugham’s reference 101 is not a Cochrane review. Second, absence of evidence is not evidence of absence [15].

In our Cochrane review (ref. 100 in Maugham’s paper), we wrote that from a methodological perspective, therapeutic trials are much more complicated than regular supplementation trials [11]. We gave examples of factors that may influence the efficacy of vitamin C, such as the timing of supplementation initiation, the duration of supplementation, and the dosage. Inappropriate selection of any of these factors might give rise to false negative findings in a therapeutic trial. We should therefore be cautious in the interpretation of the published therapeutic trials. Furthermore, we pointed out that “The larger effect observed using 8 g [of vitamin C] compared with 4 g as a single dose in the Anderson 1974f trial and the dose dependency in the Karlowski 1975a trial suggest that future therapeutic trials with adults should use doses of at least 8 g/day” [11]; see also [16].

It thus misleads readers to claim that our Cochrane review (ref. 100 in Maugham’s paper) “show[s] no benefit of initiating vitamin C supplementation after [the] onset of URS” [1]. In contrast, we conclude in our abstract that “given the consistent effect of vitamin C on the duration and severity of colds in the regular supplementation studies, and the low cost and safety, it may be worthwhile for common cold patients to test on an individual basis whether therapeutic vitamin C is beneficial for them. Further therapeutic RCTs are warranted” [11].
References

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