JEPonline

Journal of Exercise Physiology online

ISSN 1097-9751

An International Electronic
Journal for Exercise Physiologists

Vol 1 No 2 July 1998

Nutrition and Exercise

Vitamin C supplementation and upper respiratory tract infections in marathon runners

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Himmelstein, S. A. , Robergs, R. A., Koehler, K. M., Lewis, S. L., & Qualls, C. R. Vitamin C supplementation and upper respiratory tract infections in marathon runners. JEPonline

Vol. 1, No. 2, 1998. This study was funded in part by a grant from the University of New Mexico Clinical Research Center: MO1-RR-00997 1994, and from the University of New Mexico, College of Education, 1994 Graduate Research, Project and Travel Grant. ABSTRACT The purpose of this study was to determine whether vitamin C supplementation reduces the incidence of upper respiratory tract infections (URTIs), and attempt to explain the variability in URTIs among marathon runners and sedentary subjects. Marathon runners (n=44) and sedentary subjects (n=48) were randomly assigned either 1,000 mg vitamin C or a placebo daily for two months prior to and one month following a marathon race. Baseline (pre-supplementation) plasma vitamin C concentrations were higher among the vitamin C treated runners (VR, n=30) and placebo treated runners (PR, n=14) (78.5 ±2.7 and 84.0 ±3.6 mmol/L, respectively) compared to vitamin C treated sedentary (VS, n=23) and placebo treated sedentary (PS, n=25) subjects (61.1±4.7 and 52.8 ±5.0 mmol/L, respectively). Vitamin C concentrations increased with supplementation (81.0±2.1 mmol/L for VR and 72.6 ±2.9 mmol/L for VS). No treatment differences were found for URTI incidence (33.3%, 42.9%, 43.5%, and 32.0% among VR, PR, VS, and PS, respectively). Multiple logistic regression revealed the following factors to be significantly related to an increased risk of URTIs: (1) faster training pace, (2) greater number of marathons run, (3) shorter distance for the longest run of the week, and (4) female gender. The data indicate that vitamin C supplementation of 1,000 mg/day did not decrease the incidence of URTIs in marathon runners. Training and gender were more influential than vitamin C supplementation in explaining the incidence of URTIs.

Key Words:COLD, ASCORBIC ACID, RUNNING, GENDER, TRAINING

Introduction

Exercise is accompanied by hormonal and immunological changes that are associated with psychological stress. Psychological stress has been associated with an increase in susceptibility to the common cold (1,2). Similarly, prolonged exercise results in an increased risk of upper respiratory tract infections (URTIs) (3-5). High intensity, long endurance exercise such as marathon running has been shown to suppress immune function (6). In

particular, the incidence of URTIs has been shown to be dramatically increased among marathon and ultramarathon runners prior to and following competition (4,5,7).

Currently, it is unclear what mechanism is responsible for an increased risk of URTIs following heavy training and competition. Endurance exercise results in a transient decrease in natural killer cell activity which has been suggested as a potential mechanism for the increased susceptibility to URTIs during the post-exercise period (6). Other potential mechanisms offer somewhat less satisfactory explanations and less research evidence, such as findings of reduced salivary immunoglobulin A levels in athletes (8) or decreased serum interferon levels (9).

Many athletes and non-athletes alike take vitamin C supplements in an attempt to ward off the common cold. In general, studies of vitamin C supplementation by athletes and non-athletes have shown mixed results, with little or no decrease in incidence of URTIs (10-14), a decreased incidence of URTIs (7), and a relatively small reduction in the duration of a cold (10-12,14,15).

Peters et al. (7) presented the most convincing evidence for vitamin C supplementation to decrease the incidence of URTIs. These authors presented data that indicated that vitamin C supplementation of 600 mg decreased the incidence of URTIs in ultrarunners by 50%. However, several faults were inherent in the design of this study. Incidence of URTIs was based on telephone interview without clinical substantiation, a moderate supplementation of 600 mg/day of vitamin C was used without control of self-supplementation, only two female subjects completed the study, and the high incidence of URTIs in the sedentary subjects was not explained.

The conflicting research on vitamin supplementation and the incidence of URTIs, combined with the many flaws evident in past research, indicated to us that additional research was needed on whether vitamin C supplementation influenced the incidence and duration of URTIs. Therefore, the intent of the present study was to determine the effects of vitamin C supplementation on the incidence of URTIs in marathon runners. A secondary purpose of this study was to identify factors, other than vitamin C supplementation or plasma vitamin C concentrations, that are associated with increased risk of URTIs.

Methods

Subjects

The participants were recruited from all registered participants in the Duke City Marathon (Albuquerque, NM, elevation = 5,000 ft above sea level), which was held on September 11, 1994. An age and gender-matched sedentary group was obtained by including friends and coworkers of the marathon runners whenever possible. Sedentary subjects did not regularly participate in any aerobic exercise, as determined by interview.

Initially, 104 potential marathon runners and 87 sedentary subjects agreed to participate. Of these, 137 read and signed an informed consent approved by the University Medical School Human Subjects Review Committee prior to enrollment in the study. The subjects were randomly assigned into either the vitamin C or the placebo treatment (n = 52 for both VR and PR, n = 42 for VS and n = 45 for PS). Of the 137 subjects who consented to participate, only 92 subjects completed the study (VR = 30, PR = 14, VS = 23, PS = 25). Reasons for drop out included injury, relocation, side-effects to supplementation, time constraints, and poor compliance with supplementation as determined from a pill count performed at the end of the study.

Research Design
A double-blind, placebo-controlled design was used to determine the influence of vitamin C supplementation on the incidence of URTIs among marathon runners and sedentary subjects during the two months prior to and one month following the marathon. Data collected during the study included demographic and training history data, vitamin C intake, a training and URTI symptom log, plasma vitamin C concentrations, and lymphocyte proliferation.

Data were collected at baseline (BL) which corresponded to two months prior to the marathon, one week prior to the marathon (PRE), and at two days (POST1) and 1 month (POST2) after the marathon. Randomization of subjects to the vitamin C (VC) and placebo (PL) groups was conducted at BL.

Questionnaires
Questionnaires were distributed to the subjects by a combination of mail delivery or in person at BL.

Vitamin C Intake
Usual dietary intake was determined at BL using the Health Habits and History Questionnaire: Diet History and Other Risk Factors Dietary Analysis System (HHHQ-DIETSYS Analysis Software, Version 3.0, National Cancer Institute, 1993). Completed questionnaires were computer scored by Survey & Ballot Systems, Inc. (Eden Prairie, MN). The dietary questionnaire was modified to include foods commonly eaten in the Southwest that are high in vitamin C (16-18). Any vitamin C supplement use was also recorded.

Subjects were restricted to no more that 200 mg/day vitamin C self-supplementation during the study period. However, vitamin C supplementation was not controlled prior to the start of the study.

Upper Respiratory Tract Infections
Symptoms and duration of URTIs were assessed throughout the study period using a semi-quantitative list of respiratory symptoms (Hoffman-LaRoche, Nutley, NJ). Subjects were asked to fill out the respiratory symptoms report sheet on each day that they had a runny nose, cough, or sore throat. In addition, subjects were encouraged to report to the nurse practitioner at Urgent Care at the University Hospital for diagnosis of URTI when they suspected that they had a cold to provide clinical evidence of URTI. Only one subject pursued this option; therefore this part of the study was not included in the analysis.

Incidence (total number of cases), duration, and the percentage of subjects in each treatment group with at least one URTI during the two months prior and one month following the marathon were determined from the respiratory symptoms log data. The severity score was determined by summing the severity of any symptoms present for each day of a cold on a scale of 0 (not present), 1 (mild), 2 (moderate), and 3 (severe). Symptoms included: cough, nasal discharge, sneezing, stuffy nose, sore throat, headache, malaise, chilliness, shaking chills, fever, hoarseness, aching muscles or joints, or watery or burning eyes.

Training Logs
Running logs were developed based on similar logs used by Nieman et al. (4) to determine training mileage and intensity. Each subject was given a training log for the two month period prior to and one month period following the race. Subjects were instructed to log their training distances and running times daily. Additional descriptive data, such as prior running history and marathon experience were also collected.

Body Composition
Body fat was determined from anthropometric

measurements at BL for sedentary subjects using the equation of Durnham and Womersley (19), and for runner subjects using the equation of Jackson and Pollock (20,21).

Vitamin C Supplementation

Subjects were instructed to take two tablets of either vitamin C (500 mg/tablet) or placebo (similar looking and tasting tablets containing lactose) (Hoffman-La Roche, Nutley, NJ) each morning with breakfast; and specifically at 8 a.m. on the mornings of the day immediately prior to blood draws. Supplementation continued from BL to POST2.

Blood Samples

Blood samples were only obtained from a subset of volunteers from each research group, as only the local runners had access to our testin facilities. Volunteer subjects reported to the University Clinical Research Center (CRC) after a 12 hour fast and prior to the ingestion of the daily supplement. Blood samples were obtained by phlebotomy performed on an antecubital vein. Samples of 5 mL were used for vitamin C, and a 7 mL sample was obtained from the subset of subjects randomly selected for lymphocyte proliferation measurements. For subjects from groups VS, PS, and PR, blood was obtained at BL and PRE. For subjects from the VR group, blood was obtained at BL, PRE, and POST1.

Analytical Procedures

Blood samples were immediately centrifuged at 4 degrees C, and plasma was removed and stored at -80 degrees C for subsequent assay for vitamin C. Plasma vitamin C was determined by an automated procedure using 2,6 dichloroindophenol (22-23). Blood samples for lymphocyte proliferation were delivered to Spectra Cell Inc. (Houston, TX). Samples were exposed to the mitogen PHA (2 ug/mL) and incubated for four days. Tritiated thymidine is then added and the lymphocytes were cultured for 24

hours (24-26), resulting in a measure of lymphocyte proliferation expressed as cpm x 10-3. Assays of lymphocyte proliferation were performed on 8 VR and 8 PR subjects at BL and PRE.

Statistical Analyses
The Statistical Analysis System (SAS Institute, Cary, NC) was used to perform the statistical analyses. McNemar's test was used to determine whether subjects knew which treatment they were on.

Incidence (total number and % of subjects), duration, and severity of URTIs in each subject group were assessed by one-way ANOVA. Mean differences for URTIs were assessed by t-test. Fisher's Exact Test was performed on the marathon runners and sedentary subjects to determine whether there were any treatment differences in the number of URTIs.

Multiple logistic regression was used to determine the factors associated with an increased incidence of URTI. While the study subjects actually received the supplements for a total of 92 days (3 months), for analytical purposes, only days 7 through 90 of the intervention were counted in the logistic regression. The entire 3 months (BL to POST2) of the study was used in the determination of duration and severity of colds. Finally, any colds which occurred on marathon day were considered to occur after the race.

Repeated-measures three factor (runner versus sedentary, vitamin C versus placebo, and PRE versus POST1) ANOVA were performed on the plasma vitamin C data. Mean differences were either performed using paired comparisons using specific error terms from ANOVA, or by t-tests for variables at BL. Repeated-measures two factor (vitamin C versus placebo, and PRE versus POST) ANOVA were performed on the lymphocyte proliferation data. Mean differences were assessed as previously described. Data are reported as mean ±SD.

Spearman partial correlation coefficeints were used to determine the relationship between dietary, supplemental, and total vitamin C intake and BL plasma vitamin C concentrations.

Results

Subjects

Demographics and Running History

Subject characteristics are shown in Table 1. Based on data of running history, the subjects of this study were moderately trained marathon runners, with a large range of previous marathon experience and performance times.

Table 1. Subject characteristics at baseline (data are expressed as mean±SD).

Characteristics	Marathon Runners (n=44)	Range	Sedentary Subjects (n=48)	Range
Females	11 (25%)		17 (35.4%)	
Placebo Treated	14 (31.8%)		25 (52.1%)	
Vitamin C Treated	30 (68.2%)		23 (47.9%)	
Age (yr)	42 ± 5.4	24 - 64	44 ± 4.9	22 - 65
Height (cm) **males (n=33)** **females (n=11)**	 177 ± 6 166 ± 7	 165 -196 157 - 175	 180 ± 6 167 ± 4	 168 - 198 157 - 175
Weight (kg) **males** **females**	 73.6 ± 10* 57.9 ± 3.9*	 55.3 - 97.5 51.3 - 63.5	 87.0 ± 20.8 67.7 ± 13.7	 59.0 - 130.0 49.9 - 94.3
Body fat (%) **males** **females**	 14.3 ± 6.2* 22.6 ± 4.5*	 4.6 - 22.0 17.9 - 30.5	 27.3 ± 7.2 35.8 ± 6.9	 14.0 - 38.0 25.0 - 47.0
Distance Run/week (km)	47.4 ± 2.9	13 - 113		
Longest Run of Week (km)	18.9 ± 7.7	8.1 - 35.5		
Average Training Pace (km/hr)#	11.0 ± 1.4	6.0 - 15.3		
Years of Running	13.4 ± 4.6	3 - 32		

Marathon Best (min)^	205.5 ± 29.6 137 - 299
Marathons Completed	16.9 ± 19.5 0 - 140

*p<0.05 from sedentary
^33 of the 44 runners had previously completed a marathon
#data from training logs completed during the study

Attrition and Compliance

Since fewer PR completed the study compared to VR, an analysis of the number of dropouts (after giving informed consent) was performed and revealed no significant treatment or running group differences (Fisher's Exact test, p = 0.08).

Compliance with the study was determined by performing a pill count for each subject (n = 94). The pill count revealed that two subjects, both VS, had taken less than 60% of the study supplements. This finding was vastly different from the remainder of the study subjects and a post-hoc decision was made to drop them from the analysis (final sample size = 92).

No significant differences between treatment groups were found in the number of tablets left over at the end of the study (beyond extras) (Kruskal-Wallis nonparametric test, p = 0.13). PR and VR had 9.9 ± 16.3 and 4.0 ± 5.4 supplements left, respectively, at the end of the study while PS and VS had 7.7 ± 11.4 and 14.9 ± 18.5 tablets left, respectively. Subjects were queried regarding which treatment they believed that they were taking during follow-up appointments at the CRC or by questionnaire (data not shown). Subjects without any idea which treatment they were on were excluded from this analysis. In the sedentary group, no significant differences were found between actual and believed treatment (McNamara's test, p = 0.51 for sedentary group). In contrast, more of the marathon runners tended to be wrong when asked which treatment they believed that they were on (p = 0.07 for

runners). In particular, more VR believed that they were on placebo.

Vitamin C Intake
Estimated usual dietary intake of vitamin C over the past year was determined on the 135 subjects who were recruited at BL. Six subjects were excluded from the dietary analysis due to questionable accuracy of their responses.

ANOVA was performed for dietary, supplemental, and total intake of vitamin C (Table 2). Logs of actual intake were used due to unequal variances in the untransformed values. In order to avoid performing logs on zeros, the log (x + 1) was used for supplemental vitamin C. Supplemental vitamin C refers to self-selected vitamin C supplementation prior to study intervention.

Table 2. Data of mean (±SD) estimated usual dietary, supplemental, and total intake of vitamin C (mg/day) for the year prior to the study.

Vitamin C Intake	Vitamin Treated Runners, VR (n=41)	Placebo Treated Runners, PR (n=30)	Vitamin Treated Sedentary Controls, VS (n=29)	Placebo Treated Sedentary Controls, PS (n=35)
Dietary	207 ± 131*	169 ± 112*	210 ± 203	149 ± 80
Supplemental	234 ± 423	209 ± 518	102 ± 293	78 ± 212
Total	442 ± 457	378 ± 518	312 ± 360	227 ± 226

Although no significant difference was found for treatment group (vitamin C versus placebo), a treatment-by-gender interaction was found for dietary vitamin C ($p = 0.03$) (153 ± 87 mg and 176 ± 126 mg for placebo-treated males and females respectively, and 229 ± 176 mg and 149 ± 104 mg for vitamin C-treated males and females, respectively). Thus, the

placebo-treated females had a higher intake of vitamin C than the placebo-treated males, whereas the vitamin-C treated males had a higher intake of vitamin C than the vitamin C-treated females. ANOVA of total vitamin C intake (supplemental plus dietary intake) revealed a significant difference between the marathoners and the sedentary subjects for total vitamin C intake ($p = 0.02$). As shown in Table 2, the marathon runners had a higher total intake of vitamin C compared to sedentary subjects.

Biomedical Parameters

Plasma Vitamin C

Among the runners, 33 subjects had blood drawn at BL, Post1, and Post2 (25 VR and 8 PR). ANOVA of BL and Post1 vitamin C concentrations revealed a significant effect for running category (marathoners versus sedentary subjects) ($p = 0.0001$) and for treatment-by-running category ($p = 0.03$), whereas no effect was found for treatment alone ($p = 0.10$) (Figure 1). Thus, a treatment effect was found, but it differed between the runners and the sedentary subjects. For VR subjects, BL versus Post1 vitamin C concentrations were not significantly different ($p = 0.12$) whereas Post1 vitamin C concentrations were significantly different from Post2 (repeated measures ANOVA, $p = 0.04$).

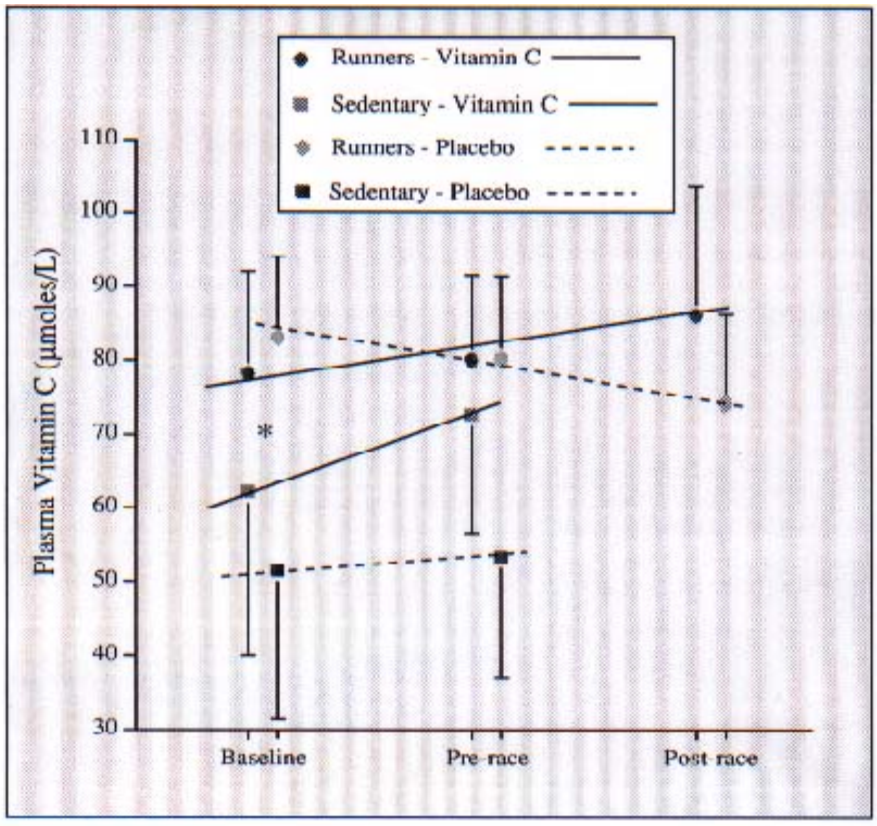

Figure 1. The change in plasma vitamin C concentrations for the subjects of each group during the study phases. At baseline, runners (VR and PR) had significantly higher plasma vitamin C than sedentary subjects (* $p<0.05$). The change in plasma Vitamin C from supplementation between baseline and post-race was significantly different between VR and PR (* $p<0.05$). Note, that pre-race blood samples were obtained between two to eight days pre-marathon, and post-race data were collected two days following the marathon.

The relationship between usual dietary intake and total intake of vitamin C and baseline plasma vitamin C concentrations were examined in 92 subjects with available data (including dropouts from the study). Dietary and total vitamin C intake were positively related to BL plasma vitamin C concentrations (Spearman correlation coefficients $r = 0.32$, $p = 0.01$ and $r = 0.35$, $p = 0.001$, respectively). However, supplemental vitamin C intake was not significantly related to baseline plasma vitamin C concentrations ($r = 0.20$, $p = 0.006$). The results were similar when

the data were adjusted for gender.

Upper Respiratory Tract Infections
Fifty-three cases of URTIs were reported during the study, 31 among vitamin C-treated subjects (15 VR and 14 VS) and 25 among placebo-treated subjects (12 PR and 12 PS). Fisher's Exact Test revealed no differences in reported URTI incidence between the four treatment groups ($p = 0.79$). When treatment alone was examined by combining the runners and sedentary subjects, no differences were found in reported URTI's ($p = 1.0$).

Duration and Severity of URTI Symptoms
The ANOVA of the duration of URTI symptoms revealed no differences between running groups (marathoners versus sedentary subjects) ($p = 0.46$) or treatment groups ($p = 0.41$). However, a significant treatment-by-running group effect was found ($p = 0.02$). Among the marathon runners, a significant treatment difference was found for the duration of URTI symptoms (t-test, $p = 0.01$), with VR having a longer duration of URTI symptoms than PR (Table 3). By contrast, no treatment difference was found among the sedentary VS and PS subjects for duration.

Table 3. Data of the incidenceof URTIs for the subject groups.

Subject Group	Subject Number	Total Number of URTIs	Number (%) of Subjects with URTIs	Mean (±SD) Duration of URTIs (days)	Mean (±SD) Number of Symptoms of URTIs
VR	30	15	10(33.3%)	5.4 ± 3.5*	42.6 ± 28.7
PR	14	12	6(42.9%)	2.7 ± 2.1	17.8 ± 26.0
VS	23	14	10(43.5%)	2.5 ± 1.1	16.1 ± 14.6
PS	25	12	8(32.0%)	4.2 ± 3.5	37.4 ± 52.7

See Table 2 for the definitions of group code abbrevations.
*p<0.05 from PR
^some subjects had more than one URTI

Analysis of the number of symptoms revealed no running group effect (p = 0.83) or treatment difference (p = 0.43), but did find a running group-by-treatment interaction (p = 0.02). A significant treatment difference was found for the number of symptoms for runners (t-test, p = 0.01), with VR reporting more symptoms than PR . Among the sedentary subjects, no treatment difference was found for the number of symptoms (t-test, p = 0.23).

Post-Race Results
URTI incidence was examined for the two weeks immediately following the marathon. Seven marathon runners (15.9% of the runners) reported URTIs during these two weeks, whereas only four sedentary subjects (8.3% of the sedentary subjects) had cold symptoms during this time period (Fisher's Exact test, p = 0.34). When the marathoners and sedentary group were examined together 12.0% had cold symptoms during the two weeks following the race (95% confidence interval from 6.1 to 20.4%). However, no treatment differences were found in the number of reported URTIs during the two weeks following the marathon when the marathoners and sedentary group were examined together (Fisher's Exact test, p = 0.19). Interestingly, no URTIs were reported among the sedentary group during the week immediately following the marathon, whereas four (three VR and one PR) marathon runners (9.1% of the runners) reported URTIs during this week (95% confidence interval from 2.0 to 18.9%).

Multivariate Analyses
Logistic regression revealed an increased risk of colds with increasing age, and a reduced risk with increased alcohol intake (Table 4). However, the majority of the subjects (82.6%) reported drinking

less than one drink per day, and only 4.4% reported drinking more than 2 drinks per day. Therefore, this finding does not imply that drinking large amounts of alcohol is of any benefit. No relationship was found between training mileage and risk of cold symptoms. However, marathon runners that reported a faster average training pace during the 12 weeks of the study, as determined by daily running logs, had a significant relationship to risk of cold symptoms ($p = 0.04$).

Table 4. Data from logistic regressionfor select variables likely to influence the incidence of URTI's, adjusted for month of the study.

Variable	Parameter Estimate	Odds Ratio	Probability > Chi-Square	Confidence Interval
Treatment	0.0757	1.079	0.89	0.4 - 3.1
Gender	1.1182	3.059	0.05	1.0 - 9.6
Number of Prior Marathons	0.0187	1.019	0.03	1.0 - 1.04
Longest Run of Week	-0.1504	0.860	0.03	0.8 - 1.0
Training Pace	0.8308	2.295	0.04	1.0 - 5.1

Additional factors among the marathon runners which were related to risk of cold symptoms included the number of marathons previously run, marathon personal best time, and the distance of the longest run of the week (Table 4). Specifically, the more marathons previously run, the slower the marathon personal best, and the shorter the distance of the longest run of the week were related to increased risk of URTIs. In addition, females were at greater risk of URTIs compared to males. However, marathon personal best was no longer significant when gender was added to the model, implying a relationship between these two factors. Therefore, marathon personal best was omitted from the model.

No treatment or running group differences were significant in any of the regression analyses. Furthermore, plasma vitamin C concentrations following two months of supplementation were not related to the incidence of URTIs using multiple logistic regression among the sub-sample (n = 69, p = 0.22 for one week pre-marathon and p = 0.20 for two days post-marathon for marathon runners, p = 0.65 for sedentary subjects).

Discussion

Vitamin C Supplementation and URTIs

The major finding of this study was that vitamin C supplementation did not reduce the incidence of colds in VR compared to PR during the two months prior to and one month following a marathon. Similarly, vitamin C supplementation did not reduce the incidence of colds among the sedentary subjects. However, comparison between R and S subjects is complicated by additional differences such as body composition, as identified in Table 1.

Our finding that vitamin C supplementation had no effect on the incidence of colds is in agreement with the vast majority of the literature (10,13,14,27-29). In general, vitamin C appears to be ineffective in reducing the incidence of colds, with the possible exception in cases of severe stress (7,28,30), whereas it does seem to modify cold symptoms and severity (10,29,31). Some authors have described this benefit of vitamin C supplementation as marginal at best and not adequate to justify supplementation (13,14). However, other researchers have stated that the risks of vitamin C supplementation are negligible and the benefits, including chronic disease prevention as well as possible effects against the common cold, may warrant supplementation (32-34). Nevertheless, no recommendation for vitamin C supplementation for the prevention of URTIs prior to or after a marathon can be made based on results of the present study.

Our findings are in contrast with those of Peters et al. (7) who found that vitamin C supplements reduced the incidence of URTIs by 50% in ultramarathoners. However, the ultramarathoners had a much greater incidence of cold symptoms (68% in the placebo group and 33% in the vitamin C group during the two weeks following an ultramarathon) and a larger sample size (92 runners and 92 sedentary subjects). Peters et al. (7) found no differences in the duration of symptoms between the vitamin C-treated runners and the placebo-treated runners, which is contrary to most of the literature on vitamin C. In addition, the incidence of colds among non-runners was extraordinarily high. In fact, there were more colds among vitamin C-supplemented non-runners (53% of subjects) than vitamin C-supplemented runners (33% of subjects). However, the duration of cold symptoms was shorter in the vitamin-C supplemented non-runners compared to placebo-treated non-runners. The findings of Peters et al. (7) are also surprising since they provided only 600 mg of vitamin C, did not control additional vitamin C supplementation, and relied on subject recall of cold symptoms in a telephone interview two weeks following the ultramarathon to determine incidence of URTIs. On the other hand, the ultramarathoners ran greater distances than the marathoners in the present study, and participated in a winter race, which may have made them more prone to URTIs. In addition, the higher stress of training among the ultramarathoners may have increased the likelihood of benefiting from supplemental vitamin C.

In the present study, seven runners (15.9%) and four sedentary subjects (8.3%) reported URTI symptoms during the two weeks following the marathon. While not significantly different, this finding suggests the possibility of increased cold symptoms following the marathon, which is in agreement with other studies of marathon and ultramarathon runners (4,5,30). For example, Nieman et al. (4) found that 12.9% of

marathoners had cold symptoms during the week following the Los Angeles Marathon, while 9.1% of the runners in the present study reported cold symptoms during the week following the marathon. Nieman et al. (4) reported that 43.2% of the marathoners had URTIs during the two months before the marathon, which is similar to our findings (33.3% of the vitamin C-treated runners and 42.9% of the placebo-treated runners had cold symptoms during the three month study). The finding that the runners in the present study were not overtraining (Table 1) may also have reduced the likelihood of finding any benefits with vitamin C supplementation.

Vitamin C Supplementation and Plasma Vitamin C Concentration

Dietary and supplemental vitamin C intake are shown in Table 2. Mean dietary intake of vitamin C was at or above 2.5 times the RDA for each of the groups. Runners had a significantly higher mean dietary vitamin C intake compared to sedentary subjects. Runners also tended to have a higher supplemental intake of vitamin C compared to sedentary subjects, although there was greater variation in these data.

Another important finding of this study was that usual estimated dietary and total vitamin C intake for the year prior to the study were positively related to BL plasma vitamin C concentrations, thus validating the food frequency questionnaire (HHHQ-DIETSYS).

An additional finding of this study was that after supplementation VR and VS subjects had plasma vitamin C concentrations in excess of 68.1 mmol/L (Figure 1). Levine et al. (35,36) showed a dietary intake of about 200 mg/day produced about 80% plasma saturation. Further, Levine et al. (35,36) also reported that neutrophils, monocytes, and lymphocytes were saturated with only 100 mg of vitamin C. Data of vitamin C intake, including supplemental intake, for all subjects revealed that

average vitamin C intake was above 200 mg/day and therefore would be close to plasma saturation. Therefore, since mean plasma vitamin C was near plateau, additional vitamin C intake from the intervention would not be expected to raise plasma concentrations substantially. This was seen in Figure 1. Consequently, it is not surprising that supplementation did not influence URTIs. Unfortunately, plasma vitamin C data were not provided by Peters et al. (7). However, the subjects of their study also had mean vitamin C intakes in excess of 200 mg/day. Once again, based on the data of Levine et al. (35,36) and also Garry et al. (23) it would seem unlikely that the vitamin C supplemented subjects of the Peters et al. (7) study should have benefitted from such large additional doses of vitamin C.

Other Factors Related to URTI Symptoms

In addition to vitamin C, other factors have been reported to influence the incidence of URTIs in runners (7,3,4). Therefore, the present study examined demographic, dietary, and training parameters in an attempt to explain the variation in incidence of URTIs in runners and sedentary subjects.

Logistic regression revealed an increased risk of colds with increasing age, and a reduced risk with increased alcohol intake. However, the majority of the subjects (82.6%) reported drinking less than one drink per day, and only 4.4% reported drinking more than 2 drinks per day. Therefore, this finding does not imply that drinking large amounts of alcohol is of any benefit.

No relationship was found between training mileage and risk of cold symptoms, which is in contrast with other studies (3,4). For example, Nieman et al. found a two-fold increase in risk of URTIs in runners that ran more than 97 km per week compared to runners

who ran under 32 km per week. Our sample size may have been too small to find such an effect (there were 2,016 runners in the study by Nieman et al.). In addition, running mileage was noted to be rather low for marathon runners in the present study (median 47 km , 75th percentile = 56 km). Nieman et al. (37) proposed a U-shaped curve for the risk of acquiring colds versus exercise level, where both very low and very high levels of exercise compromise immune function while moderate exercise enhances immune function. Thus, the moderate amount of training our subjects reported may have actually improved their immune function.

Logistic regression showed that a faster average training pace during the 12 weeks of the study, as determined by daily running logs, was significantly related to risk of cold symptoms ($p = 0.04$). As noted above with running mileage, the marathon runners did not appear to be training excessively hard. The median running pace was 11.1 km/hr (with 50% of the subjects running between 10.2 and 11.9 km/hr).

Additional factors among the marathon runners which were related to risk of cold symptoms included the number of marathons previously run, marathon personal best time, and the distance of the longest run of the week (Table 4). Specifically, the more marathons previously run, the slower the marathon personal best, and the shorter the distance of the longest run of the week were related to increased risk of URTIs. In contrast, Nieman et al. (4) reported that runners who had fewer years of running experience were at greater risk of colds ($p < 0.05$). However, Nieman et al. (4) also found that runners who ran fewer miles per week (NS) and (as in the present study) ran a shorter distance during the average longest weekly run had a greater risk of URTIs ($p < 0.05$).

Finally, it should be noted that this study was

conducted at moderate altitude (5,000 ft above sea level), and in a hot and dry environment. Although subjects differed in their residential altitude most participants in the marathon were local and resided between 3,000 to 7,000 ft. In remains unclear how the interaction between training and chronic altitude exposure influences URTIs.

Conclusions

In summary, we found no apparent benefit of vitamin C supplementation on the incidence of URTIs, despite excellent compliance of the subjects with taking their supplements during the three month study. Vitamin C supplementation did not significantly affect the incidence of colds among marathon runners or sedentary subjects. In addition, vitamin C supplementation did not decrease the duration or severity of cold symptoms in the marathon runners, although it did reduce the severity of colds in the sedentary subjects. However, only about 40% of the study subjects succumbed to colds during the study and the marathon runners were moderately trained, which may have enhanced rather than impaired immune function.

Based on the present study, vitamin C appears to offer no benefit against the common cold in marathon runners. However, the current study was based on a group of middle-aged New Mexican runners who were not over-training based on an average weekly mileage of about 33 miles per week in the year prior to the study. Thus these results should not be applied to people who are exposed to extraordinary amounts of physical or psychological stress, such as elite athletes or ultramarathoners. Thus, future research on the effect of vitamin C on colds should focus on more highly stressed subjects, and ideally should include a larger sample size and fewer dropouts. In addition, the inclusion of a higher proportion of female subjects is desirable.

Other populations that warrant further study to determine whether vitamin C might improve resistance against the common cold or improve immunity include the elderly and the immune-compromised. For example, recent studies have shown improved resistance against colds in the elderly with a multivitamin/mineral supplement, but have not determined which nutrients might be responsible (38-41). In addition, vitamin C supplementation might play a role in other respiratory conditions besides the common cold, such as in the treatment of asthma or bronchitis (42-44).

ACKNOWLEDGEMENTS: The authors gratefully acknowledge Hoffman-La Roche for providing the study supplements, the staff of the University of New Mexico Clinical Research Center for collecting blood samples and anthropometric data, Patricia Stauber, M.P.H. and the staff of the Clinical Nutrition Program for conducting plasma ascorbate assays, Beth Gautier for her assistance in organizing and running the study, Bruce Hendrickson, Ph.D. for his excellent help with computer programming, and the marathon runners and sedentary subjects for participating in this study.

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Note: No reprints will be available from the authors.

This study was funded in part by a grant from the University of New Mexico Clinical Research Center: MO1-RR-00997 1994, and from the University of Nex Mexico, College of Education, 1994 Graduate Research, Project and Travel Grant.

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