Vitamin C as effective as combinations of anti-oxidant nutrients in reducing symptoms of upper respiratory tract infection in ultramarathon runners.

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Abstract

The effect of anti-oxidant supplementation on the incidence of symptoms of upper-respiratory-tract infection (URTI) was determined during the fortnight following the 1993 Comrades Marathon (90km). Runners (n=178) and sedentary matched controls (n=162) were randomly divided into groups receiving 500mg Vit C (C; n=86), 500mg Vit C and 400IU Vit E (CE; n=90) or 300IU Vit E, 300mg Vit C and 18mg Beta Carotene (CEB; n=73) or placebo (P; n=93) daily for 21 days prior to participation in the ultramarathon. Total pre-race dietary vitamin and mineral intakes and post-race self-reported URTI symptoms were recorded in all subjects (n=340). The incidence of the URTI symptoms in P runners (40.4%) was significantly higher ($p<0.05$) than that in C (15,9%) and CEB (20,0%) runners, and also greater than that in matched, non-running controls receiving placebo (24,4%). The group of runners reporting the lowest incidence of URTI symptoms during the post-race period, had the lowest mean age and the highest (i) total mean daily Vit C intake (1004 mg); (ii) pre-race training status and (iii) percentage of black runners.

This study suggests that Vitamin C alone is as effective as combinations of Beta Carotene, Vitamin E and Vitamin C in reducing the incidence of post-race URTI symptoms and that age, training status and genetic make-up also may influence the susceptibility to the development of URTI symptoms in ultramarathon runners.

Key Words: Anti-oxidant Vitamins, Upper Respiratory Tract Infections, Ultramarathon Runners.

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Introduction

Two separate epidemiological surveys performed on ultradistance runners[1,2] have reported an increased incidence of symptoms of upper respiratory tract (URTI) following participation in ultramarathon events. A subsequent study[3] found that daily administration of 600mg Vitamin C for three weeks prior to the 90km Comrades Marathon, resulted in a significantly lower ($p<0.05$) incidence of symptoms of infection in runners during the fortnight after the race, compared to runners ingesting placebo. This was attributed to the anti-oxidant properties of Vitamin C, which suggests that athletes participating in prolonged exercise have an increased daily Vitamin C requirement.[3]

Evidence from more recent studies[4,5] is that the anti-oxidant nutrients may be more effective when used in combination. The aim of this study was therefore to compare the efficacy of supplementation with combinations of Vitamin E, Vitamin C and Beta Carotene and Vitamin C alone in reducing the incidence of post race URTI in ultra marathon runners.

Method

The protocol was approved by the Committee for Research on Human Subjects of the University of the Witwatersrand. Two hundred and twenty entrants for the 1993 Comrades Marathon volunteered to participate in the study. Each runner was matched (n=220) with a control of similar age who resided with the runner, but did not participate in running regularly. A double-blind, placebo-controlled study design was used in which the runners, in addition to their matched, non-running controls, were randomly divided into four groups. Each group received either anti-oxidant supplements or placebos for three weeks prior to the race. The pre-race training status, state of health and dietary vitamin and mineral intake of athletes and their age-matched controls was recorded by means of a questionnaire which each runner and control subject completed prior to the race. Demographic data including running distance per week, average running speed, number of weeks spent training and the number of other ultramarathons in which the athlete had recently participated were also recorded. In addition, the pre-race incidence of self-reported symptoms of URTI was documented. Runners with a history of sinusitis, hay-fever or both were excluded.

Each runner and matched control (n=55) was required to take three tablets of similar appearance daily. These contained either 500mg Vit C (C), 500mg Vit C & 400IU Vit E (CE), 300mg Vit C & 300IU Vit E, 18 mg Beta

Carotene (CEB) or lactose as placebo (P).

The total daily vitamin A, C and E intakes including that derived from any additional vitamin and mineral used by the athlete of all subjects was determined by using the Dietary Manager computer programme (Program Management, Randburg, South Africa). For the purpose of this study, the total vitamin A, C & E intake of each subject was thus calculated from the sum of the (i) daily dietary intake, (ii) additional supplements used and (iii) the anti-oxidant supplements given to the subjects.

Two weeks after the race all runners and controls who had originally volunteered to participate in the study were telephonically interviewed and questioned regarding: (i) whether the prescription of supplements had been adhered to or not; (ii) the race distance covered and the time taken by each athlete to complete this distance; (iii) the incidence and duration of symptoms of URTI. The number and duration of self-reported symptoms including sneezing, running nose, sore-throat, cough and fever were documented. All reports of trivial symptoms were excluded by including in the final analysis only reports of single URTI symptoms which lasted >1 day or a combination of at least 2 URTI symptoms each of which lasted < 1 day.

The training status ratio of each runner was calculated from the following formula:

$$\frac{\text{Weekly training distance (km)} \bullet \text{no of weeks spent in training}}{\text{average speed at which those kilometres were covered}}$$

As in our previous study[3], runners who reported a ratio of > 450 fell into the high-training status category, whereas those with a ratio < 300 were classified in the low training status category.

Statistics

A chi-square statistic was used to establish whether the incidence of symptoms of URTI was significantly different between the four groups of runners and controls. Multivariate analysis of variance and several one-way analyses of variance were used to analyze the significance of the difference between the four groups in terms of age, Vitamin C, E and Beta Carotene intake and training status ratio. For all statistical analyses the Statgraphics and Excel computer software programs were used and the level of significance were set at 0.05.

Results

Of the initial 220 runners and matched controls, 178 runners (23 female; 155 male) and 162 (116 female ; 46 male) controls compiled fully with the requirements of the study. Reasons for exclusion from the study included a previous history of allergic rhinitis, failure to take the prescribed medications, failure to complete at least 60 km of the race and inability to establish contact with the subjects after the race.

The size, gender distribution and mean age of the 4 groups of runners and their matched controls is given in Table 1. Among the runners who ranged in age from 19 to 65 years, 46 were < 30 y old, 119 were aged between 31 and 50 y and 13 were > 50 y in age. Although the two groups with the highest incidence of reports of URTI possessed the highest mean age, this was not significantly different from the mean age of the groups with lower incidence of infection (p>0.05).

Table 1: *The size, gender distribution and mean age (+/- SD) of the 4 study groups (n=340).*

EXPERIMENTAL GROUP	RUNNERS (n = 178)			CONTROLS (n = 162)		
	N		Age	N		Age
	M	F	(Years)	M	F	(Years)
Group C	44		34,3	41		33,1
	36	8	(5,2)	11	30	(9,5)
Group CE	47		37,6	43		33,7
	41	6	(8,4)	11	32	(9,2)
Group CEB	40		35,1	33		29,7
	36	4	(10,0)	8	25	(11,9)
Group P	47		39,2	45		32,8
	42	5	(9,5)	16	29	(11,8)

The total mean Vitamin A, E and C intakes of the runners in each of the four groups is shown in Table 2. The highest total mean intake of Vitamin C was reported in group C, whereas the P group reported a mean intake of 585mg of Vitamin C. Groups CE & CEB also reported high mean intakes of this Vitamin. Group CEB was the only group with a Vitamin A intake which exceeded the RDA for sedentary individuals[6], whereas group CEB was the only group which exceeded the RDA[6] of Vitamin E for sedentary individuals. The group with the lowest incidence of infection (C) reported a total mean Vitamin C intake of 1004mg.

Table 2: *The mean Vitamin A, C and E intakes of the runners (n=178) in the 4 groups.*

		GROUP C	GROUP CE	GROUP CEB	GROUP P
Food	Vit A (IU)	3170	4405	3915	3110
Sources	Vit C (mg)	72	93	95	80
	Vit E (IU)	25	22	26	18
Additional	Vit A (IU)	1446	1737	2348	2992
Supplements	Vit C (mg)	432	305	271	505
	Vit E (IU)	12	22	8	43
Anti-oxidant	Vit A (IU)	-	-	30 000	-
Supplements	Vit C (mg)	500	500	300	-
provided	Vit E (IU)	-	400	300	-
Total	Vit A (IU)	4616	6142	36 263	6102
	Vit C (mg)	1004	893	665	585
	Vit E (IU)	37	444	334	61

The incidence of symptoms of URTI in the runners and controls are given in Figure 1. The difference between the incidence of symptoms of infection in the runners ingesting placebo (40.4%) and their sedentary, matched controls (24.4%) was not significantly different (X^2=1.99; p = 0.16). The lowest incidence of infection amongst the runners (15.9%) was reported in group C. This was significantly different (X^2=5.54; $p < 0.05$) from the incidence of URTI symptoms in group P. A 20% incidence of infection was reported in group CEB. The incidence of symptoms of URTI in group CE was also significantly lower than in group P (X^2 = 6.24; $p > 0.05$). The incidence of symptoms of infection in group CE (25.6%) was not significantly different ($p > 0.05$) than the incidence in group P (40.4%).

The incidence, nature and mean duration of the symptoms of URTI among runners and control subjects is presented in Table 3. The most common URTI symptoms reported by runners in the 4 groups were nasal (n = 35). Included in this category were reports of running noses and sneezing. Symptoms lasting more than 7 days occurred in 20 cases (nasal), 13 cases (sore throat) and 12 cases (coughing). Twelve of the runners reported fever in conjunction with their URTI symptoms. Only 24,2% of the reported runners symptoms lasting 1-3 days. The mean duration of symptoms in the runners was not significantly different from the mean duration of symptoms in the control subjects ($p > 0.05$). Although the mean duration of symptoms was higher in runners on placebo than in runners who received the different combinations of anti-oxidants, this difference was not statistically significant ($p > 0.05$).

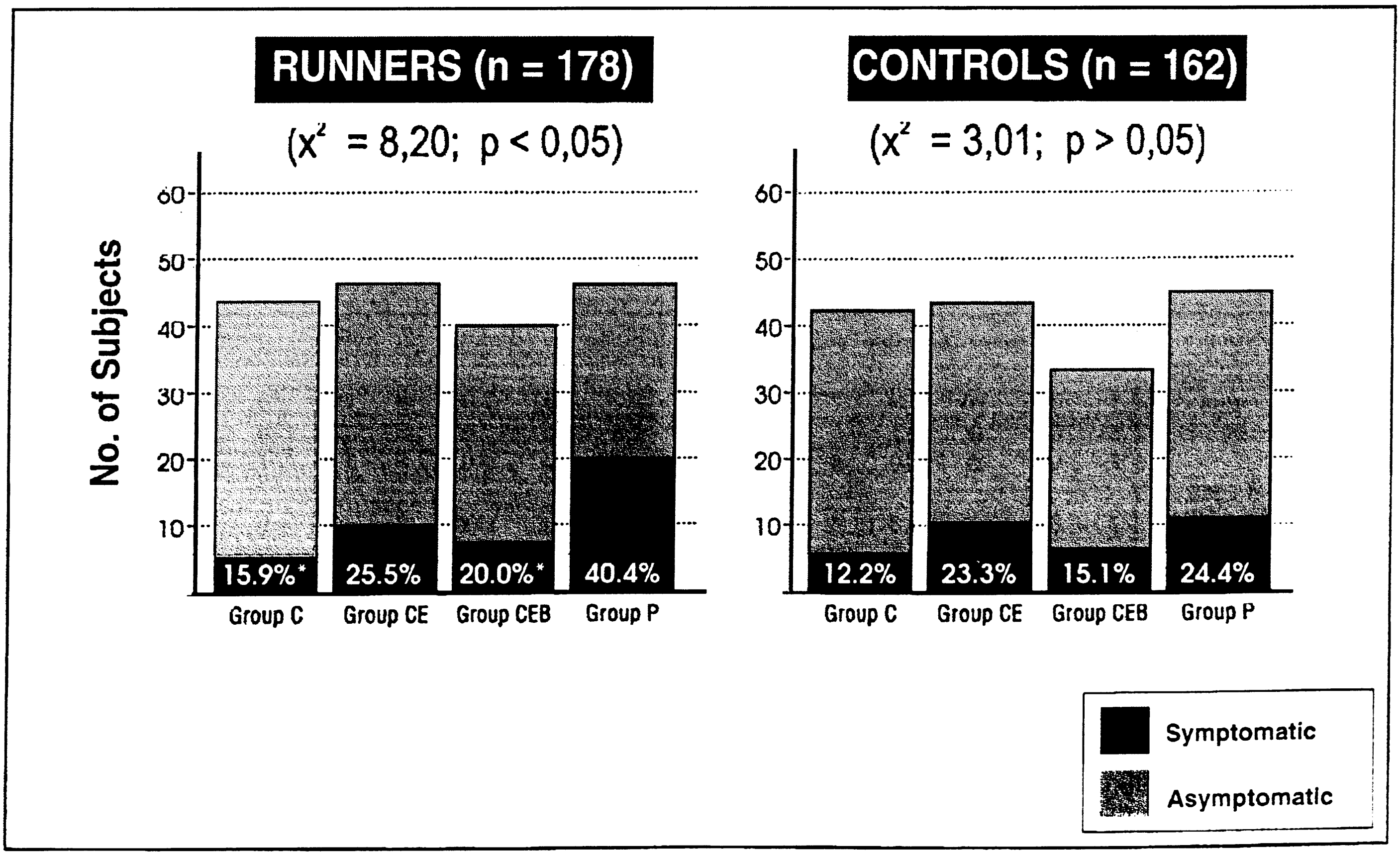
Table 3: *Incidence, nature and duration of post-race symptoms of URTI among runners and control subjects.*

EXPERIMENTAL GROUP	N	% SYMPTOMATIC	MEAN (± SD) TRAINING STATUS RATIO
Group C	42	20,2*	311 (±150)**
Group CE	47	25,8	274 (±127)
Group CEB	40	16,7*	328 (±166)**
Group P	47	40,4	236 (±111)

* P < 0.05 vs Group P
** P <0.01 vs Group P

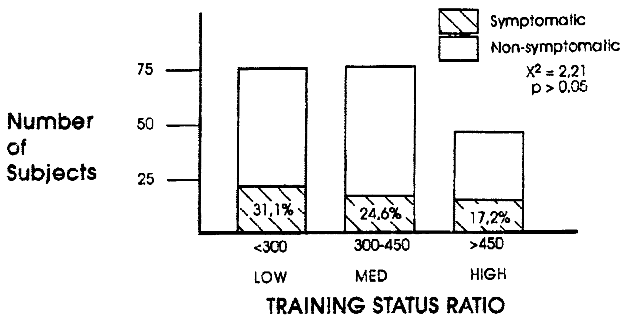
The incidence of infection in the low, medium and high training status groups is shown in Figure 2. Those runners who reported a low pre-race training status (<250) group reported the highest incidence of infection symptoms. This finding was confirmed when the incidence of post-race URTI symptoms was related to the mean training status of the 4 groups of runners (Table 4). The two groups with an incidence of URTI symptoms of more than 25%, reported the lowest mean training status. The difference between the training status of groups C and CEB (possessing the lowest incidence of infection) and groups CE and P (possessing the highest

Figure 1: *Incidence of Symptoms of URTI in runners (n = 178) and controls (n = 162) during the 14 day post race period.*



*** Significantly different from Group P (p<0,05)**

Figure 2: *The incidence of post-race URTI symptoms in low, medium and high training status groups (n=176)*



incidence of infection) was highly significant ($p > 0.01$). When the incidence of URTI symptoms were related to weekly training distance completed in preparation for the race, this trend was confirmed. Once again, the runners who had done the least pre-race training, reported the highest incidence of URTI symptoms.

A total of 16 black runners participated in the study. None of these athletes reported symptoms of URTI. When excluding the black runners from their respective groups, the percentage incidence of infection symptoms in the respective groups was 25,7(C); 41,3(P); 26,7(CE) and 23 (CEB). The difference between the three groups receiving additional anti-oxidant supplementation was not significant ($p > 0.05$). Despite a substantial difference in percentage incidence in the placebo group and the groups receiving anti-oxidant supplementation, this difference was no longer significant ($p > 0.05$).

No relationship between running time and incidence of URTI symptoms in the four groups was found in this study. Although the incidence was highest (35,5%) in those runners who took >10hrs to complete the race, this incidence was not significantly greater than the incidence in groups taking 7-8 hrs (23.5%) and 8-9 hrs (27,8%) to finish the race.

Discussion

The data obtained in this study confirms our previous findings[1,2,3,7] of a greater incidence of post-race symptoms of infection in ultramarathon runners compared to sedentary controls (Figure 2). The comparatively lower general incidence of symptoms in this study than in our previous study[3] must be seen in the light of the fact that (i) in this study, reports of symptoms lasting one day or only part thereof were not included in the final calculation and (ii) prevailing virological or bacteriological counts may have varied greatly at the time that these two separate studies were undertaken.

This study confirms previous findings[3] that daily intake of an excess of 1g of Vit C is effective in lowering the incidence of symptoms of URTI during the post-race period. Although the incidence of symptoms of URTI was substantially lower in all three groups of runners receiving anti-oxidant supplementation than in the group of runners receiving placebos, no correlation was obtained between the total amount of anti-oxidant nutrients ingested and the incidence of symptoms of URTI. Rather, it was the group with the highest total daily intake of Vit C which had the lowest incidence of URTI symptoms. Several factors could account for this.

Table 4: *The mean training status ratio and incidence of post race URTI symptoms in the 4 groups of runners (n=176)*

EXPERIMENTAL GROUP	A : RUNNERS								B : CONTROLS							
	Group C (n=44)		Group CE (n=47)		Group CEB (n=40)		Group P (n=47)		Group C (n=41)		Group CE (n=43)		Group CEB (n=33)		Group P (n=45)	
Post Race Symptoms	n	duration	n	duration	n	duration	n	duration	n	duration	n	duration	n	duration	n	duration
Nasal Symptoms	4	5,3	10	5,8	7	7,6	14	8,6	5	7,0	8	22,8	5	3,2	11	7,8
Sore Throat	5	5,8	9	4,7	5	5,8	12	4,5	5	7,8	8	9,3	3	1,3	8	8,1
Cough	2	9,0	2	7,0	4	4,8	8	7,8	4	9,6	8	11,1	1	7,0	7	10,3
Fever and URT Symptoms	1	3,0	2	1,8	4	4,3	5	6,4	1	14,6	2	17,5	6	0,0	4	2,0
Total Symptomatic**	7		12		8		19		5		11		5		11	
Mean Duration of Symptoms		5,8		4,8		5,6		6,8		9,4		15,2		2,3		6,9

Nasal symptoms include runny nose and sneezing.
** No. of persons in the group who presented with 1 or more symptoms lasting≥ 1 day or 2 more symptoms lasting ≤ 1 day
Duration = mean no. of days

Vitamin C is regarded as a first line anti-oxidant in the defence against phagocyte- derived reactive oxidants[8,9,10]. These immunosuppressive free radicals are known to be autotoxic, causing inhibition of chemotaxis, phagocytosis, the proliferation of T-lymphocytes and B-lymphocytes as well as the cytotoxic activity of natural killer cells [11,12,13]. Evidence is mounting in favour of Vitamin C- mediated neutralization of these reactive oxidants[8,9,10].

The relatively smaller protective effect of vitamin E and Beta Carotene supplementation may, be partially attributable to the slow elevation in plasma Vitamin E and Beta Carotene levels[15] and the fact that a 21 day supplementation period is too short to elevate plasma levels to reach protective levels. Secondly, variance in age[14], training status[15], environmental training conditions[16], and genetic make-up between the groups studied, may have obscured the effect of the other anti-oxidant nutrients.

As in our previous study[3], age does not appear to have played a significant role in the risk of infection. Training status, however, appeared to be an important factor. The highest incidence of symptoms of URTI was found in those runners who fell into the low training status category (Figure 2). Further confirmation of a possible beneficial effect of training is found when examining the mean training status of the four groups. It was found that the two groups possessing the highest training status had the lowest incidences of infection symptoms (Table 4). These findings were further supported when the incidence of URTI symptoms was analysed as a function of weekly training distance.

Two factors might support this finding. First, endurance training results in a lower catecholamine levels at a given exercise workload. This is potentially important as catecholamines affect free radical production[16]. Second, endurance training increases concentrations of endogenous antioxidant enzymes in skeletal muscle[15]. That endurance training exerts a protective effect on oxidative stress thus warrants further investigation in humans.

The finding that Black runners who participated in this study did not develop infection symptoms, also requires further investigation. This difference might be explained by chance; socio-economic or hereditary factors may also have played a role.

To conclude, the findings of this study appear to indicate that large intakes of Vitamin C alone (>1000mg) are more effective than combinations of Vitamin E, Vitamin C and Beta Carotene in lowering the incidence of URTI in ultradistance runners. This study, however, also indicates that besides Vitamin C ingestion, training load and ethnic background, are important variables which may influence the susceptibility to infection in ultramarathon runners.

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