A RANDOMIZED CONTROLLED TRIAL OF THE THERAPEUTIC EFFECT OF VITAMIN C IN THE COMMON COLD

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THE value of large doses of ascorbic acid in the prevention and treatment of the common cold is still uncertain. A double-blind, randomized controlled trial of the therapeutic effect of ascorbic acid was conducted therefore in a large representative population sample.

METHOD

A large number of women living in two towns in South Wales, and their husbands, were asked to cooperate in the trial. These women had been identified several years previously in a study of child growth and nutrition and had already cooperated in a prophylactic trial of vitamin C (Elwood *et al.*, 1975).

The subjects were visited in September and October and those who agreed were given ten effervescent tablets of either vitamin C (1 G) or an inert placebo. Allocation of households to vitamin C or placebo was random, but each husband received the same tablets as his wife. This was done to avoid confusion if tablets were shared. The smoking habit of each subject was recorded.

Instructions were given that, when symptoms suggestive of a cold commenced, the tablets were to be started, three tablets per day until the 10 tablets had been taken. Symptoms were to be recorded each day for the duration of the cold. Sufficient detail was requested to enable colds to be classed as 'simple', that is nasal symptoms with or without general symptoms such as fever or malaise but without any symptom referable to the chest such as cough. 'Chest' colds were recorded as any symptom-complex which included cough, wheezing, or other chest symptoms.

A stamped addressed envelope was given to each subject for the return of the record card. An arbitrary date was chosen approximately six months after the trial commenced, and any subject who had not returned a card

by then was assumed not to have had a cold. Subjects who had agreed to cooperate and who did not in fact do so cannot, therefore, be identified.

RESULTS

Of the 688 women who had cooperated in the earlier prophylactic trial, 675 were contacted. Eighty-three per cent of these agreed to participate in the further trial and, of the husbands, 78% cooperated. A breakdown of the total number of events observed into the three categories 'simple cold', 'chest cold' and 'no cold' are shown in table I.

Table II sets out the duration of simple colds which occurred in the two treatment groups. Men who had received vitamin C had an average duration

	Men	Women
Number taking part in trial	524	558
Number who had a simple cold	65	64
Number who had a chest cold	64	71
Number who reported no cold	395	423

TABLE I.—Numbers of subjects and numbers of colds

Duration (days)	Men		Women	
	Ascorbic acid	Placebo	Ascorbic acid	Placebo
1	1	1	0	0
2	6	2	1	1
3	8	3	5	7
4	8	6	10	3
5	3	4	5	4
6	3	5	3	6
7	1	6	7	1
8	1	2	1	2
9	0	1	1	0
10	1	2	1	1
11+	0	1	5	0
Total no. of colds	32	33	39	25
Mean duration	3·97	5·70	6·05	4·97
Standard deviation	(1·94)	(2·50)	(2·96)	(1·97)

Differences between means for treatment groups significant ($P < 0.01$) in men

TABLE II.—Duration of 'simple' colds

of simple colds almost 2 days less than in those who had received placebo ($t = 3{\cdot}1$; $P < 0{\cdot}01$). The difference in women goes the other way. These, and all subsequent significance tests are 'one-sided', being a test of the null hypothesis that vitamin C treatment is not effective in shortening colds against the alternative hypothesis that it is in comparison with placebo treatment.

Table III shows the duration of chest colds in the two treatment groups. Both men and women in the vitamin C group had a longer mean duration of colds than those in the placebo group.

Duration (days)	Men		Women	
	Ascorbic acid	Placebo	Ascorbic acid	Placebo
1	0	0	0	0
2	1	0	0	0
3	3	3	4	3
4	7	6	5	5
5	5	3	5	4
6	4	3	7	1
7	4	2	2	3
8	3	4	3	1
9	2	1	1	2
10	4	0	2	5
11+	6	3	6	12
Total no. of colds	39	25	35 (32)*	36 (35)*
Mean duration	7·10	6·32	8·89 (6·53)*	8·75 (8·23)*
Standard deviation	(3·47)	(2·90)	(8·65) (3·24)*	(4·79) (3·68)*

Differences between means for treatment groups not significant in either sex

*If colds of duration greater than 20 days are considered anomalous and ignored the alternative figures are appropriate. (No colds of more than 20 days duration occurred in men.) The comparison between means in women then becomes significant ($P < 0.05$).

TABLE III.—Duration of 'chest' colds

	Men		Women	
	Ascorbic acid	Placebo	Ascorbic acid	Placebo
Simple colds				
Non-smokers	4·0 SD 2·15 (23)	5·7 SD 2·63 (24)	6·0 SD 3·00 (33)	4·6 SD 1·67 (19)
Smokers	3·8 SD 1·39 (8)	5·6 SD 2·24 (9)	6·2 SD 3·31 (6)	6·0 SD 2·61 (6)
Chest colds				
Non-smokers	7·3 SD 3·61 (27)	7·1 SD 3·26 (9)	8·8 SD 9·59 (24)	9·6 SD 5·28 (20)
Smokers	6·6 SD 3·23 (12)	6·0 SD 2·83 (16)	9·0 SD 6·53 (11)	7·8 SD 4·04 (16)

TABLE IV.—Mean duration in days (with standard deviation [SD]) of simple and chest colds by sex, smoking habit and treatment. Numbers of subjects shown in brackets.

The proportion of smokers differed between the treatment groups for both simple and chest colds. The mean cold duration and its standard deviation for each treatment group, sub-divided by smoking habit, is shown in table IV. Examination of this table does not reveal any consistent

effect, due to smoking, which may mask the effect of vitamin C and thus bias the results.

Quite a few chest colds were reported to have lasted for a very long time and the vitamin C group, by chance, had an undue proportion of these. When all chest colds of duration greater than 20 days are excluded from both treatment groups it turns out that, with or without smokers, the mean duration of chest colds in the women given vitamin C is, stastically, significantly less than in the placebo group of women. The difference in mean duration is nearly two days. It is not legitimate to claim that this last analysis established a beneficial effect for vitamin C but it does suggest that if there is it could be hidden by poor definition of chest colds which leads to too many of long duration being included, thereby inflating the mean and variance and thus decreasing the sensitivity of the comparisons. Detailed examination of subjects' record cards suggests that some of the apparently very long-lasting colds may be two or more colds strung together, or perhaps that a distinction must be drawn between a cold giving rise to transient cough and a cold giving rise to chronic cough.

DISCUSSION

Trials of ascorbic acid in the common cold have not proved to be easy to conduct, nor the results easy to interpret. Indeed, as the literature grows, so do the inconsistencies.

There are a number of published trials claiming a beneficial effect for vitamin C on the duration or the severity of colds (Franz *et al.*, 1956; Ritzel, 1961; Charleston and Clegg, 1972; Wilson and Loh, 1973), although other workers have failed to detect benefit (Dahlberg *et al.*, 1944; Tebrock *et al.*, 1956; Walker *et al.*, 1967; Clegg and MacDonald, 1974).

Anderson and his colleagues (1972) initially reported that in illnesses in a group of 818 students who had been given 4 G ascorbic acid during a cold (in addition to a previous prophylactic dose of 1 G per day) there was less constitutional upset and fewer days of disability than in a group which had been given placebo. The difference was equivalent to about half a day per subject during the 118 days of the trial. An effect in the same direction but of much smaller magnitude was detected in two further trials (Anderson *et al.*, 1974; Anderson *et al.*, 1975) although, in one of these, treatment was with 4 or 8 G vitamin C per day. Similarly, Karlowski and his colleagues (1975) described the effect of 3 G ascorbic acid per day on the duration and severity of colds as '. . . at best only a minor influence'.

The present data are consistent with a 3 G daily dose of vitamin C having a therapeutic effect on simple colds in men. However, as this effect was found neither for simple colds in women nor for chest colds in either sex, there is inadequate evidence to justify the conclusion that vitamin C in the dosage employed here has a therapeutic effect on the common cold.

The lack of clear agreement in all the studies cited above is not easy to understand. The subjects in Anderson's trials were highly selected and

they estimate that they represented only about 10% of the available population (Anderson *et al.*, 1974). It could be, therefore, that a vulnerable sub-group exists in whom ascorbic acid is of benefit but we have presented evidence which goes some way towards refuting this (Elwood *et al.*, 1975). On the other hand Karlowski and his co-workers suggest that their own results and, by inference, favourable results of other workers, could be explained by a break in the double-blind conduct of the trial.

It is becoming clear from this and other work that the effect of ascorbic acid on the common cold is at best elusive and probably trivial.

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