Hesperidin and Ascorbic Acid in the Prevention of Upper Respiratory Infections

George J. Boines, M.D.* *and Steven Horoschak, B.S.*†

This study stems from observations made on a number of poliomyelitis patients treated with hesperidin and ascorbic acid (Hesper-C‡) five years ago as a prophylactic measure to maintain normal capillary integrity. We originally treated 48 patients, ranging in age from 15 to 35 years, with 800 mg. each of hesperidin and ascorbic acid daily, to correct capillary fragility, and then continued these patients on 200 mg. of each substance as a prophylactic measure to maintain normal capillary integrity.

At the end of the winter months, a number of these patients inquired if the pills "prevented colds." They found that they had been free of colds, while members of their families had to be treated for colds. These reports aroused our interest and stimulated us to survey all 48 patients given hesperidin and ascorbic acid in order to maintain normal capillary integrity, but without intending to prevent the common cold.

Our first survey disclosed the following data: (1) 48 patients were started on hesperidin and ascorbic acid; (2) of these, 40 reported no colds or experienced only one or two mild attacks; (3) the remaining 8 said their colds were as bad as or worse than those of the previous winter; and (4) 35 family contacts of these patients sought medical advice and attention from their physicians on an average of three times during this period.

It was decided to follow these patients for another year to observe what effect hesperidin and ascorbic acid would have on the incidence of colds in these same patients. They were advised to continue with the capsules of hesperidin and ascorbic acid (100 mg. of each substance per capsule), two capsules daily, throughout the year.

Following the second winter season, we obtained reports from 42 of the 48 patients, as follows: (1) of the 42 patients, 37 were adequately "protected," since they reported no colds or one to two mild colds; (2) 4 patients each reported three colds, lasting an average of three days in each instance; (3) 1 patient reported five colds, each lasting five to seven days; and (4) family contacts not taking hesperidin and ascorbic acid sought relief for colds on an average of three times during this period.

* Attending Chief of Communicable Diseases and Poliomyelitis at the Wilmington General and St. Francis Hospitals, Wilmington, Del. Lecturer at the Department of Biological Sciences, University of Delaware, Newark, Del.

† Medical Research Department, The National Drug Company, Philadelphia, Pa.

‡ The trade name of the Medical Research Department, National Drug Co., for a capsule containing 100 mg. each of hesperidin and ascorbic acid is Hesper-C. Hesperidin was originally administered in a tablet containing 50 mg. of each of hesperidin and ascorbic acid. The hesperidin and ascorbic acid used in this study were supplied through the courtesy of the Medical Research Department, National Drug Co., Philadelphia, Pa.

The data obtained in our second survey are intriguing; however, we cannot argue with the reports given by the patients. We appreciate the variable incidence of upper respiratory infections from year to year and the fluctuation of resistance to infection. It was decided to set up a controlled study in this series of patients.

For the third year, the 37 patients were divided into group I and group II. Group I was represented by 18 patients who had apparently been "protected" against the common cold while taking hesperidin and ascorbic acid for the previous two years. These patients were advised to discontinue the capsules of hesperidin and ascorbic acid and to take orange juice three times daily. This was our control group.

Group II consisted of 19 patients, including the 5 patients who reported colds during the last survey. They were continued on 200 mg. of hesperidin and ascorbic acid daily.

A review of the information obtained from these patients revealed the following: in group I, (1) 10 reported no colds or one to two mild attacks; and (2) 8 had two or more colds requiring medical attention. We did not prescribe any hesperidin and ascorbic acid in these cases because we were using the combination as a prophylactic and not as a therapeutic agent.

In group II (1) 15 patients reported no colds or one to two mild attacks of an average of two days; and (2) 4 patients reported three to five colds, but none severe enough to call a doctor.

This survey indicates that the combination of hesperidin and ascorbic acid is apparently able to "protect" against the common cold. In order to substantiate this rinding, it was decided to reverse the two groups observed during the third year.

For the fourth year, we established these two groups: group I, represented by the 18 patients used as controls in the third year were placed on 200 mg. of hesperidin and ascorbic acid daily and group II, represented by 19 patients in whom dosage of hesperidin and ascorbic acid was substituted for orange juice, were now the control group.

A follow-up survey of these two groups resulted in the following data: in group I, (1) 13 reported no colds or one to two mild colds; (2) 1 reported three colds and another, five colds of three days' duration; and (3) 3 patients gave no report.

Group II, (1) 9 reported no colds or only several mild attacks; (2) 8 patients reported two to three attacks of three to five days' duration; and (3) 2 patients did not report.

We have made it a routine practice to place all of our poliomyelitis patients on hesperidin and ascorbic acid, starting in the hospital as a therapeutic measure to correct abnormal capillary resistance and then in outpatients as a prophylactic measure to maintain normal capillary integrity. The aforementioned trend seems to prevail in a vast majority of patients.

DISCUSSION

A clearer understanding of the importance of the capillary system and its physiologic function will convince even the skeptic that "an intact capillary system means a solvent body."[1] The capillary system, among its other functions, acts as "a pro-

tective mechanism against disease."[2] Whether in health or in disease, the capillary system is an important factor.

Impaired nutrition and infection contribute to injury of the capillary walls.[3] The barrier function of the endothelial cells may be impaired by various factors, but, we believe, particularly by a deficiency in protein and certain vitamins. Depletion of ascorbic acid contributes to lowered body resistance to infection.[4] We have pointed out that in poliomyelitis patients, the infection creates a tissue deficiency,[5] and, we now add, a tissue deficiency predisposes to infection.

Capillary resistance depends on the adequate formation and maintenance of intercellular ground substance. According to Youmans,[6] "The primary structural change in vitamin C deficiency is a disturbance in the formation and maintenance of the intercellular ground substance. Apparently ascorbic acid is essential for the integrity of this tissue. In the intercellular ground substance are the collagen bundles. In the absence of a sufficient supply of ascorbic acid, the collagen bundles disappear and the ground substance takes on a thin 'watery' appearance and may eventually disappear." The nature of the dietary factors contributing to the maintenance of vascular integrity has not been unequivocally elucidated. Wolbach[7] stated that vitamin C seems to play a specific role by functioning in some manner to incorporate the vascular cement substance.

Bronte-Stewart[8] emphasized that "ascorbic acid by itself has no proved effect in combating any condition other than scurvy." According to Scarborough,[9] a deficiency of vitamin C is not necessarily complicated by low capillary resistance. Warter et al[10] confirmed reports that there is no correlation between capillary fragility, as measured by various methods, and plasma vitamin C levels.

A substance of similar importance and related activity was postulated[11] to accompany cellular vitamin C. This substance was isolated from citrus fruits and extracts of Hungarian red pepper and was labeled "citrin,"[12] which on analysis was found to be a mixture of hesperidin and eriodictin.[13]

The permeability activity of hesperidin was studied by Scarborough,[14,15] who found that this substance increased capillary resistance in man when given by mouth.

A synergism of vitamin C and vitamin P is suggested by some studies.[16] Warter et al[10] suggested that hesperidin is essential for the absorption and retention of vitamin C, acting synergistically in maintaining normal capillary resistance. The demonstration of a relationship between hesperidin and ascorbic acid by Beiler and Martin[17] shed some light on the basic mechanism involved. Selsman and Horoschak[18] suggested, on the basis of their experiences, that the presence of hesperidin is necessary in the utilization of vitamin C for the intercellular substance.

There is sufficient evidence to support this concept that the full activity of vitamin C depends on the presence of hesperidin for the formation and maintenance of the intercellular cement substance.

COMMENT

Our primary reason for using the combination of hesperidin and ascorbic acid was and continues to be to improve and maintain capillary resistance in poliomyelitis

patients and not to determine how effectively the product influences resistance to upper respiratory infection. It is our firm conviction that a pathologic condition of the capillary system is one of the underlying factors in many acute and chronic ailments. Reversal from abnormal to normal capillary resistance is essential for good therapeutic results. There is adequate clinical evidence that the hesperidin and ascorbic acid is an effective agent for this purpose.

We appreciate the variability of seasonal incidences and severity of upper respiratory infections. The above data are presented as observations based on our poliomyelitis therapeutic program, which may have some definite significance. These data are not offered as clinical conclusions that establish the prophylactic capacities of hesperidin and ascorbic acid against the common cold. However, we do believe the results suggest that a large-scale study is justified.

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