EFFECT OF EXCESSIVE DOSES OF VITAMIN C ON SOME MECHANISMS OF NATURAL IMMUNITY

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The effects of prolonged (for 21 days) administration of excessive doses of vitamin C (4 ml of a 5% solution daily) on certain of the most important mechanisms of natural immunity were studied in experiments on rabbits. After 7 days there was a significant decrease in the total bactericidal activity of the animals' blood serum, a decrease in its content of properdin and lysozyme, and sharp inhibition of the phagocytic activity of the peripheral blood leukocytes. By the end of the period of administration of the excess ascorbic acid to the animals the above parameters of natural immunity had returned to normal except the phagocytosis. It is concluded that administration of massive doses of vitamin C could have unfavorable effects during outbreaks of infectious diseases or immediately before them.

During recent years authoritative scientists have insistently advocated the taking of excessive doses of vitamin C as a nonspecific prophylactic measure against infectious diseases, especially acute respiratory infections. Some of them [8, 9] recommend the daily administration of 5-10 g ascorbic acid for this purpose.

Meanwhile the effect of prolonged administration of massive doses of vitamin C on the resistance of the body to infection and on individual immunologic mechanisms has not yet been studied experimentally to any significant degree. Only a few contradictory articles can be found on this subject in the literature [1-4, 6, 7].

The object of this investigation was to make an experimental analysis of the action of large doses of vitamin C, administered over a long period of time, on certain of the more important mechanisms of natural immunity.

EXPERIMENTAL METHOD

Experiments were carried out on 25 chinchilla rabbits weighing 3-3.5 kg. Daily for 21 days the experimental animals received intravenous injections of 4 ml of a 5% solution of vitamin C. Control rabbits received 4 ml physiological saline by intravenous injection daily for the same period. The dynamics of the following immunologic parameters was studied separately in each animal: the total bactericidal and lytic activity of the blood serum, the properdin concentration in the blood serum, and phagocytosis by peripheral-blood neutrophils. Blood for investigation was taken before and 7, 14, 21 and 28 days after administration of vitamin C.

The bactericidal activity of the blood serum (as exhibited against Staphylococcus aureus) was estimated from results obtained by a modified Pillemer's method; the serum properdin content was determined by the zymosan method in the modification of Mashkov and Mikhailova; the serum lysozyme concentration was calculated by the method of Kagramanova and Ermol'eva; the phagocytic activity of the neutrophils (using

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TABLE 1. Dynamics of Parameters of Natural Immunity in Rabbits during Administration of Massive Doses of Vitamin C (M ± m)

Parameter studied	No. of rabbits	Before adminis.	After 7 days adminis.	After 14 days adminis.	After 21 days adminis.	After 28 days adminis.
Bactericidal index of blood serum	20	5,7±0,3	3,3±0,3 $P<0,001$	4,8±0,5	6,0±0,5	6,6±0,35
Lytic activity of blood serum	11	14±1,9	9,0±1,0 $P<0,05$	12±2,2	14±2,2	16±2,3
Serum properdin concentration	9	5,0±0,3	3,1±0,4 $P<0,01$	2,6±0,6 $P<0,01$	3,7±0,45	4,8±0,4
Percentage of neutrophils engaged in phagocytosis	16	54±0,5	40±1,6 $P<0,001$	34±1,6 $P<0,001$	42±1,2 $P<0,001$	54±0,6
No. of bacteria ingested by one leukocyte	16	2,8±0,1	2,1±0,1 $P<0,001$	1,8±0,07 $P<0,001$	2,1±0,08 $P<0,001$	2,8±0,1

Staphylococcus aureus as the test organism) was studied by the usual method and both the percentage of cells phagocytosed and the mean number of microorganisms ingested by one leukocyte were calculated.

The results were subjected to statistical analysis (using Student's tables).

EXPERIMENTAL RESULTS

The results (Table 1) show that administration of massive doses of ascorbic acid very rapidly induces unfavorable changes in the state of the mechanisms of natural immunity studied. For instance, after 7 days all the parameters studied were significantly (and as a rule, considerably) below their initial level. Some of them continued to decline in the future, to reach a minimum after 14 days, whereas others (bactericidal and lytic activity of the serum) showed a tendency to return to normal in the later stages, or even to rise slightly (not significantly) above the initial value.

The depression of the phagocytic activity of the leukocytes was particularly persistent, for it was observed for 3 weeks, i.e., throughout the time that the animals received the vitamin. This is a particularly interesting fact in connection with the important role of phagocytosis in the body's fight against infection, especially infection by the pathogenic cocci and bacilli.

It would be a mistake not to allow for this possible adverse effect of prolonged administration of excessive doses of ascorbic acid on immunity to viruses also. Although properdin and, still more, lysozyme cannot be regarded as dominant factors in the protection of the body against viruses, nevertheless their importance (especially that of properdin) in this respect ought not to be ignored.

The decrease in the concentration of these protective proteins in the blood serum (by almost one-half in the case of properdin, for example, on the 14th day of the experiment) may definitely weaken the natural immunity of the body to pathogenic viruses.

So far as the control animals are concerned, at no time of the investigation were any significant variations in the activity of the mechanisms of natural immunity studied observed in any of the animals.

Administration of known excessive doses of ascorbic acid for a long period thus leads to a more or less considerable and prolonged inhibition of several important reactions of natural immunity and this must be not only of theoretical, but also of direct practical interest. The results not only call into question the desirability of administration of large doses of vitamin C at times before an expected outbreak of infectious diseases (such as acute respiratory infections) or even during epidemics themselves, but in the writers' view they provide a sufficient basis for an even stronger assertion – that such nonspecific "prophylaxis" is actually dangerous.

When these results are examined from the general theoretical point of view, the similarity between the dynamics of the responses of the animal to massive doses of vitamin C and the general principles of development of the adaptation syndrome cannot fail to be recognized: the phase of clear depression of functions is followed by a stage of adaptation, when they gradually return to normal. Consequently, large doses of the vitamin have an effect on the organism similar to that of stress.

Unfortunately little can yet be said about the intimate mechanisms of the effects now observed. To shed more light on them, special precise biochemical investigations are necessary. By way of an hypothesis it can be postulated that an excessive concentration of ascorbic acid in the blood sharply intensifies the "slag-disposing" function of the serum γ globulins, one possible result of which could be a decrease in the formation of nonspecific protective proteins and opsonins. The possibility of the production of vitamin-binding antibodies under these conditions likewise cannot be ruled out, and this ultimately must lead to the same results as are observed at the height of the productive phase of immunogenesis following vaccination of man and animals [5].

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