Physiol. Res. 41: 403 - 405, 1992

SHORT COMMUNICATION

Protective Effect of Ascorbic Acid in High Altitude Hypoxia in the Rat

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Received June 17, 1992
Accepted August 17, 1992

Summary

Control (physiological saline treated) and ascorbic acid (AA) treated (1 mg . g^{-1} b.w. one hour before exposure) 18-day-old rats were exposed for 1 hour to high altitude in a hypobaric chamber and the mean lethal altitudes were calculated. AA displayed a protective effect, so that in two identical experiments the mean lethal altitude was 10 900 and 10 150 m in controls, while it was 11 500 and 11 450 m in AA treated animals.

Key words

Hypoxia – High altitude – Ascorbic acid – Hypoxia survival

The role of ascorbic acid (AA) in those mammals which do not synthesize it (and in which it is a vitamin) is – besides the protection against scurvy – rather controversial. The reports on a protective effect of high doses of AA against common cold (Pauling 1976) and in advanced cancer (Pauling 1982) in humans have not generally been accepted (Schroeder *et al.* 1988, Wittes 1985). On the other hand, there is no doubt that AA is a free radical scavenger and an antioxidative agent (Mayes 1990) and recently (Editorial 1991) its use in chronic diseases and for prevention of genetic defects has been suggested.

The brain may be an organ with a special relation to AA: brain concentration of AA rises after repetitive hypoxia stress in young rats (Schreiber *et al.* 1989), probably as a result of increased production of AA in the liver. This could have a survival value in hypoxia of the brain. We therefore tested a possible protective effect of endogenous AA in rats exposed to high altitude hypoxia.

In two identical experiments, 18-day-old rats (b.w. 39-46 g) were divided into two groups. Controls received physiological saline s.c. in the same volume as were animals of the second group. These animals were given AA in a dose of 1 mg.g^{-1} b.w. in a 10 % solution in apyrogenic water s.c. One hour after the injections both groups were first exposed to high-altitude hypoxia

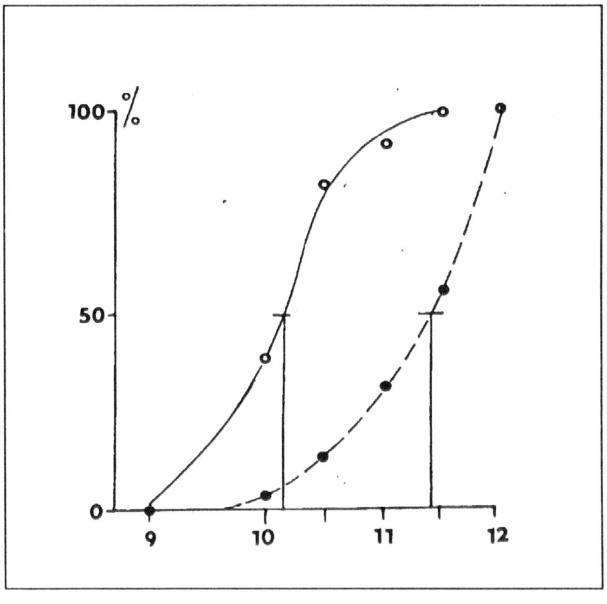

Fig. 1

The protective influence of ascorbic acid on the survival of rats at high altitudes (abscissa = $m.10^3$ above sea level, ordinate – percentage of dead in individual groups). Open symbols: controls, full symbols: AA treated. Data from Exp. No. 2. after transformation according to Behrens (1957). Mean lethal altitudes (equivalent to Behrens LD 50) are indicated by vertical lines in both.

Table 1

Experiment No. 1. Nine control (physiological saline treated, C) and 9 ascorbic (AA) treated rats were exposed to repetitive high altitude hypoxia and the mortality at individual altitudes was counted.

Altitude	Exposed		Dead		Surviving		Percentage of mortality (Behrens)	
	C	AA	C	AA	C	AA	C	AA
9 000	9	9	0	0	9	9	0	0
10 000	9	9	2	0	7	9	20	0
11 000	7	9	6	0	1	9	88	0
11 500	1	9	1	2	0	7	100	22
12 000	0	7	0	7	0	0		100

Mean lethal altitude: Controls 10 900 m, AA treated 11 500 m

Table 2

Experiment No. 2. Eleven control (physiological saline treated, C) and 11 ascorbic acid (AA) treated rats were exposed to repetitive high altitude hypoxia and the mortality at individual altitudes was counted.

Altitude	Exposed		Dead		Surviving		Percentage of mortality (Behrens)	
	C	AA	C	AA	C	AA	C	AA
9 000	11	11	0	0	11	11	0	0
10 000	11	11	5	1	6	10	38	3
10 500	6	10	5	2	1	8	83	14
11 000	1	8	0	2	1	6	91	31
11 500	1	6	1	1	0	5	100	54
12 000	0	5	0	5	0	0		100

Mean lethal altitude: Controls 10 150 m, AA treated 11 450 m

in a hypobaric chamber for 1 hour. To spare the animals (and minimalize the cost of the experiment) we used a modified approach: animals surviving at lower altitudes were exposed to higher altitudes after a one hour pause, during which they were moving freely at ambient barometric pressure.

The number of dead and surviving animals was counted at each altitude and the "mean lethal altitude" was estimated according to Behrens (1957). Essentially, this is equivalent to Behrens LD 50 in pharmacological (toxicity) experiments. The numbers of exposed, dead and surviving (and then exposed to the next higher altitude) animals are given in the tables.

The results are shown in Tab. 1 and Tab. 2 and Fig.1. Administration of AA clearly protected the animals against the lethal effect of high altitude hypoxia. The effect is obvious at all altitudes beginning with 10 000 m. The "mean lethal altitude" in the controls was 10 900 m in the first and 10 150 m in the second experiment, while in AA treated animals it was 11 500 m and 11 450 m respectively.

The mechanism of the protective effect of AA in high altitude hypoxia remains to be elucidated. One possibility is the scavenging of free radicals in the hypoxic or post-hypoxic brains. This could also play a role also in humans with brain ischaemic (stroke) and post-ischaemic (ischaemic penumbra) lesions. Since the administration of AA in high doses is most probably harmless (perhaps except in individuals with oxalate nephrolithiasis or iron overload) the clinical testing of the protective effect of AA or tocopherol (Trojan 1991) or both in brain hypoxic (neonatal) or ischaemic (stroke) conditions, as well as in myocardial infarctions (reperfusion toxicity in the ischaemic penumbra) should be considered.

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