

SHORT COMMUNICATION

Protective Effect of Vitamin E on Brain Ischaemia during Ontogenesis

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Summary

Vitamin E in a dose of 150 mg and 300 mg/kg of body weight, administered i.p., has a protective effect – in the course of the whole ontogenesis – against stagnant hypoxia induced in the laboratory rat by positive radial acceleration +10xg. The favourable influence of vitamin E is relatively greater in older animals.

Key words

Vitamin E – Brain ischaemia – Positive radial acceleration 10xg – Ontogenesis

Yamamoto *et al.* (1983) and Yoshida *et al.* (1985) demonstrated that vitamin E has a favourable effect in brain ischaemia as a non-enzyme antioxidant. Previously, we described a favourable effect of the i.p. administration of vitamin E to mature laboratory rats on their resistance to brain oligaemia induced by radial acceleration of +5xg (Trojan 1991). In this report we present the results of the experiment in which we studied the influence of vitamin E on the resistance to ischaemia induced by radial acceleration of +10xg at different stages of postnatal development.

Experiments were carried out on 375 laboratory rats of the Wistar strain of our own breed. They were fed a Velaz diet and kept at a temperature 23 ± 1 °C with regular illumination. The animals were 5, 12, 18 and 25 days old and the mature animals were 3 months old. Brain ischaemia (stagnant hypoxia) was evoked by radial acceleration of +10xg in the centrifuge (Trojan and Jílek 1967).

Maximum acceleration was attained within 3 s and braking lasted the same period of time. The animals were placed on the electrically heated pad after being taken out of the centrifuge and their respiration rate was monitored in case they breathed spontaneously. The criterion of survival was the irreversible respiratory arrest during stagnant anoxia (+10xg). We administered vitamin E in the form of Tocopherolum aceticum (Erevit, Biotika) i.p., 150 mg or 300 mg/kg of body weight one hour before the

animals were exposed to acceleration. These doses proved to be most effective against similar anoxia in mature rats (Trojan 1991). The results were evaluated according to Behrens and Schloss (1957) as LD₅₀.

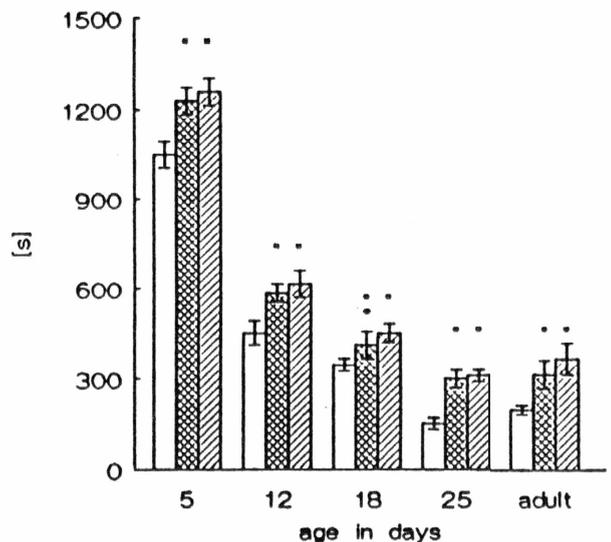


Fig. 1

Changes in the resistance of respiratory centre (in seconds) in laboratory rats of various ages to stagnant anoxia (acceleration +10xg) after of vitamin E administration (cross-hatched columns, 150 mg/kg; hatched columns, 300 mg/kg) 1 h before exposition.

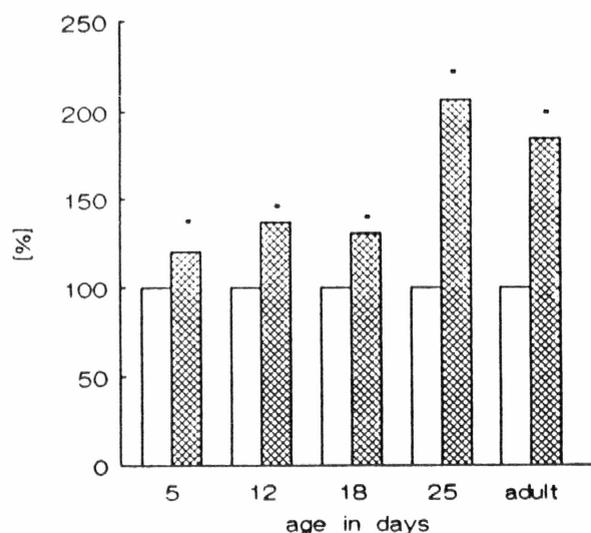


Fig. 2
Relative variations of the resistance of laboratory rats to stagnant anoxia (acceleration +10xg) after the administration of vitamin E (cross-hatched columns, 300 mg/kg) during postnatal ontogeny.

Vitamin E exerted a protective effect against stagnant anoxia during the entire ontogenesis; there

was no significant difference between the dose 150 or 300 mg/kg of vitamin E (Fig. 1). The favourable effect of vitamin E was relatively greatest in 25-day-old rats (Fig. 2).

The basic biological significance of vitamin E is to protect poly-non-saturated fatty acids (unctuuous acids) in the prosholipids of cell membranes against the activity of reactive oxygen products (Wilson 1983). The present experiments have demonstrated that high doses of vitamin E administered one hour before ischaemisation of the brain by means of positive radial acceleration 10xg significantly prolonged the survival of the respiratory centre of experimental rats. The result corresponds to the clinical findings with brain ischaemia (Yamamoto *et al.* 1983, Yoshida *et al.* 1985). The protective effect of vitamin E is obviously caused by the increased stability of cell membranes (Imaizumi *et al.* 1988). Thus the lower permeability of capillaries (Chiswick *et al.* 1983) and the direct antioxidant effect of tocoferol (Fukuzawa *et al.* 1985) should be taken into account. The fact that vitamin E is more effective in older animals with ischaemia can be explained as follows: the nervous tissue of mature and namely of 25-day-old rats has a lower ratio of anaerobic glycolysis to the whole energetic balance (Trojan and Štátný 1988) and hence the protection of oxygen metabolism can be more effective.

References

- BEHRENS B., SCHLOSSE L.: Beitrag zur Bestimmung der LD 50 der Berechnung ihrer Fehlerbreite. *Arch. Exp. Pathol. Pharmacol.* **230**: 59–68, 1957.
- CHISWICK M.L., JOHNSON M., WOODHALL C., GOWLAND M., DAVIES J., TONER N., SIMS D.: Protective effect of vitamin E on intraventricular haemorrhage in the newborn. In: *Biology of Vitamin E*, PORTER, J. WHELAN (eds), Ciba Found. Symp., Vol. 101, Pitman Press, London, 1983, pp. 186–197.
- FUKUZAWA K., TAKASE S., TSUKATANI H.: The effect of concentration on the antioxidant effectiveness of alfa-tocopherol in lipid peroxidation induced by superoxide free radicals. *Arch. Biochem.* **240**: 117–120, 1985.
- IMAIZUMI S., SUZUKI J., KINOCHI H., YOSHIMOTO T.: Superior protective effects of phenytoin against hypoxia in a pharmacological screening test. *Neurobiol. Res.* **10**: 18–24, 1988.
- TROJAN S.: Protective effect of vitamin E in stagnant hypoxia of the brain. *Physiol. Res.* **40**: 595–597, 1991.
- TROJAN S., JÍLEK L.: Methodical notes to the influence of radial acceleration on the central nervous system. In: *Some Problems of Aviation and Space Medicine*. M. MORÁVEK, J. DVOŘÁK (eds), Charles University, Prague, 1967, pp. 94–97.
- TROJAN S., ŠTÁSTNÝ F.: Hypoxia and the developing brain. In: *Handbook of Human Growth and Developmental Biology*. Vol. I., Part C, E. MEISAMI, P. TIMIRAS (eds), CRC Press, Florida, 1988, pp. 101–123.
- WILSON R.L.: Free radical protection: why vitamin E, not vitamin C, beta-carotene or glutathione? In: *Biology of Vitamins*, E. R. PORTER, J. WHELAN (eds), Ciba Found. Symp., Vol. 101, Pitman Press, London, 1983, pp. 19–44.
- YAMAMOTO M., SHIMA I., UOZUMI T., SOGABE T., YAMADA K., KAWASAKI T.: A possible role of lipid peroxidation in cellular damages caused by cerebral ischaemia and the protective effect of alfa-tocopherol administration. *Stroke* **14**: 977–982, 1983.
- YOSHIDA S., BUSTO R., WATSON B.D., SANTISO M., GINSBERG M.D.: Postischaemic cerebral lipid peroxidation in vitro: modification by dietary vitamin E. *J. Neurochem.* **44**: 1593–1601, 1985.

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