

〈特別講演〉

NO の 生 理 作 用

——活性酸素およびステロイドとの協調作用——

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Physiology of Nitric Oxide (NO)

—Co-evaluation with oxyradicals and steroids—

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Abstract

Brief review on patho-physiological role of NO, was followed with the presentation of our recent works. EDRF, which was proposed as smooth muscle relaxing factor in 1980, was proved to be NO in 1986. Muscle-relaxing action by NO through cGMP, had been reported in 1977. These three discoveries won Nobel Prize in 1998. Nitroglycerine, an explosive invented by Nobel, relax the blood vessels and rescues the attacks of angina pectoris through the formation of NO in the body. There are three types of NO synthases. Endothelial eNOS augument blood flow, neuronal nNOS works as signalling tool and retains the memory of the rodents. Inducible (i) NOS, attacks bacteria, tumor cells *etc.*, but also results in harmful sepsis, inflammation, arthriosclerosis, diabetes *etc.* NO acts together with oxyradicals (O_2^- , H_2O_2 , $\cdot OH$), not only on cell membrane lipids and functional proteins, but also as modulators of transcription factor in neucleus.

Natural antioxidants (tannic acid, α -tocopherol *etc.*) had no effect by itself on ischemic and histamine paw edema of mice in our recent studies. However, they fortified the suppressive effect of dexamethasone (Dex, 0.1 mg/kg). Relation among NO, oxyradicals and steroid could not be ignored. Glucocorticoid receptor (GR)-mediated anti-inflammatory proteins (vasoregulin *etc.*) synthesis must be controlled by NO and oxyradicals. Immunosuppressants (cyclosporin A, FK 506, rapamycin, deoxyspergualin) and a multifunctional cytokine, TGF- β_1 , accelerated, fortified and prolonged the suppression by low dose of Dex. NOS inhibitors, SOD, catalase *etc.* impaired these actions, suggesting that NO and/or oxyradicals are stimulating Dex action any where in the body. An elegant protocol considering the relation of NO, oxyradical and NO, might offer an interesting and beneficial data in the area of skin function studies.

Key words: nitric oxide (NO), oxyradicals, patho-physiology, natural antioxidant, steroid, immunosuppressant, TGF- β_1 , vasoregulin, ischemic paw edema.