

A DIET WHICH IS LOW IN SODIUM AND CONTAINS FISH OIL ENHANCES THE ANTIHYPERTENSIVE EFFECT OF ENALAPRIL, AN ANGIOTENSIN CONVERTING ENZYME (ACE) INHIBITOR, IN STROKE PRONE SPONTANEOUSLY HYPERTENSIVE RATS (SHRSP)

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The genetically pre-determined development of hypertension in SHRSP can be prevented by chronic oral administration of enalapril (25mg/kg/day) from an early age (Black et al. 1989). By feeding SHRSP a diet containing 5% MaxEPA, a fish oil rich in n-3 fatty acids, a more modest attenuation of the development of hypertension is achieved but this hypotensive effect can be counteracted by increasing dietary sodium (Na) intake (Howe et al. 1989). We have now examined whether diets which are low in Na and contain fish oil can enhance the antihypertensive effect of enalapril.

Thirty five SHRSP were divided into five groups and fed different diets from four weeks of age for 15 weeks. The control group were fed a synthetic diet containing 5% (by dry weight) olive oil and normal (0.2%) Na. The other 4 groups were given a sub-maximal dose of enalapril (2.5mg/kg/day) in their drinking water and were fed diets containing either 5% olive oil, with normal or low (0.04%) Na, or 5% fish oil (NIH, containing 80% n-3 fatty acid ethyl esters), with normal or low Na. The progressive rise of blood pressure (BP) with age was monitored by the indirect tail-cuff method and the rate of rise was determined by linear regression analysis of fortnightly measurements. Finally, aortic catheters were implanted for direct measurement of mean arterial pressure (MAP) in conscious, unrestrained animals.

Group	Treatment	Tail-cuff BP (mm Hg)		Rate of rise (mm Hg/week)	MAP (mm Hg)
		Initial	Final		
1	Untreated + Olive oil/normal Na	98 ₊₆	190 ₊₈	8.4 _{+0.6}	161 ₊₅
2	Enalapril + Olive oil/normal Na	98 ₊₂	142 _{+2^a}	4.3 _{+0.2^a}	130 _{+4^a}
3	Enalapril + Olive oil/low Na	94 ₊₄	141 ₊₂	4.2 _{+0.2}	130 ₊₄
4	Enalapril + Fish oil/normal Na	98 ₊₅	127 _{+2^b}	2.8 _{+0.3^b}	123 ₊₂
5	Enalapril + Fish oil/low Na	96 ₊₆	107 _{+2^c}	1.1 _{+0.4^c}	112 _{+2^d}

Values are means \pm SEM (n=7). Superscripts denote significant differences (a) from group 1, (b) from group 2, (c) from group 4 ($p < 0.01$) and (d) from group 4 ($p < 0.05$), Student's t-test.

The tail-cuff BP measurements demonstrated a steady rise in BP of 8mm Hg per week in the untreated SHRSP during the period of observation. Chronic administration of a sub-maximal dose of enalapril attenuated the development of hypertension in the young SHRSP. This antihypertensive effect was enhanced by adding fish oil to the diet but not by lowering Na intake. However, when enalapril was combined with a diet low in Na and containing fish oil, the development of hypertension was almost completely suppressed. Observations made by the tail-cuff method were confirmed by intra-arterial BP recordings.

The results suggest that the combination of two dietary measures (viz. sodium restriction and fish oil supplementation) may benefit patients being treated for hypertension with an ACE inhibitor in that it may be possible to reduce the dose of drug required for the management of their blood pressure.

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