DECLINE IN PREVALENCE OF DD GENOTYPE IN HYPERTENSIVE PATIENTS WITH AGE. B Cheung, C P Lau, C R Kumana. University Department of Medicine, the University of Hong Kong, Hong Kong

An insertion/deletion polymorphism in the angiotensin-converting enzyme (ACE) gene has been linked to the risk of myocardial infarction. Hence, ACE genotype was determined in 75 patients attending the hypertension clinic. Genomic DNA was extracted from peripheral leucocytes and amplified by PCR using standard primers and conditions. Insertion (I) and deletion (D) alleles were identified as distinct bands after polyacrylamide gel electrophoresis. A significant correlation between ACE genotype and age was found ($p = 0.03$).

Age	n	DD	ID	II
<50	28	21%	39%	39%
50-59	16	6%	44%	50%
≥60	31	3%	32%	65%

These results confirm and extend those of Morris *et al.* (J Clin Invest 1994; 94: 1085-9), who found that in patients with severe early-onset familial hypertension, there was a decline in the proportion of DD genotype with age, and raise the possibility that the DD genotype may increase the risk of premature death, at least in the population studied.

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DOSE-DEPENDENT GLUCOCORTICOID REGULATION OF HYPOTHALAMIC SOMATOSTATIN, GROWTH HORMONE RELEASING HORMONE AND THEIR PITUITARY RECEPTORS. KSL Lam*, SP Tam & G Srivastava[1]. Departments of Medicine and Pathology[1], The University of Hong Kong, Queen Mary Hospital, Hong Kong.

Glucocorticoid excess inhibits somatic growth, acting in part via a reduction in growth hormone (GH) secretion, with impaired GH responses to various physiological stimuli being observed in man as well as in the rat. In this study, we investigated whether such inhibition of GH secretion was mediated via changes in the gene expression of hypothalamic somatostatin (SS), growth hormone releasing hormone (GHRH) and their pituitary receptors.

Male rats, 6 weeks of age, were treated with injections of either saline or varying doses of dexamethasone (40, 200, 500 or 1000 μg/kg/d) ip for 3 or 8 days before they were sacrificed by rapid decapitation and their hypothalami and pituitaries obtained for mRNA measurement using Northern hybridization, slot blot hybridization or in-situ hybridization. Dexamethasone treatment for 3 days was not associated with any significant change in total hypothamic SS mRNA content. However, a dose-dependent significant increase ($p<0.01$) in SS mRNA levels was found in hypothalamic fragments consisting predominantly of the paraventricular and periventricular nuclei. In-situ hybridization confirmed this increase to be present in the periventricular nucleus. A dose-dependent reduction in hypothalamic SS mRNA content ($p<0.01$) was seen in rats treated for 8 days, in keeping with previous reports of enhanced SS mRNA degradation following prolonged high dose dexamethasone treatment in vitro. Pituitary mRNA levels of the SS receptor subtype SSTR2 showed a dose-dependent reduction ($p<0.001$) following 3 or 8 days of dexamethsone treatment. On the other hand significant dose-dependent reductions in total hypothalamic GHRH mRNA levels ($p<0.01$) were accompanied by significant increases in pituitary GHRH receptor mRNA levels ($p<0.001$) irrespective of the duration of dexamethasone treatment.

We concluded that the inhibitory effect of glucocorticoid excess on GH secretion was mediated, at least in part, via a reduction in hypothalamic GHRH gene expression. A reduction in SS gene expression in the periventriculat nucleus also contributed to the GH inhibition in rats with shorter duration of glucocorticoid excess.