THE ROLE OF TESTICULAR ADENYLATE CYCLASE IN THE HYPOGONADISM OF RENAL INSUFFICIENCY

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Hypergonadotrophic hypogonadism has been found commonly in uraemic man. Absolute free testosterone levels are low in the face of elevated hypo-physisal gonadotrophins, pointing to testicular gonadotrophin resistance in uraemia [1,2].

Since the effect of hCG on testicular steroidogenesis is mediated by an adenylate cyclase system [3], basal and hCG stimulated-cAMP levels were studied in the testes of prepubertal rats.

Methods

Infantile (30-40 g b.w.) male Wistar rats underwent nephrectomy (NX) or sham operation (Co) 24 hours prior to the experiment. Human chorionic gonadotrophin (hCG) was administered intravenously. After 30 minutes, testes were removed and quickly frozen for determination of cAMP (by radioimmunoassay) and of protein kinase activity.

Results

Figure 1 shows that basal cAMP levels in NX animals (4.4 ± 1.0 pmol/mg protein) were not significantly different from controls (4.6 ± 0.8). However, after stimulation with submaximal doses of hCG (5IU) cAMP response in uraemic animals was impaired (NX: 20.0 ± 3.1, Co: 51.2 ± 7.8, p<0.01). At a maximal dose of hCG (50IU) this difference was abolished (NX: 69.1 ± 9.7, Co: 72.7 ± 10.2). In a similar way, cAMP - dependent protein kinase activity ratio (-cAMP / + cAMP ; i.e. protein kinase activity in the absence or presence of exogenous cAMP added in vitro) was significantly different only at 5 IU hCG (NX: 0.76 ± 0.06, Co: 0.57 ± 0.03 p<0.01), whereas basal (NX: 0.4 ± 0.04, Co: 0.43 ± 0.03) and maximally stimulated protein kinase activity (NX: 0.8 ± 0.02; Co: 0.77 ± 0.08) were not significantly different. (Figure 2). In addition, phosphodiesterase activity was not influenced by uraemia.
Figure 1. Effect of hCG stimulation on cAMP generation in the testes of prepubertal uraemic rats in vivo.

Figure 2. Effect of hCG stimulation on protein kinase activity ratio in the testes of prepubertal uraemic rats in vivo.
Discussion

These results demonstrate decreased cAMP levels after hCG stimulation in acute experimental uraemia. This may be relevant for the finding of impaired testicular steroidogenesis despite elevated hypophyseal gonadotrophins, as seen in chronic renal failure in man. Moreover, unresponsiveness to exogenous hCG in uraemic males [1] may be explained by such end organ resistance due to diminished testicular cAMP generation.

The reduced testicular cAMP response to hCG in the face of unchanged phosphodiesterase activity in uraemia points to an alteration of the adenylate cyclase system or steps prior to it, e.g. changes at the receptor level.

References

3 Dufau, ML, Watanabe, L and Catt, KH (1973) Endocrinology, 92, 6-11