Testosterone inhibition of growth hormone release stimulated by a growth hormone secretagogue

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Anabolic steroids are frequently taken by athletes and bodybuilders together with recombinant human GH (rhGH), though there is some scientific evidence that the use of anabolic steroids reverses the rhGH-induced effects. Recently, we have shown that treatment with rhGH (0.2 IU/kg s.c., daily x 12 days) in the dog markedly reduced the canine GH (cGH) responses stimulated by EP51216, a GH secretagogue (GHS), evaluated after 3 and 5 daily rhGH injections, and that the inhibition was still present a few days after rhGH discontinuation.

The aim of the present study was to evaluate in the dog the GH response to EP51216 (125 µg/kg i.v.) in a condition of enhanced androgenic function (i.e. acute injection or 15-day treatment with testosterone at the dose of 2 mg/kg i.m. on alternate days), and in the hypophysectomized rat the hypothalamic and hippocampal expression of ghrelin, the receptor of GHSs (GHS-R), GH-releasing hormone (GHRH) and somatostatin (SS) after specific hormonal replacement therapies (testosterone, 1 mg/kg/day s.c.; hydro-cortisone, 500 µg/kg/day s.c.; rhGH, 400 µg/kg/day s.c.; 0.9% saline 0.1 ml/kg/day s.c.; x 11 days). In the dog experiments, under baseline conditions, a single injection of EP51216 elicited an abrupt rise of plasma cGH. Twenty-four hours from the acute bolus injection of testosterone, C max and AUC 0–90 of the GHS-stimulated cGH response were significantly lower than baseline cGH response; 5 days later, there was still a significant decrease of either parameter versus the original values. Short-term treatment with testosterone markedly reduced the GHS-stimulated cGH responses evaluated during (5th bolus) and at the end (8th bolus) of testosterone treatment. Four and 8 days after testosterone withdrawal, the EP51216-stimulated cGH response was still significantly reduced when compared with that under baseline conditions. Plasma concentrations of insulin-like growth factor 1 (IGF-1) were stable until the 5th bolus of testosterone and decreased progressively in the remaining time of the testosterone treatment; 4 and 8 days from treatment withdrawal, IGF-1 levels were still suppressed. In rat studies, hypothalamic mRNA levels of GHS-R were significantly reduced by treatments with testosterone and hydrocortisone, whereas hippocampal expressions of ghrelin, GHRH and SS were reduced by rhGH replacement therapy. In conclusion, these studies show that a single administration of testosterone can abrogate the cGH response ensuing acute stimulation by a GHS; the inhibitory effect of testosterone on the cGH response to GHS is present during and even 8 days after termination of a short-lived treatment with testosterone; these events occur via a downregulation of hypothalamic GHS-R.