patients with mUFC ≤ ULN at month 7 in patients who did not uptitrate at month 4; changes in UFC, plasma ACTH, and serum cortisol; changes in quality of life, and signs and symptoms of Cushing's disease; tolerability and safety.
Conclusions
This phase III study will provide the basis for the evaluation of long-acting pasireotide as a medical therapy for patients with mild-to-moderate Cushing's disease.
Declaration of interest
The authors declare that there is a conflict of interest.
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Steroid metabolism + action

P1543

Anti-inflammatory effect of a high dose of corticosteroids is associated with some paradoxical pro-inflammatory effects

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We have previously demonstrated that a low dose of hydrocortisone (100 mg) given intravenously suppresses intranuclear NFκB and AP-1 binding and the expression of pro-inflammatory genes like MMPs. We have now investigated the effect of a high dose of hydrocortisone (300 mg = 60 mg prednisolone) on NFκB binding and the expression of TLRs, the mediators of TLR signal transduction, MyD88 and TRIF and HMG-B1. Ten normal subjects were injected intravenously with 300 mg of hydrocortisone or saline in 2 separate visits one week apart in a randomized crossover study. Blood samples were obtained at 0,2,4,8 and 24 h after the injection. Mononuclear cells (MNC) were prepared by standard techniques and were tested for NFκB binding and the expression of TLRs, MyD88, TRIF, chemokines and chemokine receptors and HMG-B1. Plasma concentrations of glucose, FFAs, NO metabolites, chemokines and HMG-B1 were also measured. Following the injection of this dose, there was a significant increase in glucose concentration from 92 ± 4 to 116 ± 6 mg/dl, a marked increase in FFA concentrations from 0.38 ± 0.1 to 0.804 ± 0.15 mM. While NFκB binding and the mRNA expression of MyD88, TRIF, chemokines and chemokine receptors was suppressed significantly in MNC, the mRNA expression of TLR 2, TLR 9 and HMG-B1 was increased (by 103 ± 24%, 107 ± 19%, 56 ± 13% above baseline, respectively) in the MNC as was the concentration of HMGB1 (by 78 ± 12%) and MMP-9 (125 ± 22%) in plasma. Thus, while this high dose of HC has a powerful anti-inflammatory effect as shown above, it also exerts certain paradoxical pro-inflammatory effects. Since both glucose and FFAs have been shown to be pro-inflammatory, it is possible that they contribute to these effects. These paradoxical pro-inflammatory effects may account for the inability of these drugs to show benefit in clinical trials of septicemia and other severe pro-inflammatory states.
Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research project.
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P1544

Acute and chronic effects of low dose prednisolone on carbohydrate metabolism in subjects with inflammatory rheumatologic disease

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Large glucocorticoids reduce hepatic and peripheral insulin sensitivity and insulin secretion. However, the metabolic consequences of typical therapeutic corticoid doses (e.g. prednisolone < 10 mg/day) are poorly characterised. We was to determine the acute effect of low dose prednisolone on carbohydrate metabolism and then assess whether subjects taking chronic prednisolone had increased adiposity that amplified carbohydrate metabolism perturbations.
Controls (4 female, age 58 ± 11 years, BMI 27.5 ± 5.8 kg/m^2) with inflammatory rheumatologic disease who were not taking oral glucocorticoids were studied before and after prednisolone 6 mg/day for 7 days. Baseline data were compared with 12 matched subjects (6 female, age 61 ± 8 years, BMI 27.4 ± 3.3 kg/m^2) taking long-term prednisolone (6.3 ± 2.2 mg/day). Peripheral insulin sensitivity was assessed by hyperinsulinaemic–euglycaemic clamp (80 mU/m^2 per min for 120 min) and insulin secretion by 60 min intravenous glucose tolerance test (IVGTT, 25mg/kg glucose). Total and visceral adiposity were quantified by DXA and abdominal CT. Quantification of hepatic glucose output (using 6,6-$^2H_2$ glucose) and insulin concentrations are underway (data to follow).
Glucose infusion rate during hyperinsulinaemic–euglycaemic clamp fell from 79.6 ± 5.9 to 68.9 ± 5.2 μmol/min per kg FFM ($P = 0.02$) after 7 days of prednisolone. Glucose AUC during IVGTT acutely increased after prednisolone (504 ± 14 to 579 ± 19 mmol/L*min, $P = 0.01$). There were no significant differences in total (27.8 ± 2.8 vs 26.5 ± 3.8 kg, $P = 0.78$) or visceral (97 ± 11 vs 108 ± 27 cm^2, $P = 1.00$) fat mass between chronic prednisolone users and controls. Glucose infusion rate during hyperinsulinaemic–euglycaemic clamp (68.7 ± 6.6 vs 68.9 ± 5.2 μmol/min per kg FFM, $P = 0.78$) and glucose AUC during IVGTT (564 ± 18 vs 579 ± 19 mmol/l*min, $P = 0.67$) were not significantly different in subjects taking chronic prednisolone and following acute prednisolone administration.
In conclusion, low dose prednisolone acutely reduces peripheral insulin sensitivity and may reduce insulin secretion. Perturbations of carbohydrate metabolism during chronic prednisolone therapy match those found acutely. These findings provide insight into targeting treatment of glucocorticoid-induced diabetes at the underlying metabolic abnormality.
Declaration of interest
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P1545

The influence of aromatizable and non-aromatizable steroids on anthropometric parameters

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Objective
It is known sex steroids affect fat distribution with men and women. With men there is a tendency to deposit fat abdominally. Men are more likely to have more visceral fat than premenopausal women, with whom the preferential fat distribution is gluteofemoral and the percentage of body fat overall higher. Androgens may affect fat tissue with men either directly by androgen receptor stimulation, or indirectly by oestrogen receptor stimulation after aromatization. Interesting relationships between the parameters of metabolic syndrome and non-aromatizable metabolites of testosterone have been discussed in literature.
Aim of the study
The analysis of the relation between anthropometric parameters, lipid spectrum, glycemia, insulin resistance and the level of testosterone and dihydrotestosterone.
Methods
We examined a set of 195 men and determined their testosterone, dihydrotestosterone, SHGB, lipid spectrum, glucose metabolism parameters and the oral glucose tolerance test; also measured were their anthropometric parameters (weight, height, waist, hips, waist to hip ratio, 14 skin folds) and body composition was calculated.
Results
Comparing the hormone levels and anthropometric parameters, we found a negative correlation between weight, skin folds, waist, hips, waist to hip ratio, BMI, total cholesterol, LDL cholesterol and insulin resistance on one side and the level of both testosterone (T) and dihydrotestosterone (DHT5α) and SHBG on the other side. We found a positive correlation between HDL cholesterol and muscle mass on one side and the T, DHT levels and SHBG on the other side.
Conclusions
We found a negative relation between anthropometric parameters and both testosterone and dihydrotestosterone. We did not find any difference between aromatizable and non-aromatizable steroids with healthy, normosthenic men.
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Declaration of interest
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