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Thyroid dysfunction and Klinefelter syndrome: a multicenter study from the KING group

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Introduction

Data from the literature have suggested that thyroid abnormalities may be a common feature of Klinefelter syndrome (KS). The patients seem to have inadequate hypothalamic-pituitary control of thyroid and secondary thyroid insufficiency may be part of the KS phenotype.

Aim

To clarify if this feature is related to the 47XXY condition or to other factors, such as the influence of hypogonadism on hypothalamic-pituitary control of thyroid, we planned to study the thyroid function in KS and in non-KS hypogonadal patients. Exclusion criterion was secondary hypothyroidism.

Methods

A case-control, multicenter study from KING group enrolled 158 KS and 61 non-KS hypogonadal men was structured. The primary outcome was the prevalence of thyroid diseases in KS and in non-KS. Changes in hormonal, and ultrasound parameters were evaluated. Exclusion criterion was secondary hypothyroidism. Analyses were performed using Student's t test. TSH and testosterone were analyzed using Mann-Whitney test and, for TPO antibodies, chi-square test .

Results

KS and non-KS presented similar TSH [1.61 (1.1 - 2.3) vs 1.75 (1.35 - 2.72) mcUI/ml] and testosterone [262 (150 - 426) vs 217 (144 - 388.8) ng/dl] levels. Hashimoto's thyroiditis (HT) was diagnosed in 6,5% of KS. Five KS developed hypothyroidism. FT4 was significantly lower in KS vs non-KS [10.6 (0.2) vs 11.7 (0.4) ng/dl, p< 0,001], but the ratio FT3/FT4 was similar in KS vs. non-KS. TSH index was 1,9 in KS and in non-KS was 2,13. Adjustment for differences in age, sample size and concomitant disease in multivariate models did not alter the results.

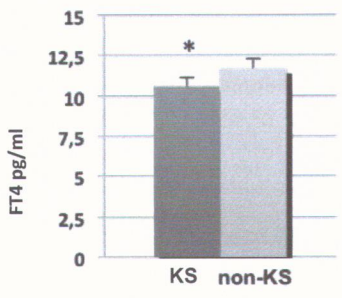

Fig. 1 – Correlation between FT4 levels in KS vs non-KS
*** p<0,001**

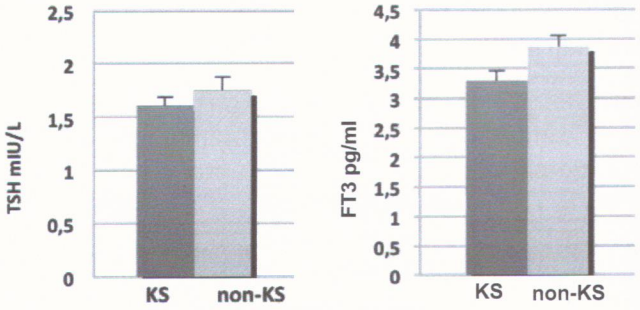

Fig. 2–TSH and FT3 levels in KS vs non-KS

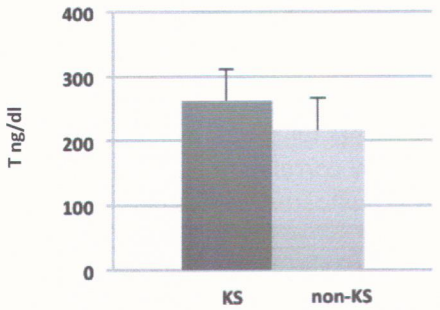

Fig. 3– Correlation between testosterone levels in KS vs non-KS

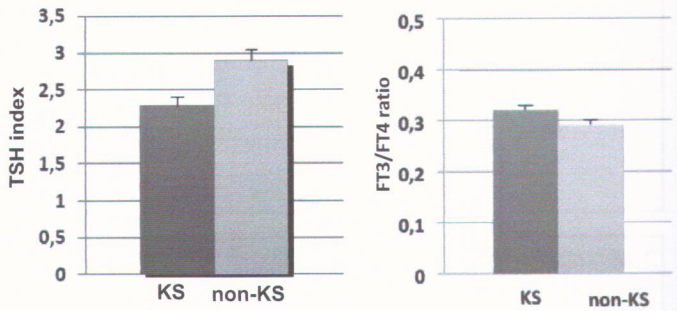

Fig. 4– Correlation between TSH index and FT3/FT4 ratio in KS vs non-KS

Conclusions

We found an altered FT4 production in KS, suggesting a deiodinase impairment, with no evidence of etiopathogenetic link to hypogonadism, or change in the set point of thyrotrophic control. All these results indicate that the thyroid dysfunction here described is a specific feature of KS, not to be underestimated.

References

Bjørn AM, Bojesen A, Gravholt CH, Laurberg PJ. Hypothyroidism secondary to hypothalamic-pituitary dysfunction may be part of the phenotype in Klinefelter syndrome: a case-control study. *J Clin Endocrinol Metab*. 2009;**94**(7):2478-2481.