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8567

Clinical Use of the Androgen Receptor Sensitivity CAG Repeat Polymorphism to Refine and Improve the Diagnosis of Male Hypogonadism

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Male hypogonadism is a syndrome comprising symptoms and biochemical evidence of testosterone (T) deficiency. The

prevalence of male hypogonadism differs due to different cut-offs in total T (TT) levels used by different guideline committees. TT is a combination of three T sub-fractions: Free T (FT), albumin-bound T, and SHBG-bound T . The FT and albumin-bound T are biologically active (BioT). The biological effects of androgenisation are not only dependent on circulating testosterone but also on the sensitivity of the androgen receptor (AR). The AR sensitivity correlates negatively with the number of CAG repeats in exon 1 of the AR gene (normal range 9 - 37 repeats). The objective of the study was to compare hypogonadal symptoms with the TT:CAG, BioT:CAG, and FT:CAG ratios compared to TT, BioT and FT alone as biochemical tests for the diagnosis of hypogonadism. All blood samples were taken fasting in the morning before 1100h. Subjects were divided, regardless of testosterone level, into Group 1 (G1) (N = 25), those with symptoms of hypogonadism; and Group 2 (G2) (N = 15), those without symptoms of hypogonadism. The Aging Male Symptom (AMS) score was used for symptom assessment. The Receiver Operating Characteristic (ROC) Curve Analysis was generated where testosterone levels (TT, BioT, FT) and TT:CAG and BioT:CAG, and FT:CAG ratios were used as variables. **Results:** Mean age (years) in G1 and G2 were 55.8 ± 2.0 (range 33 - 74) and 65.3 ± 2.7 (range 48 - 80), respectively. Mean values in ng/dl are included in square brackets after ranges. Mean TT (nmol/L), BioT (nmol/L) and FT (pmol/L) levels in G1 were 8.54 ± 0.48 (range 4.7 - 13.5)[246.3ng/dl], 2.83 ± 0.13 (range 1.86 - 4.28)[81.62ng/dl], and 189.2 ± 9.8 (range 95 - 300)[5.45ng/dl], respectively. Mean TT, BioT and FT levels in G2 were 15.41 ± 1.69 (range 6.4 - 29.5)[444.45ng/dl], 4.24 ± 0.34 (range 2.19 - 6.55)[122.9ng/dl], and 241.7 ± 18.5 (range 133 - 387)[6.97ng/dl], respectively. Mean AR CAG in G1 and G2 were 21.2 ± 0.7 (range 14 - 27) and 22.4 ± 0.6 (range 16 - 26), respectively. The ROC Curve showed that the area under the curve (AUC) for diagnosing male hypogonadism was the greatest for FT:CAG (.317), followed by FT (.289), BioT/CAG (.208), TT/CAG (.187), BioT (.173), and TT (.164). This exploratory study found that the TT:CAG, BioT:CAG and FT:CAG ratios compared to TT, BioT and FT alone may be better biochemical tests for diagnosis of Male Hypogonadism. The higher the value of the ratios the greater the biological androgen status is. Moreover, it could potentially provide a more accurate test to diagnose men with hypogonadism.

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