

Topic: G. Testosterone Deficiency Syndrome

CONTINUOUS IMPROVEMENTS OF FEATURES OF THE METABOLIC SYNDROME OVER 48 MONTHS UPON NORMALIZATION OF SERUM TESTOSTERONE IN THREE COHORTS, IN TOTAL 410 MEN.

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Purpose: Men with lower-than-normal serum testosterone often show features of the metabolic syndrome. This study tested the effects of normalization of testosterone over a period of 48 months in three cohorts of men, studied in three different German clinics, following the same treatment protocol.

Materials and methods: The study was an observational uncontrolled study. Cohort 1 (Muenster), consisted of 281 men of whom 137 hypogonadal men (aged 40 ± 13 years) were followed up for 48 months. Of the total of 281, 59 men had late onset hypogonadism (LOH). Cohort 2 (Bremerhaven) consisted of 143 men, aged 34-78 years (mean \pm SD: 62 ± 8 yrs), of whom 119 had LOH. Cohort 3 (Norderstedt) consisted of 130 men aged 46-79 years (mean \pm SD: 61 ± 9 yrs) of whom 104 had LOH. The cut-off point for inclusion in the study was serum testosterone <12 nmol/L.

The three cohorts were treated with parenteral testosterone undecanoate for 48 months as the sole intervention. Statistical analysis: (STATA (Stata Corp, College Station, Texas, USA): linear mixed model for longitudinal data.

Results: Plasma levels of testosterone rose from a range of 5.6- 9.7 to a range of 15.4- 19.0 nmol/L upon testosterone treatment, reaching their maximum at 9 months and remaining stable over the next 33 months. There was a remarkable progressive decline of body weight and waist circumference over the entire study period, most notably over the first 24 months. Plasma cholesterol, triglyceride, and LDL-cholesterol decreased significantly over the study period. Plasma HDL increased significantly over the first 24 months and then declined in cohort 2 but increased over 48 months in cohorts 1 and 3. Plasma glucose declined over the first 12-18 months and then stabilized. Systolic blood pressure declined over 48 months in cohort 1 and 2 and declined over 24 months to stabilize thereafter in cohort 3. In cohort 1 at baseline 240/281 men fulfilled the harmonized criteria of the metabolic syndrome¹, falling to 114/281 after two years. At baseline 88/143 men in cohort 2 and 93/130 men in cohort 3 met the criteria of the metabolic syndrome by the harmonized definition. After 48 months of testosterone treatment this number had declined to 48/143 in cohort 2 and to 62/130 in cohort 3.

Conclusion: In men with hypogonadism testosterone treatment over 48 months, normalizing testosterone levels to the mid-normal range led to an improvement of features of the metabolic syndrome. The improvements in the younger men with 'classical' primary or secondary hypogonadism (cohort 1) were of a similar magnitude as in men with LOH (cohorts 2 and 3). The most significant improvement of variables of the metabolic syndrome was noted over the first 12-24 months with further improvement over the following 24-36 months. Body weight and waist circumference declined further paralleled by improvements of cholesterol, LDL and triglycerides and systolic/diastolic blood pressure.

Reference: Alberti KGMM et al., Harmonizing the Metabolic Syndrome; Circulation 2009; 120: 1640-1645