

**Maximum: 500 words.presently 422 words**

**Effects of 4 Year Testosterone Treatment on Weight, Waist Circumference and Other Features of the Metabolic Syndrome**

**Topic: Metabolic syndrome, Diabetes, Obesity**

**Objective: Obesity negatively affects almost every aspect of health and its treatment is largely unsuccessful. Obesity is associated with low serum testosterone (T), and, conversely, low T leads to weight gain and the metabolic syndrome. This study tested the effects of normalization of testosterone in men with T deficiency.**

**Methods: 104 hypogonadal men (38 – 83 years, mean  $60.6 \pm 8.0$  years), with testosterone levels between  $0.14 - 4.51$  ng/mL ( $N > 4.90$  ng/ml) were treated with parenteral testosterone undecanoate for 4 years as the sole intervention.**

**Results: Plasma testosterone rose from  $3.3 \pm 1.9$  ng/mL to  $4.1 \pm 1.5$  ng/mL ( $P < 0.01$ ) at 3 months, then stabilized at  $6.8 \pm 1.3$  ng/mL after the first 6 months. Results at respectively 0, 24 and 48 months are presented. Statistically significant differences between 0 and 24 months\*, between 24 and 48 months#. There was a remarkable progressive linear decline of body weight ( $107.6 \pm 16.2$ ,  $99.1 \pm 13.6^*$ ,  $94.3 \pm 11.0\#$ ), waist circumference ( $109.1 \pm 10.0$ ,  $103.4 \pm 8.7^*$ ,  $100.9 \pm 7.7\#$ ), serum cholesterol ( $297.7 \pm 37.7$ ,  $197.4 \pm 21.1^*$ ,  $194.5 \pm 14.2\#$ ), triglyceride ( $290.4 \pm 54.6$ ,  $198.9 \pm 29.2^*$ ,  $194.2 \pm 16.2\#$ ), LDL-cholesterol ( $160.4 \pm 42.7$ ,  $121.1 \pm 37.8^*$ ,  $118.3 \pm 34.7\#$ ) and C-reactive protein ( $7.1 \pm 9.3$ ,  $3.3 \pm 4.7^*$ ,  $1.6 \pm 2.6\#$ ) over the 4 year period. Plasma glucose ( $105.8 \pm 18.4$ ,  $96.2 \pm 12.0^*$ ,  $97.0 \pm 3.7$ ) declined over the first 18 months. There was a significant decrease of levels of serum aspartate aminotransferase (AST) ( $43.9 \pm 18.6$ ,  $22.0 \pm 6.5^*$ ,  $21.6 \pm 3.9$ ) and alanine aminotransferase (ALT) ( $46.6 \pm$**

20.1,  $22.8 \pm 7.7^*$ ,  $21.3 \pm 5.0$ ) over the first 24 months, then values leveled off. Both systolic ( $157.6 \pm 15.2$ ,  $142.7 \pm 12.0^*$ ,  $141.4 \pm 11.3$ ) and diastolic ( $95.7 \pm 11.0$ ,  $83.1 \pm 8.4^*$ ,  $81.9 \pm 7.7$ ) blood pressure decreased over the first 30 months.

**Conclusions:** With testosterone treatment over four years, the most significant improvement of obesity and features of the metabolic syndrome, including blood pressure, was noted over the first 24 months but over the following 24 months improvements were at least maintained or even improved further. Decreases in AST and ALT are likely to indicate improvement of non-alcoholic fatty liver disease. Testosterone treatment of hypogonadal obese men may be a viable option in weight management.

**Keywords:** late onset hypogonadism, testosterone, metabolic syndrome