Side effect profile of long-term treatment of elderly hypogonadal men with testosterone undecanoate

A Haider, F Saad

Introduction: Testosterone therapy for hypogonadal men has been used for decades. However, there are still concerns regarding the safety of this treatment, particularly in elderly men.

Methods: Prospective registry study of 255 men (mean age 60.6 ± 8.0 years), with testosterone levels between ≤ 3.5 ng/ml. They received parenteral testosterone undecanoate 1000 mg at day 1, week 6 and every 12 weeks thereafter for up to 66 months.

Results: After 60 months the following changes were observed:
Erythropoiesis: haemoglobin increased from14.44 ± 0.72 to 14.99 ± 0.45 g/dl ($p<0.0001$ vs baseline). Haematocrit increased from 43.22 ± 2.84 to 48.78 ± 1.7% ($p<0.0001$ vs baseline). Four patients had haematocrit levels > 52% which resolved without intervention.
Prostate: PSA increased from 1.77 ± 0.96 to 1.82 ± 0.96 ng/ml ($p<0.0001$ vs baseline) with a plateau after 24 months. Prostate volume increased from 28.51 ± 11.2 to 30.23 ± 12.4 ml ($p<0.0001$ vs baseline). 3/255 patients were diagnosed with prostate cancer following elevated PSA (< 4 ng/mL) at 18 weeks of treatment. Tumour grade was T2 in all three and Gleason score 3+3 in two and 3+2 in one patient, resp. They all underwent radical prostatectomy. The proportion was 1.18% with an incidence of 30.334 per 10.000 patient years. For comparison: in the PLCO trial with a 7-year follow-up, the proportion of prostate cancer was 7.35% with an incidence of 116 per 10.000 patient years [1], in the ERSPC trial with a follow-up of 11 years, 96.6 [2]. – The International Prostate Symptom score (IPSS) improved from 6.73 ± 4.21 to 2.83 ± 1.25 ($p<0.0001$).
Liver enzymes: aspartate transaminase (AST) decreased from 43.05 ± 17.29 to 20.16 ± 3.21 U/L ($p<0.0001$ vs baseline) reaching a plateau after 24 months, alanine transaminase (ALT) from 43.89 ± 18.11 to 20.54 ± 3.92 U/L ($p<0.0001$ vs baseline) with a plateau after 36 months.

Conclusions: The incidence of 3/255 patients with prostate cancer does not suggest an increased risk of prostate cancer in elderly men on long-term testosterone treatment. Long-term treatment with testosterone undecanoate with monitoring according to the guidelines is acceptably safe.

References:
[1] Andriole G et al. New Engl J Med 2009; 360(13): 1310-1319
[2] Schröder F et al. New Engl J Med 2012; 366(11): 981-990