The controversy around testosterone therapy

By Kalli Spencer

Like the ageing woman develops menopause due to the waning levels of oestrogen so too does the ageing man develop andropause or testosterone deficiency. Some men remain symptom free despite this change while others develop significant symptoms. These symptoms may include mood changes (depression), memory and sleep disturbances and lower energy levels. This condition may result in osteoporosis (increased risk of fractures), anaemia, loss of libido, sexual dysfunction and increased risk of metabolic syndrome (diabetes, cardiovascular disease, stroke, high cholesterol). Many other conditions can cause this group of symptoms and thorough investigation by a general practitioner is required. If a diagnosis is confirmed, then referral to an endocrinologist (doctor who manages conditions related to hormones) is required for testosterone replacement therapy.

As discussed in numerous blogs up until now, testosterone is thought to drive the growth and spread of prostate cancer. This is why androgen deprivation therapy is used to starve the cancer of testosterone by blocking its production and effect in those with advanced stages of disease or in combination with radiation therapy. However, the testosterone therapy used as treatment for testosterone deficiency is different to the testosterone naturally found in the body. For almost 80 years it has been believed that testosterone therapy could cause progression of cancer in those not diagnosed with prostate cancer yet or worsening of disease in those already diagnosed. Emerging evidence over the last decade says otherwise.

Morgentaler and Traish found that prostate cancer grows despite having low testosterone levels such as in those who are medically or surgically castrated or on oestrogen treatment[1]. Its also been shown that raising serum testosterone levels did not raise testosterone levels within the prostate[2]. Reports from men treated with testosterone therapy for localised cancer have shown low to absent recurrence rates[3]. Natale et al reported that those treated previously with either radical prostatectomy or radiation therapy don't seem to have an elevated risk of cancer recurrence or progression because of testosterone therapy[2]. Some evidence even suggests that a low testosterone state may have adverse effects on oncological outcomes with another study suggesting that bipolar androgen treatment may even be used to control prostate cancer through normalisation of testosterone concentrations[4]. Current thought is based on the saturation model which postulates that prostate cancer response to variations in testosterone levels at castration or near castration range reaches a point of maximal prostate stimulation beyond which further increases produce little or no further effect on the prostate[4].

Testosterone therapy still remains controversial and a careful approach should be considered balancing risk of cancer with undue harm caused by failing to address sexual health, metabolic, cardiovascular, and other effects of testosterone deficiency. There is a need for long-term large-scale placebo-controlled trials to definitively assess the safety of this therapy but in the interim a useful set of guidelines may include[5]:

1) Clinicians should confirm that the clinical history is consistent with a laboratory diagnosis of testosterone deficiency

2) Disclosure that there are limited data confirming testosterone safety and that the true risks are unknown
3) Confirm that there are no medical contraindications to therapy (e.g erythrocytosis [High red blood cell count])
4) PSA should be either undetectable (after prostatectomy) or stable (after radiation) for at least 6-12 months
5) Be aware there may be prostate cancer recurrence (this may or may not be related to the testosterone therapy)
6) It should be used with extreme caution in men at high risk for prostate cancer recurrence or progression
7) It should not be administered at the same time as ADT.

References

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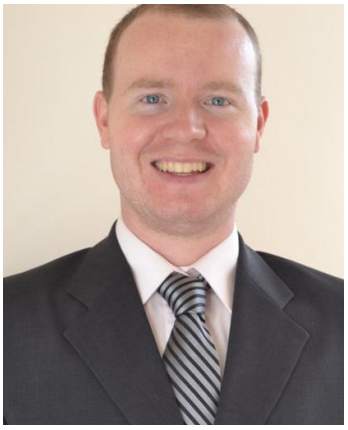

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Kalli is an internationally renowned Urological Surgeon, specialising in oncology and robotic surgery. He trained and worked in South Africa, before relocating to Australia where he has worked at Macquarie University Hospital and Westmead Hospital. His passion for what he does extends beyond the operating room, through publichealth advocacy, education and community awareness of men's health, cancer and sexuality.

Kalli has been involved with the Prostate Cancer Foundation of Australia for many years, advocating for improved cancer care and facilitating community prostate cancer support groups.