Clinical pharmacology of testosterone pellet implants

- David J. Handelsman 1998

Abstract

Androgen therapy may be divided into physiological and pharmacological applications. The pharmacological applications usually involve non-physiological doses of synthetic androgens as second-line, empirical treatment where more specific medical therapy is not yet available. The physiological applications consist of androgen replacement therapy, the treatment of androgen deficiency in hypogonadal men. Androgen replacement therapy aims to replicate physiological actions of endogenous testosterone by steadily maintaining physiological blood levels of testosterone. Since the underlying disorders are virtually always irreversible, this requires life-long administration of testosterone, making it desirable that the testosterone formulations be long-acting. Reliable therapeutic compliance over the lifetime of the patient depends heavily on a convenient formulation which ensures the continuity of treatment. The pharmacological properties of testosterone, notably its rapid hepatic metabolism and very low oral bioavailability, dictate the need for development of depot, sustained-release testosterone formulations (Parkes 1938; Wilson 1980). The perfect depot would be safe, effective, inexpensive, convenient, and long-acting with a reproducible, zero-order release profile. Not surprisingly, even six decades after entry of testosterone into clinical use (Foss 1939; Hamilton 1937), this ideal has not been achieved. Nevertheless one of the oldest testosterone formulations, the subdermal testosterone implant, provides a very close approximation to this ideal in providing stable blood testosterone levels lasting 4–6 months after a single implantation. Curiously this cheap, safe and effective treatment modality was neglected for decades despite its many advantages for androgen replacement therapy but is now undergoing a revival of interest, particularly since its desirable pharmacological properties have been outlined (Cantrill et al. 1984; Conway et al. 1988; Handelsman et al. 1990, 1997; Jockenhövel et al. 1996; Nieschlag 1996; Zacharin and Warne 1997).