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Intramuscular Testosterone and the Gel in the Current Treatment Era

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ABSTRACT

New treatment modalities for testosterone deficiency have evolved, such as the gels and the long-acting parenteral testosterone undecanoate (TU). Both fulfill the criteria of adequate androgen therapy, have proven to be effective in ameliorating sexual functions in young and elderly men, and are safe. Their mode of administration could not be more divergent; the gel requires daily application, but TU is administered every 12 weeks intramuscularly. A patient receiving long-acting TU being at higher risk when diagnosed with prostate carcinoma than one being treated with a gel is no longer believed, because the delay between diagnosing and treating prostate carcinomas almost always exceeds the duration of action of TU, which is 12 to 14 weeks. So, TU appears to be a viable alternative to the gels and will be preferred by many patients as a lesser interference with their daily lives.

Abbreviations: TU: Testosterone Undecanoate; DHT: 5-Dihydrotestosterone; ED: Erectile Dysfunction; IIEF: International Index of Erectile Function

Introduction

For androgen deficiency, testosterone therapy aims to replace physiological actions of endogenous testosterone by steadily maintaining physiological blood levels of testosterone [1,2]. Testosterone replacement is often a life-long therapy, because many of its underlying etiologies are generally irreversible. The consequence is that life-long androgen treatment is required. Patient compliance with life-long androgen administration depends on convenient pharmaceutical formulations that ensure continuity of androgen administration. Experts agree that the major goal of testosterone substitution is "to replace testosterone levels at as close to physiologic concentrations as is possible" [1,2]. Testosterone, naturally produced by the testis, is also generally accepted as the best androgen for substitution in hypogonadal men. The reason behind the selection is that testosterone can be converted to 5-dihydrotestosterone (DHT) and estradiol, thus developing the full physiological spectrum of testosterone activities in long-term substitution, and that, unlike some of the chemically modified androgens (17 methyltestosterone), it is not toxic. Testosterone compounds have been available for almost 70 years, but the pharmaceutical formulations have been less than ideal [1,2]. But over the past two decades, two testosterone formulations have been developed that largely meet the above specified requirements for testosterone treatment: the transdermal testosterone gel and the parenteral long-acting testosterone undecanoate (TU). This review discusses their profiles and their merits and disadvantages.

Testosterone Gel

Testosterone gel is 1% hydro-alcoholic (10 mg of testosterone per gram of gel) and administered between 5 and 10 g of gel per day, amounting to 50 and 100 mg testosterone applied to the skin. The pharmacokinetics of testosterone gel have been extensively studied [3,4]. Serum testosterone levels rose two- to three-fold 2 hours after application and rose further to four- to five-fold after 24 hours. Thereafter, serum testosterone remained steady in the upper range of normal [4]. Mean DHT levels followed the same pattern as testosterone and were at or above the normal adult male range. Serum estradiol levels rose and followed the same patterns as testosterone. Later studies showed that 9% to 14% of the testosterone administered is bioavailable. Steady state testosterone levels are achieved 48 to 72 hours after the first application [5]. The formulation of the testosterone gel allows easy dose adjustments (50, 75, 100 mg of testosterone gel) [6]. The clinical efficacy of transdermal testosterone gel on various androgen-dependent target organ systems has been very well documented [6,7]. The safety profile showed that prostate-specific antigen levels rose in proportion to the increase of testosterone levels but did not exceed normal values. Skin irritation was noted in 5.5% of patients in the study [6]. Four years ago, a new testosterone gel preparation was introduced, and profiles of pharmacokinetics, clinical efficacy, and safety are largely identical with the existing testosterone gels [8,9]. The value for restoring sexual functions in hypogonadal men receiving treatment with testosterone gel is well documented [5,6,8-10]. A recent study shows the adjunctive role of testosterone gel with sildenafil [11].

Parenteral Testosterone Preparations

Conventional parenteral testosterone preparations are far from ideal, even for young hypogonadal males. Plasma testosterone levels fluctuate strongly following administration [12]. The most widely used pharmaceutical forms are the intramuscularly administered hydrophobic long-chain testosterone esters in oily depot. Testosterone enanthate and cypionate, at a dose of 200 to 250 mg per 2 weeks, are the common formulations. They yield transient supraphysiologic levels the first 2 to 3 days after injection, followed by a steady decline to sub physiologic levels 4 to 6 days prior to the next injection if the injection interval is 2 weeks and proportionally longer if the injection interval is 3 weeks [12]. These fluctuations in testosterone levels are experienced by some of the patients as unpleasant and accompanied by changes in energy, libido, and mood. This phenomenon is known as the 'roller coaster effect.' The transient supraphysiologic levels may increase the frequency of side effects, such as polycythemia [13,14].

Long-Acting Parenteral TU

Parenteral Testosterone Undecanoate 1000 mg, is a new treatment modality for androgen therapy. The active pharmacologic principle of TU is the unmodified testosterone molecule itself. The kinetics for side-chain cleavage of the saturated aliphatic fatty acid undecanoic acid (with 11 carbon atoms) turn out to be considerably longer, permitting much longer injection intervals [15-17]. At the same time, the supra- or sub physiologic serum testosterone levels, so characteristics of the traditional testosterone esters are not observed [16,18,19]. Because of a few studies [15-18]. The administration regimen recommended for TU therapy in hypogonadal men is as follows: after the first injection of 1000 mg of TU, the second is to be administered 6 weeks later (loading dose), followed by injections every 12 weeks. An individualization of the TU therapy is recommended [17]. Intervals adjustment should be considered according to testosterone level before the fourth injection. When the testosterone level lies between 10 and 15 nmol/L (290–430 ng/dL), the injection interval should be once every 12 weeks. When testosterone currently is lower than 10 nmol/L (290 ng/dL), the injection interval is once every 10 weeks. With the testosterone level greater than 15 nmol/L (430 ng/dL), the injection interval should be extended to once every 14 weeks. Additionally, clinical symptoms should be taken into consideration to optimally adjust injection intervals with TU therapy [20].

The loading dose of TU achieved by the first two injections with an interval of 6 weeks is also recommended for patients who\ are being transferred from short-acting testosterone injections (e.g. 250 mg of testosterone enanthate) to treatment with long-acting TU. The attraction of TU lies in the long duration of action. After adequate loading, most patients are well substituted with administration every 12 weeks. Further, the resulting plasma testosterone levels are almost always in the physiological range, so the roller coaster effect is rarely experienced by patients. Also, side effects of supraphysiologic testosterone levels, such as polycythemia [18,19], are only rarely observed. The natural metabolites of testosterone, estradiol and DHT are also in the normal range of adult men. Long-term experience up to more than 8 years with TU in 22 hypogonadal men was studied [17]. Individual dosing intervals ranged from 10 to 14 weeks. Serum trough levels of testosterone, measured immediately before the new injection, were generally within the low-normal range, indicating sufficient substitution over the total injection interval. In contrast with short-acting testosterone esters, sensations of fluctuations in androgen serum concentrations were rarely observed. If this was the case, it occurred during the last 2 weeks before the next injection, indicating loss of androgenic psychotropic effects.

Revival of Testosterone for Treatment of Erectile Difficulties

When testosterone became pharmaceutically available, systemic studies were undertaken to define more precisely the role of testosterone in a man's sexual functioning. The early observations led to the belief that androgens primarily had effects on libido or motivation [20,21]. The influence on the penis was thought to be indirect through the effects on libido, rather than direct on penile tissues. Consequently, androgens were assumed not to be very therapeutically useful for men with erectile difficulties and unimpaired sexual desire, which

was specifically the reason for medical consultation for many men. Another reason why testosterone was not regarded as a therapeutic option in men with erectile dysfunction (ED) was the finding that the blood level of testosterone critical for restoring sexual interest, though varying between individuals, appeared to be 60% to 70% of the reference values for eugonadal men [22]. These observations were made in men with a wide range of ages. Consequently, additional testosterone was assumed likely to be of no help in men with ED and low-normal or slightly lower than- normal androgen levels, as is common in elderly population. This agreed with the clinical experience of many practitioners. When the PDE5 inhibitors were introduced in 1998, patients who had failed to respond to androgen or other types of treatment could now be successfully treated.

The success of the PDE5 inhibitors rendered androgens as treatment for erectile problems as something of the past, which seemed rational in view of the assumption that the primary effects of testosterone were on libido (i.e., on the central nervous system), and further that lower-than-normal circulating levels of testosterone were sufficient to exert that function, which is no longer tenable. However, based on their vast clinical experience, Schiavi and Rehman [22] hypothesized that the threshold for the biologic actions of testosterone might be higher in elderly men, compared with young men. Their hypothesis was recently convincingly and experimentally confirmed by Gray et al. [23], who showed that in elderly men, libido and erectile function respond only to higher levels of circulating testosterone when compared with those of younger men. New research has presented convincing evidence, so far mainly in laboratory animals, that testosterone has profound effects on tissues of the penis involved in the mechanism of erection, and that testosterone deficiency impairs the anatomic and physiologic substrate of erectile capacity [24]. Restoring plasma testosterone to normal is now widely believed to be beneficial in the treatment of ED. The full therapeutic potential of PDE5 inhibitors will only manifest in a eugonadal state. The above provides some alterations of the earlier beliefs that the effects of testosterone are primarily and predominantly exerted on libidinous aspects of the male and not directly on the penis.

Animal experiments and human observations suggest that androgens are necessary to maintain the integrity of the anatomic structures of the penile erectile tissue, and further that androgens are significant in the biochemical mechanisms subservient to penile erection [25]. Animal studies now provide ample evidence that androgen deprivation produces changes in the histological properties of penile structures. The dependence of PDE5 on androgens in the muscular and endothelial compartment of the corpus cavernosum has been confirmed in the rat but also in human tissue [26,27].

Studies on Treatment of Hypogonadal Men

With Sexual Dysfunctions with TU

Our studies with TU have mainly focused on the elderly male. Our studies have focused on the potential benefits of restoring plasma testosterone levels to normal for sexual functioning and the potential effects of normalization of plasma testosterone on penile dysfunction, such as venous leakage. In a recent study, the effects of restoring testosterone levels to normal with long-acting TU were investigated in 22 hypogonadal men (mean age, 58 years) with complaints of low sexual desire and ED [27]. Fifteen patients had serum testosterone below 6.9 nmol/L (200 ng/dL) and seven patients between 7.2 and 11.7 nmol/L (210–337 ng/dL), with normal values greater than 12.0 nmol/L (345 ng/dL), and significant comorbidities occurred. The duration of sexual complaints was on average 3.8 years. In all patients, serum testosterone levels were restored to normal within 6 to 8 weeks following the administration of TU. Twelve patients reported significant improvement in the sexual desire domain of the International Index of Erectile Function (IIEF), from 4.5 to 8.4, and experienced an improvement in the erectile function domain, from 12 to 25 (questions 1–5 plus 15), following treatment with this long-acting testosterone. The remaining 10 patients reported an improvement in sexual desire (from 4.5 to 7.5) but no significant improvement in erectile function (from 12 to 14). No changes in serum prostate-specific antigen or prostate volume were noticed in patients receiving this long-acting testosterone preparation.

Restoring testosterone levels to normal in men with proven subnormal testosterone levels appeared to improve libido in most subjects and erectile function in more than 50% of these men. An important clinical observation was that it may take 12 to 24 weeks before the effects of testosterone becomes manifest, so treatment with testosterone must not be regarded as unsuccessful after too short periods of administration. This encouraged us to extend our observation to a larger group of 771 patients consulting for ED. The average period they had experienced ED was 3.6 years. Blood tests included total testosterone, DHT, lipid profile, blood glucose and hemoglobin A1c, as well as prostate specific antigen. A total of 141 patients turned out to be hypogonadal men (18.3%; mean age, 56 years). Their baseline testosterone levels were 190 ± 50 ng/dL (6.7 ± 1.7 nmol/L). Of these 141 men, 122 received intramuscular injections of long-acting TU at day 1, again after six weeks, and thereafter trimonthly and were prospectively evaluated for a mean of 5 months (3–11 months). Digital and sonographic examinations of the prostate were performed every 3 months. Sexual functions were assessed using the several domains of the IIEF, at baseline and after 12 weeks of testosterone administration. No patient dropped out of the study during this period. No patient reported irritation or pain in the gluteal injection area or any other adverse events.

Of the total of 122 patients following treatment for at least 12 weeks, 71 patients reported significant improvement in the sexual desire domain (main value, 4.5 to 8.0), and in the erectile function domain from 12 to 25 The remaining 51 patients who had ED longer than 7 years reported an improvement of sexual desire but no signif-

icant improvement in the erectile function domain, despite the fact that their testosterone values were normalized (460 ± 50 ng/dL or 15.9± 1.7 nmol/L). All subjects are still follow-up. No significant alterations in prostate parameters have been noticed so far [27]. These results confirmed that testosterone-only therapy restored erectile function in the majority of the hypogonadal patients of this group, particularly in patients whose complaints of ED had not been long-standing. The success of testosterone treatment is less in men with comorbidities, but significant improvements have been observed in the latter men. These results suggest that testosterone should be considered more often as first line therapy in hypogonadal men and in elderly men. In case the treatment with testosterone is not successful, PDE5 inhibitors or the combination of PDE5 inhibitors with testosterone might be helpful. Within the observation period, we did not see any side effects of testosterone administration [27]. We have further examined the role of testosterone on the anatomic and functional integrity of penile structures. A 56-year-old man with diabetes mellitus type II and metabolic syndrome had complaints of severe ED because of venous leakage, confirmed by Pharmaco-cavernosography.

He was also testosterone deficient (180 ng/dL or 6.2 nmol/L). Upon testosterone administration, his erectile function improved dramatically. After 3 months, repeated cavernosography showed no more venous leakage [28]. This led us to extend our observations to a group of 12 hypogonadal men with low plasma testosterone and moderate to severe ED. Comorbidities were diabetes mellitus type I or II, metabolic syndrome with hypertension, dyslipidemia, obesity, or a combination. Oral PDE5 inhibitor therapy had failed to improve their erectile function. Each patient underwent baseline dynamic infusion pharmacocavernosometry and cavernosography, revealing various degrees of corporal Veno occlusive dysfunction. The patients underwent treatment with injectable TU. Dynamic infusion pharmacocavernosography was repeated in all 12 patients after at least 3 months of treatment. Five of the 12 patients reported significant improvement in erectile function within 12 to 20 weeks of androgen treatment. Compared with baseline pharmacocavernosography, repeat radiologic studies in patients who reported improvement in erectile function no longer showed venous leakage, with veins draining the corporal bodies. The patients who responded to androgens also noted improvement in sexual desire domain (IIEF scores increased from 4 ± 0.7 to 8 ± 0.3) and erectile function domain (IIEF scores increased from 6 ± 2 to 24 ± 1) [29].

These observations were in a limited series of cases, but they suggest that testosterone improves erectile function in hypogonadal patients by restoring Veno occlusive function in patients who had earlier not responded to PDE5 inhibitors and alprostadil injections [29].

Long-Acting TU and the Prostate

This preparation is arguably less suitable for initiation of testosterone treatment of aging men [30]. The long duration of action may constitute a problem in case an intercurrent prostate malignancy is diagnosed. Experienced urologists have pointed out that reasonable delay after diagnosing prostate cancer and its therapy until 12 weeks does not affect treatment outcome [31]. In addition, current recommendations for administration of testosterone to elderly men advocate initial follow-up at 3-month intervals for the first year [32], which fits very well into the schedule of TU injections. In the hypothetical case that a tumor is discovered, further treatment should be discontinued, and the use of antiandrogen may be considered. After the first uneventful year of androgen administration, administering long-acting testosterone preparations to elderly men seems reasonable.

Risks of Interpersonal Transfer of Dermal Testosterone

Three reports (a total of five children) of inadvertent transfer of dermal application of testosterone from father to child have been published [33]. Considering the degree of virilization of these children, the degree and duration of exposure must have been substantial. Transfer from one person to another was found to be insignificant [34]. No increase of serum testosterone was found after intense rubbing of skins of a person who had applied testosterone gel with other persons whose endogenous testosterone levels had been suppressed [35]. Washing the skin 10 minutes after application of testosterone gel did not influence the pharmacokinetic profile, and this was interpreted as to significantly reduce the risk of contamination of female partners or infants [35].

The Role of Intramuscular Testosterone Injection in the Gel Era

The introduction of testosterone gels has been a major innovation of treatment with testosterone. Many of the disadvantages of traditional parenteral testosterone esters can be bypassed, such as the strong fluctuations strongly following administration [13,14] of the transient supraphysiologic levels during the first 2 to 3 days after injection, followed by a steady decline to sub physiologic levels 4 to 6 days prior to the next injection, which has been experienced by some of the patients as unpleasant and accompanied by changes in energy, libido, and mood (roller coaster effect). The transient supraphysiologic levels may increase the frequency of side effects, such as polycythemia [16,18,19].

For more information on the effect of TTh on different organ systems and/or prevention even in older men, we can refer to the recent published literature in this concern [36-40]. For the question: how long should TTh continue? Data suggest that interruption could cause recurrence in symptoms and signs of hypogonadism. So researchers agree to continue as lifetime treatment such as with Thyroxine or Insulin [41].

Conclusions

Parenteral TU is a new treatment modality for androgen therapy. Two of its distinctive features are its prolonged duration of action. After two initial loading injections 6 weeks apart, as a rule, only one injection every 12 weeks is needed. Over the full interval between two injections, plasma testosterone levels are in the physiological range. Several studies have documented its use in hypogonadal men. Parenteral TU has none of the problems associated with the traditional parenteral testosterone esters and has all advantages of the testosterone gels. The infrequent administration of parenteral TU is an asset: four injections per year after the initial loading doses. This feature must be set against the daily application of the gel, which is time consuming and possibly difficult to integrate into the daily routine, particularly when traveling when a few testosterone gel sachets must be carried. TU is an infrequent reminder of the state of testosterone deficiency, which may be an advantage for the psychology of the patient. In our view, the safety aspects of parenteral TU do not need to be questioned more seriously than testosterone gels. According to our clinical experience, patients may be opinionated about the mode of administration and make idiosyncratic choices in treatment. Both options are available and serve patients well.

References

1. Gooren LJ, Bunck MC (2004) Androgen replacement therapy: present and future. Drugs 64(17): 1861-1891.
2. Nieschlag E (2006) Testosterone treatment comes of age: new options for hypogonadal men. Clin Endocrinol (Oxf) 65(3): 275-281.
3. Wang C, Berman N, Longstreth JA, B Chuapoco, L Hull, et al. (2000) Pharmacokinetics of transdermal testosterone gel in hypogonadal men: application of gel at one site versus four sites: a General Clinical Research Center Study. J Clin Endocrinol Metab 85 (3): 964-969.
4. Meikle AW, Matthias D, Hoffman AR (2004) Transdermal testosterone gel: pharmacokinetics, efficacy of dosing and application site in hypogonadal men. BJU Int 93(6): 789-795.
5. Wang C, Swerdloff RS, Iranmanesh A, A Dobs, P J Snyder, et al. (2000) Transdermal testosterone gel improves sexual function, mood, muscle strength, and body composition parameters in hypogonadal men. J Clin Endocrinol Metab 85(8): 2839-2853.
6. Wang C, Cunningham G, Dobs A, Ali Iranmanesh, Alvin M Matsumoto, et al. (2004) Long-term testosterone gel (AndroGel) treatment maintains beneficial effects on sexual function and mood, lean and fat mass, and bone mineral density in hypogonadal men. J Clin Endocrinol Metab 89(5): 2085-2098.
7. Swerdloff RS, Wang C (2003) Three-year follow-up of androgen treatment in hypogonadal men: preliminary report with testosterone gel. Aging Male 6(3): 207-211.
8. Steidle C, Schwartz S, Jacoby K, T Sebree, T Smith, et al. (2003) AA2500 testosterone gel normalizes androgen levels in aging males with improvements in body composition and sexual function. J Clin Endocrinol Metab 88(6): 2673-2681.
9. McNicholas T, Ong T (2006) Review of Testim gel. Expert Opin Pharmacother 7(4): 477-484.
10. Seftel AD, Mack RJ, Secrest AR, Smith TM (2004) Restorative increases in serum testosterone levels are significantly correlated to improvements in sexual functioning. J Androl 25(6): 963-972.
11. Rosenthal BD, May NR, Metro MJ, Richard C Harkaway, Phillip C Ginsberg (2006) Adjunctive use of AndroGel (testosterone gel) with sildenafil to treat erectile dysfunction in men with acquired androgen deficiency syndrome after failure using sildenafil alone. Urology 67(3): 571-574.
12. Behre HM, Wang C, Handelsman DJ, Nieschlag E (2004) Pharmacology of testosterone preparations. In Testosterone, Action, Deficiency, Substitution. Edited by Nieschlag E, Behre HM. Cambridge: Cambridge University Press, pp. 405-444.
13. Dobs AS, Meikle AW, Arver S, S W Sanders, K E Caramelli, et al. (1999) Pharmacokinetics, efficacy, and safety of a permeation-enhanced testosterone transdermal system in comparison with bi-weekly injections of testosterone enanthate for the treatment of hypogonadal men. J Clin Endocrinol Metab 84(10): 3469-3478.
14. Kaufman JM, Vermeulen A (2005) The decline of androgen levels in elderly men and its clinical and therapeutic implications. Endocr Rev 26(6): 833-876.
15. Behre HM, Abshagen K, Oettel M, D Hübler, E Nieschlag (1999) Intramuscular injection of testosterone undecanoate for the treatment of male hypogonadism: phase I studies. Eur J Endocrinol 140(5): 414-419.
16. von Eckardstein S, Nieschlag E (2002) Treatment of male hypogonadism with testosterone undecanoate injected at extended intervals of 12 weeks: a phase II study. J Androl 23(3): 419-425.
17. Morales A, Nieschlag E, Schubert M, A A Yassin, M Zitzmann, et al. (2006) Clinical experience with the new long-acting injectable testosterone undecanoate. Report on the educational symposium on the occasion of the 5th World Congress on the Aging Male, 9-12 February 2006, Salzburg, Austria. Aging Male 9(4): 221-227.
18. Schubert M, Minnemann T, Hubler D, D Rouskova, A Christoph, et al. (2004) Intramuscular testosterone undecanoate: pharmacokinetic aspects of a novel testosterone formulation during long-term treatment of men with hypogonadism. J Clin Endocrinol Metab 89(11): 5429-5434.
19. Harle L, Basaria S, Dobs AS (2005) Nebido: a long-acting injectable testosterone for the treatment of male hypogonadism. Expert Opin Pharmacother 6(10): 1751-1759.
20. Dobs AS, Matsumoto AM, Wang C, Kipnes MS (2004) Short-term pharmacokinetic comparison of a novel testosterone buccal system and a testosterone gel in testosterone deficient men. Curr Med Res Opin 20(5): 729-738.
21. Bhasin S, Woodhouse L, Casaburi R, A B Singh, D Bhasin, et al. (2001) Testosterone doseresponse relationships in healthy young men. Am J Physiol Endocrinol Metab 281(6): E1172-E1181.
22. Schiavi RC, Rehman J (1995) Sexuality and aging. Urol Clin North Am 22(4): 711-726.
23. Gray PB, Singh AB, Woodhouse LJ, Thomas W Storer, Richard Casaburi, et al. (2005) Dose-dependent effects of testosterone on sexual function, mood, and visuospatial cognition in older men. JCEM 90(7): 3838-3846.
24. Gooren LJ, Saad F (2006) Recent insights into androgen action on the anatomical and physiological substrate of penile erection. Asian J Androl 8(1): 3-9.
25. Morelli A, Filippi S, Mancina R, Michaela Luconi, Linda Vignozzi, et al. (2004) Androgens regulate phosphodiesterase type 5 expression and functional activity in corpora cavernosa. Endocrinology 145(5): 2253-

2263.

26. Yassin AA, Saad F (2005) Modulation of erectile function with long-acting testosterone injection (Nebido) i.m. in hypogonadal patients. Int J Androl 28: 53-55.
27. Yassin AA, Saad F (2007) Improvement of sexual functions in men with late onset hypogonadism treated with testosterone only. J Sex Med 4(2): 497-501.
28. Yassin AA, Saad F (2006) Dramatic improvement of penile venous leakage upon testosterone administration. A case report and review of literature. Andrologia 38(1): 34-37.
29. Yassin AA, Saad F, Traish A (2006) Testosterone undecanoate restores erectile function in a subset of patients with venous leakage: a series of case reports. J Sex Med 3(4): 727-735.
30. Nieschlag E, Swerdloff R, Behre HM, L J Gooren, J M Kaufman, et al. (2005) Investigation, treatment and monitoring of late-onset hypogonadism in males. ISA, ISSAM, and EAU recommendations. Eur Urol 28(3): 125-127.
31. Boorjian SA, Bianco FJ Jr, Scardino PT, Eastham JA (2005) Does the time from biopsy to surgery affect biochemical recurrence after radical prostatectomy? BJU Int 96(6): 773-776.
32. Graefen M, Walz J, Chun KH, Thorsten Schlomm, Alexander Haese, et al. (2005) Reasonable delay of surgical treatment in men with localized prostate cancer impact on prognosis? Eur Urol 47(6): 756-760.
33. Brachet C, Vermeulen J, Heinrichs C (2005) Children's virilization and the use of testosterone gel by their fathers. Eur J Pediatr 164(10): 646-647.
34. Rolf C, Knie U, Lemmnitz G, Nieschlag E (2002) Interpersonal testosterone transfer after topical application of a newly developed testosterone gel preparation. Clin Endocrinol (Oxf) 56(5): 637-641.
35. Rolf C, Kemper S, Lemmnitz G, U Eickenberg, E Nieschlag (2002) Pharmacokinetics of a new transdermal testosterone gel in gonadotrophin- suppressed normal men. Eur J Endocrinol 146(5): 673-679.
36. 36. Yassin A, Kamkoum H, Alzubaidi RT, Ramadan A, EI Akkad M, et al. (2025) Is There a Need for Testosterone Therapy in Older Men?. J Advances Med Sci 2(1):1-3.
37. Yassin A, Alzubaidi RT, Kamkoum H, Alzubaidi RT, Ramadan A, et al. (2025) Recent Update on Advancements in Testosterone Therapy (TTh). J Urol Ren Dis 10: 1413.
38. Yassin A, Alzubaidi RT, Kamkoum H, EI Akkad M, Mahdi M, et al. (2025) Effect of Testosterone Therapy (TTh) on Liver Function and Steatosis. Gastroint Hepatol Dig Dis 8(1): 1-8.
39. Yassin A, Kamkoum H, Alzubaidi RT, et al. (2025) Testosterone Prevention Role in Men's Health: Diabetes Mellitus. J Diabetes Treat 10: 10141.
40. Yassin A, Albaba B, Kamkoum H, Alzubaidi RT, Al-Qudimat AR, et al. (2025) Testosterone Prevention Role in Men's Health: Cardiovascular Dieseases. Cardiol Res Cardio vasc Med 10: 280.
41. Yassin A, Kamkoum H, Alzubaidi RT, Abdallah H, Assad O, et al. (2025) How Long Should We Treat with Testosterone: Stopping Testosterone Therapy (TTh) Wat is Next? Effects of Withdrawal and resumption of TTh. Ann Rev Resear 12(4): 555843.

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