Review
Turk J Endocrinol Metab 2018;22:254-259

Testosterone and Sexual Offending: From Pathophysiology to Treatment

Testosteron ve Cinsel Suçlar: Patofizyolojiden Tedaviye

Alev Selek, Şinasi Erol Bolu*

Kocaeli University School of Medicine, Department of Endocrinology and Metabolism, Kocaeli
*Memorial Atasehir Hospital, Endocrinology, Diabetes and Metabolic Diseases, İstanbul

Abstract

Sex offending is a debilitating public health concern owing to the serious consequences it has for the victims and their family. The evaluation of the biological profile and neurobiological aspects of sexual offenders is essential in order to understand their causal relationships and reduce recidivism. Sexual characteristics are mainly regulated by sex steroids. These hormones have also been found to be associated with aggression and psychiatric disorders, such as anxiety and depression. Testosterone has been thought to be the most suspicious hormone underlying the pathology of sex offenders. Testosterone-lowering agents have been used as a part of the treatment given to sexual offenders; the results are, however, controversial. On the other hand, a sexual offender with hypogonadism is another complex issue faced by the physician that cause difficulties in decision making for treatment. Literature does not report any evidence proving whether or not recidivism increases with T replacement. This review aimed to discuss the endocrinological, neurobiological, and therapeutical aspects of sexual offending. The treatment of sexual dysfunction in sex offenders is another dilemma that the physicians would face more often in the future. The article also discusses the legal, social and health care aspects of this controversy.

Keywords: Testosterone; sexual offending; chemical castration

Özet

Cinsel suçlar, mağdurda yol açacağı ciddi potansiyel sonuçlar nedeni ile önemli bir halk sağlığı sorunudur. Cinsel suçluların biyolojik profilini ve nörobiyolojik yönlerini değerlendirmek, nedensel ilişkiyi anlamak ve suçun yinelenmesini azaltmak için önemlidir. Seks steroid hormonları, insanlardaki cinsel karakterlerin başlıca düzenleyicisidir. Ayrıca bu hormonların, anksiyete ve depresyon gibi ve psikiyatrik bozukluklarla ve saldırganlık ile ilişkili olduğu düşünülmektedir. Testosteron, cinsel suçluların altta yatan patolojisi için en çok suçlanan hormondur. Testosteron düşürücü ajanlar, cinsel suçluların tedavisinin bir parçası olarak kullanılmıştır, ancak elde edilen sonuçlar tartışmalıdır. Öte yandan, hipogonadizmli cinsel suçlular, hekimin tedavi kararı vermesinde zorluklara neden olan bir başka karmaşık sorundur. Günümüzde testosteron replasmanı ile suçun yinelenmesi riskinin artırılıp artırılmadığı konusunda veri bulunmamaktadır. Bu çalışmada, cinsel suçluların endokrinolojik, nörobiyolojik ve terapötik yönlerinin tartışılması amaçlanmıştır. Cinsel suçlularda cinsel işlev bozukluğunun tedavisi, gelecekte daha sık karşılaşacağımız bir sorundur ve bu çalışmada bu konu; hukuki, sosyal ve sağlık bakış açıları ile de tartışılmıştır.

Anahtar kelimeler: Testosteron; cinsel suçlar; kimyasal hadım

Introduction

The biological profile and neurobiological aspects of sexual offenders (SO) are considered to play an important role in multifactorial theories of a sexual offense. The biological profile may affect individual behavioral differences and also treatment outcomes. There is little information about the role of central and peripheral gonadal hormones and biogenic amines in sex offenders, which is in debate since decades.

Address for Correspondence: Alev Selek, Kocaeli University Faculty of Medicine, Department of Endocrinology and Methabolism, Kocaeli, Turkey
Phone: +90 505 689 49 30 **E-mail:** alevselek@gmail.com **Received:** 29/05/2018 **Accepted:** 17/10/2018

DOI: 10.25179/tjem.2018-61554

Testosterone (T) had been thought to be the most suspicious hormone underlying the pathology in sex offenders. T-lowering agents have been used as a part of the treatment of SO, although there is only limited data about its effectiveness. Studies investigating the effect of T, besides sexuality along with different mechanisms and biological molecules that might relate to sexual offense, have been published recently (1–3). On the other hand, patients diagnosed as SO with hypogonadism is another complex issue for the physician as it makes decision making for the treatment very difficult. No data establishing whether or not recidivism increases with T treatment is available. Lastly, conflicting results have been reported regarding T-lowering treatment on SO. The selection of patients who would benefit from the treatment, its effectiveness, treatment duration, and management of side effects are other important controversies.

Testosterone action and sexuality

T and its more potent non-aromatizable metabolite, dihydrotestosterone, are two important androgens. T is mainly synthesized in the Leydig cells, although it can also be synthesized from cholesterol in the brain as "neuroactive steroid" (4). T affects various systems besides the gonads, such as the central nervous system, the cardiovascular, immune and musculoskeletal systems (4). T exerts its actions primarily via Androgen Receptors (ARs); however, to a lesser extent, it also acts through the Estrogen Receptors (ERs) after it has been aromatized into estradiol. ARs are found in various parts of the brain, right from cortex to the hippocampus (4,5). Furthermore, ERs and aromatase enzyme have been shown to be found in the pituitary gland, which may affect testosterone levels and its actions (6).

T exerts many effects on reactions arising as a result of sexual stimuli. It modulates involuntary physiological changes, perception and emotional components of the response to sexual stimuli. T has also been shown to interact with the mesolimbic pathway causing an increase in sexual motivation (2,7). Sexual interest, ejaculation, and even spontaneous erections seem to be related to T levels (8). On the other hand, it is well known that reduced T levels are associated with decreased sexual fantasies, arousal, and motivation (2). Treatment of hypogonadal males with T increases sexual desire and restores erectile dysfunction (9). Furthermore, testosterone levels, within the normal range of laboratory assays, are much higher than that required for normal sexual activities (7). This might explain why T treatment in eugonadal men has only limited effects. It should also be taken into account that low T levels do not always mean the total loss of sexual function and desire (10).

Testosterone and Aggression

Several animal studies have established a significant correlation between T and male aggression. These studies demonstrate that aggression initially decreases by surgical castration and increases again on treatment with exogenous androgens (11,12). Although the etiological evidence suggests that androgens might influence aggression, this relation is more complex in humans because human behavior is modulated by cognitive, emotional, social, and contextual factors (3).

A meta-analytic review indicates that males are much more physically aggressive than females (13). It is also well known that, during puberty, the male-to-male aggressive behavior is at peak (14). Studies examining the relationship between testosterone and aggressive behavior have been conducted in huge numbers in the recent past, which have revealed these indirect findings. The relationship between behavioral measures of aggression and testosterone are usually evaluated by self-reports of the patients. There are also studies comparing testosterone levels of violent versus non-violent offenders (14). These studies have concluded that there exists a positive relationship, though weak and conflicting, between baseline testosterone concentrations and various indicators of aggression. A more striking evidence is that testosterone concentrations increase rapidly as a result of human competition and this positively predicts the ongoing aggression (15).

The biological actions of T are mainly mediated by binding to AR's, therefore T action may vary according to variations of AR

genes. Recent studies have suggested that the relationship between testosterone and aggression or dominant behaviors may be moderated by variability in the number of increased CAG repeats of the androgen receptor (14). Chamberlain et al. have suggested that androgen sensitivity is inversely correlated to the length of CAG repeats (16). This evidence reminds that some human phenotypic features probably depend on androgen receptor sensitivity and structure.

Testosterone and sexual offending

Although T plays a central role in sexual behavior, most studies could not establish a distinct correlation between T levels and sexual offense (17). Furthermore, studies evaluating the association between hormonal status and sexual perversion have often included different groups of patients and measures, which renders it difficult to reach a clear conclusion.

Past studies have mainly been focused on the effect of chemical castration. However, the conflicting results of these studies have prompted an argument for SO as to whether or not testosterone is really accountable. Subsequent studies seeking the answer are limited in number and have some methodological and effect size limitations; therefore, the controversy is still ongoing. For instance, a meta-analysis by Wong et al., including 325 SO and 196 comparison participants, have investigated whether or not there is any scientific evidence to suggest that SO have higher levels of testosterone by implicating seven studies fitting their inclusion criteria and pooling the results. They concluded that there is no relationship between morning levels of T and sexual offending (2). The subgroup analyses of this study suggest that there may be differences in T levels between rapists and child molesters (2).

In a pilot study by Aromaki et al., the morning T levels of rapists and child molesters have been found to be similar to that of the healthy controls. However, the frequency of sexual activity estimated from self-reports have been significantly associated with T levels in SO but not in controls (8). Also, in SO, the mean salivary T was significantly correlated with the antisocial personality index, which is a frequent psychopathology found in SO (8,18).

Giotakos et al. evaluated the activity of pituitary-gonadal axis and biogenic amine turnover in SO and found that the serum gonadotropin levels of sexual offenders were similar to those of controls; also, there was no difference in T levels between SO and control subjects in the entire group. However, subgroup analyses have suggested that there may be differences in T levels of rapists and controls. Novelty seeking behavior has been found to be associated with the increased hypothalamic-pituitary-gonadal axis, especially in the group of rapists. They also concluded that hostility indicators are correlated with a low dopamine turnover, whereas the isolation indicators are associated with low norepinephrine turnover (1).

Another study advocated the hypothesis that T is related to the severity of expressed aggression, associated with sexual offending. The authors have concluded that serum T levels may predict sexual offense recidivism more precisely than that anticipated earlier (19). This suggests that T is not only related to aggression and sexual drive alone, but it may also be related to sexual aggression.

Chemical Castration

Testosterone is known to be the most important modulator of autonomic sexual functions like emotional and motivational behaviors. Impulse control is also mainly modulated by T. Therefore, T- lowering agents have been used to control pathological sexual behavior and to prevent recidivism in sex offenders since the 1940s (20). In some countries, Androgen deprivation treatment (ADT), also known as chemical castration, is being used as an additional treatment to psychotherapy for the management of SO. Evidence concerning the effectiveness of ADT is increasing with these practices.

Many studies have evaluated the efficiency of ADT in decreasing sexual drive, erections, and sexual fantasies of SO. These studies, in general, have reported a decrease in recidivism rates (2,21,22). However, most of these studies have severe methodological flaws and are therefore not suitable to conclude the effectiveness (2). ADT is routinely

used in the initial treatment approach for patients with disseminated prostate cancer, therefore treatment effect on T levels and side effects are well known. The available antiandrogen treatments are cyproterone acetate (CPA), medroxyprogesterone acetate (MPA) and GnRH analogs (or agonists).

Cyproterone acetate

Cyproterone acetate (CPA) is a progesterone-like synthetic steroid which directly blocks the T receptors. Therefore, CPA inhibits the physiological effects of T and its metabolites. It is available as tablets and slow-releasing injections; 50-100 mg tablets (50-200 mg/day) or 100 mg/mL injections (200-400 mg per week or every other week) can be considered (23). Several studies have shown that CPA treatment decreases sexual interest, fantasies and sexual drive in SO. CPA also decreases the frequency of masturbation and sexual intercourse in SO (24). However, its effect in reducing sexual recidivism is still a topic of debate due to the lack of enough scientific evidence (2,23,24). The effect of CPA is usually reversible; after cessation of the treatment, T levels recover in one to two months. Therefore, treatment duration and follow-up must be carefully assessed.

Medroxyprogesterone acetate

Medroxyprogesterone acetate (MPA) is another steroidal antiandrogen similar to CPA. The oral forms are available in 100 mg tablets and daily dosages range from 100 to 300 mg. The parenteral forms are also available in some countries. The suggested initial dose is 100 mg weekly and is then titrated up until the desired antiandrogenic effect is obtained. Testosterone levels can be used to monitor drug efficiency and dosage (25). The expected effects on reduction of sexual behavior can be obtained one to two months after initiation of the treatment. However, due to the side effects, the risk/benefit ratio does not favor the use of MPA (25).

GnRH analogs (or agonists)

These agents stimulate the release of luteinizing hormone and cause an initial flare in the levels of T. This initial period lasts for a week. Continued administration of GnRH analogs causes desensitization of the GnRH receptors. The final effect is a reduction in LH and testosterone, over a period of two to four weeks (23). Due to the flare in T, GnRH analogs are administered together with CPA or flutamide for the first weeks (23,26). GnRH analogs are associated with a decrease in T levels, therefore the frequency and intensity of sexual desire decrease. GRH analogs are also effective in reducing the frequency of masturbation and incidence of sexual fantasies (7,23). The response rates are more potent or identical to CPA, with better tolerance (23,27,28). In a recent study by Koo et al., the reason for suboptimal response rates has been attributed to the unexpected sudden increased hypersexual impulses associated with transient upsurges of serum T, immediately following treatment (21,22). Nevertheless, ADT is usually associated with a variety of side-effects, ranging from weight gain, hot flushes, and muscle weakness to more severe side-effects such as gynecomastia, an increased incidence of thromboembolism and decreased bone mineral density, even osteoporosis (28,29). The effects of chemical castration are reversible after cessation of treatment. However, the side effects of ongoing chemical castration treatment can increase in a time-dependent manner. Therefore, it is difficult to make a decision and physicians are indebted to closely monitor any potential complication associated with the treatment.

There are also social and medical concerns leading to the debate on chemical castration. Chemical castration may not guarantee human rights if it is performed without the patient's request and informed consent. In this case, it may be regarded as a punishment and not a treatment. In addition, increasing the population of SO who undergo chemical castration would create a tremendous socioeconomic burden owing to the cost of medications and the required monitorization (30).

Treatment of sexual dysfunction in SO

The rate of sexual dysfunction among SO is greater than that in the general population, with a prevalence of approximately 20%

(31,32). SO seek medical evaluation and treatment for sexual dysfunction frequently. However, SO are not obligated to disclose their status as offenders to the medical professionals. Therefore, many of them may be treated as otherwise healthy individuals (31).

The treatment of sexual dysfunction in SO raises an ethical and legal debate for the physicians because of the possibility of recidivism. Testosterone treatment is the most suspected intervention for this purpose, as it is an important driver of libido and sexual function (31). Recently a new argument has risen, especially among urologists. They advocate that treatment refusal, consisting of withholding testosterone treatment, is essentially equivalent to such chemical castration (31,33). The study by Philips et al. has demonstrated that SO have also been treated for erectile dysfunction with phosphodiesterase type 5 inhibitors, intracavernosal injection therapy, clomiphene citrate, penile prosthesis, and micro-arterial penile bypass (31). The authors concluded that treating sexual dysfunction may help lower the risk of sexual recidivism or at least diminish the violence of subsequent sexual attacks in some SO. However, in others, treating sexual dysfunction may increase the risk of sexual recidivism (31). Unfortunately, physicians are the only authority to decide whether to treat sexual dysfunction or not.

Sexual violence affects all individuals of society and it is much more common than expected. Sexual violence causes negative effects on personality and community; therefore prevention and reduction of recidivism require a multidimensional effort. Underlying psychopathology, the level, and type of SO and recidivism risk should be assessed in order to select the SO who would benefit from the treatment. Forensic psychiatrists should specialize on SO in order to be able to properly assess their past history and, in case of sexual dysfunction, offer guidance on whether or not treatment could be safely provided. Duration of treatment, monitoring, and management of side effects should also be determined before treatment. National guidelines should be prepared to help physicians manage these difficult conditions. Above all, physicians should not be responsible for this judicial duty.

Source of Finance: During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest: No conflicts of interest between the authors and/or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Alev Selek, Şinasi Erol Bolu; Design: Alev Selek, Şinasi Erol Bolu; Control/Supervision: Alev Selek, Şinasi Erol Bolu; Data Collection and/or Processing: Alev Selek, Şinasi Erol Bolu; Analysis and/or Interpretation: Alev Selek, Şinasi Erol Bolu; Literature Review: Alev Selek, Şinasi Erol Bolu; Writing the Article: Alev Selek, Şinasi Erol Bolu; Critical Review: Alev Selek, Şinasi Erol Bolu; References and Fundings: Alev Selek, Şinasi Erol Bolu; Materials: Alev Selek, Şinasi Erol Bolu.

References

1. Giotakos O, Markianos M, Vaidakis N, Christodoulou GN. Sex hormones and biogenic amine turnover of sex offenders in relation to their temperament and character dimensions. Psychiatry Res. 2004;127:185-193.
2. Wong JS, Gravel J. Do sex offenders have higher levels of testosterone? Results from a meta-analysis. Sex Abuse. 2018;30:147-168.
3. Kingston DA, Seto MC, Ahmed AG, Fedoroff P, Firestone P, Bradford JM. The role of central and peripheral hormones in sexual and violent recidivism in sex offenders. J Am Acad Psychiatry Law. 2012;40:476-485.
4. Hu ZY, Bourreau E, Jung-Testas I, Robel P, Baulieu EE. Neurosteroids: oligodendrocyte mitochondria convert cholesterol to pregnenolone. Proc Natl Acad Sci U S A. 1987;84:8215-8219.
5. Moraga-Amaro R, van Waarde A, Doorduin J, de Vries EFJ. Sex steroid hormones and brain function: PET imaging as a tool for research. J Neuroendocrinol. 2018;30.
6. Selek A, Cetinarslan B, Gurbuz Y, Tarkun I, Canturk Z, Cabuk B. Aromatase enzyme expression in acromegaly and its possible relationship with disease prognosis. Endocrine. 2015;49:250-257.

7. Jordan K, Fromberger P, Stolpmann G, Müller JL. The role of testosterone in sexuality and paraphilia--a neurobiological approach. Part I: testosterone and sexuality. J Sex Med. 2011;8:2993-3007.
8. Aromäki AS, Lindman RE, Eriksson CJ. Testosterone, sexuality and antisocial personality in rapists and child molesters: a pilot study. Psychiatry Res. 2002;110:239-247.
9. Corona G, Maggi M. The role of testosterone in erectile dysfunction. Nat Rev Urol. 2010;7:46-56.
10. Christiansen K. Behavioural effects of androgen in men and women. J Endocrynol. 2001;170:39-48.
11. Vom Saal FS. Models of early hormonal effects on ıntrasex aggression in mice. In: Svare BB, ed. Hormones and Aggressive Behavior (1st ed). Boston, MA: Springer US; 1983;197-222.
12. Harris JA. Review and methodological considerations in research on testosterone and aggression. Aggress Violent Behav. 1999;4:273-291.
13. Archer J. Sex differences in aggression in real-world settings: a meta-analytic review. Rev Gen Psychol. 2004;8:291-322.
14. Archer J. Testosterone and human aggression: an evaluation of the challenge hypothesis. Neurosci Biobehav Rev. 2006;30:319-345.
15. Oliveira RF. Social behavior in context: hormonal modulation of behavioral plasticity and social competence. Integr Comp Biol. 2009;49:423-440.
16. Chamberlain NL, Driver ED, Miesfeld RL. The length and location of CAG trinucleotide repeats in the androgen receptor N-terminal domain affect transactivation function. Nucleic Acids Res. 1994;22: 3181-3186.
17. Krueger RB, Kaplan MS. The paraphilic and hypersexual disorders: an overview. J Psychiatr Pract. 2001;7:391-403.
18. Tülü İA, Erden G. Crime analysis regarding sex offenders in Turkey: psychological profiling, cognitive distortions and psychopathy among rapists. Turk Psikiyatri Derg. 2014;25:19-30.
19. Studer LH, Aylwin A, Reddon JR. Testosterone, sexual offense recidivism, and treatment effect among adult male sex offenders. Sex Abuse. 2005;17:171-181.
20. Grubin D, Beech A. Chemical castration for sex offenders. BMJ. 2010;12:340:c74.
21. Koo KC, Ahn JH, Hong SJ, Lee JW, Chung BH. Effects of chemical castration on sex offenders in relation to the kinetics of serum testosterone recovery: implications for dosing schedule. J Sex Med. 2014;11:1316-1324.
22. Koo KC, Shim GS, Park HH, Rha KH, Choi YD, Chung BH, Hong SJ, Lee JW. Treatment outcomes of chemical castration on Korean sex offenders. J Forensic Leg Med. 2013;20:563-566.
23. Thibaut F. Pharmacological treatment of sex offenders. Sexologies. 2011;20:166-168.
24. Guay DR. Drug treatment of paraphilic and nonparaphilic sexual disorders. Clin Ther. 2009;31:1-31.
25. Assumpção AA, Garcia FD, Garcia HD, Bradford JM, Thibaut F. Pharmacologic treatment of paraphilias. Psychiatr Clin North Am. 2014;37:173-181.
26. Huygh J, Verhaegen A, Goethals K, Cosyns P, De Block C, Van Gaal L. Prolonged flare-up of testosterone after administration of a gonadotrophin agonist to a sex offender: an under-recognised risk? Crim Behav Ment Health. 2015;25:226-230.
27. Czerny JP, Briken P, Berner W. Antihormonal treatment of paraphilic patients in German forensic psychiatric clinics. Eur Psychiatry. 2002;17:104-106.
28. Turner D, Schöttle D, Bradford J, Briken P. Assessment methods and management of hypersexuality and paraphilic disorders. Curr Opin Psychiatry. 2014;27:413-422.
29. Turner D, Basdekis-Jozsa R, Dekker A, Briken P. Which factors influence the appropriateness of testosterone-lowering medications for sex offenders? A survey among clinicians from German forensic-psychiatric institutions. World J Biol Psychiatry. 2014;15:472-478.
30. Lee JY, Cho KS. Chemical castration for sexual offenders: physicians' views. J Korean Med Sci. 2013;28:171-172.
31. Phillips EA, Rajender A, Douglas T, Brandon AF, Munarriz R. Sex offenders seeking treatment for sexual dysfunction-ethics, medicine, and the law. J Sex Med. 2015;12:1975-1976.
32. Bownes IT, O'Gorman EC. Assailants' sexual dysfunction during rape reported by their victims. Med Sci Law. 1991;31:322-328.
33. Douglas T. Refusing to treat sexual dysfunction in sex offenders. Camb Q Healthc Ethics. 2017;26:143-158.