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Review article

MALE INFERTILITY ETHANOL "APRIME CULPRIT –A REVIEW

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A R T I C L E I N F O

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A B S T R A C T

Infertility is a major health issue in up to 15% of the sexually active population and male factor is responsible in 50% of these cases. It had been estimated that more than 152 million men around the world subjected to sexual dysfunction, and this number might increase to approximately 322 million by the year 2025. Sexual stimulation of the human male results in a series of psychological, neuronal, vascular, and local genital changes. Sexual dysfunction in men refers to repeated inability to achieve normal sexual intercourse.
It can also be viewed as disorders that interfere with a full sexual response cycle. These disorders make it difficult for a person to enjoy or to have sexual intercourse. Alcohol abuse is considered as one of the problems associated with poor semen production and sperm quality. Alcohol can interfere with the function of the hypothalamic-pituitary-gonadal [HPG] axis, thereby causing impotence, infertility, and reduced male secondary sexual characteristics. Alcohol abuse was considered as one of the problems associated with poor semen production and sperm quality. Ethanol was generally regarded as a reproductive to xin. Humans have consumed alcoholic beverage since prehistoric times for a variety of reasons. Alcoholic beverages were found to affect different system of the human body including reproductive system. Ithad been observed that chronic alcohol was common among infertile men.Besides being an important public and social issue, alcohol consumption in a one of the major cause of male reproduction. This review elaborates the impact of alcohol in male infertility.

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Introduction

Infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse [1]. Aging and stress exposure are the inevitable phenomena. A large body of evidence has demonstrated that male sexual behaviour gradually declinewith age [2]. Numerous factors including both physical and mental factors are regarded as the important etiology for sexual dysfunction in elderly. Stress is regarded as one important factor to induce sexual dysfunction. It was reported that chronic exposure to a variety of mild stressors significantly decreases male sexual behaviour [3].

Infertility is a major problem in up to 15% of the sexually active population and male factor is responsible in 50% of these cases [4]. It had been estimated that more than 152 million men worldwide subjected to sexual dysfunction, and this number might increase to approximately 322 million by the year 2025 [5].

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Male infertility is a world-wide medical and social problem. The fact that more than 15 percent couples worldwide are affected by infertility speaks volume about the worsening reproductive health globally. In India alone, the figure stands at 30 million and in half of such cases, men are responsible for the situation. Excessive alcoholism, smoking, late marriage and stress are all to be blamed. Mushrooming sperm banks and assisted reproduction centers are evident of how this is silently turning into a serious health concern. Male infertility is definitely on the rise and the average sperm count has been decreasing. The World Health Organization [WHO] recently revised its sperm countnorm from 20 million to 15 million per milliliter. Virility is sexual desire in the mind whereas fertility is the physical ability of reproducing, which can be judged on two parameters: Sperm type [sperm count and motility] and the ability to deposit the sperm into female reproductive tract during sexual act [6] [7]. There has long been a debate over whether male reproductive ability is determined by environmental factors, such as those present in the workplace or area of residence[8]. Among 25 male workers involved in producing the insecticide dibromo-3-chloropropane [DBCP], 14 are diagnosed as azoospermic or oligospermic[9]. Previous 50 years saw a marked decrease in sperm count [10]. During the period since 1970 in Scotland, sperm counts had decreased by approximately 25% compared with the period prior to 1959, a mean annual rate of 2.1% [11]. Many researchers and clinicians have asserted that societal progress in advanced countries and worsening of the natural environment have likely resulted in decreased male fertility. Long-reported risk factors include working in high temperatures[12], noise associated with manufacturing[13],exposure to radiation [14], electromagnetic waves [15],and a variety of chemical substances [16].

Numerous studies have compared patients with male infertility [oligospermia or azoospermia] to healthy subjects [normal sperm count]. To date, proposed risk factors include air temperature [17], automobile driving time per day [18], air pollution[19], regional differences in residential population density [20], mumps [Wong et al., 2003], stress [21], and alcoholism [22].

Male Sexual Function

Sexual stimulation of the human male results in a series of psychological, neuronal, vascular, and local genital changes. At least three different classifications for these changes have been described. Some authors described a psychosexual response cycle that consists of four phases: excitement, plateau, orgasm, and resolution [23]. Another classification by based on pen dynamic changes during the sexual cycle divides each of the psychosexual phases into two interrelated events as excitement into latency and tumescence; plateau into erection and rigidity; orgasm into emission and ejaculation; and resolution into detumescence and refractoriness [24]. The third classification focuses on the functional activities during the sexual cycle by adding an initial phase of desire or libido [25]. Thus, the normal male sexual response cycle can be functionally divided into five interrelated events that occur in a defined sequence: libido, erection, ejaculation, orgasm, and detumescence.

1. Libido or sexual desire- Libido is defined as the biological need for sexual activity [the sex drive] and frequently is expressed as sex-seeking behaviour. Its intensity is variable between individuals as well as within an individual over a given time. Higher serum testosterone appears to be associated with greater sexual activity in healthy older, but not younger men [26].

2. Erection- Erection is the enlarged and rigid state of the sexually aroused penis sufficient enough for vaginal penetration. It results from multiple psychogenic and sensory stimuli arising from imaginative, visual, auditory, olfactory, gustatory, tactile, and genital reflexogenic source.

3. Ejaculation- Ejaculation is the act of ejecting semen. It is a reflex action that occurs as a result of sexual stimulation. It is made up of two sequential processes. The first process called emission is associated with deposition of seminal fluid into the posterior urethra while the second process is the true ejaculation, which is the expulsion of the seminal fluid from the posterior urethra through the penile meatus.

4. Orgasm- This is the climax of sexual excitement. The entire period of emission and ejaculation is known as the male orgasm [27].

5. Detumescence- This is the subsidence of an erect penis after ejaculation.[28].

Male Sexual Dysfunction

Sex disorders of the male are classified into disorders of sexual function, sexual orientation, and sexual behaviour. In general, several factors must work in harmony to maintain normal sexual function. Such factors include neural activity, vascular events, intracavernosal nitric oxide system and androgens. Thus, malfunctioning of at least one of these could lead to sexual dysfunction of any kind. Sexual dysfunction in men refers to repeated inability to achieve normal sexual intercourse. It can also be viewed as disorders that interfere with a full sexual response cycle. These disorders make it difficult for a person to enjoy or to have sexual intercourse. While sexual dysfunction rarely threatens physical health, it can take a heavy psychological toll, bringing on depression, anxiety, and debilitating feelings of inadequacy. Unfortunately, it is a problem often neglected by the healthcare team who strive more with the technical and more medically manageable aspects of the patient's illness [29]. Sexual dysfunction is more prevalent in males than in females and thus, it is conventional to focus more on male sexual difficulties. It has been discovered that men between 17 and 96 years old could suffer sexual dysfunction as a result of psychological or physical health problems [30]. Generally, a prevalence of about 10% occurs across all ages. Because sexual dysfunction is an inevitable process of aging, the prevalence is over 50% in men between 50 and 70 years of age [31]. As men age, the absolute number of Leydig cells decreases by about 40%, and the vigour of pulsatile luteinizing hormone release is dampened. In association with these events, free testosterone level also declines by approximately 1.2% per year. These have contributed in no small measure to prevalence of sexual dysfunction in the aged. Male sexual dysfunction [MSD] could be caused by various factors. These include: psychological disorders [performance anxiety, strained relationship, depression, stress, guilt and fear of sexual failure], androgen deficiencies [testosterone deficiency, hyperprolactinemia], chronic medical conditions diabetes, hypertension, vascular insufficiency [atherosclerosis and venous leakage], penile disease [Peyronie's, priapism, phimosis, smooth muscle dysfunction], pelvic surgery [to correct arterial or inflow disorder], neurological disorders [Parkinson's disease, stroke, cerebral trauma, Alzheimer's disease, spinal cord or nerve injury], drug side effects [anti-hypertensives, central agents, psychiatric medications, antiulcer, antidepressants, and anti-androgens], life style [chronic alcohol abuse, cigarette smoking], aging [decrease in hormonal level with age] and systemic diseases [cardiac, hepat ic, renal, pulmonary, cancer, metabolic, post-organ transplant] [32] [33].

Hypoactive Sexual Desire [HSD]

Hypoactive sexual desire is defined as persistently or recurrently deficient[orabsent] sexual fantasy and desire for sexual activity leading to marked distress or interpersonal difficulty. It results in a complete or almost complete lack of desire to haveany type of sexual relation [34].

Compulsive Sexual Behaviours [CSBs]

Compulsive sexual behaviours [CSBs] constitute a wide range of complex sexual behaviours that have strikingly repetitive, compelling, or driven qualities. They usually manifest as obsessive-compulsive sexuality [e.g. excessive masturbation and promiscuity], excessive sex-seeking in association with affective disorders [e.g. major depression or mood disorders], addictive sexuality [e.g. attachment to another person, object, or sensation for sexual gratification to the exclusion of everything else], and sexualimpulsivity [failure to resist an impulse or temptation for sexual behaviour that is harmful to self or others such as exhibitionism, rape] [35].

Erectile Dysfunction [ED]

This is a problem with sexual arousal. ED can be defined as the difficulty in achieving or maintaining an erection sufficient for sexual activity or penetration, at least 50% of the time, for a period of six months [36].A human male may suffer from MSD at any stage of life but its risk increases with age. A population based study in US revealed that prevalence of MSD is 12 percent in those younger than 59 years, 22 percent in those 60 to 69 years of age, and 30 percent in those older than 69 years [37]. As per an estimate over 320 million peoplein the Westernized nations will be develop MSD by 2025 [38]. The current epidemiological data suggests that MSD needs immediate medical intervention and newer therapeutic strategies are required for its management. A number of treatment options are available for management of MSD. These options include psychological and behavioral therapy, non-surgical treatments using constructive rings and vacuum pumps, surgical treatment such as penile prosthesis, penile implants and venous ligation, hormone replacement therapy and intervention of chemotherapeutic agents [39].

There is very little evidence on the levels or patterns of male infertility in India, and in South Asia [40]. Semen quality of 57 Indian welders occupationally expose to nickel and chromium and they correlate semen abnormalities with the number of years of exposure to welding fumes containing nickel and chromium [41] . Adiga et al., [42] reported that sperm density, sperm morphology and sperm motility are deteriorating in the southern part of the India [1993-2005]. Significant decline in the sperm motility parameters as well as in the seminal volume of 3729 male of Kolkata city in between 1981-85 and 2000-06 are reported by [43].

Mechanism Involved in Aphrodisiac Potential

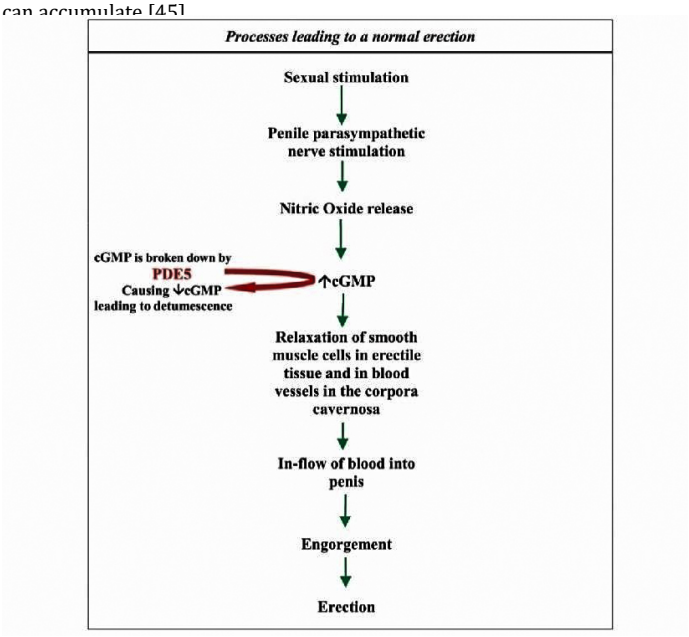
Sexual desire is controlled and regulated by the central nervous system which integrates tactile, olfactory and mental stimuli [44].

Role of Nitric Oxide

On sexual stimulation [visual [or] otherwise the famines of the axons of parasympathetic nerves release nitric oxide [NO] gas. The gas diffuses into smooth muscle cells that line those arteries of the corpus cavernosum [erectile tissues] and activates the enzymes guanylate cyclase [GC]. The later converts the nucleotide guanosine triphosphate [GTP] in to cyclic guanosine monophosphate [cGMP]. The cGMP in turn causes the smooth muscle cells around the penis to relax, leading to dilation and increased flux of blood into the penile tissues. This blood is essentially trapped in the

penis and results in an erection [Palmer, 1999]. The erection ceases after a while because cGMP is hydrolysed by phosphodiesterase type-5 enzyme [PDE-5] into inactive GMP.

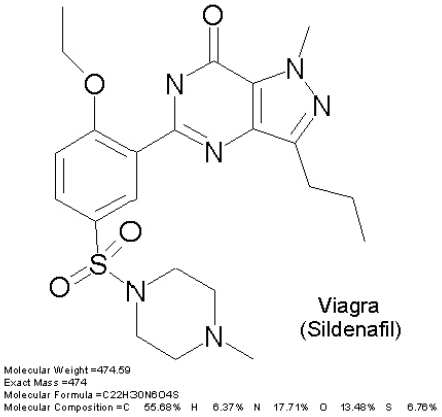
[The PDE-5 enzyme resides in the penile tissues]. Aphrodisiac potentials inhibit the hydrolysing action of PDE-5 with the result that active C.GMP can accumulate [45].



Normal erectile physiology
Source: September 1998 West Midlands DEC Report. Sildenafil - an oral drug for thetreatment of male erectile dysfunction

Synthetic Aphrodisiac Agents
Sildenafil

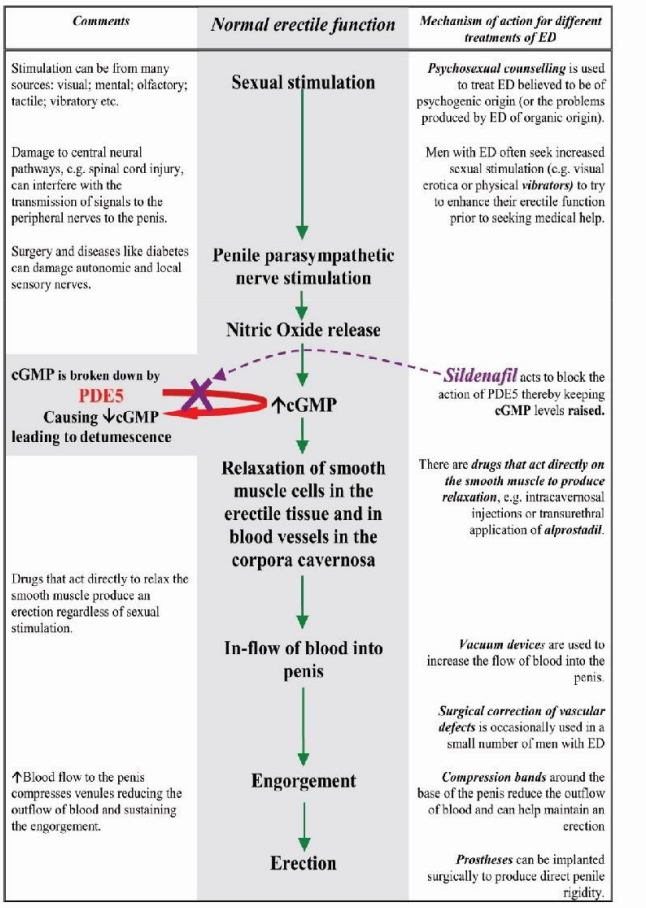
Sildenafil [VIAGRATM] is introduced by Pfizer Inc. on 27th March 1998. Sildenafil citrate is chemically 1-[[3-[6,7-dihydro-1-methyl-7-oxo-3- propyl-1H- pyrazolo [4,3-d] pyrimidin-5-yl]-4-ethoxyphenyl] sulfonyl]-4- methylpiperazine citrate with molecular formula-C22H30N604S. Unlike previously approved treatments for impotence, sildenafil does not directly cause penile erection; but affects the response to sexual stimulation. The drug acts by enhancing the smooth muscle relaxant effects of nitric oxide [46].



Mechanism of Action of Sildenafil

Unlike previously approved treatments for impotence, sildenafil does not directly cause penile erection; but affects the response to sexual stimulation. The drug acts by enhancing the smooth muscle relaxant effects of nitric oxide. The physiologic mechanism of the erection of penis involves release of nitric oxide [NO] in the corpus cavernosum during sexual stimulation. NO then activates the enzyme guanylate cyclase, which results in increased levels of cyclic guanosine monophosphotase [cGMP], producing inflow of blood.

Sildenafil has no direct relaxant effect on isolated human corpus cavernosum but enhances the effect of nitric oxide [NO] by inhibiting phosphodiesterase type V [PDEV], which is responsible for the degradation of cGMP in the corpus cavernosum. When sexual stimulation causes local release levels of cGMP in the corpus cavernosum, resulting in smooth muscle relaxation and inflow of blood to the corpus cavernosum. Sildenafil at recommended doses has no effects in the absence of sexual stimulation [47].



Erectile Function and Mechanism of Action of Sildenafil [Sildenafil forthe treatment of Male Erectile Dysfunction].

Source: September 1998 West Midlands DEC Report. Sildenafil - an oral drug forthe treatment of male erectile dysfunction

Adverse Effects of Sildenafil

Sildenafil citrate is approved by the US Food and Drug Administration [FDA] in 1998. After Sildenafil citrate is approved by the US Food and Drug Administration [FDA], several deaths are reported in patients taking sildenafil citrate. It is generally assumed that they are related to an underlying disease [e.g., ischemia] and not to a specific drug effect [48]. Nevertheless, these reports raised concerns that sildenafil citrate may increase the risk of cardiovascular events in men with ED and cardiovascular disease which led to many basic and clinical investigations of the adverse cardiovascular effects of this drug [49] Studies in rats demonstrated that PDE-5 inhibition with sildenafil attenuates the rise in pulmonary artery pressure and vascular remodelling when given before chronic exposure to hypoxia-induced pulmonary hypertension[50]. Post-marketing surveillance data after the approval of sildenafil citrate by the US FDA revealed significant cardiovascular problems, including sudden cardiac death, related to the use of sildenafil citrate[51]. One out of 10men in clinical trials developed blinding headaches. There can be sudden drops in blood pressure leading to blackouts. Although priapism never happened in trials, there is theoretical risk that men with sickle cell anaemia or leukaemia could develop priapism [46].

Hormonal Anti-infertility Agents

Gonadotropin-releasing hormone [GnRH] The pulsatile release of GnRH in the hypothalamus stimulates the release of FSH and LH from the anterior pituitary. In men, normal levels of FSH and LH are responsible for induction of spermatogenesis and maintaining high levels of testicular testosterone [52]. Pulsatile administration of GnRH is an effective treatment to replace GnRH deficiency in infertile men with hypogonadotropic hypogonadism [HH] due to a lack of secretion from the hypothalamus [e.g., Kallmann's syndrome, idiopathic HH]. Men with HH have reduced fertility that is usually restored by reestablishing the high intra-testicular testosterone and the FSH stimulation of Sertoli cells [53].

Despite the great outcomes that are experienced in pulsatile GnRH treatment, its use is limited by availability, inconvenience of delivery by carrying a pump, and the need to regularly change subcutaneous needles [54].

Dopamine Agonist for Male Infertility

For men presenting with infertility and hyperprolactinemia, prolactin - secreting pituitary adenoma [most common functional tumours] should be considered as the underlying cause. Tumours that cause stalk compression and hyperprolactinemia should not be treated with a dopamine agonist. Elevated levels of prolactin inhibit the pulsatile secretion of GnRH, men will present with hypogonadism and infertility, and they may also experience headaches or visual field changes secondary to the pituitary tumour compression. In this setting, dopamine agonists are indicated for the treatment of infertility and the pituitary tumour [55].

Ethanol and Male Infertility

Recently, the substances in the environment that can disturb male fertility have been increased. Ethanol is among the most widely abused drug, which can suppress reproductive function and sexual behaviour [56]. Alcohol abuse is considered as one of the problems associated with poor semen production and sperm quality [57]. The lack of sexual desire in long-term alcohol users has been reported from 31 to 58% [58] [59]. Whalley[59] reported that about 54% of hospitalized alcoholic men and 24% of healthy controls had erectile dysfunction. Alcohol abuse is well known to impair reproductive performance in experimental animals and also in human beings. Alcoholics are found to have fertility abnormalities, with low sperm count, impaired testosterone production, and testicular atrophy [60]. Alcohol is toxic for testes and causes fertility disturbances through low sperm count and motility in men [61]. Chronic ethanol exposure decreases plasma testosterone level and cause testicular atrophy [62], [63]. Ethanol significantly augments lipid peroxidation in the testis and inhibits the conversion of both dehydroepiandrosterone and androstenedione to testosterone by decreasing the activities of 3-beta hydroxyl steroid dehydrogenase [64].

Long-term effects of chronic alcohol abuse come along with gynecomastia, impotence, testicular atrophy, and loss of libido, as it had been reported before. [65] [66] 59]. Ethanol consumption also produces a significant decrease in the percentage of motility, concentration [61], and normal morphology in human and animal spermatozoa [67]. Martinez et al. [68] reported histological abnormalities in testicular tissue of alcoholic animals. These included intense intercellular spaces, irregular diameter of the seminiferous tubules, and high amount of necrotic cells in the lumen compared with controls. In addition, they showed that the epididymal sperm motility is decreased in ethanol-treated rats. A reduction of semen volume, density, and motility are caused by alcohol consumption [69]. In addition, it was reported that daily alcohol consumption decreases normal sperm morphology [70]. Ethanol users showed a significant decrease in mean sperm count, ranging from 113 to 66 million/mL [71].

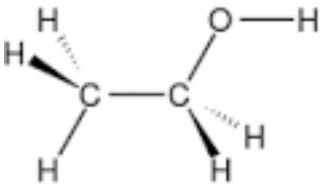
Ethanol-Risk Factors for Infertility

Ethanol [ethyl alcohol, grain alcohol] is a clear, colourless liquid with a characteristic, agreeable odour. In dilute aqueous solution, it has a somewhat sweet flavour, but in more concentrated solutions it has a burning taste. Ethanol, CH3CH2OH, is an alcohol, a group of chemical compounds whose molecules contain a hydroxyl group, – OH, bonded to a carbon atom. The word alcohol derives from Arabic al-kuhul, which denotes a fine powder of antimony used as an eye makeup. Alcohol originally referred to any fine powder, but medieval alchemists later applied the term to the refined products of distillation, and this led to the current usage. Ethanol melts at –114.1°C, boils at 78.5°C, and has a density of 0.789 g/mL at 20°C [Prof. Shakhashiri, www.scifun.org General Chemistry].
Sexual disorders have been reported in men who are long-term alcohol users, with the prevalence ranging from 8 to 58% [72]. Ethanol abuse is considered as one of the problems associated with poor semen production and sperm quality. The consumption of alcohol offers no benefits in relation to the outcomes of pregnancy, and alcohol is both teratogenic and feto -toxic in the human [74]. Numerous studies have indicated that alcohol abuse in men can cause impaired testosterone production and testicular atrophy [75]. Alcohol can interfere with the function of the hypothalamic-pituitary-gonadal [HPG] axis, thereby causing impotence, infertility, and reduced male secondary sexual characteristics [76]. Ethanol and its metabolite acetaldehyde cause a reduction in LH binding to Leydig cells, an inhibition of the enzymes responsible for the formation of sex hormone[77] [78].

Ethanol and Testosterone

Testosterone is the most important androgen in both men and women. Testosterone has androgenic, anabolic, and psychological effects. The presence of testosterone is crucial for the development of reproductive tissues and secondary male characteristics. It is essential for normal spermatogenesis, and it contributes to general growth and protein synthesis. Testosterone also effects libido, sexual potency, and behaviors such as aggressive and sexual behavior [79].

During the last half century, researchers have become very interested in the effects of alcohol, and even more specifically, in the effects of alcohol on the reproductive system. Chronic consumption of alcoholic beverages is known to for example cause liver and brain damage, mental problems, cancer. Yet, one of the most important clinical effects of alcohol is its effects on the gonads. Alcohol-induced reductions in testosterone can in theory be caused by a stimulatory effect on testosterone catabolism and/or inhibition of its synthesis. Research on the effect of alcohol on testosterone catabolism is limited in depth, while the effects of ethanol on testosterone synthesis have been widely investigated. [80].



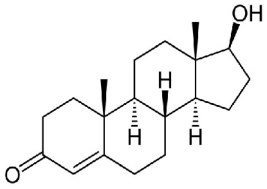
Ethyl Alcohol

Mechanism of Action of Ethanol Induced Infertility

A. Inhibition of testosterone Synthesis

Besides the ethanol molecule per se, the causes behind the alcohol induced effectson testosterone have been attributed also to the metabolism of ethanol and to an intermediate product of ethanol metabolism, acetaldehyde. Acetaldehyde has been reported being 1000-4000 times more effective than ethanol in inhibiting testosterone synthesis in vitro [81]. Even so, Eriksson and his coworkers [82] have demonstrated that acetaldehyde does not have an important role in the inhibition of testosterone synthesis in vivo. The authors assessed the role of acetaldehyde as a product of ethanol metabolism and concluded that increased acetaldehyde concentrations in blood and testicles did not inhibit testosterone synthesis. The oxidation of ethanol requires nicotinamide adenine dinucleotide [NAD+]. The competition for this cofactor between the alcohol oxidizing enzymes and the enzymes involved in steroid synthesis can cause a reduction in testosterone synthesis [80].

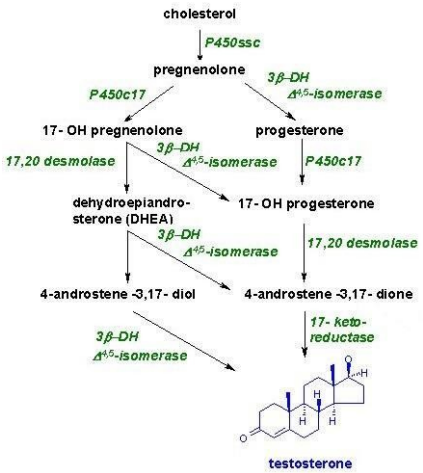
B. Effect of Ethanol on the Catabolism of Testosterone



Testosterone

Long-term alcohol use in men has been shown to increase enzyme activities of 5- α-reductase and aromatase in the liver. This, in turn, leads to an increased testosterone catabolism and turnover to estrogens [83].

C. Effect of Ethanol on the Synthesis of Testosterone



Ethanol has been shown to influence testosterone synthesis through a direct effect on the gonads. This effect has been investigated by searching for possible shifts in concentrations, which could reveal inhibited reactions of the synthesis pathway. Significant reductions of progesterone, 17α-hydroxy progesterone, and testosterone following an alcohol dose of 1.5g/kg have been reported [84].

Generally elevated testosterone levels enhance sexual behaviour. Mu-

thusami and Chinnaswamy [85] revealed that testosterone which was essential for spermatogenesis was decreased by chronic consumption of alcohol. Alcohol has a direct toxic effect on the testis which leads to decreased seminiferous tubular function. Alcohol's effects on the anterior pituitary gland produced a decrease in the production of LH and FSH. The finding of the current study correlates with [86].

Oremosu and Akang [87] states that alcohol causes testicular toxicity by increasing free radicals or reactive oxygen species and lipid peroxidation. Maneeshet al. [61] reported that the oxidative stress created in the Leydig cells as a consequence of chronic alcohol exposure diminishes the steroidogenic capacity of the testes, lowering circulating testosterone levels. The decreased testosterone in ethanol induced rats in the current study might due to oxidative stress created in Leydig cell due to adverse effect of ethanol on this type of cells.

C. Effect of Ethanol on Semen Quality and Morphology

Ethanol suppresses both blood hormonal levels and reduces semen quality. At the seminiferous tubular level, ethanol decreases semen volume, total sperm concentration, motility of sperm, number of morphologically normal sperm, and viability of sperm [85]. The sperm of ethanol consuming animals exhibit alterations in their spermatozoa concentration, abnormal motility and morphology, and a decrease of the fecundation capability [88]. A reduction in sperm concentration and in the percentage of spermatozoa with normal morphology has been detected in chronic alcoholics and in smokers. The above modifications suggest a synergistic or additive effect of both toxic habits on male reproductive function [89]. Brzek [70] found that alcohol consumption decreases semen volume, density, and motility. Goverde et al. [71] found that daily alcohol consumption decreases normal sperm morphology. Carlsen et al. [72] found a significant decrease in mean sperm count, from 113 x 106/mL to 66 x 106 / mL. Gomathi et al. [90] and Goverde et al. [91] reported decreased sperm motility in alcoholics. Goverde et al. [91] observed a significant decrease in the viability of sperm in alcoholics. Donnelly et al. [92] Gomathi et al. [90], and Nagy et al. [93] reported that alcohol consumption decreases the number of sperm with normal morphology and increases the number of sperm with morphological abnormalities.

Alcohol abuse was considered as one of the problems associated with poor semen production and sperm quality. previous studies showed that ethanol injection revealed degenerative changes of epithelial component of the seminiferous tubules [60]. El- Sokkary [94] revealed that alcohol-treated rats presented testicular lesions including a significant decrease in the diameter of the seminiferous tubules, decrease of Leydig cell number and the presence of degenerative germ cells. Nordmann et al., [95] suggested that alcohol consumption has a negative effect of testicular function through the induction of oxidative stress and the concomitant disruption of testicular antioxidant status.

Conclusion

Infertility was one of the major health problems in couples lives, approximately 30% of couple's infertilities were due to male factor [96]. Several conditions could interfere with spermatogenesis and reduce sperm quality and production. Many factors such as drug treatment, chemotherapy, toxins, air pollution, and insufficient vitamin intake might have harmful effects on spermatogenesis and the normal production of sperm [97]. It was estimated that one in 20 men has some kind of fertility problem with low numbers of sperm in his ejaculate. However, only about one in every 100 men has no sperm in his ejaculate. In about one in 100 infertile men the problem was caused by low levels of hormones made in the pituitary gland that act on thetestes. Low production of follicle stimulating hormone [FSH] and Luteinizing hormone [LH] could affect testosterone levels in the testes, and lower sperm production [98].

Alcohol abuse was well known to impair reproductive performance in experimental animals and also in human beings. Alcoholics were found to have fertility abnormalities, with low sperm count, impaired testosterone production, and testicular atrophy [60].

The testis had been shown to be highly susceptible to ethanol as it crosses the blood testis barrier. Chronic ethanol consumption causes sexual defunct. Early histological studies indicated that testis might be even more sensitive to ethanol than the liver. Recently, researchers have become very interested in the effects of alcohol on there productive system. The most important endocrineconsequences of long term alcohol use were its effects on the gonads. In human, high alcohol consumption was associated with serious disorders of spermatogenesis [99].

Ethanol was generally regarded as a reproductive toxin. Humans have consumed alcoholic beverage since prehistoric times for a variety of reasons. Alcoholic beverages were found to affect different system of the human body including reproductive system. It had been observed that chronic alcohol was common among infertile men. In this review we wish to conclude that ethanol exposure may induce reduction of sperm viability, increased sperm mortality, and increased apoptosis, with long-term effects, and may induce permanent male infertility.

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