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Alcohol and reproductive system

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Abstract
In the present study was undertaken to emotional stress, neurotransmitter imbalances and genetic factors are responsible for alcoholism. It has deleterious effect on male and female hormones leading to fecundity (fertility) and impotency. A vigilant statistical analysis indicated the above prevalence rate for alcoholism to the populations of various countries and regions. Alcohol affects male hormone levels and reproductive function such as testes, leydig cells, hypothalamus, testosterone metabolism and cell damage**.** This review considers evidence for an effect of moderate alcohol consumption on female hormone i.e. the levels of estrogen and progesterone, the timing of onset of the menopause and fecundity.

Keywords: Alcoholism male, hormones, female hormone, estrogen and progesterone

Introduction

Alcoholism is a chronic, progressive and often fatal disease. It is a primary disorder and not a symptom of other diseases or emotional problems. The chemistry of alcohol allows it to affect nearly every type of cell in the body, including those in the central nervous system. After prolonged exposure to alcohol, the brain adapts to the changes which alcohol makes and becomes dependent on it. The severity of this disease is influenced by factors such as genetics, psychology, culture and response to physical pain. People have been drinking alcohol for several thousands of years. Just drinking steadily and consistently over time can produce dependence and cause withdrawal symptoms during periods of abstinence. Physical dependence, however, is not the cause of alcoholism. To develop alcoholism, other factors usually come into play including biology, genetics, culture, and psychology.

1. Genetic factors: Genetic factors play a significant role in alcoholism and contribute 40% to 60% of alcoholism cases. The amygdala is an area of the brain thought to play a role in the emotional aspects of craving, which can lead to addiction and is smaller in subjects with family histories of alcoholism1. Asian and possibly Jewish populations may be less likely to become alcoholic because of a genetic deficiency in acetaldehyde, which produces a build-up of acetate after drinking alcohol. Acetate is toxic and in high amounts causes flushing, dizziness and nausea. Some people with alcoholism may have inherited dysfunction in the transmission of serotonin. Serotonin is an important neurotransmitter that is linked to well-being and associated behaviour (eating, relaxation and sleep).
Abnormal serotonin levels are associated with high levels of tolerance for alcohol, impulsive and aggressive behaviour, which can predispose people to drink and also increase the risk for dangerous behavior and suicide in alcoholics.

2. Chemical imbalances: Alcohol has widespread effects on the brain and can affect neurons, brain chemistry, and blood flow within the front lobes of the brain. The brain's chemistry changes after long-term alcohol use in order to adapt to the cravings and pain of withdrawal. Such chemical changes may employ two effects that lead to dependency after quitting.

a) Reducing agitation: When a person who is dependent on alcohol stops drinking, the following chemical responses create an overexcited nervous system and agitation. 1) A drop in gamma-amino butyric acid, a brain chemical that inhibits impulsivity. 2) An increase in glutamate, a brain chemical that excites nerve cells. 3) An increase in epinephrine and corticotropin releasing factor, hormones that produce stress. This hyperactivity in the brain produces an intense need to calm down with the use of more alcohol **(**Table 1).

b) Restoring pleasure: Alcohol releases the following neurotransmitters and other chemicals that produce pleasurable feelings, 1) Dopamine produces euphoria and a sensation of being rewarded and repeated alcohol use increases sensitivity to dopamine. 2) Serotonin produces feeling of well being. 3) Opioid peptides are important for well being. Over time heavy alcohol use appears to deplete the stores of dopamine and serotonin.

The effects of alcohol on female reproductive system

The pharmacokinetic response of pre-menstrual women to moderate alcohol intake has been reviewed 2. The present work considers evidence for an effect of moderate alcohol consumption on the levels of the female hormones oestrogen and progesterone, the timing of onset of the menopause and fecundity. In 1988 study of Mendelson and coworkers 3 alcohol levels of 70-75 mg/dl produced a significant increase (55-66% above predrinking levels) in the level of plasma oestrodiol. These groups of researches have also reported increase in plasma oestrogens in response to concurrent leutinizing hormone releasing hormone (LHRH) and ethanol administration and to administration of the opiod antagonist naloxone with alcohol. Mendelson4 has made two important proposals, Firstly, the effect of alcohol on reproductive hormone levels may be most evident in situations where gonadotropin levels are high, namely the early stages of pregnancy and during the pre-ovulatory surge of LH around the midpoint of the menstrual cycle Secondly, the effect of alcohol induced rise in oestrogen levels is a consequence of the metabolic breakdown of alcohol in the liver. Enzymatic degradation of alcohol is accompanied by a change in the proportions of the two forms of the co-enzyme nicotinamide and adenine dinucleotide (NAD). The accumulation of the reduced form, NADH, means that the breakdown of oestradiol to oestrone is less and so oestradiol accumulates. Reich Man showed that alcohol consumption was associated with a rise in the levels of plasma dehydroepiandrosterone sulphate during the follicular phase, plasma oestrone, oestrodiol and urinary oestradiol in the peri-ovulatory phase and urinary oestrone, oestradiol and oestriol in the luteal phase. More recent evidence supporting the proposal that alcohol intake is indeed associated with elevated oestrogen levels is provided by the report of Muti5 and Sarkola6. In oral contraceptive users, alcohol induced rise in oestradiol, but not oestrone level. In the nonusers, the evidence was less convincing. In agreement with the proposal of Mendelson, these authors suggest that a change in the redox state of liver cells induced by alcohol metabolism is responsible for increased enzymatic conversion of oestrogen to oestradiol.

Furthermore they cited the work of Tseng and Gurpide, which reported that the enzyme responsible 17-b hydrosteroid dehydrogenase type 2 is induced by the synthetic progestins contained within some oral contraceptives. Hankinson7 reported that oestrogren sulphate levels rose by 30% in women drinking at least 30 g of alcohol per day while Katsouyani noted that the levels of urinary oestradiol and oestrone in postmenopausal women increased by 16% and 20% respectively in response to a daily intake of one drink.

Gavaler and co-workers8 have also investigated a possible relationship between alcohol intake and oestrogen levels. They observed that positive correlation is evident between oestradiol levels and number of weekly drinks consumed. Another observation was that moderate drinkers were distinguished from abstainers by lower testosterone levels and oestradiol to testosterone ratios. This reflects an increased aromatization of testosterone stimulated by ethanol. Studies in this field have been elegantly reviewed by Purohit9. Studies by Ginsburg10 have shown evidence for an effect of alcohol on synthetic oestrogen administered to post-menopausal women either as a patch or orally. Alcohol (Blood level 117 mg/dl) was associated with a rise in baseline concentrations of oestradiol from 179 to 219 pg/ml 35 min after alcohol intake than those of control subjects.

Evidence is also presented that alcohol may be associated with decreased oestradiol clearance rate after removal of a patch. Teoh11 reported that alcohol suppressed progesterone levels during the early follicular phase of the cycle following naltrexone administration. It was suggested that, by decreasing progesterone production, alcohol may compromise the survival of the blastocyst. Decrease in progesterone levels in response to acute alcohol intake (0.34 to 1.02 g/kg) in a group of women comprising both oral contraceptive users and non-users. From in vitro studies using human placental cells exposed to alcohol concentrations of 20–40 mM caused a significant decrease in progesterone synthesis. Specifically, the onset of the menopause is delayed by moderate alcohol consumption. Moderate alcohol intake (100 g, 12.5 UK units per week) was reported to be associated with a significant but small increased risk of ovulatory infertility and an increased risk of endometriosis. Olsen linked high alcohol consumption to decreased fecundity. Jensen concluded that the chances of successful conception decreased with increasing alcohol intake. The fecundity ratio of conception among exposed couples divided by those not exposed fell from 0.61 (10–50 g of alcohol per week) to 0.34 (100 g of alcohol). Increased oestradiol levels reduce FSH secretion to levels which in turn, by suppressing folliculogenesis lead to anovulation. If Mendelson is correct and ovulation is indeed prevented by moderate alcohol intake, then women not wanting to become pregnant can still experience harmful effects. The cardio protective hormone characteristic of the second (luteal) phase of the menstrual cycle will not be produced. The implications of the long-term loss of these hormones in young women are considerable.

Animal studies have demonstrated the toxicity of alcohol to female gonads. Consistent with the animal findings menstrual abnormalities decreased female sexual characteristics and sterility associated with ovarian atrophy have been reported in chronic alcoholic women. Inspite of marked hypo-oestrogenization, plasma gonadotropin levels have not been elevated in chronic female alcoholics, indicating that disturbed regulation of gonadotropin secretion is an important factor in the genesis of ovarian failure in these patients, even if ovarian function may also be directly impaired. Hyperprolactinaemia is not one of the hormonal hallmarks of sexual dysfunction in chronic alcoholic women.

The effects of alcohol on male reproductive system

Hormonal system controlling testosterone production can result not only in infertility but also in other deleterious consequences, such as accelerated bone loss (i.e., osteoporosis), decreased muscle function, and lower than normal numbers of red blood cells (i.e., anemia).

Effects of alcohol on the Testes

Numerous studies have indicated that alcohol abuse in men can cause impaired testosterone production and shrinkage of the testes12. These changes can result in impotence, infertility and reduced male secondary sexual characteristics. Testicular atrophy is likely to be caused by several factors, including alcohol's damaging effects on the testes and alcohol's effects on LH and FSH, which among other factors stimulate testicular growth. Testicular atrophy results primarily from the loss of sperm cells and decreased diameter of the seminiferous tubules13. One opioid, known as beta-endorphin, has been shown to increase with acute and chronic alcohol consumption and thus may be one link between alcohol use and testicular damage. Beta-endorphin produced within the testes suppresses testicular testosterone production and release. Similarly, beta-endorphin produced in the hypothalamus results in decreased LHRH levels. In addition, opioids may increase programmed cell death (i.e. apoptosis). Apoptosis at the gonadal level would result in the death of both leydig and seminiferous cells.

Effects of alcohol on leydig cells and testosterone metabolism: Alcohol's adverse effects on leydig cell function and testosterone production were demonstrated in a study of young and healthy male volunteers with normal liver function who received alcohol over a 4-week period12. With this level of alcohol consumption, testosterone levels in the men's blood declined as early as 5 days into the study and continued to fall over the entire study period. The investigators attributed the decline in testosterone to a decrease in the production rate and an increase in the breakdown and removal of testosterone from the blood (i.e. an increased metabolic clearance rate).

Effects of alcohol on testosterone

Several studies have examined alcohol's effects on testosterone synthesis which occurs via the testosterone biosynthetic pathway. This pathway consists of a series of steroid precursors of testosterone and the respective enzymes necessary to synthesize each precursor from the previous one. Researchers are currently investigating alcohol's effects on both the molecular steps integral to manufacturing the enzymes in the testosterone pathway and the steroid precursors of testosterone. One such strategy involves giving male rat's testosterone pellets to replace testosterone. The metabolic clearance of testosterone increases only in men without alcoholic liver disease. In men with alcoholic liver disease, the metabolic clearance is decreased14. Another mechanism is the conversion of testosterone or one of its precursors in to estrogens through a process called aromatization. For example, testosterone can be metabolized to an estrogen called estradiol. Similarly, the immediate precursor of testosterone- androstenedione can be converted in to a less potent estrogen called estrone. Several studies found that some people with alcoholic liver disease have increased levels of estrogen in the blood.

Animal studies have indicated that alcohol does not directly enhance estrogen production in the testes. Instead, increased aromatization of testosterone and androstenedione to estrogens occurs in other tissues, such as the liver and fat tissue15. In those tissues, alcohol stimulates an enzyme called aromatase, which mediates the aromatization reaction. Consequently, in addition to decreased testosterone production and metabolism, higher than normal percentages of testosterone and androstenedione are converted into estradiol and estrone, respectively in heavy drinkers. This increased conversion may account for the elevated estrogen levels and abnormal breast enlargement observed in some heavy drinkers. In addition to causing breast enlargement, estrogens appear to exert a negative feedback effect on LH and FSH production and may contribute to alcohol's suppression of those key reproductive hormones. Clinical studies have demonstrated that alcohol not only alters testosterone metabolism but also diminishes testosterone production. To elucidate the mechanisms underlying the alcohol induced reduction in testosterone secretion, researchers have investigated in vitro effects of alcohol on testes or analyzed the testes independent of the rest of the body. In those experiments, testosterone production in the isolated testes decreased, as it had in studies in intact animals16. These findings indicate that alcohol exerts its effect, at least in part, by acting directly on the testes. Researchers have proposed several mechanisms that may contribute to the alcohol-induced testosterone suppression. The enzyme that mediates the breakdown of alcohol to acetaldehyde uses certain molecules that are also required by enzymes involved in testosterone production, thereby preventing testosterone generation. The adrenal hormones cortisol (in humans) and corticosterone (in rats) can suppress the reproductive system by inhibiting the ability of the leydig cells to produce and release testosterone. Studies in humans and animals found that alcohol exposure increases adrenal hormone levels, thereby interfering with reproductive functions. Alcohol has been shown to result in the production of less potent LH variants.17 Thus, alcohol's deleterious effects on LH function are qualitative as well as quantitative. Studies with young (i.e., pubertal) male rats indicate that either acute and chronic alcohol exposure result in profound testosterone suppression accompanied by lower or normal LH and FSH levels, when elevated levels are expected. An effect on FSH production and activity research also has indicated that alcohol reduces FSH levels in the blood, although this effect is not as consistent as its effect on LH levels. In light of the alcohol-induced disruption of sertoli cell function and reduction in testosterone levels, one would expect FSH levels to be elevated, because FSH is part of the same negative feedback mechanism as LH. Normal FSH levels actually should be considered toolow for the accompanying testosterone levels.

Effects of alcohol on Hypothalamus

Study in male rats' shows alcohol administration significantly lowered GnRH levels in the blood vessels connecting the hypothalamus to the pituitary gland. Alcohol decreases GnRH secretion by acting at a site outside the hypothalamus and/or that alcohol's breakdown product (acetaldehyde) rather than alcohol itself reduces GnRH secretion. In addition to interfering with GnRH secretion, alcohol also appears to affect the production of active GnRH molecules. A protein hormone, GnRH first is produced as a large, inactive precursor molecule called pre-pro-GnRH, which consists of 92 building blocks (i.e., amino acids). To generate the functional GnRH molecule, 82 of those amino acids are removed from the inactive precursor molecule. This processing reaction from an inactive precursor to an active molecule appears to be diminished after alcohol exposure.

Effects of alcohol on cell damage

Because testicular membranes are rich in molecules known as fatty acids, which are prone to oxidative injury, it is reasonable to consider that lipid peroxidation may contribute to the gonadal dysfunction that occurs as a result of acute or chronic alcohol use.18 Peroxidation injury can be attenuated with dietary vitamin A supplementation. Peroxidation of testicular lipids that occurs following alcohol consumption may be an important factor in the pathogenesis of alcohol associated gonadal injury and that diets rich in vitamin.

Table 1: Effects of alcohol on the various organs

Medical Problem	Light-Moderate Drinking	Binge Drinking and Hangovers	Heavy Chronic Drinking
Liver Disorders, Heart Disease	Beneficial. May help reduce risk for heart disease caused by artery block	Changes in liver function. High Blood Pressure. Increased heart rate. Heart Rhythm disturbances.	Alcoholic Hepatitis, Cirrhosis. High Blood Pressure. Weakened heart muscles leading to failure.
Cancer	Associated with higher risk for breast cancer in women.		Cancers in the head and neck, esophagus, stomach, liver, pancreas, and cervix and vagina (in women).
Neurologic or Mental Disorders	Insomnia. Headache.	Memory impairment and problems in thinking and concentration.	Nerve damage from severe vitamin deficiencies. Impairment in mental functioning and memory. Emotional disorders.
Genital and Reproductive Problems.	Increase sexual drive (although even modest drinking can cause impotence in men). Even moderate drinking during pregnancy increases risk for birth defects.	Any drinking during pregnancy increases risk for birth defects.	Impotence in Men. Menstrual disorders and infertility in women. Drinking during pregnancy increases risk for birth defects.
Immune System			Increased susceptibility to infections.

A can help counteract such injury. Research currently is being conducted to examine the role of oxidative injury in alcohol induced hypogonadism.

Conclusion

Chronic alcoholism causes male as well as female reproductive hormone secretion imbalance. It is considered as one of the important factor causing breast and prostate cancer. The number of alcoholics and alcohol related admissions are on a rise and are posing severe dreading issues before the world's status.

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