MedCrave
Step into the World of Research

Pharmacy & Pharmacology International Journal

Review Article

Open Access

CrossMark

Caffeine consumption and the risk of infertility among women

Abstract

Caffeine (1,3,7-Trimethylxanthine) is the naturally occurring substance that is extracted from the seeds, leaves and fruits in more than 63 species of the plant. Caffeine is extensively found in many foods & beverages including tea, coffee, energy drinks, cola and chocolate. It is rapidly absorbed and widely distributed and proves its presence in the saliva, embryo, breast milk and blood of neonates (new born babies). So, the present review was designed to unfold the myths and facts over the effect of caffeine on the development of infertility among women. Caffeine is the one of the most frequently ingested psychoactive substances worldwide. This review consists an extensive survey of literature from the Scopus, PubMed, Springer Nature and other international reputed sources. This chapter covers the diverse topics of caffeine including origin, structure and impacts on health especially on fertility among normal women and men (small extent). In most of the studies, it showed that there is no potential link between the caffeine consumption and development of infertility among women except in few studies in an equivocal way. Its overdose becomes dangerous but within the limit proves itself as a boon to human life. In conclusion, it is safe to drink coffee but in limitation and not in higher dose than 400mg per day.

Keywords: caffeine, cocoa, coffee-beverages, infertility, pregnant women

Volume 10 Issue 2 - 2022

Mohammad Asif Khan,[1] Kanchan Gangwar,[2] Saloni Srivastava,[3] Varsha Singh,[4] Akbal Ahmad,[5] Ruman Khan[6]

[1]Assistant Professor, Department of Pharmacology, Rakshpal Bahadur College of Pharmacy, India
[2]Assistant Professor, Department of Pharmacology, Kritika Pharmacy College, India
[3]Assistant Professor, Institute of Pharmacy, Kakori, India
[4]Assistant Professor,Vikrat Institute of Pharmaceutical Sciences, India
[5]Assistant Professor, Hygia Institute of Pharmaceutical Education and Research, India
[6]Professor, Department of Pharmacology, Rakshpal Bahadur College of Pharmacy, India

Correspondence: Mohammad Asif Khan, Department of Pharmacology, Rakshpal Bahadur College of Pharmacy, Bareilly-243001 (UP), India, Email asifkhanpcol@gmail.com

Received: February 27, 2022 | **Published:** March 28, 2022

Abbreviations: CNS, central nervous system; CAa, Catecholamines; US, United States; BMI, body mass index; DNA, deoxy-ribonucleic acid; FDA, food and drug administration; RR, relative risk; TTF, time to fertility; SAB, spontaneous abortion; COX, cyclo-oxygenase

Introduction

Caffeine (1,3,7-Trimethylxanthine) is the naturally occurring substance that is extracted from seeds, leaves and fruits in more than 63 species of the plant. It is rapidly absorbed and widely distributed and proves its presence in the saliva, embryo, breast milk and blood of neonates (new born babies). Apart from stimulating of Central Nervous System (CNS), caffeine is found biologically effective in different aspects such as increased heart rate to counter the hypotension, smooth muscles relaxation and production of catecholamines (CAs) needed for synthesis of diverse neurotransmitters or signal molecules. Caffeine may change ovulation and this is directly correlated with sex hormone- binding globulin proteins.[1] The history of caffeine & methylxanthines are unknown and reported in myth. Coffee became popular and widespread in the beginning of fifteenth and sixteenth centuries but in Europe it became well-known in Eighteenth and Nineteenth centuries. Coffee intake has been an upper-class drink in Saudi Arabia and a luxury drink in Europe. Caffeine is the probably a most used drug in amongst human being. It is taken as Central Nervous System (CNS) stimulant and to establish a great deal with the body and mood.[2] Coffee, tea, and chocolate are all natural sources of dietary caffeine. To improve the stimulating qualities of items, synthetic caffeine is also used. Previously, caffeine was only added to soda-type beverages, but during the last decade, caffeine has been added to a wide range of meals and non-food items to stimulate arousal, alertness, energy, and elevated mood.[3-5]

The caffeine is consumed daily in various forms such as medications of cold, pain and in mixtures of CNS stimulants called amphetamines. In America, more than 80% of population used to drink coffee or tea on daily basis. Doubtless, caffeine produces addiction but has milestone therapeutic potentials on diverse health issues.[6] Caffeine is the one of the most frequently ingested psychoactive substances worldwide. Many researchers have estimated the risk of depression after frequent coffee or caffeine use among women. In this study, a total of 50739 US women were selected with mean age of 63 years, free from depressive symptoms in 1996 and followed up through June 1, 2006. The risk was determined in women who consuming 2 to 3 cups per day, 3 to 4 cups daily and compared with women consuming 1 or less cup of caffeinated coffee per week. This research concluded that depression risk decreases with increasing in caffeine or coffee consumption.[7]

Valck & Cluydts (2001) have evaluated the effect of caffeine on the sleep deprivation among drivers by potentiating the alertness. They involved 12 drivers between 20 and 25 age groups, with 7.5 hour in bed and given 300 mg sustained caffeine release dose. The driving module was noted twice in a 45 min driving under stimulator. In results, it declared that caffeine consumption decreased the drifting in drivers suffering from sleep deprivation.[8] So, the present review was designed to unfold the myths and facts over the effect of caffeine on the development of infertility among women.

Impact on fertility among reproductive women

Bolumar et al. (1997) have estimated the effect of caffeine consumption on the infertility by the European multicenter study. They randomly selected the sample from 3187 women who have been involved in unprotected sexual intercourse. The women were chosen between August 1991 to February 1993 and from the five European countries- Denmark, Germany, Italy, Poland and Spain. Risk of subfecundity and fecundability ratio was assessed for age, frequency of coitus, smoking, alcohol intake, educational level, working status, use of contraceptives and country living. A significant increase for

subfecundity in first pregnancy was found in women taking caffeine more than 500 mg daily. The researchers concluded that high levels of caffeine may delay conception among fertile women.[9] Buck et al. (1997) have been evaluated the numerous risk factors (lifestyle) in the development of infertility. They included factors such as cigarette smoking, alcohol and caffeine consumption, body mass index (BMI), physical exercise and use of drugs/narcotics to determine their adversity on infertility. Authors declared that the obesity (increase in body size) is the risk factor for primary ovulatory infertility in women. In conclusion, the cocaine, marijuana & alcohol use, caffeine consumption, vigorous exercise and use of thyroid medications were found as possible risk factors for various subtypes of primary infertility in normal reproductive women.[10]

Ricci et al. (2017) reported the infertility relation between caffeine consumption and reproductive outcomes comprising as semen parameters, DNA characteristics of sperm and fecundability. Total they taken 19,967 men as participants in this research and most of research suggests that caffeine from coffee, tea and cocoa drinks did not make any change in quality of semen. In some studies, it declared that cola containing beverages and caffeine containing soft drinks affected the semen volume, its count and concentration. It concludes that caffeine consumption may produce adverse effect reproductive system by DNA damage in sperm. Caffeine is approved safe at level not exceeding 200 ppm (0.002%) by the US Food and Drug Administration (FDA) in cola-type beverages for flavor purposes.[11] Wikoff et al. (2017) have been published a systematic review on data from 2001 to June 2015, on the adverse outcomes of the caffeine on the healthy adults, pregnant women, adolescents and children. Total four things taken in questionnaire such as population, exposure, comparator, and outcome to address the five types of outcomes including acute toxicity, cardiovascular toxicity, bone and calcium effects, behavior, and development and reproduction among participants. This research suggests that consumption of caffeine up to 400 mg caffeine/day in healthy adults did not produce adverse effects on cardiovascular system, psychological status, reproductive system, acute and developmental effects or bone status. Caffeine consumption up to 300 mg caffeine/day has not demonstrated any link with adversity in reproductive and developmental effects among healthy pregnant women. Caffeine (10g/day) has been considered for lethality (acute outcome) among healthy adults.[12]

Chiaffarino et al. (2014) have given data on association between endometriosis and caffeine consumption in several in 6 case- control and 2 cohort epidemiological studies. They recorded relative risks of endometriosis for high, low or no caffeine intake; included 1407 women with endometriosis. The relative risk (RR) was found as 1.09 for high and low when compared to no caffeine consumption.[13] Many scientists have researched on the evaluation of effects of several lifestyle factors such as age, weight, smoking, diet, exercise, stress, caffeine & alcohol intake and exposure to environmental pollutants on fertility of human being. It resulted out that age, weight and smoking severely affected the general health and reproductive performance. However, the harmful impacts of caffeine, stress, alcohol consumption & environmental pollutants are remained equivocal or undetermined-well.[14]

Coffee and other caffeine mixed beverages are widely consumed by common women as well as pregnant women. Such consumptions reduce the chances of developing a pregnancy or may exhibit numerous harmful effects on the development of fetus are widely concern the topic for debate. Coffee consumption is very common among people across the globe. Finland has the highest consumption (12.0 kg coffee/person/year) and Denmark is considered the fourth most coffee-consuming country (8.7 kg coffee/person/year) worldwide. A cup of coffee contains about 100 mg of caffeine. Lyngso et al. (2017) investigated that if the coffee or caffeine intake may be associated with natural fertility including time to fertility (TTF) and spontaneous abortion (SAB), clinical pregnancy and live birth among women by case-control and cohort studies. The comprehensive results exhibited that coffee or caffeine consumption is associated with a significantly high risk of spontaneous abortion (SAB) for 300 mg and 600 mg caffeine per day consumption. Whether there was no association found between coffee or caffeine intake with clinical pregnancy, child birth and time to fertility (TTP).[15]

Soylu et al. (2018) have studied that whether the consumption of caffeine and tea makes the risk of generation of primary infertility in females. In this cohort study, the researchers taken nulliparous Danish women aged 20-29 years from a prospective region. From the date of enrollment (1991-1993) to 2010 (31 December) total 7574 women underwent for primary infertility analyses using Cox proportional hazard models. During follow up studies, total 822 women were diagnosed for primary infertility but not showed any link with the number or frequency of caffeine intake. Caffeine is extensively found in many foods & beverages including tea, coffee, energy drinks, cola and chocolate. Effects of caffeine on health have been seen like a double-edged sword. Bu et al. (2020) have taken men and women with the total of 12912 participants in their study and diagnosed for infertility of exposure to caffeine. The results demonstrated that there is no proof of development of infertility in the large, moderate or low caffeine consumption participants in one cohort and three case control studies.[16]

McGuire et al. 2014 have reported that in certain research, caffeine consumption is linked to fertility indices, but not in others. According to a thorough literature assessment conducted by the Oak Ridge National Laboratory, chronic caffeine consumption in humans is associated with negative effects on pregnancy and reproduction, such as delayed pregnancy and lower fecundity. These effects were observed at caffeine levels more than 200 mg/day.[17] Caffeine has been used to relieve pain for a long time. However, its pain-reduction benefits were not thoroughly investigated until 1984, when Lachance[18] discovered that adding caffeine lowered the amount of acetaminophen required to meet the aim of a 40% reduction in pain scores.[19] Caffeine's vasoconstrictive activity, caused by adenosine receptor antagonism, has now been linked to pain alleviation.[20] Acute dietary caffeine consumption has been shown in several studies to alleviate pain.[21] Caffeine, in doses ranging from 300 to 500 mg, can also alleviate post-dural puncture headaches, the most common consequence of lumbar puncture operations.[22]

Conclusion

Caffeine usage patterns, such as alcohol-mixed energy beverages, may raise the risk of injury. Some populations, such as pregnant women, youngsters, and people suffering from mental illnesses, may also be prone to the negative effects of caffeine. Caffeine consumption in excess is increasingly being recognized as possibly dangerous by health-care professionals and regulatory bodies.[23]

This review consists an extensive survey of literature from the Scopus, PubMed, Springer Nature and other international reputed bodies. This covers the diverse topics of caffeine including origin, structure and impacts on health especially on fertility among normal women and men (small extent). In most of the studies, it showed that there is no potential link between the caffeine consumption and development of infertility among women except in few studies in

an equivocal way. Apart from caffeine, the other life-style factors such cigarette smoking, alcohol consumption and use of drugs demonstrated a significant cause behind infertility in women. Coffee, cocoa butter and tea are the main sources for caffeine that is CNS stimulant and beneficial to us in many aspects of health. Its overdose becomes dangerous but within limit proves itself as a boon to human life. In conclusion, it is safe to drink coffee but in limitation and not in higher dose than 400mg per day.

Acknowledgments

Author Mr. Mohammad Asif Khan has worked on designing of this review study. The co-authors Ms. Kanchan Gangwar, Ms. Saloni Srivastava and Ms. Varsha Singh did extensive review of literature from Scopus, PubMed and other reputed international bodies. Co-author Mr. Akbal Ahmad and Dr. Ruman Khan worked on the conclusion and references. At last, Mohammad Asif Khan formatted the paper as per the template and communicated.

Conflicts of interest

This work does not contain any conflict of interest. This review study has not been supported by any funding agency/source.

References

1. Sadeu JC, Claude L Hughes, Sanjay Agarwal, et al. Alcohol, drugs, caffeine, tobacco, and environmental contaminant exposure: Reproductive health consequences and clinical implications. *Critical Reviews in Toxicology*. 2010;40(7):633–652.
2. Fredholm BB. Notes on the history of caffeine use. *Handbook of Experimental Pharmacology*. 2011;200:1–9.
3. Dews PB. Caffeine. *Annu Rev Nutr*. 1982;2:323–241.
4. Lieberman HR, Wurtman RJ, Emde GG, et al. The effects of caffeine and aspirin on mood and performance. *J Clin Psychopharmacol*. 1987;7(5):315–320.
5. Frary CD, Johnson RK, Wang MQ. Food sources and intakes of caffeine in the diets of persons in the United States. *J Am Diet Assoc*. 2005;105(1):110–113.
6. Benowitz Neal L. Clinical Pharmacology of Caffeine. *Annual Review of Medicine*. 1990;41:277–288.
7. Lucas Michel, Fariba Mirzaei, An Pan, et al. Coffee, Caffeine and Risk of Depression Among Women. *American Medical Association*. 2011;171(17):1571–1578.
8. Valck Elke De, Raymond Cluydts. Slow-release caffeine as a countermeasure to driver sleepiness induced by partial sleep deprivation. *Journal of Sleep Research*. 2001;10(3):203–209.
9. Bolumar F, Olsen J, Rebagliato M, et al. Caffeine Intake and Delayed Conception: A European Multicenter Study on Infertility and Subfecundity. *American Journal of Epidemiology*. 1997;145(4):324–334.
10. Buck Germaine M, Lowell E Sever, Ronald E Batt, et al. Life-Style Factors and Female Infertility. *Epidemiology*. 1997;8(4):435–441.
11. Ricci Elena, Paola Vigano, Sonla Cipriani, et al. Coffee and caffeine intake and male infertility: a systematic review. *Nutrition Journal*. 2017;16(1):37.
12. Wikoff Daniele, Brian T Welsh, Rayetta Henderson et al. Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children. *Food and Chemical Toxicology*. 2017;109(1):585–648.
13. Chiaffarino F, Bravi F, Sonia Cipriani, et al. Coffee and caffeine intake and risk of endometriosis: a meta-analysis. *Eur J Nutr*. 2014;53(7):1573–1579.
14. Homan GF, Davies M, Norman R. The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment: a review. *Human Reproduction Update*. 2017;13(3):209–223.
15. Lyngso Julie, Cecilia Host Ramlau-Hansen, Bjorn Bay, et al. Association between coffee or caffeine consumption and fecundity and fertility: a systematic review and dose–response meta-analysis. *Clinical Epidemiology*. 2017;9:699–719.
16. Soylu Liv I, Allan Jensen, Kirsten E. Juul et al. Coffee, tea and caffeine consumption and risk of primary infertility in women: a Danish cohort study. *Acta Obstet Gynecol Scand*. 2018;97(5):570–576.
17. Jennifer L Temple, Christophe Bernard, Steven E Lipshultz, et al. The Safety of Ingested Caffeine: A Comprehensive Review. *Front Psychiatry*. 2017;8:80.
18. Lachance MP. The pharmacology and toxicology of caffeine. *J Food Saf*. 1982;4:71–112.
19. Myers DE, Shaikh Z, Zullo TG. Hypoalgesic effect of caffeine in experimental ischemic muscle contraction pain. *Headache*. 1997;37(10):654–658.
20. Leathwood PD, Pollet P. Diet-induced mood changes in normal populations. *J Psychiatr Res*. 1982;17(2):147–154.
21. Larroque B, Kaminski M, Lelong N, et al. Effects of birth weight of alcohol and caffeine consumption during pregnancy. *Am J Epidemiol*. 1993;137(9):941–950.
22. Lee WC, Neugut AI, Garbowski GC, et al. Cigarettes, alcohol, coffee, and caffeine as risk factors for colorectal adenomatous polyps. *Ann Epidemiol*. 1993;3(3):239–244.
23. McGuire S. *Caffeine in Food and Dietary Supplements: Examining Safety-Workshop Summary*. Washington, DC: The National Academies Press; 2014.