Effects of cola intake on fertility: a review

Atsushi Imai¹*, Satoshi Ichigo², Hiroshi Takagi², Kazutoshi Matsunami², Noriko Suzuki³, Akio Yamamoto³

¹Institute of Endocrine-Related Cancer, Matsunami General Hospital, Gifu, Japan; *Corresponding Author: aimai@matsunami-hsp.or.jp
²Department of Obstetrics and Gynecology, Matsunami General Hospital, Gifu, Japan
³Department of Obstetrics and Gynecology, Gifu University School of Medicine, Gifu, Japan

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ABSTRACT

The consumption of soft drinks has increased considerably during the last decades. Among them, the cola-based preparations are possibly the refreshments with the largest sales worldwide. During the previous years, important concerns have been raised about the effects of colas on human health. In this review, we introduce the cola effects on reproduction including pregnancy miscarriages, ovulatory and menstrual disorders, and reduced semen quality. Although caffeine intoxication may be thought to play the most important role, a component of cola other than caffeine, or in combination with caffeine, may be associated with increased risk of reproductive hazards in heavy cola (> 1 L per day)-consumers. Cola discontinuation usually leads to an uneventful recovery in the most cases suggesting justification of limitations in the maximum recommended daily dose of these soft drinks. Cola is not an essential beverage, and abstaining from drinking more than 1 L per day is a minor intrusion in one's personal life. Despite these uncertainties, this growing knowledge may alarm the fertility risk of chronic cola intake in peoples of childbearing age.

Keywords: Cola; Soft Drink; Caffeine; Semen; Miscarriage; Ovulation

1. INTRODUCTION

The consumption of soft drinks has increased considerable during the last decades. Among them, the cola-based preparations are possibly the refreshments with the largest sale worldwide. During the previous years, important concerns have been raised about the effects of colas on human health. In addition to the possible detrimental effects of chronic cola consumption (enamel softening [1,2], bone demineralization [3,4], hypokalemic myopathy [5-7], development of metabolic syndrome and diabetes mellitus [8-10], and chronic kidney diseases [11,12]), several lines of evidence suggest that the chronic consumption of large amounts of cola-based soft drinks may increase the risk of reproductive problems such as decreased fetal growth, preterm delivery, and spontaneous abortion [13-16]. However, results from these epidemiological studies suggesting the association between cola consumption and such outcomes have been conflicting and the available information is incomplete and remains controversial. The observations may have important public health implications as, recently, trends of increasing the portion size of these preparations have been noticed. With the aim of evaluating the available epidemiological evidence of the effect of cola consumption on reproductive quality (see Table 1), a systematic qualitative review was conductive.

2. PHARMACOLOGICAL EFFECTS OF INGREDIENTS IN COLA

Cola contains many different chemical compounds and no certainty exists as to which ones may be associated with disease risk.

Cola soft drinks may contain large amounts of glucose (up to 11 g of sugar/dL) and high-fructose corn syrup. Highly caloric carbonated soft drinks are often sweetened with high fructose corn syrup, which makes soda inexpensive to produce. While sugary soda may be sold cheaply as a food item and yield a profit, they provide little satiety. Thus, the excessive consumption of these preparations may lead to glycemic load, resulting in osmotic diuresis and hyperinsulinemia. Fructose itself may cause kidney damage, perhaps mediated by uric acid [17].

Cola contains sufficient amounts of caffeine ranging...
Table 1. Main points of the cola (carbonated soft drink) - induced reproductive hazards.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Amount of cola consumption*</th>
<th>Suggested cause</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced sperm count (30% below the average in non-cola-drinkers)</td>
<td>&gt; 1 L per day during the past week</td>
<td>Constituents in cola other than caffeine</td>
<td>[33]</td>
</tr>
<tr>
<td>Ovulatory disorder infertility</td>
<td>&gt; 2 soft drinks a day</td>
<td>Contents in cola other than caffeine or sugar</td>
<td>[30]</td>
</tr>
<tr>
<td>Shortened menses duration and cycle</td>
<td>&gt; 300 mg of caffeine per day</td>
<td>Caffeine</td>
<td>[21]</td>
</tr>
<tr>
<td>Increased risk of miscarriage (hazard ratio of 2.23)</td>
<td>200 mg of caffeine per day during pregnancy</td>
<td>Caffeine</td>
<td>[45,50]</td>
</tr>
</tbody>
</table>

*Assumed caffeine content of 150 mg/L.

from 95 to 160 mg/L. Caffeine, 1,3,7-trimethylxanthine, is among the most frequently ingested pharmacologically active substances [18,19]. Carbonated soft drinks and coffee are the main sources of caffeine intake.

Other components in cola, such as phosphorus in dark cola, may reveal significant physiological actions.

3. OVULATION AND MENSTRUATION DISORDER

Women who consume caffeine may be less likely to have long menses. This phenomena is biologically likely plausible because caffeine is a known vasoconstrictor [20], reducing uterine blood flow. Constriction of uterine blood vessels would be expected to reduce uterine blood flow, which could reduce menstrual bleeding and shorten the duration of menses [21]. Caffeine may alter the duration of menstrual cycle via the effect of caffeine on sex hormones or the hormone receptors [22]. However, the results of studies of caffeinated beverage consumption in relation to fecundity are inconsistent. Several studies in humans have reported an association between caffeine intake and delayed time to conception [23-26], in contrast, others have shown either no association [27,28] or a relation only at very high levels of intake [29]. Most of these studies have retrospectively collected information on alcohol and caffeine intake, making the results susceptible to biases. The study by Fenster et al. [21] described the relation between caffeine intake and menstrual function was examined in 403 healthy premenopausal women who belonged to Kaiser Permanente Medical Care Program in 1990-1991. They collected information about caffeinated beverage intake as well as other lifestyle, demographic, occupational, and environmental factors. Subjects collected daily urine samples and completed a daily diary for an average of five menstrual cycles. Caffeine intake was not strongly related to an increased risk for anovulation, short luteal phase, long follicular phase, long cycle, or measures of within-woman cycle variability. Chavarro et al. [30] followed 18,555 married women without a history of infertility for 8 years as they attempted to become (or became) pregnant. Soft drinks were the only beverages positively related to ovulatory infertility. Intake of caffeinated soft drinks was associated with a higher risk of ovulatory disorder infertility among women consuming at least 2 or more soft drinks per day. Women consuming 2 or more caffeinated soft drinks per day had a 47% greater risk of ovulatory infertility than women who consumed less than 1 caffeinated soft drink per week. Their analyses suggested that neither caffeine nor fructose was responsible for this association. Extreme comparisons of caffeine and coffee intake suggested no association or an inverse association with ovulatory disorder infertility. Some constituents in cola other than caffeine or sugar may cause ovulatory disorder.

Regarding the risk of ovarian cancer developments, laboratory data suggest that caffeine or some components of coffee may cause DNA mutations and inhibit tumor suppressor mechanisms, leading to neoplastic growth. An increased risk was observed in the multivariate model for women who reported drinking five or more cups/day of caffeinated coffee compared to women who reported drinking none. Decaffeinated coffee, total coffee, and caffeine were not statistically significantly associated with ovarian cancer incidence. A component of coffee other than caffeine, or in combination with caffeine, may be associated with increased risk of ovarian cancer in postmenopausal women who drink five or more cups of coffee a day [31].

4. SEMEN QUALITY DECLINE

A recent Danish study revealed that sperm counts are lower in men who drink cola of 1 L (estimated to contain 100-140 mg of caffeine) or more per day, averaging 31% below the average in control [32,33]. This cola’s effect on sperm seems not to be attributable to their caffeine content; caffeine intake of < 800 mg per day and cola consumption of < 14 0.5-L bottles per week is not associated with reduced semen quality. The reduction in semen quality among high-quantity cola drinkers must be attributed to constituents in cola other than caffeine because the caffeine content of cola is not high. They also added that although the cola drinkers’ sperm count was still within the normal range, at 35 million/mL, cola might nonetheless dampen their fertility [33]. Among the study participants, those not drinking cola had an aver-
Caffeine can readily cross the placental barrier to the fetus [42]; its clearance is prolonged in pregnant women, and its metabolism rate is low in the fetus because of low levels of enzymes [43,44]. It may also influence cell development through increasing cellular cyclic adenosine monophosphate (cAMP) concentrations and decrease intervillous placental blood flow via increasing circulating catecholamines [18,19,45]. Caffeine intake during pregnancy has been suggested as a risk factor for adverse reproductive outcomes. Therefore, caffeine could have an adverse effect on fetal development. Indeed, caffeine intake has been reported to increase the risk of miscarriage [15,16,46-48]. Although numerous studies on maternal caffeine consumption and the risk of miscarriage have been published since the 1980s, the effect of caffeine intake on the risk of miscarriage remains controversial because of methodological limitations in past studies. Many studies have relied on retrospective information, which is subject to recall bias [15,16,46-48]. Some had only a small number of participants, which limited their power to detect an effect. Some did not take into account potential confounding factors such as smoking, alcohol consumption, and most importantly, pregnancy-related symptoms including nausea and vomiting. Some recruited women who sought prenatal care at their 13th to 28th weeks of gestation, therefore too late in pregnancy to study miscarriage. Such controversy has led to the uncertainty about the health effects of caffeine consumption during pregnancy among both clinicians and pregnant women alike.

Weng et al. [45] demonstrated, in their prospective cohort study, an elevated risk of miscarriage associated with caffeine consumption during pregnancy and a dose-response relationship with most of the risk associated with caffeine consumption at 200 mg (which approximately 1.5 L cola contains) or greater per day. This observed effect was independent of many potential confounders including pregnancy related symptoms such as nausea, vomiting, and aversion to caffeine consumption. Even among women who never changed caffeine consumption pattern during pregnancy, there was an almost 80% increased risk of miscarriage associated with caffeine consumption of 200 mg/day or greater, although it was not statistically significant because of reduced sample size by stratification. The increased risk of miscarriage appeared to be due to caffeine itself rather than other possible chemicals in coffee because caffeine intake from noncoffee sources showed the similarly increased risk of miscarriage. On the other hand, a similar cohort study, published same month, by Svavitz et al. [49] demonstrated that this can result in recall bias generating a positive results, whereas when caffeine exposure is ascertained before miscarriage, the findings indicate no effect of caffeine. To date, the literature is still inconclusive regarding the influence of caffeine on miscarriage and the available information is incomplete and remains controversial [47,50].

6. CONCLUSIONS

Although much epidemiological work has been conducted, results from studies investigating the association between cola consumption and outcomes such as reproductive hazards have been conflicting and the available information was incomplete and remained controversial. As summarized in Table 1, our reviewing recent reports suggest the association between cola consumption and increased risk of reproductive hazards. In addition to caffeine, cola contains a number of other chemical compounds, and one or more of these could be physiologically active. Further studies might attempt to disentangle a caffeine effect from a noncaffeine effect by comparing different types of beverage drinkers. Cola is not an essential beverage, and abstaining from drinking more than 1 L per day is a minor intrusion in one’s personal life.
The growing knowledge may alarm the fertility risk of chronic cola intake in peoples of childbearing age.

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