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Review

Tobacco and areca nut chewing—Reproductive impairments: An overview

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ABSTRACT

A large number of people are using smokeless tobacco and areca nut worldwide. Sufficient data on tobacco smoking have harmful effect on human health and reproduction is available. However, data on the smokeless tobacco and areca nut use on human reproduction is scanty. This overview is an attempt to compose on the consumption of smokeless tobacco and areca nut on human reproduction and some relevant experimental data were also included.

The existing studies suggest that tobacco and areca nut chewing alone, together or with other ingredients had reproductive toxic potential. Pregnant women using smokeless tobacco during pregnancy also had adverse effect on pregnancy and its outcome. Thus pregnant women must avoid consumption of any mixture containing areca nut and tobacco in order to protect the pregnancy and outcome. The data suggest that smokeless tobacco use is also harmful as smoking for reproduction and use of areca nut might have further compounded the problem.

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1. Introduction

Many reports are available on the toxic effects of tobacco consumption on reproduction. Reports on tobacco chewing in a blend of mainly areca nut on human reproduction are inadequate. Common use of tobacco blend is increasing globally. Betel quid/areca nut use is very common in South and Southeast Asia and the Asia pacific region, and is common among migrated communities in Africa and North America [1]. Both tobacco and areca nut are having addictive potential, hence populations are addicted very soon to these materials. Further, a non-perishable preparation known as panmasala, which is a dry mixture commercialized and marketed two types of panmasala; plain panmasala containing areca nut, catechu, lime, cardamom and unspecified flavoring agents (PMP), and Panmasala containing tobacco—Gutkha (PMT) are being consumed.

In addition, the habit of tobacco and areca nut chewing is increasing rapidly as smoking is prohibited at public places in the majority of the countries worldwide, and smokers are switching over to tobacco chewing habit. Very recently, Narain et al. [2] from India mentioned that tobacco addiction is emerging as a big threat among children and data indicated a recent downward shift in the age at initiation of tobacco uptake and rising prevalence of tobacco habits among girls also. Earlier, Rani et al. estimated that 30% of the population 15 years or older—47% men and 14% of women—either smoked or chewed tobacco in India alone, which translates in to almost 195 million people in India [3].

Betel quid with or without tobacco is carcinogenic to humans (Group 1 carcinogen) and areca nut is also carcinogenic (Group 1) to humans as evaluated by IARC [4]. A few reports are available, showing an increase in stillbirths and lower birth weight among offsprings of tobacco chewing mothers [5,6]. Recently, Gupta and Sreevidya also reported that there is an increase in the number of low birth babies, and pre-term deliveries among pregnant women using smokeless tobacco [7].

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Table 1
Tobacco and areca nut chewing and male reproduction.

Sl. no.	Products/toxicants	Observed effects	References
Animal study			
1	Areca nut treatment with respect to genetic toxicity in mice	The sperm deformity were significantly higher in areca nut treated mice and areca nut associated components can pass the testicular barrier to affect the mouse's sperm development, and genetic toxicity on genital cells	Xubing et al. [21]
2	Mice treated with the areca nut	Sperm number and motility decreased while deformity rate was increased and the main deformation was amorphous and fat sperm head	Yixiu et al. [22]
3	Areca nut extracts (ANE) treatment in mice	ANE induced spermatogenic damage, as indicated by declining sperm counts and motility, activity of antioxidant enzymes, an increase in sperm head abnormalities, and alterations in sialic acid and MDA levels	Wu et al. [24]
4	The antifertility activity of *Areca catechu* extract in male rats. Fertility was assessed with mating test	Reduction in fertility of *Areca catechu* treated *mice*, reduction in the number of secondary spermatocytes and spermatids, a reduction in the number of Leydig cells, increase in the diameter of seminiferous tubules with necrotic products.	Kafle et al. [23]
Human study			
1	The relationship between tobacco chewing in men—who were part of an infertile couple—and their sperm characteristics.	Sperm concentration; percentage motility, morphology, and viability were significantly higher in the mild group versus the moderate group and in the moderate group versus the severe group of chewers	Said et al. [17]
2	Compared the semen samples between addicts (smokers, chewers, and multiple addicts) with non-addicts (never consumed tobacco).	The percentage of motile sperm and total sperm count of the tobacco chewers were significantly low. The frequency of abnormal sperm was significantly high for smoking and multiple addicts as compared to non-addicts	Banerjee et al. [18]

Further, chewing any mixture containing tobacco and areca nut as major ingredients also reported to have various adverse effects on hard and soft tissues of oral cavity of human [8–12]. Snuff and chewing tobacco may affect reproduction, longevity, the cardiovascular system, and oral health. The relative risk of oral cancer in longtime users of snuff varied from 1.8 to 48 times that of its occurrence in nonusers [13]. Further, Benowitz reported that the systemic absorption of nicotine per dose is greater with the use of chewing tobacco (average 4.5 mg nicotine from an average dose of 7.9 g chewed for 30 min) or snuff (average 3.6 mg nicotine from 2.5 g moist snuff kept in the mouth for 30 min) compared with that from smoking cigarettes (average 1.0 mg nicotine per cigarette). This indicates that smokeless tobacco (ST) use might have more exposure to nicotine than smoking [14] indicating more effect of ST. Owing to these and sparse data, along with the role of these components on diverse aspects of reproduction, in this review an attempt has been made to understand the effect of tobacco and areca nut chewing on reproduction.

Literature on tobacco and areca nut consumption and reproductive health available at Pub Med, Medline, Toxline, Google, and certain other websites are reviewed in respect of both sexes. The paper is divided in different sections based on the effect of chewing on male, female reproduction and reproductive/pregnancy outcome. Both human and experimental studies are incorporated in order to understand the role of chewing habits of tobacco and areca nut in reproduction. The data on male and female reproduction and pregnancy outcome are summarized in Tables 1 and 2 respectively.

2. Tobacco and areca nut chewing and male reproductive health hazards

Tobacco smoking causes health impairments and adequate data of smoking on impairments of human male reproduction is also available. Vine reviewed the epidemiological data on smoking and reproduction and reported that cigarette smoking is associated with modest reductions in semen quality including sperm concentration, motility and morphology. The associations between smoking and sperm concentration and motility were stronger among 'healthy' men (e.g. volunteers and sperm donors) than among men from infertility clinic populations. Smoking has also been associated with alterations in hormone levels in males such as oestrone and oestradiol. He has concluded that, men with marginal semen quality who wish to have children may benefit from quitting smoking [15]. Further, Sofikitis et al. also suggested that morphological sperm abnormalities due to secretary dysfunction of the Leydig and Sertoli cells might be the cause of impaired sperms fertilizing capacity in the smokers [16].

A few reports on tobacco chewing and semen quality have also appeared in recent years. Said et al. studied the relationship between tobacco chewing in Indian men, who were part of an infertile couple, and their sperm characteristics. They have reported that sperm concentration, percentage motility, morphology, and percentage viability were significantly higher in the mild group versus the moderate group and in the moderate group versus the severe group of tobacco chewers [17]. Earlier, Banerjee et al. also compared the qualitative analysis of semen samples between different types of tobacco addicts (smokers, chewers, and multiple addicts) with non-addicts (never consumed any form of tobacco). The percentage of motile sperm and total sperm count of the tobacco chewers were significantly low ($p < 0.05$). The frequency of abnormal sperm was also significantly high ($p < 0.001$) for smoking and multiple addict groups as compared to non-addicts [18]. However, Dixit et al. from India did not find statistically significant difference in sperm parameters between tobacco chewers and non-chewers [19]. But Kumar and Gautam conducted a study by enrolling six hundred and thirty-eight male subjects aged between 18 and 40 years who were part of an infertile couple. They were grouped according to the frequency of their tobacco chewing habit into mild (<3 times/day), moderate (3–6 times/day) and severe (>6 times/day). All subjects had a history of tobacco chewing of 4–10 years. Sperm concentration (a mean of 77.95 versus 47.59 versus 27.25 million per ml), percentage motility (a mean of 60.87 versus 56.69 versus 49.29%), morphology (a mean of 33.79 versus 27.0 versus 18.62%) and percentage viability (a mean of 64.1 versus 59.38 versus 52.55%) were significantly higher in the mild group versus the moderate group and in the moderate group versus the severe group. The percentage of men with azoospermia rose with the level of addiction (1, 3 and 14%), as did the percentage of men with oligoasthenoteratozoospermia (2, 8 and 29%), although the differences were not