

Relationship between semen quality and tobacco chewing in men undergoing infertility evaluation

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Objective: Male fertility is affected by a variety of lifestyle habits that include tobacco use. A large population of Indian men is addicted to tobacco chewing. The objective of our study was to assess the relationship between tobacco chewing in these Indian men—who were part of an infertile couple—and their sperm characteristics.

Design: Retrospective study.

Setting: Private infertility clinic.

Patient(s): Six hundred thirty-eight male patients undergoing infertility evaluations were grouped according to the frequency of their tobacco chewing habit: mild (<3 times/day, n = 177), moderate (3–6 times/day, n = 264), and severe (>6 times/day, n = 197).

Intervention(s): None.

Main Outcome Measure(s): Sperm characteristics (concentration, motility, morphology, and viability).

Result(s): Sperm concentration, percentage motility, morphology, and percentage viability were significantly higher in the mild group vs. the moderate group and in the moderate group vs. 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 statistically significant.

Conclusion(s): In our study, use of chewing tobacco by a group of Indian men who were undergoing infertility evaluation was strongly associated with a decrease in sperm quality and to a lesser extent with oligoasthenozoospermia or azoospermia. Infertile men should be counseled about the adverse effects of tobacco chewing on sperm quality. (*Fertil Steril*® 2005;84:649–53. ©2005 by American Society for Reproductive Medicine.)

Key Words: Male infertility, tobacco chewing, sperm quality

Tobacco chewing constitutes one of the forms of smokeless tobacco. In the United States, smokeless tobacco consumption has increased threefold, and manufacturing output grew 8 years in a row as reported by the United States Department of Agriculture in 1993. Estimates of smokeless tobacco users in the United States range from 6 million to 22 million (1). A national survey conducted on 5,894 college and university students from different regions of the United States revealed that 8%–15% of the students used smokeless tobacco (2). Moreover, a recent study has identified that 14.8% of male high school students in the United States were current users in 2001 (3).

The habit appears to be very common among specific population groups. As an example, lower-income black and white men regularly chew tobacco more so than upper-

income classes (4). The habit also appears to be common in young amateur and professional baseball athletes (5) and in other parts of the world, such as India, China, and the southeast Asia region (6). In India, chewing tobacco is systematically associated with socioeconomic markers at the individual and household level. Individuals with no education are 2.69 times more likely to smoke and chew tobacco than those with a postgraduate education (7).

In general, smokeless tobacco is substantially less harmful than smoking (8). A meta-analysis showed that tobacco chewing increases the risk of respiratory tract cancers minimally (9). It is also true that tobacco chewing is associated with a lower risk for adverse cardiovascular effects than is smoking (10). However, the habit has been strongly associated with oral malignant diseases and is considered the most important risk factor for multiple oral premalignant lesions (11).

Several carcinogens have been identified in smokeless tobacco; the tobacco-specific N-nitrosamine (TSNA), N'-nitrosornicotine (NNN), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) are the most important. NNN and NNK are formed from nicotine during curing, aging, and

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TABLE 1**Comparison of sperm parameters in all semen samples collected from mild, moderate, and severe tobacco chewing groups.**

Parameter	Mild group (n = 177)	Moderate group (n = 264)	Severe group (n = 197)
Sperm count (10 ⁶ /mL)	77.95 ± 49.36 ^{b,c}	47.59 ± 27.39 ^{a,c}	27.25 ± 29.49 ^{a,b}
Motility (%)	60.87 ± 8.74 ^{b,c}	56.69 ± 10.4 ^{a,c}	49.29 ± 16.88 ^{a,b}
Morphology (%)	33.79 ± 12.92 ^{b,c}	27.0 ± 10.53 ^{a,c}	18.62 ± 9.27 ^{a,b}
Viability (%)	64.1 ± 8.98 ^{b,c}	59.38 ± 10.39 ^{a,c}	52.55 ± 15.51 ^{a,b}

Note: Values are expressed as mean ± standard deviation. $P < .001$ was considered significant using one-way ANOVA compared to: ^a mild group; ^b moderate group; ^c severe group.

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especially during fermentation (12). Other compounds, such as 3-methylnitrosaminopropionaldehyde (MNPA), negatively affect DNA by causing single-strand breaks and protein cross-links (13).

The relationship between tobacco consumption and male infertility remains controversial. A number of studies have shown that smoking detrimentally affects sperm concentration, motility, and morphology and damages DNA (14–17). In addition, cigarette smoking has been correlated with poor sperm function (18, 19). On the other hand, a handful of studies have found no association between smoking and sperm quality (20, 21) or sperm function (22).

An increasing number of reports suggest that chemical and physical agents in the environment may affect male fertility in humans. Scientific and public concern exists about the potential reproductive health effects of tobacco consumption. Little is known about the effect of tobacco chewing on male reproduction. Thus, the objective of our study was to evaluate the relationship between tobacco chewing and sperm quality in male partners of infertile couples undergoing infertility evaluation.

MATERIALS AND METHODS

The medical charts of patients attending the infertility clinic at the Karthekeya Medical Research and Diagnostic Center in Mumbai, India, were reviewed. Our study included 638 male partners of infertile couples undergoing infertility evaluation from November 1998 to December 2003. All participants provided informed consent.

The patients' ages ranged from 18 to 40 years. All had a history of tobacco chewing of 4–10 years' duration but no other relevant social habits. Patients were grouped according to the frequency of their habit of tobacco chewing: mild (<3 times/day, n = 177), moderate (3–6 times/day, n = 264), and severe (>6 times/day, n = 197). Semen analysis was performed manually according to the World Health Organization (WHO) standard guidelines. Azoospermia was diagnosed if sperm were completely absent in the ejaculate; oligozoospermia if sperm concentration was $<20 \times 10^6$ /mL;

asthenozoospermia if <50% of sperm were progressively motile; and teratozoospermia if >30% of sperm had abnormal forms (23).

Statistical Analysis

Comparisons between the three groups were performed using one-way analysis of variance (ANOVA), and unpaired *t* test was used for comparisons between two groups. All hypothesis testing was two-tailed with a significance level of .05. Calculations were performed with GraphPad InStat version 3.00 statistical software (GraphPad Software, San Diego, CA).

RESULTS

Sperm parameters were significantly higher in samples from men in the mild group compared to moderate, and in the moderate compared to the severely addicted group (Table 1). Semen samples from men with a mild tobacco chewing habit had normal sperm count, motility, morphology, and viability according to the WHO standards (23). On the other hand, samples from men in the moderate and severe groups were characterized by teratozoospermia (Fig. 1).

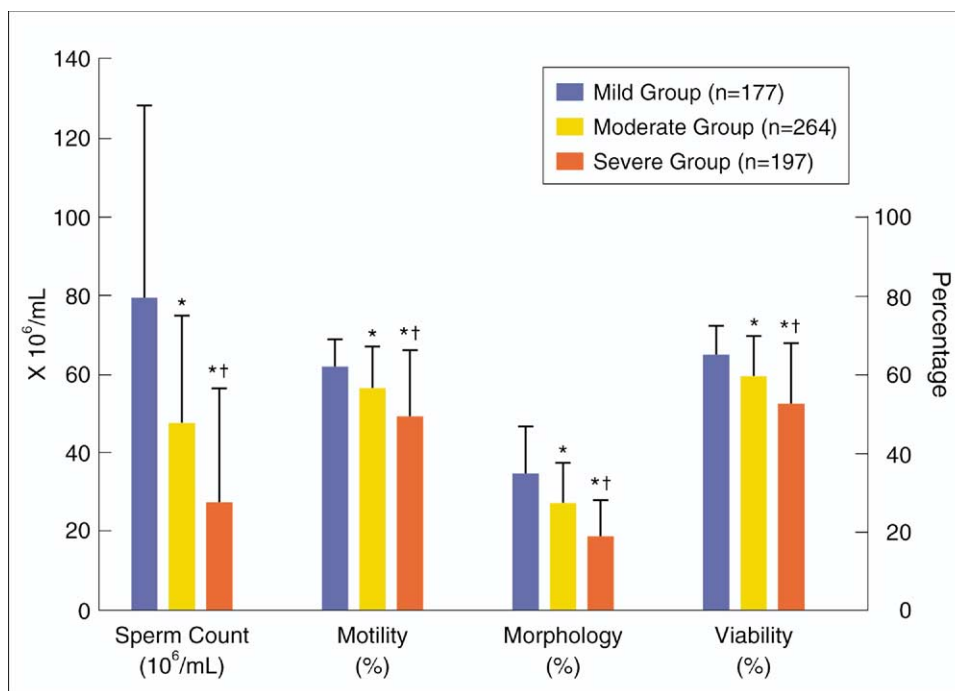
The percentage of azoospermia observed in the mild, moderate, and severe tobacco chewing groups was 1% (2/177), 3% (8/264), and 14% (28/197), respectively, indicating an increase in prevalence in the severely addicted group.

The incidence of oligoasthenoteratozoospermia (OAT) showed an increasing trend from mild (2%) to moderate (8%) to severe addiction (29%). The incidence of OAT was highly significant in the severely addicted group as compared to mild and moderate users. Within semen samples characterized by OAT, we were able to detect lower values in men with a severe tobacco chewing habit compared to those with a moderate habit as regards sperm motility ($P = .03$) and morphology ($P = .05$) (Table 2). No comparisons were made with the mild tobacco chewing group owing to the limited number of samples characterized by OAT in this group (n = 4).

When men with normal sperm count, motility, and viability from the three study groups were compared, the values of

FIGURE 1

Comparison of sperm parameters in semen samples collected from mild, moderate, and severe tobacco chewing groups. Values are expressed as mean \pm standard deviation. Using unpaired *t* test, $P < .0001$ was considered significant compared to *mild group and to †moderate group.



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sperm parameters were significantly lower in the men with a severe tobacco chewing habit versus the moderate group and in the moderate versus the mild group. The presence of normal sperm count, motility, and viability was associated with normal sperm morphology in the mild tobacco chewing group. In contrast, samples with normal sperm count, motility, and viability were characterized by teratozoospermia in the moderate and severe tobacco chewing groups (Table 3).

DISCUSSION

Regardless of how tobacco is consumed, its adverse effects on disease and mortality rates are clear. The use of smokeless tobacco products is associated with gum recession, leukoplakia, nicotine addiction, increased cardiovascular disease mortality, and cancers of the oral cavity, larynx, and pharynx (24). Furthermore, smokeless tobacco is highly addictive (25).

TABLE 2

Comparison of sperm parameters in samples characterized with oligoastheno-teratozoospermia from moderate and severe tobacco chewing groups.

Parameter	Moderate group (n = 22)	Severe group (n = 49)	P value ^a
Sperm count (10 ⁶ /mL)	4.62 \pm 1.9	4.08 \pm 2.54	.37
Motility (%)	32.27 \pm 7.33	25.88 \pm 12.93	.03
Morphology (% normal)	7.63 \pm 2.3	6.43 \pm 3.06	.05
Viability (%)	35.72 \pm 6.98	30.84 \pm 10.72	.1

Note: Values are expressed as mean \pm standard deviation.

^a $P < .05$ considered significant using unpaired *t* test.

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TABLE 3

Comparison of sperm parameters in samples characterized with normal sperm count from mild, moderate, and severe tobacco chewing groups.

Parameter	Mild group (n = 171)	Moderate group (n = 234)	Severe group (n = 120)
Sperm count (10 ⁶ /mL)	79.69 ± 48.6 ^{b,c}	51.63 ± 25.1 ^{a,c}	36.51 ± 30.26 ^{a,b}
Motility (%)	61.6 ± 7.36 ^{b,c}	59.0 ± 7.21 ^a	58.68 ± 4.71 ^a
Morphology (%)	34.46 ± 12.29 ^{b,c}	28.82 ± 9.06 ^{a,c}	23.51 ± 5.72 ^{a,b}
Viability (%)	64.84 ± 7.57 ^{b,c}	61.61 ± 7.48 ^a	61.23 ± 5.03 ^a

Note: Values are expressed as mean ± standard deviation. $P < .001$ was considered significant using one-way ANOVA compared to: ^a mild group; ^b moderate group; ^c severe group.

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Our study reports, for the first time, a significant decrease in semen quality (sperm count, motility, morphology, and viability) associated with a chewing tobacco habit in men undergoing infertility evaluation. No significant changes in sperm parameters were observed in the men with a mild habit compared to normal standard WHO values.

Our results contradict the finding of another study that consisted of 119 tobacco chewers. In that study, no significant difference was found in sperm parameters between tobacco consumers and nonusers (20). Our study included a much larger number of patients (n = 638), which may be the reason we were able to detect more significant differences. Also, we chose to demonstrate the effect of tobacco chewing by comparing patients according to their rate of consumption. The other study compared tobacco chewers to infertile men who were nonusers. However, one limitation of our study may be the lack of information regarding the exact etiology of infertility in these patients.

Chronic systemic exposure to nicotine could contribute to accelerated coronary artery disease, acute cardiac ischemic events, and hypertension (26). In the context of male infertility, nicotine is absorbed in substantial quantities as a result of tobacco chewing and could contribute to the adverse consequences of this habit. Experiments using murine models have documented virulent inflammatory reaction and marked ultrastructural changes in the testes of animals exposed to nicotine (27, 28). In addition, levels of nicotine and its major metabolites cotinine and trans-3'-hydroxycotinine in human seminal plasma negatively correlated with sperm parameters (5). However, further studies are needed to substantiate the impact of nicotine on spermatogenesis.

Men addicted to tobacco chewing also have the least access to infertility medical services. Therefore, prevention and cessation programs should be directed towards specific high-risk groups. Strategies should be developed to direct the attention of the general public towards the possible relationship between tobacco chewing and the incidence of male infertility. In addition, infertile men who have a habit of tobacco chewing should be advised about the potential adverse effects of their habit on sperm quality.

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